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ScienceDirect
Psychiatry Research: Neuroimaging 162 (2008) 39–49
PSYCHIATRY RESEARCH NEUROIMAGING
www.elsevier.com/locate/psychresns

Childhood adversity predicts earlier onset of major depression but not reduced hippocampal volume

Shannon N. Lenze[a,*], Chengjie Xiong[b], Yvette I. Sheline[c]

[a]Department of Psychology, University of Pittsburgh, 3rd Floor Sennott Square, Pittsburgh, PA 15260, USA
[b]Department of Biostatistics, Washington University School of Medicine, St. Louis, MO, USA
[c]Department of Psychiatry, Washington University School of Medicine, St. Louis, MO, USA

Received 5 April 2007; accepted 7 April 2007

Abstract

Childhood adversity may influence severity and age of onset of depression, potentially mediated by greater vulnerability to an existing biochemical or neural mechanism. Prior studies have suggested that reduced hippocampal volume is a result of childhood adversity. This study examined the relationship between childhood adversity, hippocampal volumes and clinical characteristics in women who were recruited for depression history rather than abuse experiences. Thirty-one women with remitted unipolar depression and 24 psychiatrically healthy women completed the Childhood Experience of Care and Abuse interview [Bifulco, A., Brown, G.W., Harris, T.O., 1994. Childhood Experience of Care and Abuse (CECA): A retrospective interview measure. Journal of Child Psychology and Psychiatry 55, 1419–1435]. High resolution MRI scans and hippocampal volumetric determination by stereological assessment were obtained. We found that childhood adversity was associated with a history of recurrent depression and with earlier age of depression onset. We did not find a relationship between childhood adversity and hippocampal volumes in this sample with mild childhood adversity. Our results suggest that the decreased hippocampal volume seen in Major Depressive Disorder may be mediated by additional factors. Further research is needed to more fully understand the interrelationships among childhood adversity, hippocampal morphology, neuroendocrine regulation, and other genetic and environmental factors influencing vulnerability to depression.

Keywords: Magnetic resonance imaging; Depression; Abuse; CECA

1. Introduction

The link between childhood adversity and the development of Major Depressive Disorder (MDD) has been widely studied. MDD has been associated with experiencing physical or sexual abuse, poor parenting, marital discord, and family violence in childhood (Parker, 1979; Bifulco et al., 1994, 1998; Parker et al., 1995, 1997; Harkness and Monroe, 2002). Prevalence rates of childhood abuse or adversity range from 8% to 83% in clinical samples of depressed patients and 23% to 68% in community studies depending on the sample characteristics and on the definitions used to measure the adversity (Brown and Anderson, 1991; Carlin et al., 1994; Mullen et al., 1996; Kessler et al., 1997). For example, definitions of sexual abuse range from "some kind of sexual experience with another while growing

* Corresponding author. Tel.: +1 412 624 4500; fax: +1 412 624 4428.
E-mail address: lenzesn@upmc.edu (S.N. Lenze).

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doi:10.1016/j.pscychresns.2007.04.004

up" (Sedney and Brooks, 1984) to "sexual contact between a girl under 15 and an individual at least 5 years older" (Briere and Runtz, 1988). Most research has focused on the adult outcomes of childhood sexual abuse. Other forms of childhood adversities including physical abuse, emotional abuse, or parental neglect are receiving increased attention and also have important implications for depression. It should be noted that many different terms are used throughout the literature to describe childhood adverse experiences including, adversity, abuse, and trauma. For simplicity, we will use the term 'adversity.'

Several studies have suggested that childhood adversity is associated with age of onset, course, and treatment response of MDD (Brown and Moran, 1994; Brown et al., 1994; Zlotnick et al., 1995; Kessler et al., 1997; Young et al., 1997; Bifulco et al., 1998; Bernet and Stein, 1999; Sakado et al., 1999; Kaplan and Klinetob, 2000; Lara et al., 2000). Some studies have found a link between childhood adversity and increased chronicity of depressive episodes (Brown et al., 1994; Brown and Moran, 1994; Zlotnick et al., 1995; Lara et al., 2000). Other studies have found an association between childhood adversity and earlier age of onset of depression (Kessler et al., 1997; Young et al., 1997; Bifulco et al., 1998; Bernet and Stein, 1999; Widom et al., 2007). Recent reports have suggested that early adversity is associated with an increased risk of depressive episode recurrence, decreased chance of remission, increased suicidality, and overall poorer prognosis (Dube et al., 2001; Gilman et al., 2003; McHolm et al., 2003).

Our previous work, as well as that of other studies, has found an association between MDD and hippocampal volume loss (Sheline et al., 1996, 1999; for review, see Sheline, 2003; Videbech and Ravnkilde, 2004). There have also been reports of hippocampal volume changes in adults with childhood abuse histories and other psychiatric diagnoses (Bremner et al., 1997; Stein et al., 1997; Driessen et al., 2000). Bremner and colleagues found smaller hippocampal volumes in adults meeting criteria for PTSD secondary to childhood abuse (1997). Stein and colleagues selected an abuse sample and found smaller hippocampal volumes in women who reported sexual abuse compared with those with no prior abuse (1997). Others have found an association between abuse experiences and smaller hippocampal volumes in women with Borderline Personality Disorder (Driessen et al., 2000; Brambilla et al., 2004) and Dissociative Identity Disorder (Vermetten et al., 2006). Because these studies found a relationship between childhood adversity and decreased hippocampal volumes, it was hypothesized that the observed hippocampal volume deficits in MDD may also be related to childhood adversity. To our knowledge, only one study has looked at the association of hippocampal volumes and childhood adversity in MDD (Vythilingam et al., 2002). Vythilingam and colleagues found smaller hippocampal volumes only in the women with MDD who had experienced severe and prolonged sexual and/or physical abuse in childhood. They did not find hippocampal volume differences in women with MDD without abuse histories.

The goal of this study was to investigate the differences in the severity of childhood adversity in a sample of women with a history of MDD and matched controls. Second, we investigated whether the severity of childhood adversity is related to depression severity, age of onset of MDD, number of past depressive episodes, and number of lifetime days depressed. Finally, we investigated the relationship between childhood adversity severity and depression status and hippocampal volumes. In order to minimize subjective bias in reporting early experiences, we utilized a rigorous investigator-based rating instrument, the Childhood Experience of Care and Abuse (CECA; Bifulco et al., 1994). Childhood adversity in the core scales of the CECA is conceptualized as caregiver lack of warmth or positive regard, emotional or material neglect, physical abuse, sexual abuse, and psychological abuse. The CECA offers advantages over self-report ratings in several ways (Bifulco et al., 1994). It includes detailed information on a wide range of childhood experiences for all household members, and it takes into account duration of experiences to allow for more precise hypothesis testing.

We hypothesized that women with a history of recurrent depression would report more severe levels of childhood adversity than women without histories of depression. We also hypothesized that more severe levels of childhood adversity would be associated with earlier age of onset of depression, greater number of depressive episodes, and more lifetime days depressed. Finally, we hypothesized that more severe levels of childhood adversity would be associated with lower hippocampal volumes.

2. Methods

2.1. Participants

Participants in this study were recruited to take part in one of two neuroimaging studies of depression (24 participants from Sheline et al., 1999 and 7 participants