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Abnormal T2 relaxation time in the cerebellar vermis of adults sexually abused in childhood: potential role of the vermis in stress-enhanced risk for drug abuse

Carl M. Anderson [a, b,*], Martin H. Teicher [a, b], Ann Polcari [a, b], Perry F. Renshaw [a, b]

[a] *Department of Psychiatry, Harvard Medical School, Boston, MA, USA*
[b] *Developmental Biopsychiatry Research Program and Brain Imaging Center, McLean Hospital, 115 Mill Street, Belmont, MA 02478, USA*

Abstract

Recent studies suggest that childhood sexual abuse (CSA) elicits a cascade of neurohumoral events that affect brain development and is also a risk factor for the later development of substance abuse. We hypothesize that the cerebellar vermis may be a key region linking these observations. The vermis has a protracted ontogeny and a high density of glucocorticoid receptors, rendering it highly susceptible to early stress. The vermis modulates dopamine turnover in the accumbens and receives direct dopamine input through fibers with dopamine transporters. To test this hypothesis, steady-state functional magnetic resonance imaging (fMRI) (T2 relaxometry) was performed to assess resting blood flow in the vermis of 24 young adults (18–22 years) selected by screening from a large community sample. Eight subjects had a history of repeated CSA but were unmedicated and not under psychiatric care. Sixteen subjects were age-matched controls who had no personal or family history of Axis I psychiatric disorders. All subjects were screened to exclude known abnormalities affecting brain development, and any history of drug or alcohol abuse. CSA subjects had higher T2 relaxation time (T2-RT) than controls in the vermis but not in cerebral or cerebellar hemispheres. Vermal T2-RT correlated strongly with Limbic System Checklist (LSCL-33) ratings of temporal lobe epilepsy (TLE)-like symptomatology. From 537 prescreened young adults we found that their

* Corresponding author. Address for correspondence: Developmental Biopsychiatry Research Program, McLean Hospital, 115 Mill Street, Belmont, MA 02478, USA. Tel.: +1-617-855-2972; fax: +1-617-855-3712.

E-mail address: carl_anderson@hms.harvard.edu (C.M. Anderson).

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frequency of substance use was associated with a monotonic increase in LSCL-33 ratings and depression scores. Together these findings suggest that early trauma may interfere with the development of the vermis, and produce neuropsychiatric symptoms associated with drug use.

Keywords: Cerebellar vermis; Substance abuse; Child abuse; Sexual abuse; Early stress; fMRI

1. Introduction

Early stress or maltreatment is an important risk factor for the later development of substance abuse (Ellason et al., 1996; Janikowski et al., 1997; Kendler et al., 2000; McClanahan et al., 1999; Najavits et al., 1997; Simpson et al., 1994; Wilsnack et al., 1997). We have spent the last several years pursuing the hypothesis that childhood abuse or neglect induces a cascade of neurohumoral and physiological events that affect brain development (Ito et al., 1993; Ito et al., 1998; Teicher et al. 1993, 1994; Schiffer et al., 1995). Briefly, we found that subjects reporting childhood abuse had markedly increased scores on the Limbic System Checklist-33 (LSCL-33), which was devised to ascertain the frequency of occurrence of symptoms suggestive of temporal lobe epilepsy (TLE) (Teicher et al., 1993). Childhood abuse was associated with a two-fold increased incidence of clinically significant electroencephalographic (EEG) abnormalities, which were restricted to the left hemisphere (Ito et al., 1993). Abused children had highly abnormal measures of left hemisphere EEG coherence, suggesting deficient cortical maturation and differentiation (Ito et al., 1998; Teicher et al., 1997). Bremner et al. (1997) and Stein (1997) found that women with posttraumatic stress disorder (PTSD) who were abused in childhood had a smaller left, but not right, hippocampus. Abuse was also associated with prominent thinning of the middle portion of the corpus callosum, affecting males more than females (DeBellis et al., 1999; Teicher et al., 1997). These anatomic anomalies may contribute to the psychiatric syndromes reported to occur with increased frequency in childhood trauma survivors (Teicher et al., 1994; Teicher, 2000).

Preclinical studies have experimentally established the enduring effects of early experience on brain development and have elucidated potential mechanisms and key target areas. One major finding has been the discovery that excessive levels of glucocorticoids, or stress, damage brain regions with high densities of glucocorticoid receptors, such as the hippocampus (e.g. Sapolsky et al., 1988; McEwen, 1999).

A brain region that should also be extraordinarily sensitive to the effects of early maltreatment is the cerebellar vermis. Like the hippocampus, the vermis has a protracted period of postnatal ontogeny and may produce granule cells postnatally (Altman and Bayer, 1997). The vermis also has the highest density of glucocorticoid receptors during development, exceeding that of the hippocampus (Lawson et al., 1992; Pavlik and Buresova, 1984; Sanchez et al., 2000) and may be particularly vulnerable to the effects of stress hormones (Schapiro, 1971; Ferguson and Holson, 1999).

Our interest in the cerebellar vermis stems from the work of Harlow (Harlow et