

Hippocampal volume reduced in major depression

Major depression is a common psychiatric disorder that is associated with considerable morbidity. Depressive episodes are associated with high levels of cortisol in about 40-50% of patients. Elevated levels of glucocorticoids seen in stress have been associated with damage to hippocampal neurons, and the diagnosis of posttraumatic stress disorder (PTSD) has been associated with hippocampal volume reduction and deficits in declarative memory function.

Hippocampal dysfunction may contribute to verbal declarative memory deficits in depression.

Few studies, however, have examined hippocampal volume in patients with depression. Neuro-imaging findings in affective disorders include:

- ventricular enlargement
- widening of the cortical sulci
- smaller volumes in the right hippocampus, left amygdala and temporal lobe in bipolar disorder
- increased subcortical white matter areas of increased signal intensity
- smaller caudate and putamen volumes
- alterations in hippocampal T1 relaxation time
- reductions in grey matter in the left temporal lobe in unipolar depression. Studies of hippocampal volume in unipolar depression have had conflicting findings; some studies of amygdala/hippocampal volume (combined) found no difference in comparison with control subjects, and others found a reduction. The purpose of the current study was to compare hippocampal volume of patients with treated unipolar depression and non-depressed subjects.

Aim

The purpose of this study was to measure hippocampal volume in patients with depression.

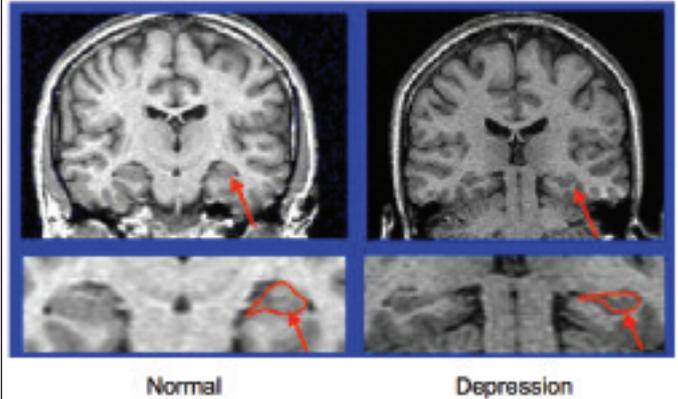
Method

Magnetic resonance imaging was used to measure the volume of the hippocampus in 16 patients with major depression in remission and 16 case-matched, non-depressed comparison subjects.

Results

Repeated measures analysis of variants (ANOVA), with side (left vs. right hemisphere) as the repeated factor, showed a significant main effect for diagnosis and no significant main effect for side or side-by-diagnosis interaction. Univariate analyses showed a statistically significant 19% smaller volume of the left hippocampus in the depressed patients than the comparison subjects; the difference remained significant after differences in whole brain volume were controlled for, but a 12% difference in right hippocampal volume between the groups was not significant. There were no differences in volume in the comparison regions with the exception of the right amygdala, which was related to a larger volume of the right amygdala in depression. This effect was not significant, however, after differences in whole brain volume were controlled for.

Atrophy of the Hippocampus in Depression



Bremner JD, et al. *Am J Psychiatry*. 2000;157(1):115-118.
Images courtesy of J Douglas Bremner, MD, Yale University.

There was no correlation between left hippocampal volume and clinical variables, including number of weeks in remission, number of previous episodes of depression, or number of hospitalisations for depression.

Multiple linear regression to control for possible confounds that may affect hippocampal volume, including age, years of education, and years of alcohol abuse, continued to show differences in left hippocampal volume between patients and comparison subjects when these potential confounders were entered in the model.

Discussion

Patients with remitted major depression in this study had a 19% smaller volume of the left hippocampus than matched comparison subjects. There were no differences in volumes of comparison regions between the groups in the temporal lobe, caudate, frontal lobe, or whole brain. There are several possible explanations for our findings of hippocampal volume reduction in depression. Elevated levels of glucocorticoids during depressive episodes could cause hippocampal damage, leading to a reduction in volume. In this model, chronic repeated episodes of depression may lead to progressive hippocampal atrophy over time, possibly increasing the risk for subsequent depressive relapse. Other factors, such as reductions in neurotrophins, could also be responsible for hippocampal volume reduction. However, the current study did not include measures of cortisol during depressive episodes, and future studies are needed to evaluate the relationship between cortisol and hippocampal volume in depression. It is also possible that smaller hippocampal volume from birth, or some premorbid environmental factor, is a risk factor for depression. There is a significant relationship between hippocampal volume and major depressive disorder that warrants further investigation.

Excerpted from: Bremner JD, Narayan M, Anderson ER, et al. Hippocampal volume reduction in major depression. *Am J Psychiatry* 2000;157:115-17.