Hippocampal volume is reduced in people with unipolar depression.

**CONCLUSIONS**

Was significant heterogeneity between studies (p = 0.01 right side) but there was no evidence of publication bias (single study skewed the results). In addition, the absence of evidence for publication bias lends further credence to the validity of the findings.

The considerable heterogeneity identified suggests that hippocampal volume reduction may be present in some but not all people with depression, or at some but not all stages of illness. Thus, studies of recurrent depression demonstrated larger reductions of right hippocampal volumes than studies of people with first episode depression. It will be important to conduct further research with more homogeneous samples in order to identify other clinical moderators of hippocampal volumes in depression (for example, early adverse experiences, comorbidity). Other possible sources of heterogeneity include differences in study design and imaging methodology that can affect sensitivity to variation in hippocampus volumes: sample size, acquisition sequences, slice thickness, and the definition and reliability of anatomical delineations. 1,2,3

Unfortunately, the authors did not examine whether any of these parameters contributed to within or between group variation in hippocampal volume. Such analyses would be useful to guide the design of future MRI studies of depression.

It is too early to conclusively establish the timing of hippocampal volume loss in major depression. One possibility is that it predates onset of affective symptoms, and thereby represents a biological risk marker. Thus far, cross-sectional studies largely have not found evidence of hippocampal atrophy in first episode or paediatric depression. 4-7 Instead, this meta-analysis is more compatible with hypotheses that hippocampal atrophy arises from a neurotoxic progression of the (untreated) disease. 8-9 This underlines the importance of intervening clinically at the first signs of acute depression, and of maintaining an aggressive treatment regimen during periods of partial or complete remission. Even so, we await the results of longitudinal studies of high risk subjects and homogeneous samples to refine our treatment targets and interventions.

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**Commentary**

Videbech and Ravnkilde’s meta-analysis has identified a significant association between major depressive disorder and bilateral volume reduction of the hippocampus. It is a hypothesis driven review that used systematic selection criteria of empirical studies, as well as stringent statistical methods (for example, analyses assuring that no single study skewed the results). In addition, the absence of evidence for publication bias lends further credence to the validity of the findings.

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