Subcortical brain volume abnormalities in major depressive disorder: prospective meta-analytic findings from the enigma major depressive disorder working group

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Abstract:
Despite overwhelming evidence that major depressive disorder (MDD) is heritable, intensive efforts to elucidate genetic variation underlying MDD have yielded only modest success, perhaps partly because genetic effects do not directly translate into dichotomous clinical phenotypes. Biomarkers, for instance measures of brain structure and function, may represent an intermediate step in the causal pathway from genetic variation to distal clinical phenotypes and may therefore help to resolve questions about the etiology of depression. The goal of our ENIGMA-Major Depressive Disorder (ENIGMA-MDD) consortium, a network of 14 research institutes from 7 different countries (for a full list of participating institutes, see: http://enigma.ini.usc.edu/ongoing/enigma-mdd-working-group/) with overlapping neuroimaging data from around 1800 MDD patients and 7200 controls, is to identify imaging markers that robustly discriminate MDD patients from healthy controls using a prospective meta-analytic approach employing the same analysis techniques and statistical models across all participating centers. Here we present the results of the first meta-analysis on differences in subcortical volumes between MDD patients and controls. MDD patients showed robust hippocampal volume reductions compared to healthy individuals (Cohen’s d=-0.14), whereas other subcortical volumes seemed to be preserved. However, when examining subcortical volume differences between healthy controls and patients with recurrent MDD and patients experiencing their first MDD episode at time of scanning, more widespread subcortical volume
abnormalities were observed in recurrent MDD patients including the hippocampus (Cohen's d=−0.14), amygdala (Cohen's d=−0.11), caudate (Cohen's d=0.21) and lateral ventricles (Cohen's d=0.16). In contrast, no differences between first episode patients and healthy individuals were observed. No associations between age of onset and use of antidepressant medication and subcortical volumes were observed. In conclusion, this currently largest worldwide effort to identify subcortical structural brain alterations showed robust reductions in hippocampus volume in MDD patients, with more widespread subcortical volume abnormalities in MDD patients with more than one depressive episode.

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