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# Understanding the pathophysiology of bipolar disorder

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Advances in magnetic resonance imaging (MRI) acquisition and analyses over the last two decades have enabled the identification of neuroanatomical abnormalities in a range of mental disorders, however one question which has consistently surfaced is the extent to which the medications used to treat such disorders may accentuate or ameliorate these abnormalities. Bipolar disorder causes substantial suffering and disability, but most patients can be successfully treated with mood stabilizing medication, such as lithium or valproate, and with antipsychotic or antidepressant medication during episodes of illness exacerbation. MRI studies comparing patients with bipolar disorder and healthy volunteers have demonstrated subtle grey matter volume deficits in patients, especially in brain regions underpinning mood regulation, as well as white matter disorganization in tracts interconnecting distributed brain regions. However studies tend to display considerable heterogeneity in their findings. In this review of in vivo neuroanatomical imaging studies of bipolar disorder to date, McDonald discusses the evidence that differential usage of psychopharmacological treatment is associated with alterations in neuroanatomy and thus an important source of this heterogeneity.

When greater weight is given to more powerful studies, with large numbers or with longitudinal design where intra-individual variation after initiation of medication is examined, substantial evidence emerges that medications used in bipolar disorder have a predominantly ameliorative affect on brain anatomy. This includes evidence that use of mood stabilizers such as lithium is associated with increased grey matter volume especially in brain regions underpinning mood regulation, as well as normalization of white matter disconnectivity. This generally normalizing effect of mood stabilizers on brain anatomy mirrors similar findings for brain physiology identified by functional neuroimaging studies. The implications of these findings for understanding the pathophysiology of bipolar disorder and future directions for research are discussed in detail in the review.

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