BRAIN MORPHOLOGY IN TWINS DISCORDANT FOR BIPOLAR DISORDER

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Brain morphological abnormalities are a robust correlate of bipolar disorder, but their etiology remains unresolved. Bipolar disorder is influenced by both genetic and environmental (e.g., perinatal complications) factors, but compared to schizophrenia few studies have examined their effects on the observed brain morphological abnormalities. Twin studies including both monozygotic and dizygotic twins, who share 100% and 50% (on average) of their polymorphic genetic material, provide a powerful method for identifying genetic and environmental influences. Regions that are more similar among monozygotic compared to dizygotic twins are thought to be influenced by genetic factors, while regional differences between ill-twins and their healthy monozygotic co-twins are though to be influenced by disease-related factors.

Examining the brains of monozygotic and dizygotic twins, using methods that either measure well-defined regions of interest or provide high-order registrations of individual shape differences among individuals, have been shown to be highly successful in identifying genetic and environmental influences in healthy twins (Thompson et al., 2001), as well as genetic and disease-related influences on regional brain morphology in schizophrenia (Cannon et al., 2002; van Erp et al., In press).

In our region of interest (ROI) based study, examining 24 twins with bipolar disorder, 15 of their healthy co-twins, and 27 control twins, both the patients and their healthy co-twins showed a significant decrease in left hemisphere white matter compared to the healthy control twins (Kieseppa et al., 2003), suggesting that left hemisphere white matter in bipolar disorder may reflect genetic factors predisposing to the disorder.

Identifying the causes of brain morphological deficits is important. Brain regions found to be influenced by environmental factors can aid in the search for specific environmental factors and their mechanisms of action. As such, they can suggest ways to prevent the impact of the environmental factors and/or avenues for treatment. Brain regions found to be influenced by genetic factors can serve as endophenotypes in linkage and association analyses in the search for predisposing genes.

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