The Bipolar Disorder Neuroimaging Database
A new tool for structural imaging research

www.bipolardatabase.org

National Institute for Health Research

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Introduction

We recently published a meta-analysis of 98 structural imaging studies in bipolar disorder[1] which revealed robust changes in brain structure such as lateral ventricle enlargement (+17%), increased rates of deep white matter hyperintensities (x2.5) and that lithium was associated with increased gray matter volume.

Here we present a freely available online database of 141 structural imaging studies in bipolar disorder and demonstrate six ways in which it may be used in planning and analysing structural imaging studies.

Method

• Study inclusion criteria: CT or MRI study of patients with bipolar disorder with a control group.
• MEDLINE, EMBASE and PSYCINFO databases were searched and a total of 1471 unique publications were examined. 141 publications fulfilled the inclusion criteria and were included in the database.

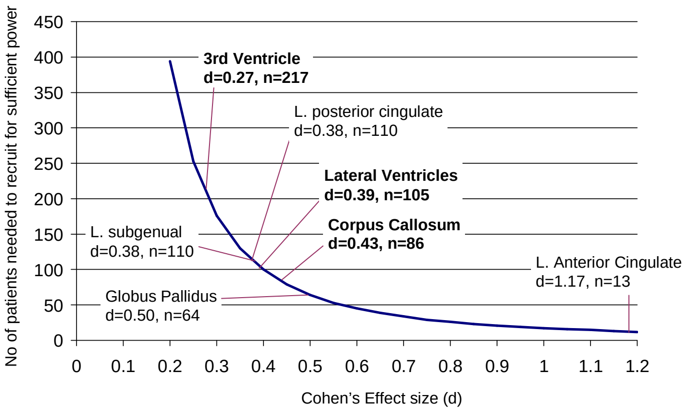
• The following were recorded from each study where available:
 - Mean age, age standard deviation, and number of females in the patient and control group
 - Diagnostic classification system (e.g. DSM-IV)
 - Number of bipolar I and bipolar II patients
 - Current medication and the number of patients previously treated with ECT
 - All brain regions measured
 - Field strength of the MRI scanner and slice thickness

• A priori power calculations were carried out using Gpower 3. Customised fixed effects meta-regressions were carried out using SPSS 15.0.

• To enable researchers to calculate an updated effect size, meta-analysis equations for a random effects, inverse weighted variance model (DerSimonian and Laird) were entered into Excel 2003.

Results

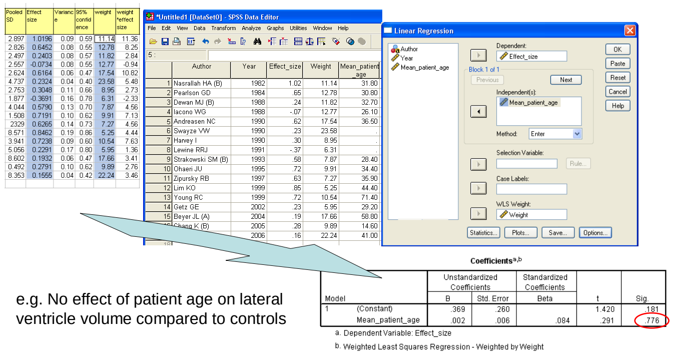
i) A priori power analysis



The graph shows the number of patients that are required to be recruited for sufficient power to detect significant differences (power=0.8, alpha =0.05). For example 105 patients and 105 controls are required to show a significant difference in lateral ventricle volume. Regions in **bold** were significant in the meta-analysis, other regions shown had large effect sizes.

ii) Performing a customised meta-regression

For a fixed effects meta-regression, effect size, weight and demographic variables may be extracted from the BiND database and analysed with SPSS in a weighted linear regression



e.g. No effect of patient age on lateral ventricle volume compared to controls

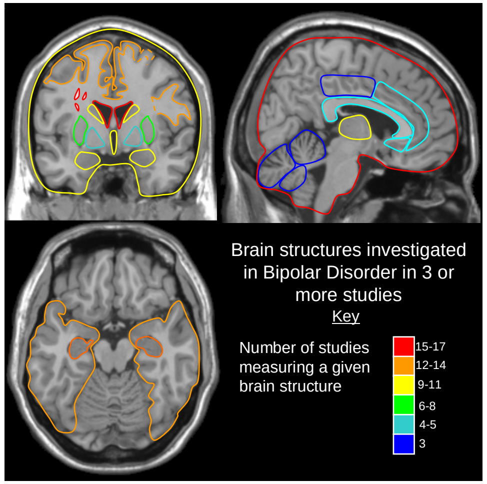
iii) Determining regions to investigate in relatives of patients with bipolar disorder

The regions with the highest significance and largest effect size from the database are listed below. We suggest studies on relatives of bipolar patients include these brain regions.

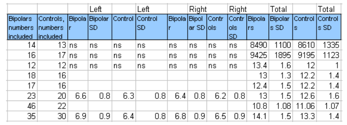
Significant Effect size	Large Effect size (non significant)
Lateral Ventricles	Left anterior cingulate
Deep white matter hyperintensities	Globus pallidus
Third ventricle	Left posterior cingulate
Corpus callosum	Left subgenual prefrontal cortex

iv) Aiding literature reviews for brain regions investigated in bipolar disorder

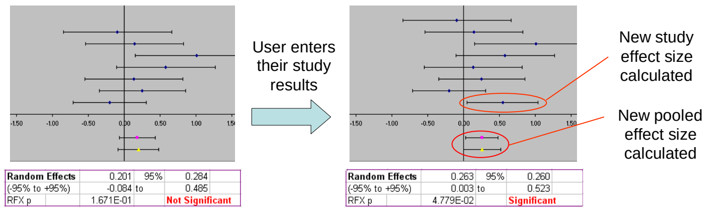
The database lists every brain region (>200) measured by the 141 studies and will aid literature reviews of a given brain structure.



v) Allowing individual researchers to calculate an updated effect size after their study is complete

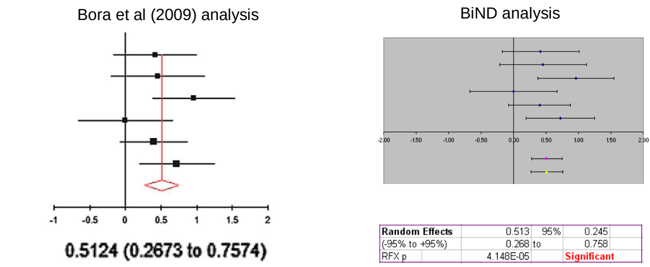


Full instructions are available on the website to show how the results of a new study can be added to the meta-analysis



vi) Use of the software to perform new meta-analyses in other fields of research

To demonstrate this we have entered data from a meta-analysis of Stroop task performance in first degree relatives of bipolar disorder[2] into the BiND database, and compared the results to the original analysis.



=> Calculated effect sizes and confidence intervals agree

Conclusion

We have demonstrated how the Bipolar Disorder Neuroimaging Database may used in a number of ways to aid researchers in planning and analysing structural MRI studies. We hope that authors who are undertaking meta-analyses of other types of data (fMRI neuropsychological, genetic, randomised controlled trials) may see the benefits of making their datasets freely available on the internet.

References
[1] Kempton MJ, Geddes JR, Ettinger U, Williams SCR, Grasby PM (2008) Meta-analysis, database and meta-regression of 98 structural imaging studies in bipolar disorder. *Archives of General Psychiatry* 65(9) 1017-1032.
[2] Bora E, Yucel M, Pantelis C (2009) Cognitive endophenotypes of bipolar disorder: A meta-analysis of neuropsychological deficits in euthymic patients and their first-degree relatives. *Journal of Affective Disorders* 133(1-2) 1-20

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