TECHNICAL COMMENTARY

Psychosocial treatments for first-episode bipolar disorder

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Introduction

The course of bipolar disorder and its treatment response tends to worsen over time, highlighting the importance of early intervention. As bipolar disorder cannot be diagnosed on the basis of depression alone, the onset of a manic episode may indicate an underlying bipolar disorder. Interventions for first-episode psychosis or depression have begun to be extended to those with bipolar disorder, however such interventions need to be tailored to suit people with first-episode bipolar disorder, and research is sparse for these patients.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2010 that report results separately for people with a diagnosis of bipolar or related disorders. Due to the high volume of systematic reviews we have now limited inclusion to systematic meta-analyses. Where no systematic meta-analysis exists for a topic, systematic reviews without meta-analysis are included for that topic. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Hand searching reference lists of identified reviews was also conducted. When multiple copies of review topics were found, the most recent and/or comprehensive review was included.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist which describes a preferred way to present a meta-analysis[1]. Reviews reporting less than 50% of items have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)[2]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found two systematic reviews that met our inclusion criteria[3, 4].

- Low quality evidence is unable to determine the benefits of interventions for people with first-episode bipolar disorder.

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McMurrich S, Sylvia LG, Dupuy JM, Peckham AD, Peters AT, Deckersbach T, Perlis R H

Course, outcomes, and psychosocial interventions for first-episode mania

Bipolar Disorders 2012; 14: 797-808

View review abstract online

Comparison	**Cognitive behavioural therapy for people with first-episode bipolar disorder who were in a euthymic state.**
Summary of evidence	**Low quality evidence (1 small study, unable to assess consistency or precision) is unable to determine the benefits of CBT for people with first-episode bipolar one disorder.**
Symptoms	
1 study (N = 7) assessed CBT adapted by including sessions devoted to discussing the meaning of a bipolar diagnosis, an increased focus on warnings signs of mood episodes, and formulating detailed relapse prevention plans. Authors report that after CBT, patients were able to identify significantly more early warning signs of both mania and depression, and they used significantly more adaptive coping strategies for the management of mania.	
Consistency in results‡	No measure of consistency is reported.
Precision in results§	No measure of precision is reported.
Directness of results‖	Direct

Vallarino M, Henry C, Etain B, Gehue LJ, Macneil C, Scott EM, Barbato A, Conus P, Hlastala SA, Fristad M, Miklowitz DJ, Scott J

An evidence map of psychosocial interventions for the earliest stages of bipolar disorder

Lancet Psychiatry 2015; 2: 548-63

View review abstract online

Comparison	**Interventions for people with first-episode bipolar disorder.**
Summary of evidence	**Low quality evidence (small studies, unable to assess consistency or precision) is unable to determine the benefits of interventions for people with first-episode bipolar disorder.**
Symptoms	
1 study (N = 7 patients with first-episode bipolar disorder 1 or 2) assessed the Think Effectively About Mood Swings (TEAMS) CBT approach for 3 months and showed reductions in depressive symptoms (effect size = 2.35) and manic symptoms (effect size = 0.89), along with cognitive and functional improvements. 1 study (N = 7 patients with first-episode bipolar disorder 1 or 2) assessed CBT for 6 months and reported improvements in depression, and coping with early warning signs of depressive (effect size = 1.97) and manic episodes (effect size = 1.62). 1 study (N = 108; 87 patients with bipolar disorder, 21 patients with schizoaffective disorder) assessed integrated intervention and medication for 12 months. Compared to patients with schizomania, patients with bipolar disorders showed significantly better functioning and fewer negative symptoms, although 30% of patients with bipolar disorder did not complete therapy. 1 study (N = 40 patients with first-episode mania with psychotic features) assessed CBT plus treatment as usual compared to treatment as usual (case management and medication) for 18 months. There were significantly greater improvements in depressive symptoms, illness severity, and functioning with CBT, although manic symptoms and overall relapse rates were similar across groups.	
Consistency in results	No measure of consistency is reported.
Precision in results	No measure of precision is reported.
Directness of results	Direct

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Explanation of technical terms

† Different effect measures are reported by different reviews.

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) which allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. 0.2 represents a small effect, 0.5 a moderate effect, and 0.8 and over represents a large effect[5].

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[6]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They are an indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

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‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula[5];

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

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§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary

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data) and 400 (for continuous data), although for some topics, these criteria should be relaxed[7].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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