TECHNICAL COMMENTARY

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Psychotic symptoms

Introduction

Psychotic symptoms are sometimes found in people with bipolar disorder, particularly in the manic phase of the illness. The severity of psychotic symptoms can significantly affect a person's day-to-day functioning, quality of life, and cognition.

Psychotic symptoms most commonly involve hallucinations and delusions. Hallucinations are defined as a perceptual experience that occurs in the absence of any corresponding external sensory input. They are most commonly auditory, but can occur in any modality. Delusions are fixed, false beliefs that persist regardless of contradictory evidence, and are not explained by cultural beliefs. Persecutory delusions involve the belief that people are attempting to harm or even kill the individual. Delusions of reference refer to beliefs that neutral events are directed specifically towards the individual. Somatic delusions involve the belief that the individual has a serious physical disease or alteration of the body. Delusions of grandeur are characterised by an exaggerated belief that the individual has extraordinary powers, abilities, or fame.

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. 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, only the most recent and comprehensive version was included. Reviews with pooled data are prioritised for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[1]. Reviews rated as having less than 50% of items checked 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, there is a dose dependent response or if results are reasonably 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].

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- Moderate quality evidence suggests the prevalence of visual hallucinations in people with affective psychosis is around 15%, and the prevalence of auditory hallucinations is around 28%. These rates are lower than in schizophrenia (visual = 27%, auditory = 59%), Parkinson's disease (15-40%), dementia with Lewy bodies (60-90%), age-related eye disease (10-60%), and death-bed visions (50%). They are higher than general population rates (7%).
- Moderate to low quality evidence suggests the lifetime frequency of delusions is higher than the lifetime frequency of auditory hallucinations (66-82% vs. 23-31%).
- Auditory hallucinations are more frequent than visual, olfactory, tactile, or gustatory hallucinations, are most common in the early stages of the disorder, and in people with a history of childhood abuse.
- Rates of delusions and auditory hallucinations are higher in people in a manic episode than in people in a depressive episode. Rates of auditory hallucinations are most common in people with mixed-manic presentations.

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Smith LM, Johns LC, Mitchell R

Characterizing the experience of auditory verbal hallucinations and accompanying delusions in individuals with a diagnosis of bipolar disorder: A systematic review

Bipolar Disorders 2017; 19: 417-33

View review abstract online

Comparison	**Psychotic symptoms in people with bipolar disorder.**
Summary of evidence	**Moderate to low quality evidence (direct, large sample) suggests the lifetime frequency of delusions is higher than the lifetime frequency of auditory hallucinations (66-82% vs. 23-31%).** **Rates of delusions and auditory hallucinations are higher in people in a manic episode than in people in a depressive episode. Rates of auditory hallucinations are most common in people with mixed-manic presentations.** **Auditory hallucinations are more frequent than visual, olfactory, tactile or gustatory hallucinations, are most common in the early stages of the disorder, and in people with a history of childhood abuse.**
Psychotic symptoms	
32 studies, N = 8,727 Delusions were more prevalent than auditory hallucinations, with lifetime frequency estimates ranging from 66% to 82%. Rates were higher in people in a manic episode (48% to 93%) than a depressive episode (12% to 77%). Lifetime frequency of auditory hallucinations was between 23% and 31%, although 34% to 67% frequency was found in samples selected for a history of psychotic episodes. Auditory hallucinations were generally reported more frequently than visual, olfactory, tactile or gustatory hallucinations, and are most common in the early stages of the disorder, and in patients with a history of childhood abuse. Auditory hallucinations are most commonly associated with mixed-manic presentations (49% to 67%), than manic episodes (12% to 58%) or depressive episodes (7% to 50%).	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Waters F, Collerton D, Ffytche DH, Jardri R, Pins D, Dudley R, Blom J, Mosimann U, Eperjesi F, Ford S, Larøi F

Visual hallucinations in the psychosis spectrum and comparative information from neurodegenerative disorders and eye disease

Schizophrenia bulletin 2014; 40 Suppl 4: S233-S45

View review abstract online

Comparison	**Prevalence and features of hallucinations in people with affective disorders vs. schizophrenia, neurodegenerative and eye disorders, and non-clinical groups.**
Summary of evidence	**Moderate quality evidence (large samples, unable to assess consistency or precision, direct) suggests the prevalence of visual hallucinations in people with affective psychosis is around 15%, and the prevalence of auditory hallucinations is around 28%. These rates are lower than in schizophrenia (visual = 27%, auditory = 59%), Parkinson's disease (15-40%), dementia with Lewy bodies (60-90%), age-related eye disease (10-60%), and death-bed visions (50%). They are higher than general population rates (7%).**

Prevalence and features of hallucinations

Affective psychosis

12 studies, N = 2,892, mean prevalence of visual hallucinations = 15%, mean prevalence of auditory hallucinations = 28%

Schizophrenia

29 studies, N = 5,873, mean prevalence of visual hallucinations = 27%, mean prevalence of auditory hallucinations = 59%

Parkinson's disease

Frequency rates range from 15-40%

Dementia with Lewy bodies

Frequency rates range from 60-90%

Age-related eye disease

Frequency rates range from 10-60%

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Death-bed visions Frequency rates around 50% General population 6 studies, N = 26,458, mean prevalence of visual hallucinations = 7.3%	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

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Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[5].

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

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) that 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 medium 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

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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.

‡ 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 be 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];

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

§ 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 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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