Characterising the experience of auditory verbal hallucinations and accompanying delusions in individuals with a diagnosis of Bipolar Disorder: a systematic review

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Abstract

Objectives

The current study aimed to inform ongoing attempts to identify clinically meaningful subcategories of auditory verbal hallucination (AVH), and to evaluate evidence that might pertain to the suitability of current psychological interventions for people with BD that experience psychotic symptoms.

Method

A comprehensive synthesis of findings on the phenomenology of AVH and delusions in Bipolar Disorder (BD) is included, alongside a critical review of clinical and cognitive correlates. Studies published in the previous twenty years until December 2016, were retrieved from the following databases: Embase, CINAHL, MEDLINE, PsycINFO and Web of Science. 32 articles were reviewed after applying a set of pre-determined inclusion criteria.

Results

Psychotic symptoms were common in both manic and depressive phases, although higher frequencies were indicated in mania. Few detailed characterisations of AVH phenomenology were identified. Delusions with persecutory, grandiose and referential themes were the most common in BD. AVH were associated with delusions and there was evidence to suggest that delusion subtype may vary according to mood state and type of AVH. Data on clinical correlates of AVH in BD were sparse. However, the results indicated that cognitive appraisals or interpretations of voices might be different in BD to those established to be predictive of clinical outcomes in schizophrenia spectrum disorders.

Conclusions

Clear gaps exist in our current understanding of the first-person experience of AVH in BD and the potential relationship to co-occurring symptoms, including delusions. Further research into cognitive interpretations of AVH in BD might inform adapted psychological interventions for psychotic symptoms in this population.

Introduction

The frequency at which the positive symptoms of psychosis are reported within the acute mood episodes of BD (mania, depression, mixed states) has by some studies been found to be almost comparable to the rates observed in schizophrenia (SCZ) [1]. Indeed, across jurisdictions individuals with a diagnosis of BD make up a sizeable proportion of hospital admissions following a psychotic episode [2-3]. Alongside this issue of prevalence, recent research trends have contributed to a rise in studies specifically investigating AVH and their relationship to other symptoms in BD. First, mental health research has moved towards increased scrutiny of psychiatric symptoms as they occur across diagnoses [4]. Once considered pathognomic for schizophrenia, the experience of AVH, in some form, has now been evidenced in other physical and mental health conditions, and in those without a need for mental health care [5-6]. A comprehensive explanation of psychotic phenomena will therefore entail a detailed understanding of the differentiating characteristics across diagnostic classifications [7].

Second, there has been a concerted effort within hallucinations research to improve existing subcategorizations of AVH [8]. Voice-hearing experiences are acknowledged for their incredible complexity and diversity [9]. Hence, AVH may be categorised at several different levels e.g. phenomenology, cognition, neurology, etiology, treatment response, diagnosis or a voice hearer's own interpretations [8]. However, the International Hallucination Research Network has given some priority to the advance of more clinically meaningful phenomenological taxonomies, as research has highlighted the shortcomings of previous attempts [10]. For example, Schneider's first rank symptoms (e.g. voices conversing in the 3rd person or the belief that one's thoughts are being controlled by an outside force), have been found neither to predict reliably a diagnosis of schizophrenia, nor need for care [11-12]. The

utility of mood congruence criteria, used to distinguish psychotic features experienced in BD from schizophrenia and to determine prognosis in both main operational diagnostic manuals (DSM-V, APA, 2013; ICD-10, WHO, 1992), also continue to be debated [13].

The potential benefits of advancing research into AVH and their correlates in BD are several. Lack of sophistication in phenotypic subcategories of AVH has been identified as a key barrier to the progress of aetiological neurocognitive research [14]. To facilitate better mapping of evidence obtained at different levels of analysis (e.g. neurobiological, cognitive and behavioural), the National Institute for Mental Health's Research Diagnostic Criteria (RDoC) initiative has provided a framework of transdiagnostic dimensions within which to organise and harmonise research [4]. Initial attempts to generate more meaningful phenomenological subtypes of AVH have been consistent with this RDoC approach and they offer the hope of improved integration of research findings [8]. However, these more recently proposed phenomenological sub-typing systems have still been restricted by a lack of reliable data on the characteristics of AVH outside of schizophrenia spectrum populations [15]. In order to avoid potential bias in developing models of AVH, phenomenological information derived from other populations will need to be assessed and assimilated [16- 17]. Specifically, within BD, the study of AVH has the potential to reveal valuable insights as to the contribution of affective and emotional state characteristics to the frequency and qualities of the experience[18]. Continuing to consider the relationship of AVH to other symptoms in BD, like delusions, may also prevent reductionist subtyping systems from diverting attentions away from meaningful connections between hallucinations as perceptual disturbances and higher-order cognitive processes [8].

A second important reason for advancing research into psychotic symptoms in BD is the potential to inform decision-making regarding differential diagnosis. Diversity in the symptoms experienced by people, particularly in the earlier stages of illness, can contribute to misdiagnosis or under-diagnosis of BD [19-20]. Whereas a clearer picture of the characteristics of psychotic symptoms as they might be experienced in BD could improve the rigour of clinical assessment and diagnosis [21]. Alternatively, research into AVH and delusions in BD might contribute to refinements in newer conceptualisations of the relationship between BD and schizophrenia-spectrum conditions, which depart from categorical diagnosis (e.g. continuum approaches) [22-23].

However, the ultimate aim of research into the AVH phenomenon in BD is to better the care and treatment that can be offered to individuals with potentially very distressing experiences. It has long been recognised that psychotic phenomena are not always experienced negatively by individuals, nor judged negatively by social communities [24-26]. Yet within the context of schizophrenia they are reported to be amongst the most debilitating aspects of illness [27]. Individual interpretations of AVH in BD may yet to be systematically examined. Psychotic experiences may or may not be appraised negatively by individuals with BD, and beliefs about AVH might differ depending on mood state [18,28]. Given the high rates of (potentially psychotic) relapse in BD and associated costs to the individual and society, there are important benefits that might be derived from a better understanding of responses to psychotic phenomena in BD and their potential impact on the longer-term course of illness [29].

Current international treatment guidelines specify the prescription of antipsychotic medication or electroconvulsive therapy for people with BD who experience psychotic symptoms within acute mood episodes [30-32]. Psychosocial interventions are indicated as an

adjunctive therapy, principally in the treatment of bipolar depression and during the maintenance, as opposed to acute or early stages [32]. Evidence supports a range of interventions, including cognitive behavioural, interpersonal and family therapies, in managing residual depressive symptoms, relapse and general social functioning, but not psychotic symptoms [30-32]. Indeed, the evidence base for targeted, specific psychosocial interventions for people with BD is still developing [31]. The prospect of better phenomenological subtyping systems and subsequent models of AVH leading to improvements in neurobiological treatments for BD is likely a distant one. However, a more nuanced understanding of the experience of AVH and delusions in BD might bring nearer-term improvements to recommended psychological interventions. At the very least, further study could inform ongoing assessment of the requirement for, and suitability of existing voice-hearing interventions, developed within schizophrenia and psychosis populations, for people with BD who experience hallucinations [33].

Aims of the review

This review was intended to update and extend previous critiques of studies investigating psychotic symptoms in BD [34-37]. The literature was examined to assess how the characteristics of AVH and delusions, as well as their relationship with one another, might change across the acute mood episodes in BD. Specific consideration was also given to available information on the clinical and cognitive correlates of AVH and delusions, to inform ongoing evaluation of the generalizability of developing psychological interventions for individuals with BD who experience psychotic symptoms.

Method

The review was conducted and reported with reference to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, PRISMA, [38].

Databases searched

A search for studies was conducted on the 29th December 2016 using the following online search platforms: i) PubMed (National Centre for Biotechnology Information). This included the most up to date MEDLINE registry of biomedical articles, 'in-process and other non-indexed citations' and citations available online ahead of print. ii) PsycINFO for psychological and behavioural sciences research and EMBASE for biomedical science research via OVIDSP. iii) The CINAHL (EBSCOhost) database for studies relevant to nursing and allied health professionals. iv) Web of Science (Thomson Reuters), including the Science Citation Index Expanded and Social Sciences Citation Index.

Search strategy

Titles and abstracts were searched. Database-specific Boolean search strings were created using variants to the following key terms: 'mania' or 'hypomania' or 'bipolar' or 'manic depression' or 'affective psychos$' AND 'hallucinat$' or 'delusion'. Full database-specific search strings are provided in Appendix 1.

Inclusion criteria

Studies were included if they met the following criteria: i) Reported empirical data on auditory hallucinations or delusions specifically. ii) Involved >10 adults with a diagnosis of BD confirmed through structured clinical interview. iii) Were published in the last 20 years

(1986 - present). iv) Were available in the English language. v) Reported results in full (conference abstracts were excluded).

Data extraction

To examine the main review questions, all results relating to the structure or content of AVH and delusions, as well as associations between these symptoms were recorded. Study sample details were also noted, including BD subtype (Type I or II) and any information reported about participant mood state relative to the expression of psychotic symptoms. Additional main findings relating to the clinical or cognitive correlates of AVH or delusions were extracted to inform a narrative synthesis to guide future research.

Quality Assessment

To inform evaluations of the comparability of results, measurement instruments used to assess psychotic symptoms were recorded from included studies. Some key strengths and weaknesses in the experimental design were also noted.

Results

Details of the search and selection process are shown in Figure 1. Thirty two papers were included in the review. Data extracted from selected studies are shown in Table 1.

Figure 1, attached

Table 1, attached

1. Frequency and course

Auditory Hallucinations

Several studies, but not all [39,] suggested that auditory hallucinations (AH, including other sounds) were the most frequent type of hallucination in BD, as opposed to visual, olfactory, tactile or gustatory [40-46]. Lifetime AH frequency estimates across BD Type 1 diagnoses were reported between 23% and 31% [46,55]. Although higher rates, between 34% and 67%, were found in samples already pre-selected for a history of psychotic episodes [1, 43, 47-49]. As expected, elevated AH rates were similarly indicated when measured during acute mood episodes, whether in depression (50%), mania (58%) or mixed states (49%), respectively [41,50-51]. Although the results supported the notion that AH in BD are more commonly associated with manic episodes (12%-58%) [1, 44-45, 50, 53-54] than with depressive episodes (7%-50%) [39, 41, 53, 56] and are potentially most frequent within mixed-manic presentations (49%-67%) [1, 40, 51.] There were comparatively fewer studies conducted with people in depressive mood states and there were only three studies that directly contrasted AH frequencies across affective subtypes [46, 57, 59]. Higher AH rates in mania were confirmed in these studies, but the differences reported were actually quite modest. Further examination of AH phenomena may therefore be required within the depressive phases of BD [41, 56].

With regards to the time point at which AH might develop in the course of illness in BD, Ryu and colleagues (2012) reported that even for those people whose most recent affective episode was free from psychotic symptoms, one fifth still experienced AH in the prodromal (early symptomatic) stages of illness [57]. Whereas for individuals who had later psychotic experiences within mood episodes, nearly one half said they also heard voices when they first became ill [57]. The results of this study suggest that the presence or absence of hallucinations in early mood episodes need not necessarily predict later recurrence or chronicity in BD.

However, the same study also estimated a significantly earlier age of illness onset for BD with psychotic features ($p = .05$, mean = 27 vs 31 years), which is often interpreted as being indicative of more severe variants of illness [57]. There is evidently a requirement for longitudinal assessment of psychotic symptoms in BD if research is to explore fully the initiation and maintenance of AH. Additionally, there may be a potential clinical opportunity to discuss the implications of psychotic symptoms experienced within early mood episodes for diagnosis and prognosis.

Four prospective studies captured by the review attempted to examine the ongoing course of hallucinations in BD. Carlson and colleagues (2012) found that most of those admitted with hallucinations (89%) went on to have at least one further psychotic admission over the next four years [58]. Similarly, Gaudiano et al., (2007) found that after an initial index psychotic episode, people with BD went on to report further psychotic symptoms, 5% of the time over a 28-month period [44]. This compared to 29% of the time when people reported acute mood symptomatology [44]. Psychotic episodes in BD may therefore be neither singular nor entirely discrete experiences. Nevertheless, the typically transient nature of AH in BD and their unique association with affective episodes was demonstrated by other studies [45, 59-60]. As was the tendency for AH to be less frequently reported over time in BD than in, for example, schizophrenia spectrum conditions [60]. Indeed, a longitudinal study by Goghari et al., (2016) found that the proportion of individuals with BD reporting AH experiences reduced over a 20-yearlong period [60]. There are many potential explanations for fewer later life experiences of AH in BD, including the longer-term effects of medication on the frequency or chronicity of mood episodes. However, the results of this study suggest perhaps that AH experiences in BD might be anticipated earlier in the course of illness.

Delusions

In general, the results indicated that delusions were a more prevalent experience for people with BD than were AH. Frequency estimates for the proportion of individuals with BD Type 1 ever having reported delusions, irrespective of mood state and not pre-selected for psychotic episodes, ranged from 66% - 82% [40, 46, 49, 52, 61]. Amongst samples of individuals specifically with mania as opposed to depression there were twice as many studies that reported on delusions. A total of 48% - 93% of those with current or past experiences of psychotic mania reported at least one type of delusional belief [1, 44-45, 50, 53, 54, 58, 62-64]. Whereas within depressive episodes, the proportions of people reporting delusions ranged from 12% to 77% [41, 53, 56, 65]. Two studies directly compared the rates of delusions in BD manic and BD depressed groups. Baethge et al. (2005) recorded less frequency in depression (70% vs 63%) and non-significant differences in delusion severity [40]. Similarly, Black and Nazarallah (1992) found that those with depression had significantly fewer lifetime delusions (44% vs 12%) [53]. However, it is notable, that certain studies of chronic depression in BD have found nearly all individuals to experience delusions (e.g. 99%) [66]. Evidently therefore illness characteristics other than the predominate valence of any mood episode, e.g. its severity, may mediate the likelihood of experiencing psychotic symptoms.

Delusional beliefs were reported from early in the course of illness by individuals with and without a most recent diagnosis of BD with psychotic features [57]. Indeed, several studies noted delusion proneness even amongst subsamples deemed 'non-psychotic' based on diagnosis or study inclusion criteria [40, 47, 52, 62, 65]. As evidenced across other disorders and in non-clinical populations, delusional ideation may therefore be experienced by individuals with BD independently of other psychotic symptoms, including AH, and need not necessarily be associated with exacerbating illness [24]. Nevertheless, several studies confirmed positive

correlations between the frequency of hallucinatory experiences and delusions in BD [40,43,47]. As expected, this demonstrates that the cascade of neurobiological processes that underpin the experience of hallucinations in BD may typically also lead to accompanying changes in the severity of delusional beliefs.

2. Form and content

Auditory Hallucinations

In the most recent study in the review, Toh and colleagues (2016) examined the prevalence of three subtypes of AVH in BD and other affective psychoses: voices with negative content, voices conversing in the third person and voices providing a running commentary [47]. All three of these subtypes were endorsed in BD, in current and lifetime estimates. Yet at lower rates than in depressive psychosis (MDD), Schizoaffective Disorder (SCD) and Schizophrenia (SCZ). Principal comparisons in the study were made between BD and MDD. Contrary to study hypotheses, lifetime AVH subtype rates were comparable across the two diagnoses and there were also no significant differences in current AVH rates [47]. However, fewer individuals with BD compared to MDD reported current negative voices or running commentary over the previous month [47]. Several additional studies confirmed that one-to-two thirds of individuals with BD and hallucinations might report hearing voices conversing or commenting on a person's actions (30% - 67%) [39, 41, 43, 46, 52, 63]. These findings are relevant because voices speaking in the third-person, using ‘he’, ‘she’ or ‘they’ as the form of address, together with hearing one's thoughts spoken out loud, were historically thought to be sufficient for a diagnosis of schizophrenia, but have now been reported across diagnoses [11, 67]. Nonetheless, across the reviewed studies there was the suggestion of a trend towards more frequent 'second-person' voices in BD, using 'you' as a form of address, particularly within manic episodes [42, 68]. This is consistent with the ICD 10's description of the typical form of

AVH in mania (WHO, 1992). Moreover, it potentially indicates avenues for future research into AVH subtypes in BD, which might include further exploration of commanding hallucinations, speaking directly to the individual, when in mania.

Kumari and colleagues (2013) were the only group to attempt to examine specific dimensions of the form of AVH using a clinical assessment instrument, the Psychotic Symptoms Ratings Scale (PSYRATS, Haddock et al., 1999) [42, 69]. Although those with 'affective psychoses' (mainly mania in BD) expectedly scored less than individuals with 'non-affective' psychoses on each of the PSYRATS domains that measure, for example, frequency, duration, amount of negative content and amount of distress, they reported greater intensity of distress from AVH[42]. They also reported higher levels of conviction in delusional beliefs [42]. However, these observations may simply represent the fact that hallucinations tend to occur in BD during the most severe periods of illness. Two studies also found that when AH were experienced in BD they tended to be mood-congruent or "*consistent with depressive themes like guilt or illness…or manic themes like inflated worth or power*" [45-46].

Delusions

Some 17 studies attested to the broad range of delusional themes observed across the illness course and in different diagnostic variants of BD [1, 40-41,43, 44-45, 47-48, 50, 52-54, 56-58, 62-63]. Indeed, there were no consistent findings differentiating BD from other psychotic disorders based on the content of delusions [1, 41, 56]. Although Pini and colleagues (2004) did find that the frequency of delusions of grandeur differentiated BD with mania, from SCZ and SZD[1]. These findings support established theories that specify shared cross-diagnostic mechanisms in the development of delusional thinking [70.] Additional studies confirmed that grandiosity reaching delusional severity was most frequently reported by individuals with manic presentations [44-

[45, 50, 58, 62-63]. Whereas, persecution and paranoid delusions were most frequently reported in studies examining depressive episodes and general samples of individuals with BD irrespective of current mood episode [40-41, 56]. These results suggest a potentially direct effect of mood on the content of delusions, such that particular delusional themes may be associated with certain mood states [63]. Negative mood states and emotions, for example, have already been well-recognized for their role in influencing the occurrence and content of persecutory delusions within the schizophrenia literature [71]. Delusions of reference were also commonly reported across BD samples [40, 41, 48, 50, 56], including cross-culturally [63], and may or may not relate to grandiose beliefs about self-worth or power. Toh and colleagues (2016) further examined the relationships between specific types of AVH and delusions in BD [47]. They observed a degree of specificity in the relationships between negative voices and persecutory delusions, and voices conversing/running commentary and delusions of thought alienation [47]. By contrast, grandiose delusions were not related to any specific type of AVH examined by their study. Similarly, Baethge et al. (2005) found that persecutory delusions, followed by delusions of reference, most frequently accompanied AVH experiences, whereas non-hallucinating individuals were more likely to present with delusions of grandeur [40.]

3. Clinical and cognitive correlates

Socio-demographics

There was some evidence to suggest that psychotic symptoms in BD [51, 60], and AVH in particular [43], might be associated with lower levels of education. Although people with BD will usually experience their first episode of illness after typical schooling age [36]. This suggests a potentially higher level of social adversity in the experiences of those who go on to develop psychotic symptoms in BD. Alternatively, it may indicate a more severe disease variant, with a longer prodromal period of illness or earlier cognitive dysfunction that might

have impacted ability to access education. Importantly, lower levels of education amongst people with BD and psychotic symptoms have been shown to predict fewer periods of recovery and employment in the future [60]. Bräunig et al. (2009) found that women with BD were significantly more likely than men to experience delusions [50]. More specifically, the researchers observed that delusions involving paranoia/reference and mood-incongruent delusions respectively were more marked in women [50]. This potentially suggests an association between female gender and more negative mood states, and indeed women in their study did have more previous episodes of depression than psychotic men. The possibility of a mediating role for depression and anxiety in explaining higher frequencies of mood-incongruent psychotic symptoms and paranoia in study samples has been cited by other researchers [1, 40, 48].

Illness outcomes

The significance of hallucinations and delusions in BD for prognosis was an additional clinical focus in several longitudinal studies [44, 51, 54, 60] and retrospective analyses [62, 66, 48-49]. Outcome measurements were examined over periods of 24 months to 20 years and variously included, but were not limited to: i) Symptomatic or illness course variables e.g. symptom recurrence, percentage time spent in mood or psychotic episodes and periods of symptom remission. ii) Indicators of chronicity including relapse, hospital re-admission, re-diagnosis and attempted suicide, and also iii) Measures of psychosocial or vocational functioning and life-satisfaction. The results were conflicted as to the importance of psychotic phenomena in predicting illness outcomes. The lack of consistency in these findings likely in part reflects the heterogeneity of BD itself, but may also be a function of variability in study design. Nonetheless, by virtue of being associated with mixed-mania, and possibly therefore greater emotional disturbance, hallucinations and delusions (general) predicted higher recurrence

rates over 2 years and higher overall mood symptom scores in Azorin et al. (2013) [51]. Indeed, a positive association between psychotic symptoms and worse outcomes in BD was reported in several studies [49, 54, 58], but not all [44, 48]. Similarly, in comparisons of illness outcomes made across BD with psychotic features and other conditions no consistent differences were reported [61, 66, 60]. These findings therefore serve to continue a long-standing and unresolved debate about the prognostic significance of psychotic symptoms in BD, as noted in several other studies [e.g. 58]. The issue is unlikely to be clarified without greater specificity and concordance in the measurement of psychotic symptoms and clinical outcomes, and without greater consistency in the sample populations being compared. Keck and colleagues (2003) for example remarked that high levels of chronicity across their sample may have explained the lack of differences in illness outcomes observed between individuals with and without a history of psychotic episodes [48]. The complicating issue of diagnostic switching was also highlighted by certain studies, with up to 22% of individuals engaged in longitudinal studies having changed diagnosis at follow-up [54, 58].

Clinical correlates

Insight and coping

An association between AH and delusions and reduced insight into illness was further reported by three studies [40, 42, 62]. Clinical insight in each study was assessed using different measures of an individual's general awareness of symptoms, judgement or openness to feedback about illness and self-reflectiveness, for example, using the Beck Cognitive Insight Scale [73] in Kumari et al. (2013) [42]. The implication being that psychotic symptoms significantly impact information processing in such a way as to impede an individual's ability to distance themselves from symptoms or cognitive difficulties [74]. Indeed, Canuso and colleagues (2008) reported that psychotic features within acute mood episodes were

associated with reduced insight, over and above the impact of mania [62]. Kumari et al. (2013) also reported that whilst outpatients with affective psychoses (majority BD) had significantly better insight into illness than those with SCZ, some 50% of their sample were still unaware of illness (by contrast to 60% in SCZ) [42]. These results suggest potentially differential but compounding influences of manic and psychotic processes on levels of insight, although any supposed causal relationship may also exist in the opposite direction. The prediction of levels of insight is clinically relevant given the acknowledged relationship between insight and responses to treatment [75]. Azorin and colleagues (2013), for example, found that medication compliance was significantly reduced in those with mixed mania by comparison to those with predominately mixed depressive episodes (30.4% complied no more than half the time by contrast with 10.4%) [51]. Several reasons were cited for the difference in medication compliance between BD subtypes, including care management, attitudes to mood states and to treatment regimes. However, the potential contribution of increased delusions in this group and associated reductions in insight were proposed as influential factors [51]. Ryu and colleagues (2012) also found that people with BD who had prodromal psychotic symptoms, by comparison to those who didn't, were more likely to engage in denial and blaming coping strategies, which they related to reduced insight and which they found was associated with a longer prodromal period and potentially therefore delayed engagement with treatment services [57].

Trauma and attributions

Two studies reported a significant association between childhood abuse and AVH in BD [46,55]. This is consistent with the literature in schizophrenia [76]. Several theories have been proposed as to the mechanisms by which trauma may lead to the development of hallucinations and how recurrent AVH may be driven by dysregulation in mood [77]. For example, early traumatic

insults have been conceptualised to result in abnormal activation of neuronal networks in the auditory cortex, resulting in altered salience (or perceptual prominence) of auditory signals [77.] Affective disturbance (as is experienced in BD, but which may be a result of different internal or environmental causes) is hypothesised to play a role in initiating cognitive processes that might interact with altered signals from the auditory cortex to result in misattributions of this information to an external source. For example, the relationship between mood dysregulation, trauma and AVH might operate through memory processes, with affective disturbance leading to changes in reality or self-monitoring in such a way as to make an individual more vulnerable to intrusions from memory and faulty source attributions [77]. Further research into the nature of traumatic events as experienced by those with BD might consider not just their potential role in initiating processes that might lead to hallucinations but also how particular traumatic incidents might influence the content and quality of AVH, people's beliefs about voices and their emotional and behavioural reactions to them [5].

Hammersley and colleagues (2010) reported clinically relevant differences in the attributions individuals with BD made about AVH by contrast to SCZ [39]. More specifically, the researchers found that beliefs that the voices intend to do harm and are all powerful, which are known to predict distress in SCZ, were comparatively rare amongst individuals with BD (30% within mood episodes, only one individual post episode). Albeit this was one small study's (n=40) findings, but the results have potential implications for models of AVH that are based on traumatic events as primary neurological insults, and subsequent processes that are driven principally by negative affective disturbance (i.e. depression and anxiety). In order to provide a comprehensive model of AVH, mechanisms and pathways will need to be identified by which voice experiences that are not perceived negatively may arise. This may require further research into the links between trauma and appraisals or attributions of voices

in BD. The results of the study by Hammersley et al. (2010) also raise questions about whether existing clinical interventions for psychosis, that target voice appraisals, could be adapted to include attributions other than those observed in SCZ to be effective in reducing distress and functional disturbance for the range of experiences of individuals with BD [55].

Discussion

This review set out to investigate the specific nature of AVH and delusions in BD. We wanted to know how the experience might differ for individuals relative to potential mood fluctuations. Specifically, we also looked to the literature for data on clinical and cognitive correlates that might be relevant to the development of more targeted psychological interventions for people with BD who experience psychotic mood episodes or ongoing residual psychotic symptoms. A broad base of evidence confirmed the frequency of AVH and delusions in BD. However, more detailed investigations of the course, phenomenology and correlates of these experiences were notably absent, particularly in the case of AVH.

Frequency and course

AH rates were reported in the studies reviewed here between 7% and 67% [1, 53]. Delusions were found in 39– 99% of people [78-79]. Expectedly, psychotic symptoms were commonly reported in acute mood states [e.g. 1, 41, 50, 66] and there was some evidence to support the assumption that AVH and delusions are more frequent in mania than depression [40, 53]. The discrepancies in rates observed between studies that examined lifetime AH experiences versus those within a recent mood episode, potentially indicate a tendency for longer-term, retrospective approaches to underestimate the proportion of people with BD who hallucinate. Although even when measured at the time of an admission, certain studies still found rates that were more conservative than others (e.g. 12%) [40, 52]. Additional factors to the time period

over which measurement was taken must therefore be considered when explaining discrepancies in AH frequencies. Most importantly, lower estimates were observed in studies that examined individuals irrespective of mood state or diagnostic mood subtype [39-40, 46]. Alongside differences in sample and mood characteristics, the use of varied measurements of AH may have affected the rates obtained. More marginal rate differences might also be attributed to an increased focus specifically on examining auditory 'verbal' hallucinations (AVH), within an AH category that might also include sounds. The results therefore highlight the need for controlled comparison studies, with better characterization of mood state and greater attention to specific subtypes of AVH and delusions.

Form and content

Examination of the data on the form and content of AVH in BD highlighted a lack of studies examining specific phenomenological characteristics of the experiences in detail. Greater information was available on the types of delusions in BD relative to mood, with mania being strongly associated with delusions of grandeur [e.g. 50, 58, 62], and paranoia being more frequent in depression and across lifetime assessments of delusional ideation in BD [40-41, 47, 54, 56]. More recent research indicated advances towards the assessment of specific subtypes of voices and their potential relationships to delusional themes [40-42, 46-47.] Several studies suggested that the content of AVH were more likely to be mood congruent than mood incongruent [45-46]. However, shortcomings in the mood congruence construct were also noted [44.] At present, mood congruence criteria, as detailed within international diagnostic statistical manuals, refer only to voice content and judge mood congruence based on objective observation (DSM-V, 2013, ICD-10, 1992). Perhaps the criteria might be improved by referring to additional specific elements of voice phenomenology, including how AVH are experienced by the individual relative to their mood, rather than clinical judgement alone.

Additionally, there was some suggestion that AVH in BD might be more likely to use a second person form of address in mania [41-42]. Although voices conversing and giving commentary in the third person were also frequently reported [39, 43, 46]. Recent research has indicated that there may be no specific feature or property to AVH that is uniquely associated with specific diagnoses [67.] The results of the current review are consistent with this finding. Nevertheless, we did also observe the possibility of shortcomings in the assessment tools available to identify potential differentiating features in AVH in BD versus other conditions [42]. There is some inconsistency to the findings that AVH may be more frequent in manic episodes, alongside delusions of grandeur; that AVH are also associated with delusions, yet delusions of grandeur were not reported by any study to correspond to the hallucinations as assessed. It may be that psychotic symptoms associated with manic episodes remain too difficult for individuals to access or researchers to assess. However, it would be worth trying to ask more specific questions about the nature of AVH experienced within acute mood episodes soon after people have stabilized. Indeed, it has recently been proposed that what might differentiate hallucinatory experiences across mental illnesses may be less likely to be found in the specific content of the perceptual experience itself, but rather in the transformations or alterations of consciousness that give rise to these mental events [80]. Given the relapsing and remitting course of BD and the preponderance of psychotic symptoms within acute mood episodes, this particular illness may offer unique perspectives on the trajectory of phenomenological changes in consciousness that give rise to hallucinatory symptoms.

Clinical implications

The review of evidence on clinical correlates of psychotic experiences in BD indicated few consistent sociodemographic differences [43, 50-51, 59]. A wealth of studies assessed if psychotic symptoms in BD were predictive of better or worse outcomes [e.g. 48, 54, 58]. However, significant variability in the studies prevented this being determined. The small number of studies that reported on cognitive correlates of AVH and delusions in BD highlighted some directions in which future research might progress to support potentially adapted psychological interventions for the BD population.

First, it was suggested that the experience of psychotic symptoms within early mood episodes in BD may be associated with less adaptive coping styles (e.g. denial/blame), which may delay engagement with treatment [57.] Several further studies reported that psychotic symptoms in BD were associated with reduced insight into illness, potentially over and above the influence of mania [40, 42, 62]. These findings are supportive of the case for early intervention in BD and the provision of tailored psychosocial treatments even at this early stage of illness. A recent 'evidence map' of early intervention psychosocial treatments for BD (assessed in high-risk, first-episode and early-onset groups) indicated several studies, reporting on a proliferation of different cognitive, behavioural, family and interpersonal therapies [83]. However, there were seemingly few interventions that targeted specific cognitive or physiological processes (e.g. mood appraisals, sleep, coping styles or psychotic experiences) [83]. Indeed, there are very few high-quality, randomized controlled trials of targeted psychological interventions that have been completed early in the course of BD [81-82]. This is despite current cognitive models indicating that psychological interventions in BD may be more efficacious if delivered prior to the complicating effects of subsequent mood episodes[81]. Yet evidence is growing to improve our understanding of experiences early in the course of

BD [84] and studies are emerging that will specifically assess the suitability and efficacy of targeted psychological interventions during the early phases of illness [e.g. 85-86]. It remains to be seen whether these forthcoming psychological interventions will require components that target, for example, potential anxieties about diagnosis or prognosis, that might follow an early psychotic mood episode, or more intensive work with interpretations of psychotic symptoms as part of more prolonged relapse prevention work.

Currently young people who experience psychotic symptoms, within the context of depression and emerging BD, should be eligible to receive evidenced-based psychological treatments (CBT and Family Interventions) from Early Intervention in psychosis services (EI), according to certain international practice guidelines and provided that they meet the assessment criteria [e.g. 87-88]. Increased sophistication in our abilities to identify people that might go on to develop BD and improvements in early interventions for people with BD might mean different care pathways and recommendations in future. However, further research would be required to assess whether there are qualitative differences in the experience of psychotic symptoms in people who develop BD versus other psychoses. The results of the current review suggested, for example, that people's interpretations or appraisals of voice experiences may be different to those that have been found to be predictive of distress and functional disturbance within the schizophrenia literature. Although the findings were from a single study, people with a diagnosis of BD reported fewer omnipotent/malevolent appraisals of voices than those with SCZ [39]. This potential difference in voice appraisals in BD is relevant because beliefs about voices remain a key target in CBT treatments delivered by EI services [33, 89]. It may be that fewer omnipotent/malevolent appraisals of voices in BD simply reflects less disturbance from AVH experiences when out of an acute mood episode, and therefore a limited requirement for intervention. However,

research into how beliefs about voices might change relative to mood fluctuations in BD could be informative. The contributions that elevated mood might make to less negative appraisals of voices, for example, have yet to be theoretically accounted for. Positively perceived voices are also of particular clinical significance as people have been found to be more likely to comply with them and to be less likely to seek out and respond to treatment [90-91]. Given the prominence of elevated mood alongside depression in BD further investigations into the diversity of AVH experiences might contribute to the development of a putative 'positive' affective pathway to psychotic symptoms.

Further considerations from the review

Overall, the results of the review raise the question as to why, in the light of several studies indicating the frequency of psychotic symptoms in BD, do there remain comparatively fewer studies investigating psychotic experiences in more depth for people with this diagnosis. One possible explanation is that researchers assume that psychotic phenomena, which tend to be more transient in BD than in SCZ, are less clinically relevant, and therefore less important as a target of research, than the mood episodes within which then tend to occur i.e. treat the mood instability and the psychotic symptoms will dissipate alongside this. However, this would be to overlook the potential need to work clinically with psychotic phenomenon retrospectively and prospectively in BD, together with the value of research for its own sake to improve our understanding of psychosis. Alternatively, research into psychotic symptoms in BD may simply represent one of the several neglected areas of research that have been previously highlighted within BD [36.]

It is likely that methodological issues associated with researching the experience of AVH in BD have posed significant barriers to the progress of research in this area. In relation to the

studies reviewed here, specific challenges have already been mentioned, including recall bias associated with retrospective assessments of hallucinations and difficulties assessing and controlling for the influence of mood state characteristics. More broadly, a central concern to the experimental design of future research is whether further examination of psychotic phenomena as they occur *within* specific diagnoses is even a useful way in which to develop research. New studies are emerging that have chosen to examine AVH as a phenomenon regardless of diagnosis [e.g. 16]. This approach seems reasonable given that recent doubts have been raised over the potential that any specific feature of AVH is pathognomic for any particular diagnosis [67]. However, it also seems reasonable to assume that the processes that lead to hallucinatory experiences in Lewy Body dementia are not equitable to those in SCZ. Indeed, whilst concepts such as Schneiderian FRS may have been jettisoned from the diagnostic statistical manual for lack of diagnostic specificity, debate continues as to their potential phenomenological and clinical importance [92]. The question for future research therefore becomes, across which diagnostic boundaries can we justify theoretically the aggregate analysis of AVH experiences, and this will of course depend on the objectives of any study. Presently SCZ typically represents a comparison group for other populations [67]. However, disputes are longstanding regarding the potential continuities and discontinuities between BD, as a mood disorder, and schizophrenia spectrum conditions [22, 93]. Indeed, the SZD diagnosis emerged to cater for the minority of people who meet diagnostic criteria for both disorders simultaneously [36]. It remains to be seen therefore whether further studies will be forthcoming that examine AVH within BD specifically, in addition to across diagnoses. However, the results may have fundamental implications for advancing conceptualisations and classifications of mental illness.

Limitations

The limited period covered (last 20 years), was intended to ensure some comparability in nomenclature and measures employed to facilitate study comparison, but may have also led to some omissions. Unfortunately, we were also restricted to the English-language press. The search terms generated were intended to capture studies using all possible variants in terminology for BD, auditory hallucinations and delusions. However, data may have been missed that was embedded in papers referring to psychotic symptoms more generally in BD, or that included BD within samples of other psychoses. No formal quality assessment of studies was conducted because of the broad aims of the review and potential diversity in study design. Hence there is the possibility of some degree of bias in our appraisals of the studies' strengths and weaknesses. Additionally, the main findings reviewed on the clinical and cognitive correlates of AVH and delusions were extracted in a less structured fashion to the data on occurrence and characteristics. It was hoped however that this provisional analysis would indicate more specific categories for data extraction in future research.

Conclusions

The occurrence of auditory hallucinations particularly within acute mood episodes in BD is well-evidenced and widely acknowledged. Indeed, the distinct mood fluctuations that individuals with BD experience alongside hallucinations add a unique layer of complexity to an already enigmatic phenomenon. Studies conducted over the past twenty years have established that people with BD frequently report certain subtypes of voices that were previously thought to be specific to SCZ. They have also highlighted limitations in the concept of mood congruence which is used to describe AVH in BD. Research has become increasing focused on studying the specific characteristics of AVH in BD. However, we still do not know how the content or form of AVH and associated delusions might differ across

predominantly depressive vs manic episodes. A better understanding of the interplay between mood changes and psychotic experiences might inform developing theories of AVH. Perhaps because of their typical transience, few studies have assessed how individuals with a BD diagnosis make sense of and respond to hallucinatory experiences to assess whether psychological interventions could be adapted to better meet the needs of this population.

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Table 1: Data Extraction: characteristics of AVH and delusions in BD

Authors	Experimental design	Participants	AVH results in BD	Delusions results in BD	Outcomes/ measures	Other main findings	Strengths/limitations
Toh et al., 2016	*Cross-sectional group comparison:* large population-based psychosis survey (Australian Survey of High Impact Psychosis, SHIP): AVH and delusions in BD vs depressive psychosis (MDD), Schizoaffective disorder (SZD) & Schizophrenia (SCZ)	n = 319, BD, **Ps, *mss* n = 81, MDD n = 293, SZD n = 857, SCZ	· 10% = current · 39% = lifetime · Trend BD < DP < SZD < SCZ for severity of all AVH types · Negative voices common · AVH associated with delusions, current & lifetime, particularly thought alienation	· Current stats: 17% = persecutory = most common, current 8% = grandiose, current · Delusions of influence associated with running commentary & conversing · Persecutory associated with negative voices · No links between grandiose delusions and specific AVH	· *Current & lifetime stats* · AVH prompts for running commentary, conversing & negative voices · ICD-10 · DIP interview · OPCRIT	· BD < DP - current running commentary and negative voices, n.s · BD ≅ DP – current voices conversing · BD ≅ DP – lifetime prevalence for negative, running commentary and conversing · BD < DP - current delusions, but ≅ over lifetime	S – large population survey incorporating analysis of subtypes of AVH and delusions L – some symptom measures recorded on binary basis, no information on mood states or mood profile within BD diagnosis
Goghari et al., 2016	*Longitudinal group comparison:* 20-yr follow-up examining different types of hallucinations across schizophrenia, schizoaffective, bipolar disorder and depression	n= 25, BD, *Ps*, **mnr* n= 25, SZD n= 51, SCZ n= 49, MDD	· 20% = AVH at baseline (inc. audible thoughts, commenting, conversing, arguing) · all subsequent rates of AVH < 20%	-	· *Current stats at multiple time points* · Research Diagnostic criteria · SADS schedule	· BD did not differ from MDD in rate of AVH · BD < SZD and SCZ at all time points · fewer periods of recovery in those with AVH to those without	S - designed to focus specifically on AVH, looks at long term course, good diagnostic reliabilities reported L - small sample size
Leonpacher et al, 2015	*Cross-sectional group comparison:* large opportunistic data collections used to compare depression-related clinical features in BD vs unipolar depression (MDD)	n = 386, BDI, *most severe depressive episode* n = 158, BDII n = 684, MDD	· 10% = 'any' Hallucination, (inc. voices, visual)	· 22% = 'any' delusional belief	· *Lifetime stats, during most severe depressive episode* · Sections from DIGS interview	· BDI (not BDII) significantly more delusions, than MDD · AH in BDI not significantly different from MDD in multiple regression, $p < .07$	S - large sample size, specifies mood state L - does not specify AH or specific delusions, no illness-related confounds
Nisha et al., 2015	*Cross-sectional group comparison:* small study of psycho-socio-demographic & clinical features between BD and Unipolar Depression (MDD) in current admissions	n = 30, BD *currently depressed* n = 30, MDD	· 50% = Auditory Verbal Hallucination (AVH), current · 33% = second person · 17 % = third person, running commentary	· 77% = 'any' delusion. · 20% = 'first-rank' · 70% = persecutory · 34% = referential · 20% = infidelity · 14% = guilt · 7% = hypochondriacal · 4% = nihilistic	· *Current stats, in depressive episode* · ICD-10 · BPRS	· Psychotic symptoms significantly higher in BD group than MDD · Delusions were predictive of BD in regression analysis, AVH were not	S - examined specific types of AVH and delusions in currently admitted patients L - insufficient detail on participation to assess selection bias, high co-morbidity, no control of confounds

Table 1: Data Extraction: characteristics of AVH and delusions in BD

Authors	Experimental design	Participants	AVH results in BD	Delusions results in BD	Outcomes/ measures	Other main findings	Strengths/limitations
Upthegrove et al., 2015	*Cross-sectional within-group correlation*: large UK study of BD, test of association between childhood trauma and lifetime-ever psychosis	n = 2019, BDI, *mnr*	· 23% = Auditory Hallucination (AH), ever · 11% = mood congruent · 6% = abusive/accusatory · 1% = running comments	· 65% = any delusional belief, ever · 15% = depressive delusions	· *Lifetime stats* · DSM-IV · SCAN-interview	· Significant association between trauma & specific AVH, mainly driven by sexual abuse category · Grandiose delusions (only) negatively corr. trauma	S - large sample size, high diagnostic inter-rater reliability, includes specific types of AVH L - representativeness, only White British included due to genetic analysis
Mancuso et al., 2015	*Cross-sectional group comparison:* large population-based psychosis survey (SHIP)*:* clinical characteristics across BD, SZD & SCZ.	n = 319, BD, *Ps*, *mss* n= 293, SZD n= 857, SCZ	· 19% = current 'any' hallucination, (inc. voices, visual) · 68% = lifetime 'any' hallucination	· 99% current delusions · 99% lifetime delusions	· *Current & lifetime stats* · ICD-10 · DIP interview	· BD had significantly fewer symptom scores for current & lifetime halls & delusions than SZD and SCZ	S - national survey dataset, random sampling L – does not specific AVH, only reports stats on 'any' hallucination
Goghari et al., 2013	*Longitudinal group comparison:* 20-yr follow-up of relationship between hallucinations, recovery and work -attainment	n= 25, BD, *Ps*, *mnr* n= 25, SZD n= 51, SCZ n= 49, UD	· 25% = 'any' Hallucinations at baseline · BD less likely than SCZ/ SZD to have frequent (8%) or chronic (0%) halls		· *Current stats at baseline* · Research Diagnostic criteria (RDC) · SADS schedule	· *Presence of halls across groups was related to the lack of a period of and poorer work attainment*	S - designed to focus on hallucinations, looks at long term course, good diagnostic reliabilities reported L - crude binary value for 'any' halls used, small sample size
Azorin et al., 2013	*Longitudinal group comparison: e*valuation of short & long term outcomes for individuals with BD mixed states	n= 341, MSM, *mixed state, mainly manic* n= 68, MSD, *mixed state mainly depressed*	Any hall/delusion (grouped) at baseline: · MSM = 49%, (149) · MSD = 28%, (18)		· *Current stats* · Clinical Global Impressions scale	· Halls/delusions & inpatient status at baseline more often associated with MSM than MSD · Higher recurrence of illness in mania over 24 month follow-up	S - cross-country, prospective study with acute & outpatients L - includes all halls, not validated clinical global impression scale used for diagnosis & symptom ratings, Hall/delusions not reported on at follow-up
Kumari et al., 2013	*Cross-sectional group comparison:* dimensions of hallucinations and delusions in affective, AP, and non-affective psychoses, NAP	n = 30, AP, *Ps** (22 BD all *in euphoric/ irritable mood)* n = 30, NAP, mostly SCZ	· 43% = AVH in AP, only second person voices · AP scores on all PSYRATS dimensions, *except intensity of distress*, significantly less than NAP	· AP differ significantly from NAP only on PSYRATS conviction in delusional beliefs	· *Current stats* · ICD-10 · PANSS · PSYRATS	· *Negative correlation between overall AVH score and insight*	S - detailed phenomenology of AVH and delusions, participants were drug-naive outpatients L - no control for symptom severity, generalisability limited by broad AP, NAP grouping

Table 1: Data Extraction: characteristics of AVH and delusions in BD

Authors	Experimental design	Participants	AVH results in BD	Delusions results in BD	Outcomes/ Measures	Other main findings	(S)trengths and (L)imitations
Carlson et al., 2012	*Longitudinal within-group correlation:* determinants of 4-year clinical outcomes following first hospitalisation in BD with psychosis	n = 126, BDI, *Ps*, *80% manic*	· 51% = 'Any' hallucination at baseline · 'Any' hallucination at baseline predicted number of manic episodes & rehospitalisation at follow-up	· 75% = manic delusions at baseline · 47% = paranoid delusions, at baseline ·46% = any 'mood-incongruent' psychotic symptom, at baseline · 29% = 'any Schneiderian' symptoms (AH & delusions) at baseline	· *Current stats at baseline* · Scale for the Assessment of Positive Symptoms, (SAPS) · DSM IV	· 89% had at least one further psychotic episode during follow-up, associated with younger age & paranoia · Type of psychotic symptom (i.e Schneiderian) more important than 'mood incongruence' in predicting worse clinical outcomes (e.g % time ill)	S - detailed sampling info and good diagnostic inter-rater reliability, controlled multiple regression L - co-morbidity could not be assessed as predictor of outcome, no comparison available for non-psychotic group
Ryu et al., 2012	*Cross-sectional group comparison:* an analysis of the prodrome and coping styles *in euthymic BDI with and without psychotic symptoms in most recent episode*	n = 41, BDI, euthymic *'psychotic'* n=42 BDI, euthymic '*non-psychotic'*	· 45% of 'psychotic' group vs 20% of 'non-psychotic' reported AH in prodrome	· both groups reported prodromal belief-related symptoms e.g thoughts are controlled, feeling strong/powerful · yet no significant differences in groups	· *Lifetime stats during prodrome* · Prodromal symptoms checklist · DSM-IV	· *Psychotic symptoms in prodrome associated with denial or blame as coping strategy* · Psychotic group reported significantly younger age of onset & longer prodrome	S - unique results on early course of illness and clinically relevant group differences L - detailed analysis of psychotic symptoms used to define groups not reported
Shinn et al., 2012	*Cross-sectional group comparison:* descriptive study of auditory hallucinations and delusions and their severity across SCZ, BDI & SZD.	n=244, BDI, *Ps, mss* n=172, SCZ n=153, SZD	· 34% lifetime history of AH · 31% at least one 'first rank' AVH in BD · 21% 'running commentary', 19% 'conversing'	· Across total transdiagnostic sample, AVH significantly associated with 'passivity' delusions of control, thought insertion, thought broadcast.	· *Lifetime stats* · DSM- IV · PANSS	· AH strongly associated with hallucinations in other modalities, overall	S - reported associations of AVH with other halls and delusions, sizeable samples, analysis of 'first-rank' AVH L - one item measure of AVH severity, associations between AVH and other variables only reported across groups, limited detail on phenomenology
Hammersley et al. 2010	*Cross sectional within-group correlation*: examination of attributions for hallucinations in and out of episode in BD predominantly euthymic	n = 40, BD, euthymic/ depressed/ *not manic*	· 20% = AH · AH reported mostly during depressive episode (88%)	-	· *Lifetime stats, in past episode* · Beliefs About Voices Questionnaire	· dual attributions for AH · majority attributed AH to illness out of episode, and some also during episode · only one third malevolent/omnipotent attributions in episode	S - clinically useful report of subjective descriptions and interpretations of hallucinations in BD L – sampling bias, retrospective descriptions of attributions

Table 1: Data Extraction: characteristics of AVH and delusions in BD

Authors	Experimental design	Participants	AVH results in BD	Delusions results in BD	Outcomes/ Measures	Other main findings	Strengths/limitations
Bräunig et al., 2009	*Cross sectional within-group correlation*: Gender differences in psychotic bipolar mania	n = 246, BDI *in current manic episode*	· 58% = AVH (n=113) · mean hallucinations (inc. non-auditory) = 1.5	· 48% = 'any' delusion · Mean delusions = 1.6 Of those with delusions: · 76% = grandeur · 16% = paranoid · 14% = reference delusions · 22% = religious delusions · 9% = erotomania · 3% = guilt	· *Current stats in manic episode* · DSM-IV · Association for Methodology & Documentation in Psychiatry system (AMDP) system	· 63% overall (155/246) presented with psychotic symptoms · *Women reported significantly more AH and delusions overall compared to men, and delusions of reference and paranoia more specifically*	S - includes analysis of types of delusions and specifically examines gender differences L - little information on characteristics of AVH, could have quoted associations with delusions
Canuso et al., 2008	*Cross-sectional group comparison*: a study of psychotic symptoms in bipolar mania	n = 264, BDI *psychotic* n =251, BDI *non-psychotic* *current manic/mixed episode*	· mean score on PANSS 'hallucinatory behaviour' significantly higher in those diagnosed as psychotic group at baseline (2 - minimal vs 1- absent)	· grandiosity reaching delusional status in 78% of BD psychotic vs 45% in non-psychotic · mean score on PANSS 'delusions' and 'suspiciousness' significantly higher in psychotic group	· *Current stats in manic/mixed episode* · PANSS · DSM IV	· psychotic features diagnosed in 51% of patients (264/251) · psychotic group had higher mania symptoms, higher PANSS severity, and lower insight compared to non-psychotic	S - emphasised spectrum of psychosis due to presence of PANSS +ve symptoms in the group diagnosed as non-psychotic L - crude measure of AVH and delusions, study sample details insufficient to interpret rates, composite sample from 2 countries
Gaudiano et al., 2007	*Longitudinal group comparison:* predictive significance of mood incongruent (MI) and mood congruent (MC) psychotic symptoms in BDI over 28 months	n = 40, BDI, MC n = 24, BDI, MI *current manic/mixed episode*	Total sample (n = 64): · 41% auditory, 20% visual, 5% tactile.	Total sample (n = 64): · 66% = grandiose · 56% = reference · 31% = persecutory · 16% = thought broadcasting · 15% = thought control	· *Current stats in baseline manic/mixed episode* · DSM IV · BPRS	· No differences were found on any longitudinal course variables between mood congruence subtypes. Few differences at baseline · 29% of follow-up time spent in a mood episode · 5% of follow-up time spent in psychotic episode	S - longitudinal design, good inter-rater reliability ratings for diagnosis and mood congruence L - not generalisable to BD where psychotic features present in depression, 20% of sample met criteria for MI and MC
Goes et al., 2007	*Cross-sectional group-comparison:* clinical correlates of mood incongruent/congruent psychotic features (MI, MC) in BD and their genetic linkage	n =291, BDI, MI n=404, BDI, MC n=866, BD, non-psychotic **pme*	· 56% = AH in BDI, MI · 33% = AH in BDI, MC	· 69% = persecutory delusions, MI · 46% = persecutory delusions, MC	· *Lifetime stats* · DIGS interview · DSM IV	· MI features associated with higher rates of hospitalisation and suicide attempts · Significant differences in frequency of AH and delusions between MI &MC	S - very large cohort study, explicit methodological details given on diagnostic and mood congruence groupings, including patient descriptions L - reliabilities for mood congruence not reported

Table 1: Data Extraction: characteristics of AVH and delusions in BD

Authors	Experimental design	Participants	AVH results in BD	Delusions results in BD	Outcomes/ Measures	Other main findings	Strengths/limitations
Baethge et al., 2005	*Cross-sectional group-comparison:* comparison in the frequency and type of current hallucinations and delusions reported in BD, SCZ and MDD	n = 244, BD *mania/mixed* n = 305, BD *depressed* n = 1937, MDD n = 2103, SCZ	· 12% (65/549) = BD who reported ≥ 1 current hallucination, of which 57% = AVH · AH in mixed BD > AH in BD manic > AH in BD depressed · AVH less often associated with grandeur	Amongst BD with halls: · 66% = any delusion · 31% = persecutory · 23% = reference · 12% = grandiose · 19% = guilt · 9% = hypochondria · significantly more delusions in BD with halls than without · yet delusions still prevalent in BD without halls (highest = grandeur, 9%)	· *Current stats at time of admission* · AMDP system · ICD-9	· *those with AH at hospital admission were more likely to be delusional, had higher anxiety scores, had less illness-insight, and longer hospitalization* · delusions less frequent, less severe in BD depressed vs BD manic · delusions less frequent, less severe in BD by comparison to SCZ	S - specific characteristics of delusions reported and their association with AH, large cohort study offering more accurate prevalence statistics L - data on characteristics of AVH not included, no attempt to control for medication effects
Pini et al., 2004	*Cross-sectional group comparison:* in the frequency and type of hallucinations & delusions reported in SCZ, SZD and BD mania or mixed mania with mood incongruent (MI) psychotic features	n = 29, BD, *manic, Ps, MI* n = 49, BD *mixed-mania, Ps, MI* n= 32, SZD n = 46, SCZ	· 55% = AH in mania group · 67% = AH in mixed-manic · No significant diagnostic group differences in rates of specific AH	· >80% of manic and mixed manic reported delusions of persecution, additional delusion proportions given in paper · Only significant difference in frequency of delusion types across groups was grandiosity, highest in BD manic (79%)	· *Current stats at discharge* · DSM III · BPRS	· Negative symptoms rather than affective symptomatology differentiates groups	S - extensive data on illness characteristics accounted for in group comparisons L - BD groups already selected for mood-incongruent psychotic features limits generalisability of conclusions, specific characteristics of AH not specified
Hammersley et al., 2003	*Cross-sectional within-group correlation:* investigating the association between childhood trauma and auditory hallucinations in BDI	n=96 BD, *81% hospitalized at some point in illness, *mnr*	· 31% = lifetime AH · 12% = 'commentary' voices	-	· *Lifetime stats* · DSM IV	· Significant association between reports of trauma and presence or absence of AVH, specifically sexual abuse · Strong association between those reporting childhood sexual abuse and AVH specifically	S - abuse ratings based on current reports as opposed to retrospective analysis, raters blind to study hypotheses L – possible sampling bias, participants approached by therapists as part of trial, no reliability ratings for trauma reports
Schürhoff et al., 2003	*Cross-sectional group comparison:* of delusional proneness amongst first degree unaffected relatives of those with SCZ and BDI diagnoses	n = 61, BD, *with & without psychosis, manic and depressed* n= 32, SCZ	· 12% = AVH · 8% = voices conversing · 3% = imperative voices	Most common items: · 64% = Double meaning · 51% = Having no thoughts · 49% = telepathy · 48% = people not as seem · 46% = persecution	· *Current stats at discharge* · DIGS · Delusions Inventory · DSM IV	· higher delusional proneness demonstrated in the relatives of SCZ and BD with psychotic features in affective episodes	S - assessment at discharge increases reliability of self-report, includes specific AVH characteristics and a range of delusional beliefs L - small sample size

Table 1: Data Extraction: characteristics of AVH and delusions in BD

Authors	Experimental design	Participants	AVH results in BD	Delusions results in BD	Outcomes/ Measures	Other main findings	Strengths/limitations
Keck et al., 2003	*Cross-sectional group comparison:* of demographic and course of illness features of BDI with and without lifetime history psychotic features	n= 114 BDI *without history of psychosis* n = 238 BDI *with at least one psychotic feature in any mood episode, pme*	• 37% = AH in BD psychotic group	In BD psychotic group: • 62% delusions of reference • 61% grandiose delusions • 51% persecutory delusions • 29% = mood incongruent • 16% thought control • 14% thought broadcasting • 13% somatic • 10% bizarre	• *Lifetime stats* • DSM IV	• *No significant differences between groups on any demographic, psychosocial, vocational, or course of illness variables* • Higher anxiety in the mood incongruent group	S - substantial cohort study, high inter-rater reliability for diagnosis, comprehensive assessment of psychosocial and clinical characteristics and co-morbidities L - overall morbidity was high in the sample, may have obscured relevant illness course or psychosocial differences
Benabarre et al., 2001	*Longitudinal group comparison:* exploration of validity of SZD diagnosis, comparison of demographic, clinical and prognostic differences between BD, SZD & SCZ over 3 years	n = 67 BDI, *pme* n = 34 SZD n = 37 SCZ	• 34% = 'any' hallucinations ever	• 82% = 'any' delusion ever	• *Lifetime stats* • RDC • SADS	• BD had better autonomy and job adaptation than other groups, yet still reported difficulties • SZD scores at 'intermediate' point between BD and SCZ on several variables, but not all.	S - examines clinically relevant outcomes across psychotic disorders L - all data gathered at interview, non-validated instruments, RDC criteria used for diagnosis, no details on diagnostic reliability, no details on types of halls or delusions
Benazzi et al., 1999	*Cross-sectional group comparison:* in clinical characteristics between bipolar psychotic depression and unipolar psychotic depression	n = 30 BDI and BDII, Ps, *depressed outpatients* n = 40 UD, Ps, *depressed outpatients*	• 17% 'any' hallucinations	• 97% 'any' delusions	• *Current stats in depressive episode* • DSM IV • BPRS	• No significant differences in clinical characteristics between groups: age at onset, duration of illness, number of depressive episodes, mean BPRS or co-morbidities	S - patients and family members interviewed about relationship between psychotic features & depressive episode, >60% BDII L - only one interviewer, outpatient group at the clinic tend to be more severe which limits generalisability
Tanenberg-Karant et al., 1995	*Cross sectional group comparison:* Study of the prevalence of bizarre and Scneiderian 'first-rank' delusions (FRS) in a first episode sample	n = 62 BD, *Ps, manic* n= 94 SCZ n = 40 MDD	• FRS (hallucinations and delusions) = 29% in BD • Majority of symptoms neither bizarre nor FRS across all groups combined		• *Current stats in manic episode* • DSM III	• None of the demographic, premorbid, or baseline clinical variables were related to FRS and/or bizarre symptoms in BD, except no. of symptoms.	S - halls and delusions coded blind to diagnosis by coders L - SCID fails to capture FRS fully, non-FRS symptoms across groups excluded

Table 1: Data Extraction: characteristics of AVH and delusions in BD

Authors	Experimental design	Participants	AVH results in BD	Delusions results in BD	Outcomes/ Measures	Other main findings	Strengths/limitations
Sethi et al., 1993	*Cross-sectional observation:* phenomenology of mania, study of psychotic features, specifically delusions	n = 100 BD, *manic*	· 6% 'first-rank' voices discussing the individual in the third person or commenting on actions	· 93% - grandiose ability · 90% - grandiose ideas/acts · 81% - grandiose identity · 69% - reference · 62% - persecution · 61% - sexual delusions · 42% - religious delusions · 37% - assistance · 7% - delusion of pregnancy	· *Current stats in manic episode* · DSM-III · Hindi translation of Present State Examination (PSE)	· No significant difference between the frequency of occurrence of any symptom in those in first episode versus those with history of episodes of mania	S - explores transcultural differences in delusion phenomenology, sizeable sample, mixed methods inc. interview at admission & case note review L - high gender imbalance (80% males), no details on selection criteria from total admissions
Tohen et al., 1992	*Longitudinal within-group correlation:* investigation of importance of mood incongruent psychotic features in predicting outcomes over 4 yrs	n = 54 BD, *Ps, manic*	· 30% = AH	· 65% - paranoid delusions · 17% - bizarre delusions	· *Current stats in baseline manic episode* · DSM-III R	· Mood incongruent psychotic features at index manic episode predicted shorter time in remission · FRS predicted poorer residential status	S - prospective design with considerable length of follow-up, independent raters blind to index assessment, high inter-rater reliability L - impact of treatment interventions not accounted for
Stephens et al., 1991	*Longitudinal group comparison:* characteristics and follow-up outcomes for patients admitted for mood disorders 1913-1940	n = 235 BD, *past or present history manic symptoms, pme* n = 782 MDD	· 17% and 18% prevalence of 'any' hallucination in BD mania and BD mixed mania and depression respectively	· 40% and 44% prevalence of 'any' delusion in BD mania and BD mixed mania and depression respectively	· *Stats at index admission* · Systematic evaluation of case notes · DSM III	· BD had an earlier age of onset than MDD and were more likely to have AH or delusions, and worse outcomes	S - comprehensive study of outcomes, large drug-naive cohort L - historic case review, reliability of case notes
Black & Nasrallah, 1989	*Cross-sectional group comparison:* prevalence of hallucinations and delusions studied in BD, MDD, SAD	n = 467, BD, *manic/mixed at index* n = 161, BD, *depressed* n = 763, MDD1 n = 324 , MDD2	· 13% = AH in BD mania · 7% = AH in BD depressed	Prevalence of 'any' delusion · 44% = BD mania · 12% in BD depression · delusions more likely to be mood congruent than incongruent in both depression and mania	· *Stats at index admission* · Systematic evaluation of case notes · DSM III	· BD manic more likely than all other groups to have delusions and AH during episode · BD manic more likely to have delusions only, and less likely to have AH only	S- large sample diagnosed at inpatient admission, BD subtypes compared L - retrospective case review, >2000 files reviewed by one individual, no reliability checks
Chatterjee & Kulhara, 1989	*Longitudinal within-group correlation:* examination of symptom resolution over 90 days post manic episode	n = 40 *manic (inc. 15 BD)*	· 12.5% = AVH 'based on affect'	· 68% - 'any' delusions · 42 % - grandiose ability · 37% - grandiose role · 27% - religious delusions · 22% - delusions of wealth · 5% - grandiose identity	· *Current stats at multiple time points* · DSM III · PSE	· All except 1 participant 'asymptomatic' of psychotic phenomenon by 90th day	S -strong design, 6 x follow-ups over 90 days from admission, includes AVH specifically L - sample size, generalisability low, mania admissions only and includes mixed sample

Table 1: Data Extraction: characteristics of AVH and delusions in BD

Authors	*Experimental design*	Participants	AVH results in BD	Delusions results in BD	Outcomes/ Measures	Other main findings	Strengths/limitations
Breslau et al., 1989	*Cross-sectional group comparison: phenomenology of psychotic depression*	n = 34 SZD, n = 39 MDD, n = 38 BD, Ps, depressive episode	· 18% = AH	· 53% - persecution · 32% - reference · 50% - depressive delusions · 16% - grandiose delusions	· Current stats in depressive episode · RDC · SADS	· SZD had greater FRS, delusions of reference and AH, but indistinguishable from BD depression on other delusions	S - diagnoses made on discharge based on group consensus, comparisons made on types of delusion L - small sample sizes, informal outpatient sample restricts implications to be drawn for other subtypes
Mitterauer et al., 1988	*Cross-sectional group comparison: in clinical characteristics between BD with and without family history of suicide (FH-S)*	n = 342 BD with FH-S n = 80 BD without FH-S	-	· 39% = 'any' delusion for those with FH-S · 52% = 'any' delusion for for those without FH-S	· Lifetime stats · DSM-III	· more delusions amongst those without family suicide history of suicide	S - verifies family history as risk marker for suicide in large cohort L - historic record review, unequal sample sizes, lack of theoretical rationale for some hypotheses

*Ps - pre-screened for psychotic symptoms
*mss - current mood assessed using symptoms scales for mania and depression
*pme - previous mood episodes given as % of sample with manic and depressive episodes
*mnr - mood not reported

DISCLOSURES

The authors of this paper do not have any commercial associations that might pose a conflict of interest in connection with this manuscript.

AUTHOR CONTRIBUTIONS

LMS performed the literature search and wrote the paper. LCJ and RLCM reviewed the paper and provided comments for editing.

Appendix 1: Database specific search-strings

i. Pub Med

((((((mania) OR hypomania) OR bipolar) OR manic depression) OR affective psychos*) AND ((hallucinat*) OR delusion))

((((((("bipolar disorder"[MeSH Terms] OR ("bipolar"[All Fields] AND "disorder"[All Fields]) OR "bipolar disorder"[All Fields] OR "mania"[All Fields]) OR hypomania[All Fields]) OR bipolar[All Fields]) OR ("bipolar disorder"[MeSH Terms] OR ("bipolar"[All Fields] AND "disorder"[All Fields]) OR "bipolar disorder"[All Fields] OR ("manic"[All Fields] AND "depression"[All Fields]) OR "manic depression"[All Fields])) OR (affective psychoses[All Fields] OR affective psychosis[All Fields])) AND ((hallucinat[All Fields] OR hallucinate[All Fields] OR hallucinated[All Fields] OR hallucinates[All Fields] OR hallucinatic[All Fields] OR hallucinatie[All Fields] OR hallucinaties[All Fields] OR hallucinatiion[All Fields] OR hallucinatiions[All Fields] OR hallucinating[All Fields] OR hallucination[All Fields] OR hallucination'[All Fields] OR hallucinational[All Fields] OR hallucinationen[All Fields] OR hallucinationer[All Fields] OR hallucinationes[All Fields] OR hallucinations[All Fields] OR hallucinations'[All Fields] OR hallucinations'than[All Fields] OR hallucinatire[All Fields] OR hallucinative[All Fields] OR hallucinatoire[All Fields] OR hallucinatoire'[All Fields] OR hallucinatoires[All Fields] OR hallucinatoiresaigues[All Fields] OR hallucinator[All Fields] OR hallucinatoria[All Fields] OR hallucinatoric[All Fields] OR hallucinatornih[All Fields] OR hallucinators[All Fields] OR hallucinators'[All Fields] OR hallucinatory[All Fields] OR hallucinatory'[All Fields] OR hallucinatroy[All Fields]) OR ("delusions"[MeSH Terms] OR "delusions"[All Fields] OR "delusion"[All Fields]))) AND ("loattrfull text"[sb] AND ("1986/12/31"[PDAT] : "2016/12/31"[PDAT]) AND "humans"[MeSH Terms])

ii. Ovid SP (EMBASE and PsychINFO)

1. ((mania or hypomania or bipolar or (manic adj depression) or (affective adj psychos$s)) and (hallucinat* or delusion)).ab.

2. limit 1 to (full text and abstracts and human and english language and yr="1986 - Current")

iii. CINAHL

TX (((((((mania) OR hypomania) OR bipolar) OR manic depression) OR affective psychos*)) AND TX (((hallucinat*) OR delusion))) **Limiters** - Published Date: 19861201-20161231; English Language; Human; Search modes - Boolean/Phrase

iv. Web of Science

(TS=((((mania) OR hypomania) OR bipolar))) **AND TS=** (((hallucinat*) OR delusion)) *AND* **LANGUAGE:** (English) *AND* **DOCUMENT TYPES:** (Article)
Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=1986-2016

OR

(TS=(("manic depression")) *AND* **TS=** (((hallucinat*) OR delusion)) *AND* **LANGUAGE:** (English) *AND* **DOCUMENT TYPES:** (Article)
Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=1986-2016

OR

(TS=((affective NEAR psychos$s)) *AND* **TS=** (((hallucinat*) OR delusion)) AND **LANGUAGE:** (English) *AND* **DOCUMENT TYPES:** (Article)
Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=1986-2016