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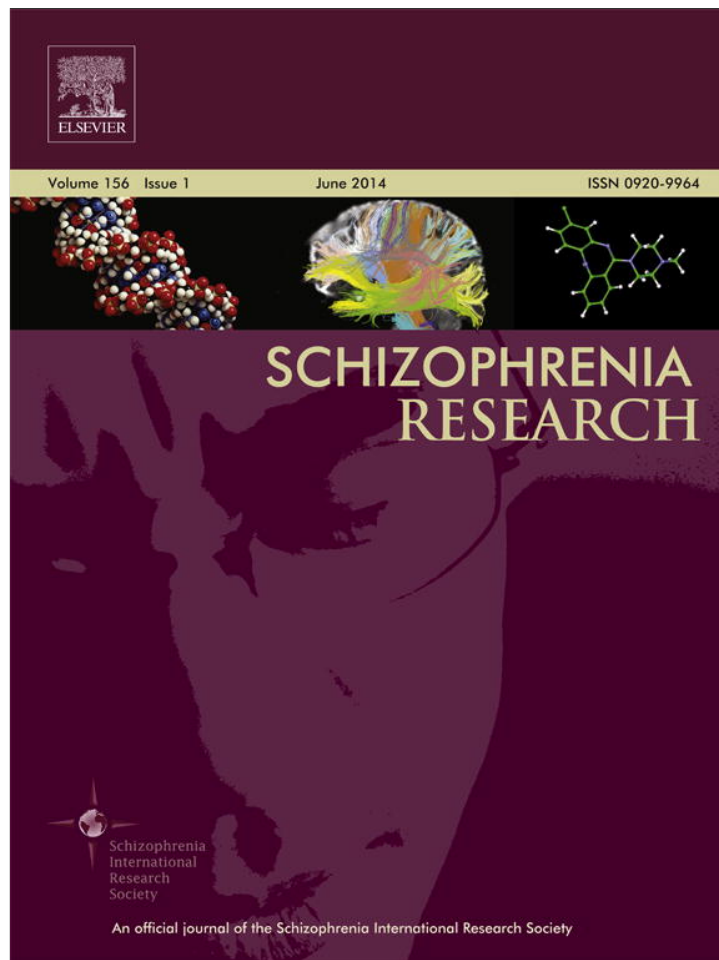
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The effects of individually tailored formulation-based cognitive behavioural therapy in auditory hallucinations and delusions: A meta-analysis



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ABSTRACT

There is no meta-analysis of cognitive behavioural therapy for delusions and hallucinations separately. The aim of this meta-analysis is to evaluate the end-of-treatment effects of individually tailored case-formulation cognitive behavioural therapy on delusions and auditory hallucinations using symptom-specific outcome measures.

A systematic search of the trial literature was conducted in MEDLINE, PSYCHINFO and EMBASE. Eighteen studies were selected with symptom specific outcome measures. Hedges' *g* was computed and outcomes were pooled meta-analytically using the random-effects model.

Our main analyses were with the selected studies with CBT using individually tailored case-formulation that aimed to reduce hallucinations and delusions. The statistically significant effect-sizes were 0.36 with delusions and 0.44 with hallucinations, which are modest and in line with other recent meta-analyses. Contrasted with active treatment, CBT for delusions lost statistical significance (0.33), but the effect-size for CBT for hallucinations increased (0.49). Blinded studies reduced effect-size in delusions (0.24) and gained some in hallucinations (0.46). There was no heterogeneity in hallucinations and moderate heterogeneity in delusion trials. We conclude that CBT is effective in treating auditory hallucinations. CBT for delusions is also effective, but the results must be interpreted with caution, because of heterogeneity and the non-significant effect-sizes when compared with active treatment.

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1. Introduction

To date meta-analyses of CBT for psychosis (CBTp) have evaluated the effects in terms of effects on the frequency and severity of positive symptoms (Gould et al., 2001; Rector and Beck, 2001; Zimmermann et al., 2005; Wykes et al., 2008; NICE, 2009), negative symptoms (Rector and Beck, 2001; Wykes et al., 2008) and general symptoms (Tarrier and Wykes, 2004; NICE, 2009; Jones et al., 2012), but none focussed on and differentiated between auditory hallucinations and delusions. CBTp does not aim to reduce the frequency and severity of

symptoms, but rather to reappraise the meaning and purpose of hallucinations and delusions to reduce distress and improve coping in daily life (Birchwood and Trower, 2006). Therefore, a symptom-specific measure may be better suited to measure multiple aspects such as objective characteristics and subjective experiential aspects of delusions and hallucinations. Recent findings have shown that formulation based CBTp, tailored to the individual and carried out by a skilled therapist is the most efficacious (Steel et al., 2012).

In this review we present the results of a meta-analysis on published trials that report on the effects of CBTp using individually tailored case-formulation on hallucinations and/or delusions with the use of a symptom-specific measure. We expect that individually tailored case-formulation CBT will show larger effect-sizes than broad CBT including standard training programmes. We anticipate larger effect sizes in studies comparing CBTp with treatment as usual (TAU) to those comparing

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CBT to an active treatment condition. Furthermore, we expected larger effect size in studies that were not blinded compared to those, which were blinded.

2. Methods

2.1. Eligibility criteria

To be included in the review studies had to meet the following criteria: 1) had to be randomised controlled trials, 2) the experimental treatment was (formulation-based) CBT for psychosis, 3) any control condition was accepted, 4) patients were diagnosed with a psychotic disorder with at least 75% schizophrenia patients, 5) were published in peer reviewed journals, and 6) no conference abstracts, only full papers were selected. Individually tailored case-formulation CBT was expected to yield better results in comparison to broadly defined CBT (Steel et al., 2012). The criteria used to define individually tailored case-formulation CBT were quite strict: studies using CBT techniques in a training format without individually tailored case formulation were only included in sensitivity analyses. We considered these studies with broad CBT still “apples”. Studies that were associated with different cognitive techniques, such as Competitive Memory Training, Acceptance and Commitment Therapy, Mindfulness training, and Cognitive Bias Modification were considered “oranges” and were not included in the meta-analyses. We limited the meta-analysis to end-of-treatment data, because too few studies reported longer-term effects or with varying follow-up periods.

2.2. Information sources

Literature searches were conducted following the PRISMA guideline (Liberati et al., 2009) using three databases: Ovid MEDLINE and

EMBASE, both from 1996 to July 2013, and PsycINFO from 1987 to July 2013. We also examined published reviews and meta-analyses. The search was conducted at August 3rd 2013. Within each of the databases three searches were carried out.

2.3. Search

The first search was on “CBT” (17385) OR “cognitive therapy” (54629) OR “cognitive behavioral therapy” (16589) OR “cognitive behavioural therapy” (5526).

The second search was on “auditory hallucinations” (4283) OR “auditory verbal hallucinations” (663) OR “AVH” (612) OR “psychosis” (97486) OR “psychotic symptoms” (16154) OR “delusions” (15394) OR “paranoia” (7957) OR “paranoid” (15337).

The third search was on “RCT” (20233) OR “randomised controlled trial” (22216) OR “randomized controlled trial” (610869).

Combining the three searches and the examination of the reviews resulted in 685 references (see Fig. 1). Removing duplicates left 462 papers and 4 papers were added from other sources.

2.4. Study selection

All papers were screened on titles and abstracts. Seventy-two papers were read and assessed for eligibility. Eighteen papers described randomised controlled trials of CBT versus a control condition and used delusions or hallucinations measured separately. One study was removed because they measured hallucinations with only one item (England, 2007). One study did not primarily aim for symptom reduction but relapse prevention (Garety et al., 2008) and was included for sensitivity analysis. Four studies did not use individually tailored formulation-based CBT, but were manualised training programmes

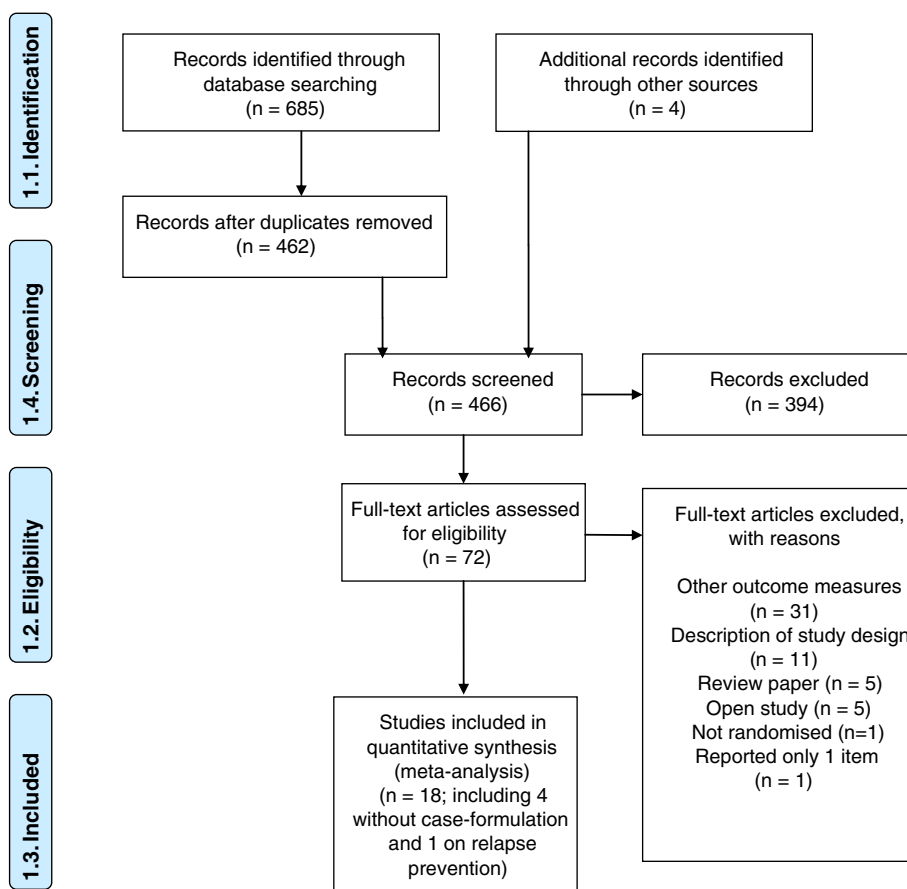


Fig. 1. Flowchart of selected studies.

aimed at coping behaviour (Cather et al., 2005; Wykes et al., 2005; Penn et al., 2009) or worry (Foster et al., 2010). These studies were used in sensitivity analyses too. Excluded studies were not reporting symptom specific measures at end-of-treatment (Turkington et al., 2002, 2006); were not randomised (Morrison et al., 2004); and were not CBTp but other interventions (Chadwick et al., 2009; Shawyer et al., 2012; van der Gaag et al., 2012). See Table 2.

2.5. Synthesis of results

The most commonly used symptom-specific instruments that measure multiple aspects are the Psychosis Rating Scale (PSYRATS) (Haddock et al., 1999; Steel et al., 2007), the MacArthur-Maudsley Delusions Assessment Schedule (MADS) (Appelbaum et al., 1999), The Peters Delusion Inventory (PDI) (Peters et al., 1999), the Comprehensive Assessment of Psychiatric Symptoms (CPRS) (Asberg et al., 1978) and the Beliefs about Voices Questionnaire (BaVQ-R) (Chadwick and Birchwood, 1995; Chadwick et al., 2000).

Some studies reported not full-scale PSYRATS data. The study by McLeod and colleagues reported three items (McLeod et al., 2007a,b); the study by Trower and colleagues reported five items (Trower et al., 2004). Other studies reported all PSYRATS hallucination items divided into the three subscales: (a) physical characteristics, (b) emotional characteristics and (c) cognitive interpretation. Hallucination total scores were calculated using the formula suggested by Borenstein et al. (2009). If no PSYRATS scores were available or if only one item was reported, we choose one of the other symptom-specific measures we mentioned above or if absent excluded the study.

Two studies reported all PSYRATS delusions items divided into two subscales: (a) emotional characteristics and (b) cognitive characteristics. Sum scores and variance were calculated. The study with the MADS did not report full-scale results and limited the analysis on an item level (O'Connor et al., 2007). We have calculated a combined measure on the items measuring strength of belief, reaction to hypothetical contradiction, affect with delusion, preoccupation with delusions and systematisation of delusion. Most studies report on hallucinations and delusions, but not all patients in the studies had hallucinations, delusions, or both. As the number of patients (n) we used the proportion of the patients with hallucinations or delusions at baseline and who reported hallucinations or delusions at the end of treatment measurement.

The outcomes across the trials were expressed in Hedges' *g* (the standardised mean difference, *d*, corrected for small sample bias) and meta-analytically synthesized using Comprehensive Meta-Analysis version 2.2 (www.meta-analysis.com/) with the random effects model. We have chosen end-of-treatment data, because not all studies reported follow-up data, or used quite variable follow-up periods. For the meta-analysis, the random effects model was chosen, because heterogeneity was expected owing to samples differing across studies and therapy formats varying from individual to group, and being shorter or longer.

Heterogeneity is a concern in meta-analysis as it may introduce the problem of 'comparing apples with oranges'. Heterogeneity was tested with a χ^2 test. We also report the I^2 statistic. When $I^2 = 0\%$, 25% , 50% or 75% , then no, low, moderate or high heterogeneity must be assumed (Higgins et al., 2003).

Meta-analysis may be subject to publication bias. We conducted Egger's regression test to quantify the bias captured by the funnel plot and to test whether it was statistically significant (Egger et al., 1997). If Egger's test was significant, then the publication bias was further evaluated using Duval and Tweedie's trim and fill procedure, which yields an adjusted estimate of the pooled effect-size after the publication bias has been taken into account (Duval and Tweedie, 2000a, 2000b). Another way to examine publication bias was to use the fail/safe *N* analysis, which indicates the number of missed studies that would render the pooled effect size to a statistically insignificant effect ($\alpha > 0.05$).

2.6. Moderator selection

Several moderator analyses explored the data in more detail. Comparing with active treatment was expected to yield smaller effect-sizes than comparing with treatment as usual (TAU) as a control condition. Blinded studies were expected to reduce the effect-sizes compared with studies that were not blinded.

2.7. Risk of bias and blind studies

Risk of bias is examined as a dichotomous moderator and as a continuous measure in a meta-regression analysis. The quality of the studies was assessed with the Clinical Trials Assessment Measure (CTAM) (Tarrier and Wykes, 2004; Wykes et al., 2008). This instrument has been developed to assess the quality of clinical trials of psychosocial interventions and is based on the CONSORT statement. In addition, we dichotomized the studies in blinded and not blinded studies for moderator analysis.

2.8. Sensitivity and moderator analyses

The main analysis comprises trials directed at symptom reduction with individually tailored case-formulation CBT. Additional sensitivity analyses were conducted; examining symptom reduction in broad CBT with other goals, e.g. worry reduction or coping skills enhancement and symptom reduction of broad CBT focussed on relapse prevention. Other moderator analyses were directed at comparing CBT with TAU or with active treatment, and assessing the effects of blinded trials.

3. Results

3.1. Characteristics of the included studies

Eighteen studies were included in the meta-analyses (Lewis et al., 2002; Durham et al., 2003; Trower et al., 2004; Cather et al., 2005; Valmaggia et al., 2005; Wykes et al., 2005; McLeod et al., 2007a, 2007b; O'Connor et al., 2007; Garety et al., 2008; Haddock et al., 2009; Penn et al., 2009; Foster et al., 2010; Peters et al., 2010; Lincoln et al., 2012; Krakvik et al., 2013; Leff et al., 2013; Rathod et al., 2013; Morrison et al., in press). Fifteen studies reported on hallucinations and twelve on delusions. Of these, two studies had three arms (Lewis et al., 2002; Durham et al., 2003). We pooled the control conditions in the overall analyses to prevent double counting of subjects. In the sensitivity analyses for active treatment or TAU, we just selected a single control condition relevant for that particular analysis. The overall database comprised 1418 patients with auditory hallucinations and/or delusions; 653 had been randomised to the CBT condition and 765 to the control condition. Table 1 presents a comparison of the studies included in these two meta-analyses. The number of participants, age and sex are presented by condition. Table 2 presents the reasons for studies added in sensitivity analyses and the reasons to exclude studies from analysis to prevent including apples and oranges.

3.2. Hallucination studies

3.2.1. Overall analysis and sensitivity analyses

Fig. 2 presents the results of all hallucination studies with individually tailored case-formulation aimed at symptom reduction combined in a forest plot. Table 3 (upper part) shows the effect-sizes of the overall meta-analysis in the hallucination trials and two sensitivity analyses and three moderator analyses. All analyses showed significant effect-sizes ranging from 0.31 to 0.49.

3.2.2. Heterogeneity in the hallucination studies

The Chi-square (*Q*) was not significant in any of the analyses, pointing to the absence of heterogeneity, as does I^2 . There was moderate

Table 1
Description of the interventions, patient characteristics, location, transition criteria, and quality of the studies.

Author	Year	Format	Duration intervention	Experimental condition				Control condition				Country	CTAM score	Blind rating	Selected outcome measure
				CBT format	Subjects	Age mean (SD)	Male sex %	Control format	Subjects	Age mean (SD)	Male sex %				
Lewis et al.	2002	Indiv	15–20 h in 5 weeks	CBT	101	29.1	71%	[1] SC [2] TAU	[1] 106 [2] 102	[1] 27.2 [2] 27.0	[1] 71% [2] 68%	UK	93	Yes	PSYRATS
Durham et al.	2003	Indiv	9 months	CBT	22	36.0 (10.0)	68%	[1] SC [2] TAU	[1] 23 [2] 21	[1] 37.0 (11.2) [2] 36.0 (10.2)	[1] 65% [2] 71%	UK	79	Yes	PSYRATS
Trower et al.	2004	Indiv	6 months	CT CH	18	36.6 (10.3)	56%	TAU	20	35.1 (10.4)	70%	UK	66	Yes	PSYRATS
Wykes et al.	2005	Group	10 weeks	CBT	45	39.7 (10.8)	53%	TAU	40	39.7 (10.1)	65%	UK	56*	Yes	PSYRATS
Valmaggia et al.	2005	Indiv	6 months	CBT	35	35.5 (10.8)	77%	SC	23	35.5 (11.4)	61%	NL	67	Yes	PSYRATS
Cather et al.	2005	Indiv	16 weekly sessions	fCBT	16	45.9 (10.2)	25%	PE	12	33.1 (10.3)	67%	USA	57*	No	PSYRATS
McLeod et al.	2007	Group	8 weekly sessions	CBT	10	n.a.	n.a.	TAU	10	n.a.	n.a.	UK	34*	No	PSYRATS
O'Connor et al.	2007	Indiv	24 weekly sessions	CBT	12	40.0 (9.4)	45%	APC	12	36.8 (13.5)	67%	CAN	49*	No	MADS
Garety et al.	2008	Indiv	20 sessions in 9 months	CBT	60 H 85 D	39.1 (10.3)	71%	TAU	60 H 85 D	37.1 (10.9)	72%	UK	88	Yes	PSYRATS
Penn et al.	2009	Group	12 weeks	CBT	32	41.7 (11.8)	53%	SC	33	39.6 (15.7)	49%	USA	88	Yes	PSYRATS
Haddock et al.	2009	Indiv	17 sessions	CBT	38	35.7 (12.5)	86%	SAT	39	33.9 (9.7)	86%	UK	88	Yes	PSYRATS
Peters et al.	2010	Indiv	6 months	CBT	36	34.0 (9.8)	72%	TAU	38	39.6 (10.2)	53%	UK	68	No	BAVQ
Foster et al.	2010	Indiv	4 sessions	Worry-CBT	12	40.0 (10.0)	58%	TAU	12	39.1 (9.2)	58%	UK	38*	No	PSYRATS
Lincoln et al.	2012	Indiv	16 weekly sessions	CBT	40	33.2 (10.4)	55%	TAU	40	33.1 (10.9)	57%	GER	82	Yes	PDI
Krakvik et al.	2013	Indiv	6 months 20 sessions	CBT	23	35.3 (8.9)	65%	TAU	22	37.5 (11.2)	64%	NO	48*	No	PSYRATS
Rathod et al.	2013	Indiv	16 weekly sessions	Ca CBT	17	31.4 (12.4)	63%	TAU	18	35.6 (10.7)	59%	UK	58*	No	CPRS Del. Hall. Scale
Leff et al.	2013	Indiv	6 weekly sessions	Avatar CT	14	n.a.	n.a.	TAU	12	n.a.	n.a.	UK	58*	Yes	PSYRATS
Morrison et al.	2014	Indiv	9 months	CBT	37	33.0 (13.1)	46%	TAU	37	29.7 (12.0)	59%	UK	81	Yes	PSYRATS

CBT = Cognitive behavioural therapy; SC = Supportive counselling/supportive therapy; TAU = Treatment as usual/Waiting list; CTCH = Cognitive Therapy for Command Hallucinations; fCBT = Functional CBT; APC = Attention Placebo Control; SAT = Social activity treatment; CaCBT = Culturally adapted CBT; UK = United Kingdom; NL = Netherlands; USA = United States of America; CAN = Canada; GER = Germany; NO = Norway; CTAM = Quality rating; * = Risk of bias; PSYRATS = Psychotic symptom rating scale; MADS = MacArthur-Maudsley Delusions Assessment Schedule; BAVQ = Beliefs about Voices Questionnaire; PDI = Peters Delusion Inventory; CPRS = Comprehensive Psychiatric Rating Scale Delusion and Hallucination Scales.

Table 2
Reasons for including studies in sensitivity analyses or excluding from the analyses.

Study	Year	
<i>Reason for inclusion in sensitivity analysis</i>		
Cather et al.	2005	Not formulation-based CBT: Coping skills based training: "Patients are taught skills for managing persistent positive symptoms that interfere with accomplishing certain activities or goals; only symptoms that interfere with goal attainment or role functioning are targeted"
Wykes et al.	1999, 2005	Not formulation-based CBT: Six group sessions were based on a cognitive behavioural approach, followed a semi-structured format and lasted for an hour. Each session dealt with a particular theme: (1) sharing of information about the voices, (2) models of psychosis, (3) models of hallucinations, (4) effective coping strategies, (5) improving self-esteem, and (6) an overall model of coping with voices.
Penn et al.	2009	Not formulation-based CBT: Coping skills based training: "We modified the Wykes et al. (1999) manual in the following ways: 1) emphasizing coping skills rather than cognitive restructuring; 2) deemphasizing self-esteem work; and 3) expanding the protocol from 6–12 sessions so that more time can be spent on each of the above themes."
Foster et al.	2010	Not formulation-based CBT, primary outcome worry reduction: "Participants in the W-CBT arm of the trial were offered four sessions over one month. The worry reduction strategies included were (i) indicated in the literature to be effective at reducing worry, either alone or in conjunction with other anxiety management strategies; (ii) did not challenge or review the delusion itself; and (iii) had been used by the authors in clinical practice."
Garety et al.	2008	Primary outcome relapse prevention: Some CBT, but most effort on relapse prevention, only 2 items used: "The last stage involved developing a set of self-regulatory strategies to manage relapse. This would include a pragmatic relapse management plan and the identification of particular behavioural strategies to manage risk situations and early signs as they emerged."
<i>Reason for exclusion</i>		
Turkington et al.	2002, 2006	No hallucination and delusion data at end-of-treatment, just at follow-up
Morrison et al.	2004	Not randomised
England et al.	2007	Reported only one item
Chadwick et al.	2009	No CBT, but Mindfulness meditation and discussion
Van der Gaag et al.	2012	No CBT, but imagery techniques targeted at depression reduction, not hallucinations
Shawyer et al.	2012	No CBT, but Acceptance and Commitment therapy

heterogeneity in the moderator analysis with active control treatment. Still, the data must be interpreted with some caution as the number of trials was quite small and most studies were also underpowered.

3.2.3. Publication bias in the hallucination studies

Egger's regression test did not suggest asymmetry in the funnel plot of the main and moderator analyses. The effect-sizes did not co-vary with the blinded ratings. Fail-safe N (alpha = 0.05, 2 sided) shows that 61 studies with null findings are necessary to reduce the pooled effect-size to a non-significant one and 36 null findings to do the same to blind trials using case-formulation CBT aiming at symptom reduction. Including broad CBT and relapse reduction studies in the sensitivity analyses did show publication bias and the Hedges' g was corrected from 0.31 to 0.27 in broad CBT with other outcomes.

3.3. Delusion studies

3.3.1. Overall analysis and sensitivity analyses

Fig. 3 presents the results of all delusion studies combined in a forest plot.

Table 3 (lower part) shows the effect-sizes of the overall meta-analysis in the delusion trials and two sensitivity analyses and three moderator analyses. The pooled effect is slightly reduced compared with those in hallucinations, and lost statistical significance in contrast with active treatment.

3.3.2. Heterogeneity in the delusion studies

The Q-statistic was significant in almost all analyses, suggesting that the null-hypothesis of homogeneity had to be rejected. Likewise I²

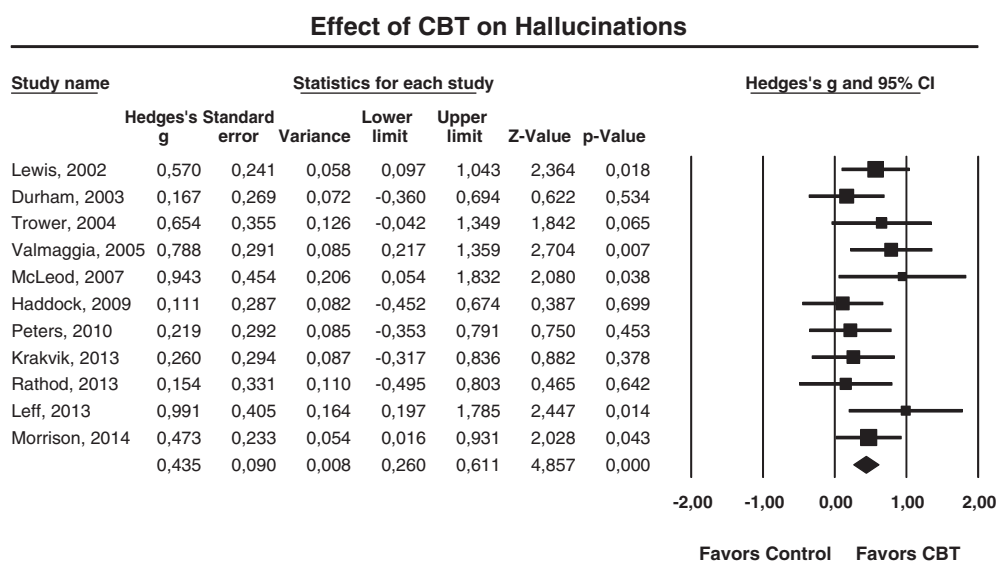


Fig. 2. Forest plot of studies using CBT and evaluating the effect on auditory hallucinations.

Table 3
Random effect-sizes, heterogeneity and publication bias in the main and sensitivity analyses.

Analysis	Random effect-sizes				Heterogeneity			Publication bias	
	Number of contrasts	Hedges' g	Z	p-value of Z	Q (df)	p-value of Q	I ²	Egger's regression (corrected g)	Fail-safe N
<i>Auditory hallucinations</i>									
Main: SR + CF	11	0.44***	4.857	0.000	9.221 (10)	0.511	0/NO	0.225	61
<i>Sensitivity analyses</i>									
Broad CBT also training approaches	14	0.35***	4.519	0.000	12.886 (13)	0.457	0/NO	0.130	68
Broad CBT with any primary outcome	15	0.31***	4.114	0.000	15.296 (14)	0.358	0/NO	0.033 (0.27)	69
<i>Moderator analyses</i>									
SR + CF compared with TAU	9	0.39***	3.793	0.000	6.330 (8)	0.610	0/NO	0.123	29
SR + CF compared with active treatment	4	0.49*	2.541	0.011	5.072 (3)	0.167	40.9/MOD	0.930	8
SR + CF + blind	8	0.46***	4.482	0.000	7.015 (7)	0.427	0/NO	0.507	36
<i>Delusions</i>									
Main: SR + CF	9	0.36*	2.549	0.011	17.993 (8)	0.021	55.5/MOD	0.394	26
<i>Sensitivity analyses</i>									
Broad CBT also training approaches	11	0.36**	2.749	0.006	20.786 (10)	0.023	51.9/MOD	0.364	36
Broad CBT with any primary outcome	12	0.31**	2.653	0.008	23.656 (11)	0.014	53.5/MOD	0.149	36
<i>Moderator analyses</i>									
SR + CF compared with TAU	6	0.33*	2.015	0.044	10.256 (5)	0.068	51.2/MOD	0.565	8
SR + CF compared with active treatment	5	0.33	1.501	0.133	10.556 (4)	0.032	62.1/MOD	0.915	–
SR + CF + blind	6	0.24*	2.368	0.018	12.603 (5)	0.027	60.3/MOD	0.982	3

SR + CF = Symptom reduction + individually tailored case-formulation; Q = value for heterogeneity tested by Chi-square; I² = degree of heterogeneity; NO = No heterogeneity; MOD = Moderate heterogeneity; HIGH = High heterogeneity; – = non-significant contrast and no fail-safe N.

* p < .05.
** p < 0.01.
*** p < 0.005.

points to moderate heterogeneity. Therefore the data must be interpreted with some caution.

3.3.3. Publication bias in the delusion studies

Egger's regression test showed no publication bias. Fail-safe N indicated that 36 null findings would be necessary to reduce the observed effect-size to a non-significant one in case-formulation CBT aiming for symptom reduction.

3.4. Quality of the included studies

The CTAM score (Table 1) describes the methodological quality of the primary studies. The trials were rated by two independent senior researchers in psychosis (ABP. S. and S.C.) and minor differences were discussed and resolved in a consensus meeting. Nine studies were scored as of poor quality according to CTAM criteria. A meta-regression analysis of the quality assessment on the effect-size in the

trials found no evidence that higher quality was associated with a lower effect-size (Delusions: Point estimate of the slope = –0.004; SE = 0.006; z = –0.562; p = 0.574; Hallucinations: Point estimate of the slope = –0.004; SE = 0.006; z = –0.641; p = 0.521).

4. Discussion

The results of this meta-analyses support the general conclusion that CBTp is effective in treating auditory hallucinations and delusions. The effect-sizes vary from small to medium and are in line with other meta-analyses (Pfammatter et al., 2006; Wykes et al., 2008; Jauhar et al., 2014; Turner et al., in press). There was no statistically significant heterogeneity in the hallucination trials, while moderate heterogeneity was found in the delusion trials. All trials had improved hallucinations in the CBTp condition, but two trials reported adverse impacts on delusions while the remaining seven trials showed an improvement in delusions in the CBTp condition. Both studies by Durham and colleagues and

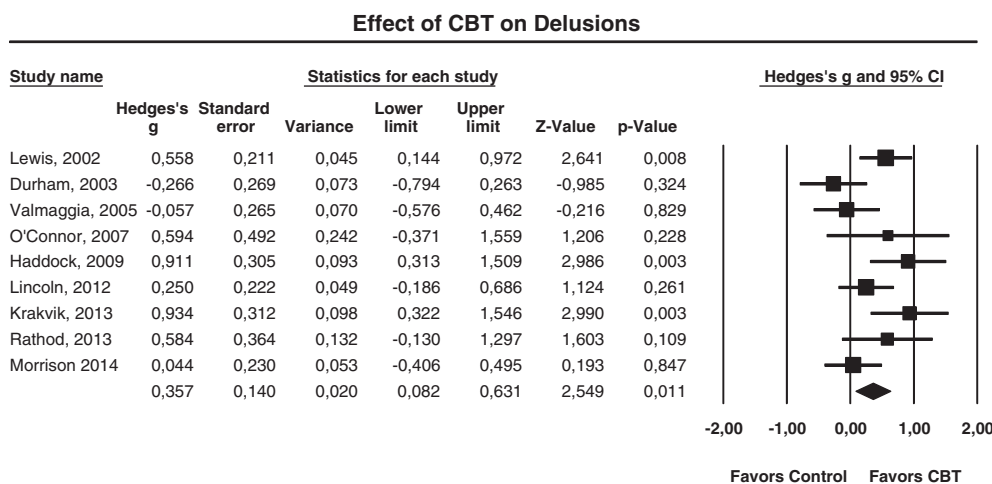


Fig. 3. Forest plot of studies using CBT and evaluating the effect on delusions.

Valmaggia and colleagues specifically focussed on chronic patients with medication-resistant patients and had an active treatment in the control condition (Durham et al., 2003; Valmaggia et al., 2005). These studies may indicate that delusions are less amenable to change than hallucinations in patients on antipsychotic medication with refractory psychosis.

Individually tailored case-formulation CBT had better results than broad CBT as expected.

CBTp for delusions compared with active treatment did not attain statistical significance, and had reduced but significant effect-size in blinded studies. CBTp for hallucinations was slightly more effective in contrast with active treatment and in contrast with blinded studies.

Contrary to our expectation, we did not find an effect of the quality of the trials on the effect-sizes in meta-regression, but blinded versus not blinded studies were associated with a difference in delusions and not in hallucinations.

4.1. Strength

The strength of this meta-analysis is that eighteen trials were included encompassing 1418 patients allowing for relatively detailed evaluation of effects. Nevertheless, more long-term studies are needed to strengthen the evidence-base and to shed light on the efficacy.

4.2. Limitations

As highlighted above, a limitation is the small number of blind studies or studies with an active control condition. Our meta-analytic results regarding these sub-sets must be interpreted with some caution.

Another limitation was that it is not certain from the published papers whether the symptom-specific measure reported in the results was chosen at the study design as a primary outcome measure. This may have resulted in selective outcome reporting where significant results were reported more often than non-significant results.

A final limitation is our application of the selection criteria for the primary studies. Our focus on published studies may have introduced publication bias, but publication bias was not found in the analyses neither in delusions nor in hallucinations.

4.3. Concluding remarks and recommendations

We join other authors before us who have advocated the effectiveness of individual tailored therapy based on case-formulation (Morrison and Barratt, 2010; Steel et al., 2012). The effect-sizes might increase if more sensitive outcome measures are developed, while more specific outcome measures may also generate more informative feedback on what types of CBTp work best for whom and in what clinical outcome dimensions.

The field may be also be furthered by the development of more targeted forms of CBT, for example Trower and colleagues developed an intervention targeting command hallucinations, which has shown positive results (Trower et al., 2004). The focus of their intervention was on modifying the appraisal about the power of the voices, and the change in appraisal resulted in a decrease of compliance with the command hallucinations. Also recommended are further studies in the emotional and cognitive processes involved in the development and maintenance of auditory hallucinations and delusions, which can inform the development of tailored CBTp (Garety et al., 2013).

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Contributors

The design of the study and the selection of studies were done by L Valmaggia and M van der Gaag.

The analyses were conducted by M van der Gaag and ff Smit.

The paper was drafted by M van der Gaag and co-authored by L Valmaggia and F Smit.

Conflict of interest

The authors declare that they do not have conflicting interests.

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