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Efficacy of Cognitive-Behavioral Therapy in Pediatric Obsessive-Compulsive Disorder: A Meta-Analysis

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Study Design A

Data Collection B Statistical Analysis C

Data Interpretation D

Manuscript Preparation E

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Background:

Pediatric obsessive-compulsive disorder (OCD) is a debilitating psychological anxiety disorder. Cognitivebehavioral therapy (CBT) has been shown to be an effective therapy for OCD, but the evaluation results from various studies are inconsistent and incomprehensive. This meta-analysis examined the efficacy of CBT in treatment of OCD.

Material/Methods:

A literature search identified 13 studies that met the inclusion criteria. The efficacy of CBT on OCD was evaluated by comparing post-treatment and pre-treatment Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) scores. Weighted mean difference (WMD) was generated for the statistical evaluation. Heterogeneity was evaluated by I2 index.

Results:

A decrease in WMD and a statistical significance (p<0.0001) in both CY-BOCS and CGI scores between pre- and post-CBT treatment were observed in both overall database (-11.73) and USA subgroup (-11.371), which indicates a dramatic relief of OCD symptoms after CBT treatment. Heterogeneity was detected in overall database and USA subgroup, which resulted in an application of the random-effects model to both groups. Publication bias was examined by both Begg's funnel plot and Egger's test and no publication bias was detected.

Conclusions:

We concluded that CBT is efficacious in treating children's OCD.

MeSH Keywords:

Cognitive Therapy • Meta-Analysis • Obsessive-Compulsive Disorder

Full-text PDF:

http://www.medscimonit.com/abstract/index/idArt/895481











Background

Obsessive-compulsive disorder (OCD) is a complex psychological disorder that is characterized by recurrent obsessions and/ or compulsions. Obsessions are defined as intrusive, repetitive thoughts, images, or impulses. Compulsions are purposeful, repetitive, overt and covert behaviors or rituals performed in an effort to relieve obsessional distress [1]. OCD affects approximately 1% to 4% of children and adolescents [1,2], which causes marked distress and interferes with daily functioning [3]. As reported, the age of onset for pediatric OCD varies considerably; early onset as early as 3 years of age has been reported[1], but the mean age of onset is around 10.4 years (range, 6.9-12.5 years) [1]. Pediatric OCD is often associated with other psychological disorders, such as tics, attention deficit/hyperactivity disorder (ADHD), depression, multiple anxiety disorders, eating disorders, pervasive developmental disorders, and externalizing behavioral disorders [1]. The comorbidity has been associated with a lower treatment response and a greater percentage of relapse after treatment, both in medication and psychological interventions [4]. Thus, the occurrence of OCD and its comorbidity during childhood is very pernicious in its impact in disrupting functions across multiple domains, including family relationships and everyday life routines, school functioning, and peer relationships, and compounding its negative impact over time to derail normal development, which leads to lifelong suffering if left untreated [5-7]. Thus, the severe consequences of OCD in lives of children and adolescents have motivated physicians and researchers to improve pharmacological and psychological interventions, as well as to develop new assessment instruments.

Cognitive-behavioral therapy (CBT) is the only psychological therapy that has been demonstrated to be effective in treating pediatric OCD in many studies [1,8]. CBT refers to a class of interventions that were developed from the basic premise that psychological disorders are maintained by cognitive and behavioral factors. CBT for OCD in youth involves 4 primary components: psycho-education, cognitive training, mapping of OCD, and exposure with response prevention [9], which aims to weaken the association between obsessions and increased anxiety, and between compulsions and the relief of anxiety. Despite the positive outcome of CBT on OCD treatment, the results delivered by current articles are inconsistent and not comprehensive, mainly because of the huge variations among studies in sample sizes, various ethnic groups, and different outcome assessment tools used. To generate a more comprehensive evaluation of the efficacy of CBT on the treatment of OCD, we carried out this meta-analysis covering 13 studies and 415 OCD patients.

Material and Methods

Literature search

Published reports were searched in the NCBI Global database, including PubMed, PubMed Central, and Google Scholar, using "children's obsessive-compulsive disorder", "pediatric OCD", "cognitive-behavioral therapy", and "CBT" as key words. Reference lists of articles that were included for review were also examined to further identify reports that were potentially relevant. Unpublished studies were not considered.

Inclusion and exclusion criteria

Studies were included if they: (1) included only children and/ or adolescents (age <18) with a primary diagnosis of OCD; (2) had enough participants (10 or more); (3) the participants were only treated with CBT, without any pharmacological interventions; (4) used randomization; (5) used at least 1 reliable and valid measurement for primary outcome; and (6) presented sufficient information to enable calculation of effect sizes.

Exclusion criteria were: (1) books and other literature that were not therapy evaluation studies; (2) studies of which the primary goal was not the investigation of the efficacy of CBT in OCD; and (3) articles without comprehensive statistical information or without the retrievable original data. When the studies that were covered in different articles overlapped, only the ones showing the most extensive results were included in this study.

Two investigators independently extracted the data from each eligible study. Disagreements between reviewers were resolved by discussion and a consensus was reached on all items.

Effect size calculation

An effect size θ based on means usually considers the standardized mean difference between 2 populations. In the equation: $\theta = \frac{\mu_1 - \mu_2}{\sigma}$, where μ_1 is the mean for population, μ_2 is the mean for the other population, and σ is a standard deviation (SD) based on either or both populations. For clinical trials covered in our meta-analysis, effect sizes were calculated within each trial. Similar to the 2-sample Cohen's d, the effect size is an estimate of the true difference between pre-treatment and post-treatment outcome divided by SD.

Data collection and synthesis

The primary outcome measure of interest was the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS), which is a psychometrically sound [10], clinician-rated, semi-structured interview assessing the severity of obsessive-compulsive

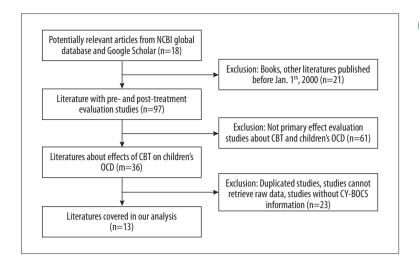


Figure 1. Flow chart of selection of studies and specific reasons for exclusion from the meta-analysis. We identified 118 studies for the first-round exclusion, out of which 13 studies were included in the final meta-analysis.

symptoms. The CY-BOCS rates the severity of obsessions and compulsions across 5 items each and provides a total severity score. The score of different scales reflects a difference in the severity of symptoms: 0–7 is sub-clinical, 8–15 is mild, 16–23 is moderate, 24–31 is severe, and 32–40 is extreme. Patients with a mild range or higher score are more likely to experience a significant negative impact on quality of life and should receive professional help in alleviating the symptoms.

The Clinical Global Impression – Severity (CGI-S) score as a secondary outcome measurement was also assessed among studies for which CGI-S score was available. CGI-S is a single-item 7-point clinician rating of severity of OCD. The CGI-S allows the clinician to rate the global severity of anxiety, with scores ranging from 0 ("no illness") to 6 ("serious illness"), and were completed at baseline and post-treatment. In our analysis, a decrease of CGI-S indicates improvement of the condition. For continuous variables, the mean, standard deviation, and sample size in each group are known. The weight given to each study (how much influence of each study has on the overall analysis result) is determined by the precision of its estimate of effect [11].

Weighted mean difference (WMD) will then be calculated with groups before and after an intervention. In this case, WMD was generated to test the efficacy of CBT, which was calculated by comparing mean and standard deviation of pre- and post-treatment CY-BOCS score and CGI-S score. A positive WMD indicates an increased CY-BOCS or CGI-S score for post-treatment compared to the pre-treatment score. On the other hand, a negative WMD shows a decrease in CY-BOCS or CGI-S score after treatment, indicating an improvement in OCD symptoms. For each study, mean value and standard deviation of CY-BOCS score and the number of patients involved in the trail were used as pooled data.

Statistics

The statistical analysis of the pooled data was conducted using STATA 12.0 (Stata Corp LP, College Station, TX, USA). P-value <0.05 was considered as statistically significant. In addition to the overall database, a subgroup that covered all studies performed in USA was created. For continuous data, inverse variance method should be applied. The Mantel-Haenszel (M-H) fixed-effects model should be used to analyze databases without significant heterogeneity. On the other hand, DerSimonian and Laird (D-L) random-effected model should be used for databases with evident heterogeneity. In our analysis, the heterogeneity between studies was tested using I2 index, with the equation of $l^2 = \frac{\sigma - df}{1} \times 100\%$, where Q is statistical data and DF is its freedom. The higher the I², the more significant the heterogeneity is. Values of I² as 25%, 50% and 75% represent low, medium, and high heterogeneity, respectively. When I2 ≤50%, there is no significant heterogeneity between pooled data. In this meta-analysis, the M-H fixed-effects model was used to test the heterogeneity first, and then different models were chosen based on the results. WMD was calculated with each model within 95% confidence intervals. Forest plots were generated to evaluate OR and summarize the results. To evaluate publication bias, Begg's funnel plots were generated based on the analysis results and database size, and Egger's test was also performed.

Results

Study characteristics

A total of 118studies were retrieved after the first search, and 105 of them were excluded from the analysis for reasons listed in the Methods section and as shown in the data collection flow chart of Figure 1. As a result, 13 studies [9,12–23] that met the inclusion criteria were included in the final meta-analysis,

Table 1. Pooled Data for evaluation of CY-BOCS score for patients with CBT.

Study	V	Age	Pre-treatment			Post-treatment			FC	
	Year		Mean	Std	n	Mean	Std	n	ES	Country
Benazon, 2002	2002	8-17	22.56	6.45	16	11.79	6.58	16	1.65	USA
Farrell, 2011	2011	9–13	20.45	6.82	43	12.43	8.18	43	0.92	Australia
Farrell, 2010	2010	10–15	23.54	5.79	35	10.06	6.82	35	2.13	Australia
Franklin, 2011	2011	7–17	26.08	5.12	42	25.45	5.18	42	0.85	USA
Freeman, 2014	2014	5–8	25.13	4.46	63	12.5	2.4	63	0.84	USA
Keeley, 2011	2011	10–16	25.73	4.59	25	8.27	7.19	25	2.89	USA
Lenhard, 2014	2014	11–16	21.33	3.54	21	12.05	4.51	21	2.29	Sweden
POTS, 2004	2004	7–17	26	4.6	28	14	9.5	28	0.97	USA
Rudy, 2014	2014	10–16	26.54	4.54	78	10.85	6.74	78	2.73	USA
Storch, 2013	2013	7–17	23.64	4.48	14	15.43	9.72	14	1.01	USA
Storch, 2011	2011	7–16	25.38	3.61	16	11.13	10.53	16	1.36	USA
Storch, 2006	2006	7–17	25.9	5.6	20	9.5	6.9	20	2.62	USA
Whiteside, 2014	2014	7–18	25	5.55	14	15.67	5.24	14	1.37	USA

Table 2. Meta-analysis for overall database and USA subgroup.

Period	Analysis	Heterogeneity			W	Publication bias			
	method	l² (%)	p-value	Overall	Lower	Upper	p-value	Begg	Egger
Overall	Random	91.9	0	-11.37	-14.11	-8.63	<0.0001	0.3	0.974
USA	Random	93.5	0	-11.73	-15.25	-8.21	<0.0001	0.049	0.953

in which 415 OCD patients were covered. Table 1 shows the characteristics of all studies, including the age range and the countries of the patients employed in each trial, as well as year published.

Evaluation of heterogeneity

A heterogeneity analysis was conducted to test the variation in study outcomes between studies. I² index was calculated in this study and significant heterogeneity was detected in both overall database (I²=91.9%) and USA subgroup (I²=93.5%). Thus, the random-effects model, as a more natural choice that allows the study outcomes to vary in a normal distribution between studies, was applied to both groups.

Quantitative synthesis

The meta-analysis was carried out on both the overall database and the USA subgroup. The pooled data was made up of mean value and standard deviation of the CY-BOCS scores for OCD patients before and after CBT treatments, the total number of patients employed in each trial, and the calculated effect sizes. The 95% confidence interval for effect sizes of the CBT were relatively large and did not contain zero across all 13 studies covered in this meta-analysis, indicating that the effect of CBT on OCD symptoms severity was significantly greater than zero. WMD was calculated and Forest plots of WMD between pre- and post-treatment of CBT on children's OCD for either entire database or USA subgroup were generated to summarize the results (Figure 2). Significant difference was detected in the CY-BOCS scores between pre-treatment and post-treatment data as judged by WMD. Overall WMD in the entire database was estimated to be -11.371 [95% CI: -14.11 to -8.631, p<0.0001], which indicates that the post-treatment CY-BOCS score decreased by more than 11 compared to the pre-treatment score, demonstrating a significant relief in the OCD symptoms after CBT treatment. Similarly, the WMD in the USA subgroup was estimated to be -11.73 [95% CI: -15.25 to -8.21, p<0.0001], as shown in Table 2 and Figure 3, which also suggests a dramatic efficacy of CBT in improving OCD symptoms of patients in USA.

A secondary outcome measurement using CGI-S score was also performed. The pooled data are shown in Table 3, and the results are given in Table 4 and Figure 4. A significant difference was detected in the CGI-S scores between pre-treatment and

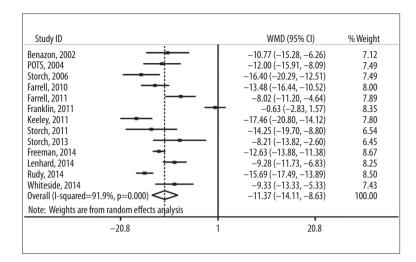


Figure 2. Forest plot of WMD of CY-BOCS score between pre- and post-treatment of CBT on children's OCD for entire database.

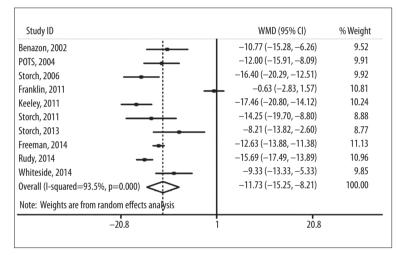


Figure 3. Forest plot of WMD of CY-BOCS score between pre- and post-treatment of CBT on children's OCD for USA subgroup.

Table 3. Pooled Data for evaluation of CGI-S score for patients with CBT.

CALLAL	V	Ann	F	re-treatmen	t	Post-treatment			
Study	Year	Age	Mean	Std	n	Mean	Std	n	
Rudy, 2014a	2014	13.2	4.16	0.76	19	1.21	0.71	19	
Rudy, 2014b	2014	13.2	4.1	0.61	30	2.03	0.93	30	
Rudy, 2014c	2014	13.2	4.69	0.6	29	2.14	1.09	29	
Storch, 2013	2013	7~17	4.63	0.72	16	3.37	0.89	16	
Storch, 2011	2011	7~16	3.75	0.93	16	1.56	1.75	16	
Storch, 2006	2006	7~17	4.2	0.8	20	1.4	0.9	20	

post-treatment data as judged by WMD, which was estimated to be -2.318 [95% CI: -2.808 to -1.827, p<0.0001], as shown in Table 4 and Figure 4.

Publication bias

It has been suggested that a potential discrepancy could exist between the number of published trials and the total number of studies that has been carried out. Thus, some non-significant studies could have been missed in a meta-analysis of published studies, so the overall effect size could be overestimated [24]. Therefore, the publication bias of the present meta-analysis was examined and both Begg's and Egger's tests were performed to the overall database, as well as the USA subgroup. The funnel plots for either overall database or USA subgroup were also generated. No publication bias was

Table 4. Meta-analysis for overall database on CGI-S score.

Analysis	Heter	Heterogeneity		W	Publication bias			
method	l² (%)	p-value	Overall	Lower	Upper	p-value	Begg	Egger
Random	81	0	-2.318	-2.808	-1.827	<0.0001	1	0.8

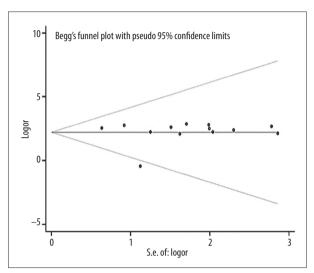


Figure 4. Forest plot of WMD of CGI-S score between pre- and post-treatment of CBT on children's OCD for studies included.

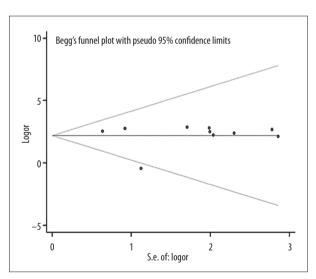


Figure 5. Funnel plot of entire database.

observed among these studies as judged by the results of funnel plots shown in Figures 5–7.

Discussion

In the present study, efficacy of CBT for treatment of pediatric OCD was investigated by a meta-analysis, in which 13 studies

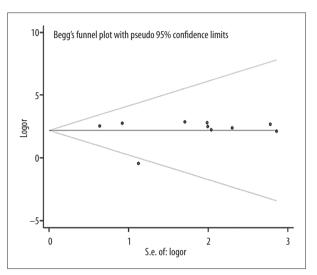


Figure 6. Funnel plot of USA subgroup.

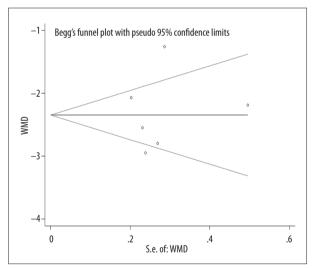


Figure 7. Funnel plot of studies with CGI-S score.

and 415 OCD patients were included. The results showed that there was a significant decrease in WMD in overall database (-11.371, p<0.0001) and USA subgroup (-11.73, p<0.0001), and the effect size is large across all studies included, suggesting that OCD symptoms were significantly relieved after CBT treatment. In addition, no publication bias was observed.

Findings from the present study substantiated the results from previous meta-analyses showing that CBT is efficacious in treating pediatric and adult OCD [25–31]. Interestingly, the

efficacy for OCD treatment was compared between CBT and certain pharmacological therapeutic strategies, such as the use of serotonergic antidepressants in some of these studies. The results of these comparisons demonstrated that CBT out-performs pharmacotherapy by showing a greater effect size and better improvement in clinical symptoms [25-28]. In addition, potential adverse effects generated by pharmacotherapy still remain a major concern for clinicians when considering the optimal therapeutic strategy for pediatric OCD patients [32]. Thus, CBT is regarded as the first-line therapeutic strategy for pediatric OCD. This was one of the major motivations for us to focus on the efficacy of CBT for OCD in this meta-analysis. One of the merits of the present study is that a number of very recent randomized clinical trials [15,17,19,20] have been for the first time included in our meta-analysis, which made the results very up-to-date. Another merit of the present study is that in addition to the overall database, a metaanalysis was also carried out on the 10 studies that focused on USA patients as a subgroup. Thus, the finding from the present study will definitely add new supplementary information to the evidence base of CBT for pediatric OCD treatment, and contribute to the translation of efficacy research into clinical community practice. A strength of the present study is that to minimize the bias caused by a single assessment tool, we used not only CY-BOCS score as a primary outcome measurement, but also CGI score as a secondary tool to assess the outcome of certain studies.

A major limitation of the present study is that although the findings suggest that CBT is efficacious for treatment of pediatric OCD, many of the studies included were uncontrolled trials that did not have controls for effects of time and other nonspecific factors, which might also contribute to the relief of symptoms.

Conclusions

A significant difference (a decreased WMD) in CY-BOCS and CGI-S score between pre-treatment and post-treatment was observed in the overall database and USA subgroup, suggesting that CBT is efficacious in treating pediatric OCD.

Conflict of interest declaration

No conflict of interest.

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