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Article

Cognitive-Behavioral Therapy and Anxiety and Depression Level in Pediatric Obsessive-Compulsive Disorder: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Although some meta-analyses have identified potential moderators associated with treatment outcomes for pediatric obsessive-compulsive disorder (OCD), there is as yet no consensus regarding the influence of anxiety and depression symptoms on the recovery from pediatric OCD. A meta-analysis was conducted to investigate the effects of depression and anxiety symptoms and their comorbidities on the efficacy of CBT in pediatric OCD, as well as other potential moderators that may be associated with outcomes. **Method:** An exhaustive literature search from 1983 to March 2021 located 22 published articles that applied cognitive-behavioral therapy (CBT) to pediatric OCD, producing a total of 26 treatment groups. Some of the moderator variables analyzed included age, gender, comorbidity baseline in anxiety, depression and obsession, and methodological quality. **Results:** Results showed that the psychological treatment of OCD achieves clinically significant effectiveness, both for measures of obsessions and compulsions (d_+ = 2.030), and for anxiety (d_+ = 0.613) and depression (d_+ = 0.451). An explanatory model for the CY-BOCS effect sizes showed that three moderator variables were statistically related: the mean of the CY-BOCS (Children's Yale Brown Obsessive Compulsive Scale) in pretest, the effect size for anxiety, and the mean age of the sample. **Conclusions:** CBT reduced obsessive-compulsive symptoms and, to a lesser extent, anxiety and depression symptoms. Since anxiety symptoms are reduced with the same therapy, resources would be saved compared to other treatments.

Terapia Cognitivo-Conductual y Niveles de Ansiedad y Depresión en el Trastorno Obsesivo-Compulsivo Pediátrico: una Revisión Sistemática y Meta-Análisis

Palabras clave:
Terapia cognitivo-conductual
TOC pediátrico
Síntomas de ansiedad
Síntomas de depresión
Comorbilidad ansiedad
Depresión.

RESUMEN

Antecedentes: Aunque algunos metanálisis han identificado posibles moderadores asociados con los resultados del tratamiento en el trastorno obsesivo compulsivo (TOC) pediátrico, todavía no existe consenso sobre la influencia de los síntomas de ansiedad y depresión en la recuperación de éste. Se realizó un metanálisis para investigar los efectos de los síntomas ansioso-depresivos y sus comorbilidades sobre la eficacia de la TCC en el TOC pediátrico, así como otras posibles variables moderadoras que pudieran estar asociados con el resultado. **Método:** Realizamos una búsqueda exhaustiva de la literatura desde 1983 hasta marzo de 2021 que nos permitió localizar 22 artículos publicados que aplicaban la terapia cognitivo-conductual (TCC) en el TOC pediátrico, produciendo un total de 26 grupos de tratamiento. Algunas variables moderadoras analizadas fueron: edad, sexo, comorbilidad, linea base en ansiedad, depresión y obsesion-compulsión, calidad metodológica. **Resultados:** Los resultados mostraron que el tratamiento psicológico del TOC consigue una eficacia clínicamente relevante, tanto para las medidas de obsesiones y compulsiones (d_+= 2.030), como para la ansiedad (d_+= 0,613) y la depresión (d_+= 0,451). Un modelo explicativo para los tamaños del efecto CY-

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BOCS (Escala obsesiva compulsiva de Yale-Brown para niños) reveló que tres variables moderadoras estaban relacionadas estadísticamente: la media del CY-BOCS en el pretest, el tamaño del efecto para la ansiedad y la media de edad de la muestra. **Conclusiones:** La TCC redujo los síntomas obsesivo-compulsivos y, en menor medida, los síntomas de ansiedad y depresión. Dado que los síntomas de ansiedad se reducen con la misma terapia, se ahorrarían recursos con respecto a la implementación y adición de otros tratamientos.

Obsessive-compulsive disorder (OCD) is characterized by obsessions (recurrent and intrusive thoughts) and/or compulsions (repetitive behaviors or mental acts) having serious consequences in an individual's daily life (APA, 2013). Epidemiological studies have shown that OCD is relatively prevalent in children and adolescents, yielding similar rates (around 2%) to those observed in adults (Canals et al., 2012; Kessler et al., 2012). OCD is also often associated with other psychological disorders, such as tics, attention deficit-hyperactivity disorder, anxiety or depression, which increase the degree of discomfort and complicate treatment and prognosis (Lavell et al., 2016; Murray et al., 2015; Storch et al., 2010).

Treatment options for children with OCD include cognitive-behavioral therapy (CBT), pharmacotherapy or both (Barret et al., 2008; Geller & March, 2012). However, some children and adolescents do not respond adequately to these first-line treatments, highlighting the need to identify predictors of poor response, such as comorbidity with other disorders, age, OCD severity at baseline, age at onset of the treatment, parental psychopathology, behavior management skills (parent tools), family accommodation, and family history of OCD, among others (Lebowitz, 2016; Wu & Storch, 2016).

Anxiety and depressive disorders and their symptoms have shown high comorbidity with OCD (Peris et al., 2017; Turner et al., 2018). Some authors have reported different reasons for the high co-occurrence of these disorders such as the practice of ascribing additional diagnoses to psychiatric patients, shared genetic risk factors, and direct causal mechanisms through which changes in OCD symptoms give rise to changes in symptoms of anxiety and depression, and viceversa (Rickelt et al., 2016; Voltas et al., 2014)

Other studies have examined the impact of depression and anxiety on CBT response in pediatric OCD populations, obtaining heterogeneous findings. Thus, some studies reported poorer treatment response due to co-occurring anxiety (Piacentini et al., 2002), while others reported no impact on treatment outcomes (Olatunji et al., 2013). McGuire et al. (2015) found that comorbid anxiety predicts treatment outcome in CBT, while attention deficit hyperactivity disorder (ADHD), depressive disorders, baseline OCD severity, and age were not associated with treatment outcomes. Other meta-analyses have found that older age and pre-treatment OCD severity were negative moderators of treatment outcome, while comorbid anxiety was a positive moderator of treatment effect (Öst et al., 2016).

Comorbid depression has been associated with greater OCD symptom severity (Canavera et al., 2010; Storch et al., 2008; 2011; Turner et al., 2018). As for the effect of depression on CBT outcomes, some authors have found that the presence of depression was not associated with a poorer response to treatment (Farrell et al., 2012). Nevertheless, other authors have shown that higher average OCD severity was associated with greater depressive symptoms across treatment but that regardless of initial depressive symptom severity, these decreased in line with reductions in OCD symptom severity (Meyer et al., 2014; Turner et al, 2018).

Højgaard et al. (2018) found that pretreatment OCD severity and levels of comorbid anxiety predict post-treatment OCD severity. However, when controlling for the effect of these predictors, only lower pretreatment OCD severity showed a significant, positive predictor of post-treatment OCD severity. Anxiety and depression scores were not significant predictors of treatment response in the multiple regression model. Torp et al. (2015) observed differences according to the type of informant whit anxiety and depression symptoms being predictors of poorer treatment outcome when parents answered, while when children answered these symptoms were not significant predictors of outcome. Cervin et al. (2020) reported that the severity of obsessions were linked to depression in youth with OCD. It was observed that specific OCD symptom dimensions (obsessing and doubting and checking) were linked to panic and generalized anxiety and, furthermore, these were related to depression. A limitation in these studies was that they have largely based on diagnostic interviews in which mental disorders are categorized as present or absent.

Therefore, as far as we are aware there is no meta-analytical study which analyzes both variables, anxiety and depression, as predictors of the efficacy of treatment in children and adolescents..

Other moderators variables associated with treatment outcomes have been the baseline OCD severity. This has been associated with poorer response to CBT (Piacentini et al., 2002; Scahill et al., 1997) or without any association with pre-treatment severity (Olatunji et al., 2013), or high and low pre-treatment severity predictive of a better outcome (Veale et al., 2016). Regarding the age of the patients, some authors have concluded that pre-adolescent children benefit more from treatment than adolescents (Ginsburg et al., 2008; Torp et al., 2015). Parental involvement has shown to be a predictor relevant to improving the benefits of CBT in reducing obsessive-compulsive symptoms (Iniesta-Sepúlveda et al., 2017; Rosa-Alcázar et al., 2015), while Öst et al. (2016) showed that CBT for pediatric OCD is effective when delivered in different formats, and that the active involvement of parents is not a crucial factor for the treatment effects.

Due to discrepant results in the literature, the overall aim of the present work was to perform a meta-analysis to analyze whether depression and anxiety pretest-posttest changes are statistically associated to the effect size for obsessive-compulsive symptoms (assessed with the Children Yale-Brown Obsessive-Compulsive Scale, CY-BOCS; Scahill et al., 1997) when applying CBT to children and adolescents with OCD. This study aims to report whether there are significant differences when measuring anxiety and depression as quantitative symptoms or when they are analyzed as disorders through diagnostic interviews in which mental disorders are categorized as present or absent. A further aim was to test the efficacy of CBT to ameliorate the obsessive-compulsive, depression, and anxiety symptoms.We were also interested in identifying characteristics of the samples of participants that could be used as potential predictors of the CY-BOCS effect size, such as the mean of the CY-BOCS in the pretest, effect sizes for anxiety and depression

symptoms, average depression and anxiety in the pretest, % anxiety and % depression in the sample, and OCD history. We also aimed to assess the influence of moderators related to how CBT was delivered (e.g., treatment duration, intensity and magnitude, treatment focus, mode, parent involvement), as well as the methodological quality of the studies, on the CY-BOCS effect sizes, and sociodemographic characteristics of the samples of participants (mean age and gender distribution). Finally, we intended to find an explanatory model with the moderators that better explain the variability of the CY-BOCS effect sizes.

Methods

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA 2020) guidelines.

Selection Criteria

For inclusion in this research, studies had to fulfill the following criteria based on PICOS statement (Moher et al., 2009): (a) to examine the efficacy of cognitive-behavioral treatments on a sample of participants younger than 19 years old with a diagnosis of OCD according to standardized diagnostic criteria (DSM; APA, 1994; 2000; 2013); (b) to include at least one treatment group with pretest and posttest measures; (c) the study was required to include the CY-BOCS as outcome measure for obsessive-compulsive symptoms, as well as depression and anxiety measures, both mandatory; (d) the sample size in the posttest should comprise more than four participants; therefore, single-case designs were excluded; (e) statistical data reported in the study had to allow us to compute the effect sizes, and (f) the study had to be written in English or Spanish.

Search strategy

We used several literature search procedures to locate studies which met our selection criteria. First, several electronic databases were consulted: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, and PsycINFO. The following keywords were combined, in English and Spanish, in the electronic searches: ([obsessive-compulsive] or [OCD]) and ([cognitive behavioral therapy] or [CBT] or [exposure response prevention] or [ERP]) and ([pediatric] or [child*] or [adolesce*]), which should be in the title or abstract. Second, the references of some meta-analyses and systematic reviews were consulted (Barret et al., 2005; Himle et al., 2003; Iniesta-Sepúlveda et al., 2017; March et al., 2001; McGuire et al., 2015; Rosa-Alcázar et al., 2012; 2015; Sánchez-Meca et al., 2014; Thompson-Hollands et al., 2014; Torp et al., 2015; Turner, 2006; Turner et al., 2018; Wu et al., 2016). Third, the references of the located studies were also reviewed. Finally, emails were sent to 10 experts in this area to locate unpublished studies. A flow chart of the literature search process is shown in Figure 1. The search strategy produced a total of 655 references, finding 22 articles that fulfilled the selection criteria, all written in English and published between 1983 and March 2021. The 22 articles produced a total of 26 treatment groups. Table 1 presents moderator variables of the studies included in the meta-analysis.

Coding of moderator variables

In order to examine the potential influence of characteristics of studies on effect sizes, potential moderator variables were coded: (1) mean age of the sample (in years); (2) sex distribution (percentage of males); (3) OCD history (average in years); (4) percentage of participants in the sample with comorbid disorders; (5) baseline obsessive-compulsive symptoms severity assessed with the CY-BOCS; (6) baseline in depression assessed with Children's Depression Inventory (Kovacs, 1992); (7) baseline in anxiety assessed with the Multidimensional Anxiety Scale for Children, MASC (March et al., 1997); (8) treatment duration (number of weeks); (9) treatment intensity (number of weekly hours); (10) treatment magnitude (total number of intervention hours per participant); (11) parental involvement, (12) treatment focus (child or family); (13) mode of CBT (individual, group, mixed); (14) therapist's training, and (15) methodological quality of the study (on a scale of 0–6 points). The items comprising the methodological quality scale were: (i) random versus non-random assignment of participants to the groups; (ii) the internal validity of the design (active control group, non-active control group or no control group); (iii) the sample size in the postest; (iv) attrition in the treatment group; (v) the use of intent-to-treat analysis, and (vi) the use of blinded assessors in measuring the outcomes. Each one was rated from 0 to 1. The items included in this scale were selected from other methodological quality scales: Chacón-Moscoso et al. (2016) scale, risk of bias items of the Cochrane Collaboration (Higgins et al., 2021), and PEDro scale (Verhagen et al., 1998).

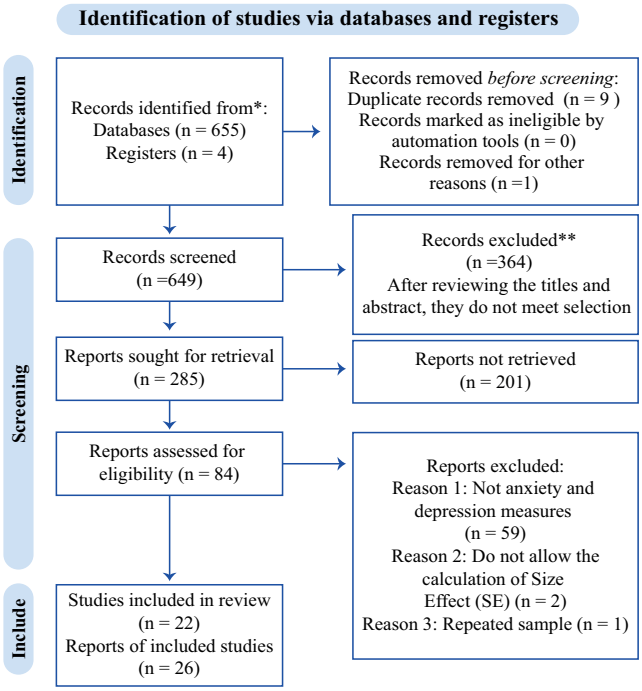

Figure 1.
PRISMA 2020 Flow Diagram.
*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

Table 1.
Moderator Variables of the Studies Included in the Meta-analysis

Study	N	Age	Sex	History	CY-BOCS pretest mean	Duration	% anxiety	% depression	g´s Hedges anxiety	g´s Hedges depression	g`s Hedges CY-BOCS
Barrett et al. (2004)a	24	10.8	50.0	--	23.64	14	70.80	.00	0.12	0.26	3.43
Barrett et al. (2004)b	29	12.9	45.0	--	21.38	14	75.86	6.89	0.86	0.57	2.27
Benazon et al. (2003)	23	11.7	52.2	3.2	22.56	12	11.54	7.69	1.41	1.39	1.61
Björgvinsson et al. (2008)	23	15.3	52.2	--	23.90	9.5	13.00	35.00	0.81	0.54	1.07
Bolton et al. (2011)a	36	15.0	42.0	3.8	22.30	12			1.09	0.86	2.50
Bolton et al. (2011)b	36	14.4	36.0	3.0	22.00	5			0.75	0.45	1.27
Farrell et al. (2010)	35	12.3	54.3	2.0	23.54	11.5	38.00	12.00	0.30	0.24	2.27
Farrell et al. (2016)	10	13.6	60.0	--	29.10	8	90.00		0.61	0.27	3.09
Lenhard et al. (2014)	21	14.4	38.1	3.9	21.33	12			0.58	-0.02	2.52
Martin &Thienemann (2005)	14	11.3	31.0	2.5	22.50	14	28.00	.00	0.36	0.39	0.99
Olino et al. (2011)	41	12.4	47.0	--	19.42	12.1	12.20	14.60	0.09	0.24	0.84
Ramos et al. (2005)	20	13.7	75.0	4.8	26.30	12	30.00	10.00	2.65	0.60	3.97
Reynolds et al. (2013)	25	14.4	--	--	24.32	14			0.41	0.67	2.17
Reynolds et al. (2013)	25	14.6	--	--	23.84	14			0.40	0.67	1.52
Saleminnk et al. (2015)	12	15.6	44.4	6.2	23.90	1.57			0.15	0.19	0.50
Söchting & Third (2011)	7	15.5	57.0	--	28.30	10	.00	14.30	-0.07	0.06	1.32
Storch, Bagner et al. (2007)	5	9.6	80.0	4.6	32.00	3	.00		0.65	0.60	4.45
Storch, Geffken et al. (2007)	18	14.5	50.0	--	25.38	14	37.03	14.80	0.32	0.69	2.07
Storch, Geffken et al. (2007)b	18	12.0	50.0	--	25.38	3	32.14	10.71	0.79	0.37	2.79
Storch, Murphy et al. (2006)	7	11.1	57.1	4.6	28.00	3	42.85	28.50	1.69	0.17	3.30
Storch et al. (2010)	30	13.4	50.0	--	26.93	3	40.00	26.70	0.50	0.65	3.06
Storch, et al. (2011)	16	11.10	61.0	--	25.38	12			0.41	0.19	4.03
Storch et al. (2013)	16	12.6	68.8	--	23.64	14			0.85	0.42	1.71
Thienemann et al. (2001)	18	15.2	66.7	4.9	24.80	14	22.20	16.70	0.42	0.28	1.09
Whiteside & Jacobsen (2010)	16	13.13	56.3	--	25.00	0.7			0.56	0.10	1.62
Williams et al. (2010)	10	13.6	61.9	--	23.09	12	50.00	4.54	1.33	1.62	2.57

N: sample size posttest. Age: mean age of the sample (in years). Gender: percentage of males. History: mean years suffering the OCD. Duration: treatment duration (in weeks). g´s Hedges: Effect size Hedges

It is worth note the reasons for focusing our attention on the CDI and the MASC to assess depression and anxiety symptoms. One of our purposes was to examine whether the beaseline levels of depression and anxiety symptoms were predictors of the CBT effectiveness by means of meta-regression models. Thus, the pretest means for depression and anxiety symtoms were extracted from the studies and this involved to obtain these means from the same measurement tools to make them comparable among studies. We decided to extract the means from the CDI and the MASC because these measurement scales were the most frequently used in the studies of the meta-analysis. A table with the study characteristics can be obtained from the corresponding author upon request.

The coding process was performed in a standardized and systematic way. With this purpose, a codebook and a protocol for registering the study characteristics was produced. To assess the reliability of the coding process, 20% of studies were randomly selected and subjected to a double coding process by two previously trained coders (Both documents can be obtained from the corresponding author upon request). Inconsistencies between the coders were resolved by consensus. Results showed very satisfactory inter-coder reliability, with kappa coefficients ranging from 0.85 to 1 for categorical variables, and intra-class correlations between 0.99 and 1 for continuous variables. A table with the study characteristics can be obtained from the corresponding author upon request.

Computation of effect sizes

As the main purpose of this meta-analysis was to search for correlates of the pretest-posttest change of OCD patients that received CBT, our analysis unit was defined as a CBT group with pretest and posttest measures. The effect size index was the standardized mean change index, defined as the difference between the pretest and the posttest means divided by the pretest standard deviation: $d = c\,(m)(\overline{Y}_{post} - \overline{Y}_{pre})/S_{pre}$, with c($m$) being a correction factor for small sample sizes (Morris, 2000). Positive values for d indicated a favorable change in the group from the pretest to the posttest, and vice versa.

Separate effect sizes (d indices) were calculated for obsessive-compulsive symptoms (assessed with CY-BOCS), as well as for anxiety and for depression symptoms. In 17 of the 26 studies, depression was assessed with the CDI, and 16 studies assessed anxiety with MASC scales. For reliability assessment of effect size calculations, the same random sample of studies used in the coding reliability study was subjected to a double process of effect size calculations, obtaining excellent inter-coder reliability, with intra-class correlations over 0.90. To assess the clinical significance of the average effect sizes, we used the results of a meta-review of 50 meta-analyses on the effectiveness of clinical psychology treatments (Rubio-Aparicio et al., 2018). In particular, d values around 0.64, 0.98, and 1.26 were interpreted as reflecting low, moderate, and large clinical relevance, respectively.

Data Analysis

Separate meta-analyses were carried out with the effect sizes for each outcome measure: for the CY-BOCS and depression and anxiety outcomes. Random-effects models were assumed in order to accommodate the variability exhibited by the effect sizes (Borenstein et al., 2009). To assess the heterogeneity of the effect sizes, the Q statistic and the I^2 index were calculated. I^2 indices around 25%, 50%, and 75% were interpreted as reflecting low, moderate, and large

heterogeneity, respectively (Higgins et al., 2003). For each outcome measure, a weighted mean effect size with its confidence interval was calculated. To assess publication bias on the CY-BOCS effect sizes, a funnel plot was constructed, the Egger test was calculated, and the trim-and-fill method for imputing missing effect sizes was applied (Rothstein et al.,2005). The influence of moderator variables on the effect sizes was carried out by assuming mixed-effects models. ANOVAs and meta-regressions were applied for categorical and continuous moderator variables, respectively (Borenstein et al., 2009). In place of the Q_B and Q_R tests, the improved *t*- and *F*-statistics developed by Knapp and Hartung (2003) were applied to assess the statistical association of each moderator with the CY-BOCS effect sizes. Q_W and Q_E statistics were computed to assess the model misspecification in ANOVAs and meta-regressions, respectively. In addition, an estimate of the proportion of variance accounted for by the moderator variable/s was calculated. Multiple meta-regressions were also applied to search for the subset of moderator variables exhibiting the largest statistical associations with the CY-BOCS effect sizes. Statistical analyses were carried out with the statistical program *Comprehensive Meta-analysis 3.3*, CMA 3.3 (Borenstein et al., 2014).

Results

Distribution of effect sizes and heterogeneity

Average effect sizes with 95% confidence intervals and heterogeneity statistics for the 26 CY-BOCS, anxiety and depression effect sizes are presented in Table 2. The average effect size for the CY-BOCS was of a very large magnitude and statistically significant (d_+ = 2.030). Depression and anxiety symptoms also exhibited statistically significant mean effect sizes, but of medium clinical relevance (d_+ = 0.451 and d_+ = 0.613, respectively). Forest plots for CY-BOCS effect sizes are presented in Figure 2. Figure 3 and 4 present forest plots for anxiety and depression. Effect sizes for the CY-BOCS exhibited large heterogeneity (I^2 = 83.23%). The heterogeneity found among the effect sizes justified the search for moderator variables that can be statistically associated with effect size variability.

Table 2.
CY-BOCS, Anxiety and Depression Effect Sizes.

Outcome variable	*k*	d_+	95% CI		*Q*	I^2
			LL	UL		
CY-BOCS	26	2.030	1.698	2.362	149.059***	83.23
Anxiety	26	0.613	0.453	0.774	93.993***	73.40
Depression	26	0.451	0.333	0.569	52.207**	52.11

d_+ = average standardized mean change. Hedges' g coincides with the d index reported in the text. LL and UL = lower and upper limits of the 95% confidence interval for d_+. *Q* = Cochran's heterogeneity *Q* statistic. I^2 = heterogeneity index. ** $p < .001$. *** $p < .0001$.

Publication bias

To assess publication bias as a threat against the average effect sizes for CY-BOCS, anxiety, and depression, funnel plots were constructed. Figure 5 presents these graphs. The trim-and-fill method imputed six additional effect sizes to symmetrize those of the CY-BOCS, so that the average effect size obtained with the 26 originals (d_+ = 2.030) reduced to d_+ = 1.494 (95%CI: 1.370 and 1.670). In addition, the Egger test reached statistical significance for the CY-BOCS effect sizes, $t(24) = 6.887$, $p < .001$.

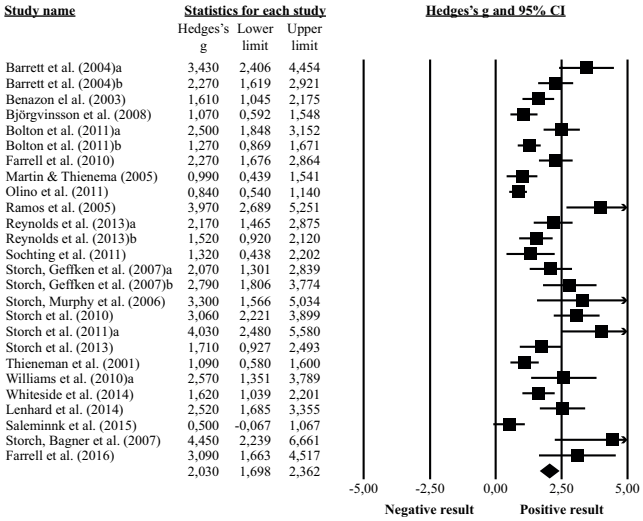

Figure 2.
Forest Plot Displaying the Standardized Mean Changes for the CY-BOCS. Hedges' g coincides with the d index reported in the text.

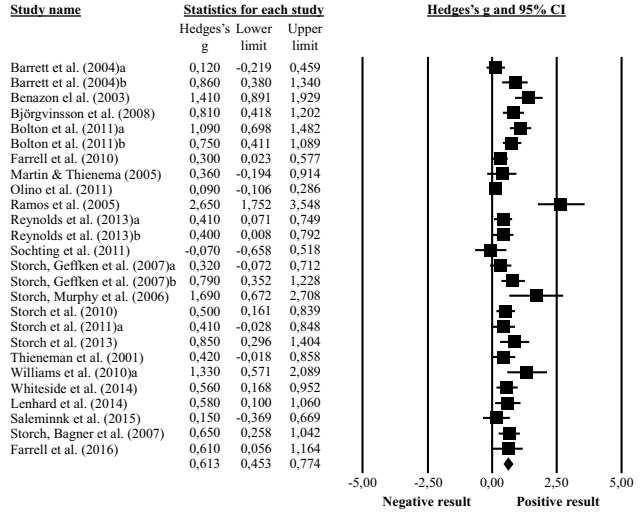

Figure 3.
Forest Plot Displaying the Standardized Mean Changes for Anxiety. Hedges' g coincides with the d index reported in the text.

Predictors/Moderators of the CY-BOCS effect sizes

A first step in the search for moderator variables statistically associated to the variability of the CY-BOCS effect sizes consisted of applying simple meta-regressions for each of the continuous moderator variable (i.e., CY-BOCS pretest mean, effect sizes for anxiety and depression symptoms, mean for depression in the pretest assessed with CDI, mean for anxiety in the pretest assessed with MASC, % anxiety and % depression in the sample, OCD history, treatment duration, magnitude, and intensity, mean age of the sample, gender (% male), and quality score), and ANOVAs for categorical moderators (i.e., parental involvement, treatment focus, mode of CBFT, and therapist´s training).

Tables 3 and 4 present the results of the simple meta-regressions and ANOVAs for the continuous and categorical moderators, respectively. Regarding simple meta-regressions, four of them revealed a statistically significant relationship with the CY-BOCS

effect sizes: the average CY-BOCS scores in the pretest (p = .016, R^2 = .19), the effect size for anxiety (p = .037, R^2 = .19), % anxiety (p = .041, R^2 = .40), and mean age (p = .037, R^2 = .11). In particular, larger CY-BOCS effect sizes were associated to large average CY-BOCS scores in the pretest, large effect sizes in anxiety, large anxiety comorbidity, and low mean age of the participants. Regarding categorical moderators (Table 4), none of them reached statistical significance.

One aim of this investigation was to examine the potential predictive value of the depression and anxiety levels in the pretest on the CY-BOCS effect sizes. Seventeen studies reported depression symptoms with the CDI and 16 studies reported anxiety symptoms with the MASC in the pretest. The mean for the CDI scores in the pretest ranged from 0.87 to 17.85 through the studies, with an average of 11.06. These figures indicated low depression symptoms, on average, in the pretest for OCD samples. In addition, the mean for the MASC scores in the pretest ranged between 36.98 and 86.60, with an average of 52.81, revealing a medium anxiety level. As shown in Table 3, the average CDI and MASC scores in pretest did not exhibit a statistically significant relationship with the CY-BOCS effect sizes.

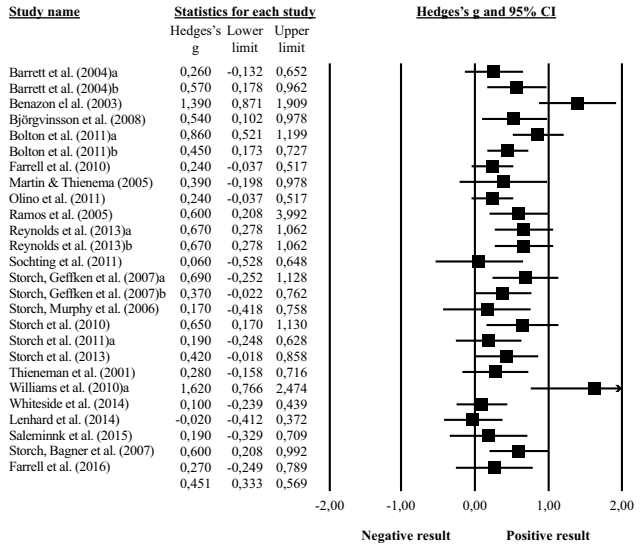

Figure 4.
Forest Plot Displaying the Standardized Mean Changes for Depression. Hedges' g coincides with the d index reported in the text.

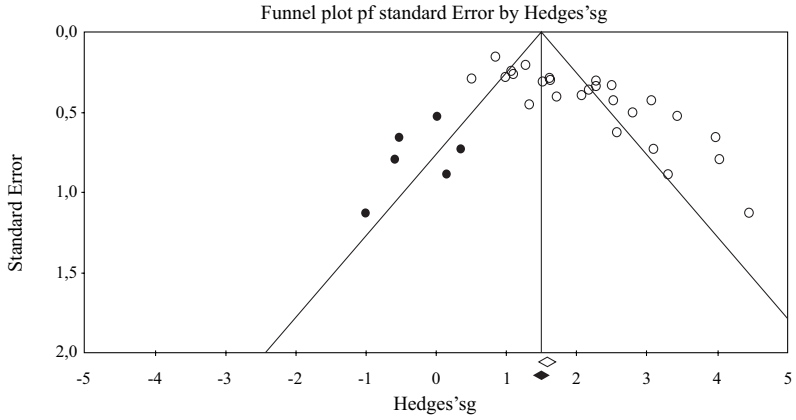

Figure 5.
Funnel Plot of the 26 Standardized Mean Changes for the CY-BOCS. Hedges' g coincides with the d index reported in the text.

Table 3.
Results of the Simple Meta-regressions Applied on the CY-BOCS Effect Sizes.

Moderator variable	*k*	*bj*	*t*	*p*	R^2
CY-BOCS pretest mean	26	0.187	2.60	.016	.19
Effect size for depression	26	0.255	0.47	.641	0.0
Effect size for anxiety	26	0.751	2.21	.037	.19
Mean depression in the pretest (CDI)	17	-0.061	-1.01	.327	0.0
Mean anxiety in the pretest (MASC)	16	-0.002	-0.09	.931	0.0
% anxiety	17	0.021	2.24	.041	.40
% depression	15	-0.070	-0.26	.802	0.0
Treatment duration	26	-0.007	-0.17	.865	0.0
Treatment intensity	21	-0.007	-0.10	.925	0.0
Treatment magnitude	21	-0.019	-0.50	.625	0.0
Mean age (years)	26	-0.266	-2.21	.037	.11
Sex (% male)	24	0.027	1.45	.162	.03
OCD history (years)	11	0.020	0.06	.949	0.0
Quality score	26	0.293	1.66	.109	.13

k = number of studies. bj = unstandardized regression coefficient of each predictor. *t* = Knapp-Hartung's t-statistic for testing the significance of the moderator variable. *p* = probability level for the *t* statistic. R^2 = proportion of variance accounted for by the moderator. *** $p < .0001$. Hedges' g coincides with the d index reported in the text.

Table 4.
Results of the ANOVAs for Categorical Variables

Moderator variable	*k*	d_+	95%C. I. d_l d_u	ANOVA results
Parental involvement:				F(2,23) = 1.93, p = .168 R2 = .16 QW(23) = 106.81, p < .001
Large	13	2.37	1.93 2.82	
Medium	10	1.58	1.12 2.03	
Low	3	1.97	1.29 2.64	
Treatment focus:				F(1,24) = .09, p = .772 R2 = .00 QW(24) = 149.05, p < .001
Children	10	1.967	1.55 2.38	
Family	16	2.130	1.55 2.71	
Mode of CBFT:				F(2,21) =2,65, p = .09 R2 = 0.21 QW(21) = 92.13, p < .001
Individual	14	2.38	1.98 2.78	
Group	5	1.80	1.00 2.59	
Mixed	5	1.38	0.72 2.04	
Therapist´s training:				F(1,22) = 1.63, p = .214 R2 = .07 QW(22) = 120.32, p = .002
Psychologist	20	2.19	1.82 2.57	
Psychology and psychiatrist	4	1.545	0.77 2.32	

K = number of studies. d_+ = mean effect size for each category. 95% C.I. = 95% confidence interval for d_+. d_l and d_u = lower and upper confidence limits around d_+. F = Knapp-Hartung's F statistic for testing the significance of the moderator. Q_W = statistics for testing the model misspecification. R^2 = proportion of variance explained by the moderator. CBFT = Cognitive Behavioral Family Therapy. Hedges' g coincides with the d index reported in the text.

Another purpose of this investigation was to examine whether CY-BOCS effect sizes were statistically associated to depression and anxiety effect sizes, all of them assessed as the standardized average pretest-posttest change. As shown in Table 3, only anxiety effect size reached a statistically significant relationship with the CY-BOCS effect sizes, with 19% of variance accounted for. In addition, we applied a multiple meta-regression model taking the effect sizes for anxiety and depression as moderator variables and the CY-BOCS effect sizes as the outcome. The results are presented in Table 5. As in the simple meta-regressions, only the anxiety effect size was statistically associated to the CY-BOCS effect sizes (p = .037), with depression effect sizes not showing a significant relationship (p = .537).

Table 5.
Multiple Meta-regression Applied on the CY-BOCS Effect Sizes Taking Anxiety and Depression Effect Sizes

Predictor variable	b_j	*t*	*p*	Model fit
Intercept	1.638	5.08	<.001	*F(2, 23) = 2.58, p = .097*
Effect size for depression	-0.358	-0.63	.537	R^2 = *.16*
Effect size for anxiety	0.873	2.21	.037	Q_E*(23) = 117.63, p < .0001*

b_j = unstandardized partial regression coefficient of each predictor. *t* = Knapp-Hartung's statistic for testing the significance of each predictor. *p* = probability level for the t statistic. *F* = Knapp-Hartung's statistic for testing the significance of the full model. R^2 = proportion of variance accounted for by the full model. Q_E = statistic for testing the model misspecification. Hedges' g coincides with the d index reported in the text.

An explanatory model for the CY-BOCS effect sizes

The above described meta-regressions revealed that only four moderator variables were statistically related with the CY-BOCS effect sizes: CY-BOCS scores in the pretest, the effect size for anxiety, % anxiety, and mean age of the sample. As % anxiety was reported in only 17 studies, this moderator was excluded from this multiple meta-regression, in order not to reduce the number of studies (k = 26). The results of a multiple meta-regression of the remaining three moderators are shown in Table 6. The full model reached statistical significance (p = .002), with a 48% of variance accounted for (R^2 = .48). In addition, the three moderators exhibited a statistically significant relationship with the CY-BOCS effect sizes, once the influence of the other moderators was controlled. Therefore, studies exhibited better CY-BOCS effect sizes as larger was the baseline CY-BOCS mean and for younger children. Additionally, large CY-BOCS effect sizes were assoiated to large anxiety effect sizes.

Table 6.
Results of the Multiple Meta-regression Model Applied on CY-BOCS Effect Sizes

Predictor variable	b_j	*t*	*p*	Model fit
Intercept	0.427	0.22	.828	*F(3,22) = 6.88, p = .002*
Effect size for anxiety	0.628	2.21	.038	R^2 = *.48*
CY-BOCS pretest mean	0.181	2.93	.008	Q_E*(22) = 79.60, p < .0001*
Mean age	-0.238	-2.42	.024	

b_j = unstandardized partial regression coefficient of each predictor. *t* = Knapp-Hartung's statistic for testing the significance of the predictor. *p* = probability level for the t statistic. *F* = Knapp-Hartung's statistic for testing the significance of the full model. R^2 = proportion of variance accounted for by the predictors. Q_E = statistic for testing the model misspecification.

Discussion

The aim of this research was to investigate whether anxiety and depression symptoms moderate the efficacy of CBT on pediatric OCD. A meta-analysis was conducted on 26 treatment groups. The effect size index was the standardized pretest-posttest mean change for obsession and compulsion symptoms, as well as for anxiety and depression. Consistent with our predictions, the effect size for the CY-BOCS was of very large magnitude (d_+ = 2.030). When the trim-and-fill method to assess the influence of publication bias was applied, a more conservative average effect size was found (d_{adj} = 1.494), although still statistically significant and of large magnitude following Rubio-Aparicio et al. (2018) guidelines. This finding is consistent with previous meta-analyses showing that CBT is highly effective in reducing OCD symptoms (Meyer et al., 2014; Rosa-Alcázar et al., 2015; Sánchez-Meca et al., 2014). Follow-up analysis of outcomes was not possible as only 16 studies reported follow-up data.

Our results showed that CBT also produced changes in secondary outcome measures, such as depression and anxiety, although to a lesser extent than CY-BOCS. The effect size for anxiety symptoms was greater than for depression (d_+ = 0.613 and d_+ = 0.451, respectively). The efficacy of CBT on anxiety when applied to pediatric OCD participants can be explained by the fact that CBT is also indicated for ameliorating fear and other anxiety symptoms present in anxiety disorders. Therefore, skills learned to cope with OCD by children and their parents can be generalized to manage other situations that generate anxiety (Wu & Storch, 2016).

Regarding depression, CBT also achieved statistically and clinically relevant benefits, but to a lesser extent than for anxiety and obsessive-compulsive symptoms. Several tentative explanations can be considered for this result. One is that depression is a consequence of OCD, severity of symptoms being low-to-

moderate. In fact, our results showed low severity for depression at baseline, so that large pretest-posttest reductions cannot be expected. In line with that found in some previous research, as depression is a product of OCD, improvements in obsessive-compulsive symptoms also lead to improvements in depression, but to a lesser degree (Anholt et al., 2011; Olatunji et al., 2013). In addition, clinical practice reveals that children and adolescents with OCD begin with obsessive-compulsive symptoms, and only when it grows in seriousness do large depression symptoms appear.

Another objective was to find potential predictors of the CY-BOCS effect sizes, such as the average CY-BOCS in the pretest, effect sizes for anxiety and depression symptoms, average depression in the pretest assessed with the CDI, average anxiety in the pretest assessed with the MASC, % anxiety and % depression in the sample,, OCD history, as well as sociodemographic (mean age, % male), treatment (duration, intensity, magnitude, mode, treatment focus, parent involvement), and methodological (quality score) variables.

Simple meta-regressions showed that four variables revealed a statistically significant relationship with the CY-BOCS effect sizes: the average CY-BOCS scores in the pretest, the effect size for anxiety, % anxiety and mean age.

The average CY-BOCS scores in the pretest were associated to larger CY-BOCS effect sizes, being a different result from that obtained in some studies (Højgaard et al., 2018; Torp et al., 2015). High pretreatment OCD severity predicts improvements in post-treatment. This suggests that children improve regardless of their initial severity in obsessions and impulses. Veale et al. (2016) found that both high and low pre-treatment severity predictive of a better outcome. Our results could be due to the existence of a mediating variable such as age, showing a negative correlation with the CY-BOCS in pretest and effect size CYBOSCS in posttest. Specifically, some studies with the largest effect size in pretest present a sample of young children (Storch et al., 2006; 2011; Storch, Bagner et al., 2007). However, this should be studied in greater detail.

These results support that improvements in anxiety are related to improvements in CY-BOCS. This leads us to affirm that CBT is also an effective procedure for ameliorating other anxiety symptoms, as other authors concluded (McGuire et al., 2015; Öst et al., 2016). CBT is a therapy used not only for OCD but also for anxiety disorders, thus capable of improving both disorders.

Depression symptoms at baseline did not predict the treatment efficacy in terms of obsessive-compulsive symptoms, coinciding with previous research (Farrell et al., 2012; Olatunji et al., 2013). Nevertheless, it is worth noting that the baseline levels of depressive symptoms were very low. Therefore, more research on this issue should investigate whether high levels of depression in OCD patients would hinder treatment improvement. In the same line, and coinciding with previous research, neither the presence of comorbidity nor the OCD history affected the CY-BOCS effect sizes (Ginsburg et al., 2008; Olatunji et al., 2013).

Another result was that older age were negative moderator of treatment outcome, agreement with previous studies (Ginsburg et al., 2008; Öst et al., 2016; Torp et al., 2015). This finding could be explained by various reasons such as that OCD symptoms in younger children would more easily modified since compulsions are mainly present, or there could be a greater involvement and motivation of parents and children in the treatment. This could lead us to highlight the importance of early detection and intervention of OCD.

The final objective consisted of proposing an explanatory model for the CY-BOCS effect sizes. Based on previous moderator analyses, a multiple meta-regression model was applied with three moderators: the average CY-BOCS score in the pretest, the effect size for anxiety, and the average age of the sample. The full model explained a large proportion of variance (R^2 = .48). The anxiety effect size revealed a positive relationship with the CY-BOCS effect size. In addition, the younger samples with larger average CY-BOCS scores in the pretest exhibited larger CY-BOCS effect sizes.Therefore, it seems that CBT offers better results for young OCD children and when the baseline of obsessive-compulsive symtomathology is large.

The current study has important implications for clinical practice with pediatric OCD patients. Firstly, the CBT reduced obsessive-compulsive symptoms and, to a lesser extent, anxiety and depression symptoms. In pediatric samples with low levels of depression, it is not necessary to add a specific treatment to reduce depressive symptoms, since the CBT could decrease them. On the other hand, as anxiety symptoms are reduced with the same therapy, resources would be saved regarding implementation and addition of other treatments.

Despite the important implications of our findings, this research is not without limitations. Firstly, we are aware that there are more studies assessing the effectiveness of CBT on pediatric OCD than those we included in our meta-analysis. However, one of our selection criteria was that the study had to report data on anxiety and depression measures necessarily, as one of our purposes was to investigate the correlates between obsessive-compulsive symptoms and depression and anxiety. Unfortunately, not all of the primary studies that assess the benefits of CBT for pediatric OCD reported depression and anxiety assessments. As a consequence, only 26 studies assessing the effects of CBT were included. In addition, although we initially wanted to analyze the influence of the mean scores for anxiety and depression in the pretest assessed with the MASC and the CDI on the CY-BOCS effect sizes, only 16 and 17 studies included in this meta-analysis reported this information, such that our findings regarding the predictive value of these variables on the CY-BOCS effect sizes must be interpreted cautiously. Secondly, primary studies reported limited information about important characteristics related to family accommodation (n = 8) or illness duration (n = 10) or type of obsessions/compulsions. Third, treatment effect on the anxiety and depression variables in follow-up could not be carried out as only 13 studies reported such measures at that point in time. Four, our results showed the existence of potential publication bias in the treatment effects of CY-BOCS and anxiety symptoms, leading to cautious interpretation of the results. In addition, the meta-regression models in meta-analysis cannot be employed to establish cause-effect relationships, but only statistical associations between the predictors and the effect sizes. Finally, a larger number of empirical studies that assess depression and anxiety symptoms with the same measurement tools would allow us to better generalize these results (Chacón et al., 2013). A more comprehensive reporting of the relevant variables in the primary studies would not only facilitate performing meta-analyses, but also the replication of empirical studies.

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