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ORIGINAL ARTICLE

Assessing Acute Secondary Treatment Outcomes in Early-Onset Obsessive–Compulsive Disorder

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Abstract

Obsessive–compulsive disorder (OCD) in children under 8 years of age, referred to as early-onset OCD, has similar features to OCD in older children, including moderate to severe symptoms, impairment, and significant comorbidity. Family-based cognitive behavioral therapy (FB-CBT) has been found efficacious in reducing OCD symptoms and functional impairment in children ages 5–8 years with OCD; however, its effectiveness on reducing comorbid psychiatric symptoms in this same population has yet to be demonstrated. This study examined the acute effects of FB-CBT vs. family-based relaxation treatment over 14 weeks on measures of secondary treatment outcomes (non-OCD) in children with early-onset OCD. Children in the FB-CBT condition showed significant improvements from pre- to post-treatment on secondary outcomes, with a decrease in overall behavioral and emotional problems, internalizing symptoms, as well as overall anxiety symptom severity. Neither condition yielded significant change in externalizing symptoms. Clinical implications of these findings are considered.

Keywords OCD · Early-onset · Comorbidity · CBT · Treatment

Introduction

Obsessive–Compulsive Disorder (OCD) is a heterogeneous, neurobiological condition that frequently emerges in childhood and continues through adulthood [1]. It has a lifetime estimated prevalence of 1–3% among children and adolescents [2–4] and is frequently associated with significant impairment within academic, familial, and social domains [5–7]. OCD is typically under-diagnosed [8]; however, records indicate that onset can occur in children as young as 3 years old [5, 9]. Most often, youth affected by OCD also have other psychiatric disorders including anxiety disorders, tic disorders, attention-deficit/hyperactivity disorder (ADHD), disruptive behavior disorders [oppositional defiant disorder (ODD) and conduct disorder (CD)], and depressive disorders [10–12]. In fact, because there is such a high rate of comorbidity reported in OCD samples, it is now seen as the norm for this disorder [10, 12–15].

OCD Comorbidity and Impairment

Prior studies of youth with OCD (often referred to as *juvenile-onset OCD*) report mean onset at approximately 10 years old, with high rates of psychiatric comorbidity, severe symptomatology, and functional impairment [12,

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14–16]. For example, Storch et al. [12] looked at comorbidity and symptom severity in children with OCD ages 7–18 years ($M = 12.85$; $SD = 2.63$) and found that 56% had a comorbid disorder. Study findings also revealed that youth with comorbid psychiatric disorders exhibited more severe OCD symptoms and worse psychotherapy outcomes than those without comorbid disorders. Moreover, in a cross-sectional study of 322 youth with OCD ages 7–17 years (M age = 12.28, $SD = 2.75$), the investigators found that 50% of the overall sample met criteria for an anxiety disorder, 12% for a depressive disorder, 16% for an externalizing disorder (i.e., ADHD, ODD, CD), 11% for a tic disorder, and 3% for autism spectrum disorder (ASD) [17], whereby the number of comorbid diagnoses ranged from zero to six ($M = 1.15$, $SD = 1.16$). However, when the same co-occurring diagnoses were divided across three age bands (children ages 7–9, pre-adolescents ages 10–13, and adolescents ages 14–17), the investigators found that the sample did not vary on the occurrence of anxiety disorders or externalizing disorders. Instead, it was found that the adolescent group showed greater depressive disorders (24 vs. 4% and 5%), both the adolescents and pre-adolescents groups indicated a higher prevalence of tic disorders (10 and 13% respectively vs. 6%), and the children group showed greater ASD (6 vs. 1% and 3%). Similarly, in a study of youth with OCD (ages 7–17) evaluated after 14 weekly sessions of exposure-based cognitive behavioral therapy (CBT), it was found that high rates of comorbidity compromised OCD treatment, thus signaling greater impairment and a need for treatment to target OCD while at the same time targeting other co-occurring symptomatology and disorders [18].

OCD in children under the age of 8 years, herein referred to as *early-onset OCD*, has been described as having many of the same characteristics of juvenile-onset OCD, including multiple comorbid psychiatric conditions and the further development of more severe psychopathology [19–21]. In a study of children with early-onset OCD (4–8 years; age of onset $M = 4.95$ years), symptom severity was observed to be between moderate to severe, with substantial comorbidity (about 55% meeting criteria for a disruptive behavior disorder, 30% for a tic disorder, 96% for an anxiety disorder, and 8% for a mood disorder) [20]. Despite the similarities to juvenile-onset OCD, this sample of early-onset OCD had lower rates of depression (around 8%, compared to juvenile-onset OCD ranging from 10 to 73%), though this may be an artifact of having been interviewed before typical age of onset of depression [12]. Furthermore, in a study of 31 preschool-aged children with OCD (ages 3–8 years; $M = 5.8$), sample characteristics included numerous comorbid diagnoses such as anxiety disorders (71%) and behavioral disturbance disorders (42%), but no reported depressive disorders. This information is, again, similar to juvenile OCD, with the exception of depressive disorders [22]. Lastly, in a study comparing young children with OCD ($n = 99$; 3–9 years; $M = 7.46$; $SD = 1.42$) to older youth with OCD ($n = 193$; 10–18 years; $M = 12.83$ $SD = 2.14$), it was found that overall OCD severity was similar between groups. However, in this sample, differences occurred in observed comorbidity, where the younger group of children showed higher rates of comorbid ADHD (29 vs. 16%), disruptive behavior (20 vs. 7%), and anxiety (50 vs. 44%) and the older group had a greater occurrence of depression (5% in younger group vs. 23% in the older group) [23].

Treatment for OCD

CBT with exposure and response prevention (EX/RP) is recognized as the treatment of choice for OCD in children and adolescents ages 8–17 years old [24, 25]. In a recent study, Freeman et al. [25] found evidence that in children with early-onset OCD, 14 weeks of family-based CBT with EX/RP (FB-CBT) was efficacious in reducing OCD symptoms and functional impairment when compared to 14 weeks of family-based relaxation treatment (FB-RT). Additionally, in a pilot study of children with early-onset OCD, investigators examined a 12-week OCD treatment of CBT vs. treatment as usual (e.g., psychotherapy, parent classes, social skills therapy, pharmacological) and witnessed favorable CBT group differences for primary outcomes of OCD symptoms and secondary outcomes of anxiety symptoms [22].

While no clinical trail, to our knowledge, has focused on the investigation of CBT with EX/RP for OCD with comorbidity in juvenile or early onset populations, clinical trials investigating the effects of CBT with EX/RP for juvenile OCD and secondary outcomes of comorbid conditions are well documented and may offer insight as to the reach of the treatment. For instance, Conelea et al. [26] found, in a clinical trail for juvenile OCD (children 7–17; POTS II [24]), improvements in acute secondary outcomes (non-OCD), regardless of the treatment condition. In this study, participants were randomized to medication management, medication management plus instructions in CBT, or medication management plus full CBT, and co-occurring symptom reductions were seen for anxiety, inattention, hyperactivity, and quality of life. In addition, findings showed symptom severity decreased more in the condition with full CBT, and that the child-rated depressive symptoms showed no change across conditions. Further, in a meta analysis of 18 studies [27] looking at the differential effects of treatment, CBT ($n = 11$; CBT and CBT with EX/RP); medication management ($n = 10$); and combined CBT and medication management ($n = 3$) vs. a control condition, on juvenile-onset OCD, ages 7–17, each treatment was found to be efficacious in reducing OCD symptoms and severity as well as secondary outcomes. In this meta analysis, secondary outcomes were identified as the analysis of moderating variables across

studies and showed improvements on depression and anxiety, particularly within CBT interventions.

Given the frequent documentation of OCD with comorbidity and increased symptom severity and impairment, the study of the broader effects of treatment in child early-onset OCD warrants attention. While CBT and CBT with EX/RP have been shown effective in reducing OCD symptoms and secondary outcomes in samples of juvenile-onset OCD, these findings cannot be extrapolated to younger samples of children ages 5–8 years with OCD due to developmental differences. FB-CBT has been demonstrated effective in reducing OCD symptoms and functional impairment in children ages 5–8 years with OCD; however, its effectiveness on reducing comorbid psychiatric symptoms and symptom severity in those same children is not well established.

Current Study

The current study aims to examine whether family-based CBT (FB-CBT) and family-based relaxation treatment (FB-RT) produce a differential outcome on measures of comorbid symptoms (non-OCD) in children 5–8 years old.

Methods

Participants

A sample of children ($N = 127$) ages 5–8 years ($M = 6.72$; $SD = 1.20$) was enrolled in the Pediatric OCD Treatment Study for Young Children (POTS Jr) from 2006 to 2011 [25, 28]. This study was a multi-site, parallel-group, randomized clinical trial testing the efficacy of family-based CBT with exposure and response prevention (FB-CBT) compared to family-based relaxation treatment (FB-RT). Participants were recruited from 3 academic sites: The University of Pennsylvania ($n = 44$; 34.6%), Duke University ($n = 35$; 27.6%), and Brown Medical School ($n = 48$; 37.8%). The Institutional Review Boards at each institution approved the study. Informed consent (parent) and assent (child) were obtained after eligibility was determined and prior to randomization to treatment. Of note, the IRB did not require written assent from children ages 8 and under. However, all children in the study were given the opportunity to provide written assent in order to be thorough, but not all participants "signed" the form. Study procedures, as well as potential risks, benefits, and treatment alternatives were clearly explained to both the parent and the child in a language understandable to each. No child was asked to participate if demonstrably unwilling, even if his or her parent wished it. Parents provided written informed consent and children provided written assent. A detailed description of study design considerations, measurement psychometrics, recruitment procedures, and adaptations designed to increase the developmental sensitivity of the assessment and treatment is available [25, 28].

For study eligibility, a three-gate assessment procedure was employed and typically completed in 3 weeks. Gate A included a brief description of the study and a preliminary telephone screening with a parent/guardian to assess patients' preliminary eligibility. At Gate B1 a study psychologist met in-person with the family and first obtained patient assent and parental consent. The study psychologist then assessed the patient's OCD symptoms, co-occurring symptoms, and eligibility to participate in the treatment (i.e., exclusionary and inclusionary criteria) utilizing parent self-report measures and therapist-administered questionnaires. Then, patients who were likely to be eligible to participate in the study from the information obtained at Gate B1, preceded to Gate B2, where the patient and his/her parents received a comprehensive diagnostic assessment administered by a study psychologist. Afterwards, the study team met to review all available data to establish caseness and suitability for study entry. Patients determined to be eligible, were invited back for Gate C1 with their parents. Gate C included randomization and a participant meeting for pre-treatment (week 0) assessments on child OCD symptoms and functioning. In total, of the 452 participants screened at Gate A, 127 (28%) were randomized into the study.

Participant inclusion criteria were: (1) a primary DSM-IV diagnosis of OCD, (2) a total Children's Yale-Brown Obsessive–Compulsive Scale (CY-BOCS) [29] score of 16 or greater, (3) 5–8 years of age, (4) had stable symptoms for 3 months or longer, (5) appropriate for outpatient treatment, and (6) at least one parent/guardian who could participate in the study. Exclusion criteria included: (1) other primary or co-primary psychiatric disorders requiring initiation of another active treatment, (2) pervasive developmental disorder(s), (3) intellectual disability, (4) thought disorder or psychosis, (5) conduct disorder, (6) acute suicidality, (7) concurrent psychotherapy, (8) chronic medical illness precluding active participation in treatment, (9) treatment with psychotropic medication for depression or mood stabilization, (10) treatment with medication of OCD, ADHD, &/or tic disorders that was not stable for more than 8 weeks, (11) prior failed trial of adequate CBT for OCD (defined as 10 sessions of formalized EX/RP), and (12) pediatric autoimmune disorders associated with strep (PANDAS).

Treatment

Participants were randomly assigned to 14 weeks FB-CBT or FB-RT. Randomization was determined using a computer-generated permuted blocking procedure, stratified by site, SSRI medication status, and presence of comorbid tics at pre-treatment. Treatment was twelve sessions delivered over

the 14 weeks for both treatment conditions. The first 2 sessions were parent-only sessions (with a duration of 90 min), and the remaining sessions (with a duration of 60 min each) were facilitated jointly with parents and children. The last 2 sessions were held over 4 weeks.

FB-CBT is EX/RP with components centered on providing the parent–child dyad with information to understand, manage, and reduce OCD symptomology. Primary treatment elements included (1) psychoeducation (OCD neurobiology, correction of OCD misattribution, identifying OCD behaviors, and rationale for treatment), (2) behavior management skills training for parents (behavioral management of child OCD symptoms, modeling, and scaffolding), (3) externalizing OCD and EX/RP training (active collaboration with the family by assisting in hierarchy development and implementing gradual exposure to triggers), and (4) family process components (more related to accommodation and parental distress).

FB-RT provided more general strategies focusing on lowering the child's anxiety. The primary components consisted of (1) psychoeducation (the relationship between stress management and anxiety, rationale for treatment, and the implementation of a reward system devoid of differential attention principles), (2) affective education (teaching the child how to identify their feeling states, with specific emphasis on anxiety), (3) relaxation training (instruction in progressive muscle relaxation and guided imagery).

Families with children on a stable SSRI medication regimen were seen by a child psychiatrist at each independent evaluator visit, but families did not transfer medication management to study physician. Adverse effects were closely monitored, with a special focus on suicidal ideation and/or behavior. An independent data and safety monitoring board provided regular, biannual trial oversight.

Treatment providers were clinical psychologists and clinical psychology trainees who had familiarity with CBT for anxiety. Therapists were trained in-person at study initiation and had extensive on-site and cross-site supervision in both treatment arms. Session adherence was rated on adherence to session-specific contents, and each had prescribed and proscribed targets that were rated from 1 (none/low adherence) to 3 (excellent adherence). Reliability was checked regularly on randomly selected video tapes and retraining occurred if they fell below 80% agreement. High adherence was indicated to both prescribed FB-CBT ($M = 2.86$; $SD = 0.09$) and FB-RT ($M = 2.94$; $SD = 0.07$) elements and proscribed FB-CBT ($M = 2.96$; $SD = 0.07$) and FB-RT ($M = 3.00$; $SD = 0.01$) elements.

Assessment

Independent Evaluators (IE) were doctoral-level psychologists and blind to the treatment conditions. All study IEs were trained to meet an initial reliability criteria of 0.80 (Cohen's K) and checked bi-weekly with randomly selected tapes. Assessment measures included the pre-treatment evaluation ratings and assessments by the IE assessing the participant at gate B, ratings by the IE assessing the participant at gate C, and self-and parent-report measures administered at gate C. IE evaluations were completed at weeks 0, 5, 9, and 14. For the current study, only select questionnaires from pre-treatment (gating procedures and week 0) to post-treatment (week 14) were included and discussed. All parent- and therapist-report measures were completed on scheduled visit days. Consistent with an intent-to-treat approach, all patients were assessed at each time point and included in the data analyses.

Measures

Demographics were measured using the *Conners March Developmental Questionnaire* (CMDQ) [30] and included age, grade level, gender, race, and socioeconomic status. This measure was completed by parents prior to treatment.

OCD symptoms and severity were measured using the *Child Yale-Brown Obsessive Compulsive Scale* (CY-BOCS) [29], a clinician interview incorporating child and parent report of child obsessions and compulsions with a total score (0–40, with scores > 23 indicating severe OCD). The CY-BOCS demonstrates adequate reliability and validity [29], and the literature supports the use of the measure in children as young as 6 years [31, 32]. The CY-BOCS was administered prior to treatment and at post-treatment by the IE and included child and parent report.

The *Clinical Global Improvement* scale (CGI) [33] is a 7-point scale measuring clinician-rated improvement in treatment. It has been used in multiple studies for children with OCD as young as 3 years old and shows adequate reliability and validity [20, 34, 35]. The CGI was completed prior to treatment and then again post treatment by the study clinicians.

Comorbidity was assessed using the *Kiddie Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version* (K-SADS-P/L) [36, 37]. K-SADS-P/L is a semi-structured, clinician rated interview that yields DSM-IV diagnoses and has favorable psychometric properties. Interviews were administered to the parent(s)/primary caretakers(s) regarding the child, and to children. The K-SADS is routinely used to assess psychiatric diagnoses in children as young as 5 years [38, 39]. The K-SADS-P/L was administered prior to treatment by a study psychologist.

The *Child Behavioral Checklist, Parent Report Form* (CBCL) [40] is a 118-item checklist that records responses using a Likert scale ranging from 0 = "Not True", 1 = "Somewhat or Sometimes True," 2 = "Very True or Often

True." The parent-rated scale assesses behavioral and emotional problems in children ages 6–18 years and has well-established psychometric properties. The *Child Behavior Checklist for Ages 1.5-5-Parent Report* form (CBCL/1(1/2)-5) [40] is a 100-item checklist utilizing the same Likert scale and used for children ages 1.5–5 years. Internal consistencies for both versions were strong ($\alpha = 0.93$ and $\alpha = 0.90$, respectively). The CBCL was completed by the parent prior to treatment and again at post-treatment.

The *Screen for Child Anxiety Related Emotional Disorders-Revised, Parent Version* (SCARED-R) [41] is a 66-item parent-reported scale of severity of anxiety symptoms in youth (ages 8–18 years old) using a 3-point scale from 0 = "Not True or Hardly Ever True" to 2 = "Very True or Often True" The measure has demonstrates good psychometric properties [41, 42]. Sample internal consistency was strong ($\alpha = 0.94$). The SCARED was completed by the parent prior to treatment and again at post-treatment.

Data Analysis

Preliminary analyses employing analysis of variance and crosstabs revealed no group differences. Descriptive statistics were used to summarize the sample characteristics. Continuous variables were summarized using means, standard deviations, medians, and ranges, and categorical variables were described with frequencies and percentages. Additionally, acute treatment effects from pre-treatment to 14 weeks were tested with Repeated Measures Analysis of Covariance (ANCOVA). In most instances, sample analyses are based on $N = 127$. In the event of missing data, n is the number of cases with data recorded.

Prior to analysis, missing outcome data on randomly assigned participants was replaced utilizing maximum likelihood, expectation–maximization algorithm [43]. A non-significant Little's MCAR test suggests that the data were missing completely at random [44]. Maximum likelihood imputation, using the expectation–maximization algorithm, was used to impute the missing data to improve statistical power with unbiased parameter estimates [45, 46]. Missing data were imputed using the Missing Values Analysis (normal distribution; 25 iterations) within SPSS 24.0.

Results

Recruitment and Retention

Study participants were recruited from (1) study site clinics, (2) schools, (3) primary care physicians, (4) mental health providers, and (5) paid and public service advertisements in local media. Out of the 127 randomly assigned subjects, 126 (99.2%) completed at least one post-baseline assessment.

The mean number of completed FB-CBT sessions was 11.2 and mean number of completed FB-RT sessions was 10.1 out of a possible 12 sessions for each condition. A total of 102 participants (80.3%) completed acute treatment, where post-randomization activity indicated that FB-RT participants were more likely to prematurely stop and receive out-of-protocol treatment. The original study CONSORT diagram is located in Freeman et al. [25].

Sample Characteristics

The POTS Jr demographic characteristics are outlined in Table 1 and reported on by total sample and by treatment condition. Children ranged in age from 5 to 8 with a mean age at pre-treatment of 7.22 ($SD = 1.12$). Nearly half of the sample was female (52.8%), and 95.3% of the sample described themselves as non-Hispanic and 4.7% Hispanic/Latino. Sample race was endorsed as 89.9% White, 2.4% Asian, 1.6% African American/Black, 3.1% multi-racial, and 3.1% were not endorsed/missing. The majority of participants had parents living together (90.2%) and over 80% making greater than $60,000 (annual family income). Many parents reported a college degree or higher (70.9% of fathers, 78.3% of mothers). All participants met criteria for a primary diagnosis of OCD. The CYBOCS mean total score was 25.55 ($SD = 4.23$), indicating severe OCD symptoms, and average age of onset of OCD symptoms was 5.06 ($SD = 1.65$, range 2–8). Similarly, the clinicians' rating of illness severity on the CGI scale was in the moderately to markedly severe range (i.e., ratings of 4–5) identifying overall illness severity ($M = 4.69$; $SD = 0.82$, range 0–7).

Out of the 127 children identified at pre-treatment with a primary diagnosis of OCD, 59.1% met clinical criteria for OCD with comorbidity per the KSADS. Anxiety disorders where the most observed comorbid diagnoses (47%), followed by disruptive behavioral disorders (24%), and the least observed comorbidity was depressive disorders (2%). Furthermore, there were 31 (24.4%) children with OCD and one additional diagnosis, 22 (17.3%) met criteria for two additional diagnoses, 13 (10.2%) met criteria for three additional diagnoses, three (2.4%) met criteria for four additional diagnoses, and one (0.8%) child met criteria for six additional diagnoses. See Table 2 for a complete list of pre-treatment comorbid diagnoses.

Acute Comparison Between Treatments on Secondary Outcomes

Comorbid Psychiatric Symptoms

The 14-week FB-CBT demonstrated better outcomes compared to the 14-week FB-RT in reducing acute secondary outcomes (non-OCD) in young children with early-onset

Table 1 Pre-treatment sample characteristics

Demographics	Total N	FB-CBT (n = 63)	FB-RT (n = 64)	N (%)/mean (*SD*)
Study site, No. (%)	127			
Brown University		23 (36.5)	25 (39.1)	48 (37.8)
Duke University Medical Center		18 (28.6)	17 (26.6)	35 (27.6)
University of Pennsylvania		22 (34.9)	22 (34.4)	44 (34.6)
Age, years, mean (*SD*)	127	7.4 (1.2)	7.0 (1.2)	7.2 (1.2)
Child's gender	127			
Female, No. (%)		39(61.9)	28 (43.8)	67 (52.8)
Child's ethnicity, No. (%)	127			
Not Hispanic/Latino		60 (95.2)	61 (95.3)	121 (95.3)
Hispanic/Latino		3 (4.8)	3 (4.7)	6 (4.7)
Child's race, No. (%)	127			
White		59 (93.7)	55 (85.9)	114 (89.8)
Black/African American		1 (1.6)	1 (1.6)	2 (1.6)
Asian		0 (0.0)	3 (4.7)	3 (2.4)
Multiple races		1 (1.6)	3 (4.7)	4 (3.1)
Not reported		2 (3.2)	2 (3.1)	4 (3.1)
Annual family income, range, No. (%)	116			
$30,000 and under		3 (5.2)	4 (6.9)	7 (6.0)
$30,000–60,000		5 (8.6)	9 (15.5)	14 (12.1)
$60,000–90,000		18 (31)	23 (39.7)	41 (35.3)
Over $100,000		32 (55.2)	22 (37.9)	54 (46.6)
OCD severity				
Clinician ratings, mean (*SD*)				
CY-BOCS total score	127	25.13 (4.46)	25.97 (3.98)	25.55 (4.23)
CGI	126	4.71 (0.89)	4.67 (0.76)	4.69 (0.82)
Parent on child/family, mean (*SD*)				
SCARED-R total score	127	38.24 (18.75)	40.28 (16.53)	39.27 (17.62)
CBCL total score (> 6)	108	61.57 (8.29)	62.48 (8.09)	62.01 (8.17)
CBCL total score (≤ 6)	19	61.71 (8.62)	57.17 (7.49)	58.84 (8.01)
Observed participants, No. (%)				
Baseline		63 (100.0)	64 (100.0)	127 (100.0)
Week 14		59 (93.7)	57 (89.1)	116 (91.3)

OCD on both parent report symptom measures: The CBCL (≥ 6 yo. version) and the SCARED-R. FB-CBT frequently showed clinical range (T Score ≥ 64) to sub-clinical range (T Score < 60) improvements on the CBCL (≥ 6 yo. version), where FB-RT showed modest non-significant improvements. For instance, on the CBCL (≥ 6 yo. version) total score, FB-CBT showed significantly fewer emotional and behavioral problems, F (1, 107) = 4.52, $p = 0.036$, from pre-treatment to post-treatment than FB-RT. For the CBCL (≥ 6 yo. version) Internalizing subscale, FB-CBT showed significantly fewer internalizing problems (e.g., withdrawn, somatic and anxious/depressed behavior), F (1, 107) = 12.24, $p = 0.001$, at pre-treatment to post-treatment than FB-RT. See Table 3 for means and standard deviations.

Because externalizing comorbidity made up 25% of the sample, the CBCL was examined on the total sample as well as on the subset of externalizing KSADS diagnosed comorbidities (ODD and ADD). Results revealed neither the intervention nor the control group demonstrated a significant change; however, externalizing symptoms at pre-treatment assessment for both conditions were in a sub-clinical range (See Table 3).

Parent report on the SCARED-R also revealed a shift from a clinical range to a sub-clinical range on FB-CBT vs. FB-RT [42], as seen in Table 3. For instance, on the SCARED-R total score, the FB-CBT demonstrated significantly less symptoms, F (1, 126) = 8.87, $p = 0.003$, at pre-treatment to post-treatment than FB-RT. Similarly, many of the SCARED-R subscales showed significantly fewer symptoms from pre-treatment to post-treatment on FB-CBT vs. FB-RT. This was seen on the Generalized Anxiety Disorder subscale, F (1, 126) = 12.09, $p = 0.001$, the Social Phobia

Table 2 Pre-treatment OCD Comorbidities from the KSADS

Comorbidities, No. (%)	FB-CBT (n = 63)	FB-RT (n = 64)	N (%)
Any	40 (63.5)	35 (54.7)	75 (59.1)
Anxiety	30 (47.6)	29 (45.3)	59 (46.5)
Separation anxiety	8 (12.7)	8 (12.5)	16 (12.6)
Specific phobia	16 (25.4)	11 (17.2)	27 (21.2)
Social phobia	4 (6.3)	10 (15.6)	14 (11.0)
Generalized anxiety disorder	12 (19.0)	13 (20.3)	25 (19.7)
Mood	1 (1.6)	1 (1.6)	2 (1.6)
Dysthymia	0 (0.0)	1 (1.6)	1 (0.8)
Depressive disorder NOS	1 (1.6)	0 (0.0)	1 (0.8)
Externalizing	18 (28.6)	13 (20.3)	31 (24.4)
ADHD (any type)	8 (12.7)	10 (15.6)	18 (14.2)
Oppositional defiant disorder	12 (19.0)	6 (9.4)	18 (14.2)
Elimination disorder	2 (3.2)	5 (7.8)	7 (5.5)
Enuresis	2 (3.2)	5 (7.8)	7 (5.5)
Encopresis	0 (0.0)	1 (1.6)	1 (0.8)

subscale, F (1, 126) = 4.14, p = 0.044, and the Separation Disorder subscale, F (1, 126) = 4.64, p = 0.033.

Clinician Report of Illness Severity

Clinicians' report of illness severity on the CGI showed a significant decrease from pre- to post-treatment in FB-CBT treatment condition vs. the FB-RT treatment condition, F (1, 113) = 16.66, p = 0.000 (see Table 4). In the FB-CBT condition, the CGI rating went from a mean of 4.71 (moderate to markedly ill) pre-treatment to a post-treatment CGI mean of 2.61 (borderline to mildly ill).

In an examination of the entire sample separately at pretreatment and post-treatment clinicians' rating of illness severity on the CGI by a dichotomous variable of "no comorbidity" (OCD diagnosis only) and "yes comorbidity" (OCD plus comorbid diagnoses), no significant associations were observed at pre-treatment, χ^2 (15, 126) = 10.38, p = 0.795, or post-treatment, χ^2 (25, 114) = 34.56, p = 0.097. See Table 5 for results. The post-treatment findings did, however, show improvements on

Table 3 CBCL and SCARED means and standard deviations

	Baseline		14 Weeks		Mean differences		*F*
	Mean (*SD*)	*Mean* (*SD*)	*Mean* (*SD*)	*Mean* (*SD*)	FB-CBT	FB-RT	
CBCL-R (> 6), N = 108	FB-CBT n = 56	FB-RT n = 52	FB-CBT n = 56	FB-RT n = 52			
Total score	61.57 (8.29)	62.48 (8.09)	**52.70** (9.06)	55.99 (6.74)	8.87	6.49	4.52*
Internalizing	64.17 (9.63)	64.67 (8.75)	**53.70** (8.77)	59.38 (8.06)	10.47	5.29	12.24**
Externalizing	56.48 (9.83)	57.98 (9.82)	**51.10** (10.08)	52.80 (7.44)	5.38	5.18	0.99
CBCL-R (≤ 6), N = 19	FB-CBT n = 7	FB-RT n = 12	FB-CBT n = 7	FB-RT n = 12			
Total score	61.71 (8.62)	57.17 (7.49)	**57.34** (11.77)	57.40 (8.43)	4.37	−0.23	0.00
Internalizing	64.71 (6.95)	62.17 (7.31)	**55.83** (11.27)	60.55 (8.34)	8.88	1.62	1.10
Externalizing	57.47 (13.39)	50.42 (9.17)	**57.05** (9.90)	52.81 (8.66)	0.42	−2.39	0.96
SCARED, N = 127	FB-CBT n = 63	FB-RT n = 64	FB-CBT n = 63	FB-RT n = 64			
Total score	38.24 (18.75)	40.28 (16.53)	**24.69** (12.78)	32.02 (14.84)	13.55	8.26	8.87**
Separation disorder	5.92 (3.68)	6.45 (2.89)	**3.97** (2.56)	5.11 (3.32)	1.95	1.34	4.64*
GAD	8.07 (4.32)	8.88 (4.61)	**4.92** (3.00)	6.88 (3.34)	3.15	2.00	12.09**
Social anxiety	3.30 (2.21)	3.75 (2.25)	**2.58** (1.87)	3.25 (1.87)	0.72	0.50	4.14*
Panic disorder	3.48 (3.14)	3.22 (2.89)	**2.12** (2.01)	2.93 (2.65)	1.36	0.29	3.69

Bolded items = greatest mean differences

*p < 0.05; **p < 0.01; ***p < 0.001

Table 4 CGI severity by treatment condition

	CGI pre-treatment		CGI post-treatment	
	FB-CBT = 62	FB-RT = 64	FB-CBT = 59	FB-RT
M (*SD*)	4.71 (0.89)	4.67 (0.76)	2.61 (1.33)	3.64 (1.35)
Normal, No. (%)	0	0	17 (27.0%)	5 (7.8%)
Borderline, No. (%)	0	0	10 (15.9%)	7 (10.9%)
Mild, No. (%)	5 (7.9%)	1 (1.6%)	16 (25.4%)	9 (14.1%)
Moderately, No. (%)	21 (33.3%)	29 (45.3%)	12 (19.0%)	19 (29.7%)
Markedly, No. (%)	23 (36.5%)	24 (37.5%)	3 (4.8%)	12 (18.8%)
Severely, No. (%)	13 (20.6%)	10 (15.6%)	1 (1.6%)	3 (4.7%)
Missing	1	0	4	9

Table 5 Number of comorbidies and clinician rating of clinical severity

	CGI pre-treatment (e.g., consider clinical experience with patient, how mentally ill is patient at this time?)						
	1 Normal	2 Borderline	3 Mildly	4 Moderately	5 Markedly	6 Severely	Total
No comorbidity	0	0	2	19	16	9	46
Yes comorbidity	0	0	4	31	31	14	80
Total	0	0	6	50	47	23	126
	CGI post-treatment (e.g., consider clinical experience with patient, how mentally ill is patient at this time?)						
	1 Normal	2 Borderline	3 Mildly	4 Moderately	5 Markedly	6 Severely	Total
No comorbidity	13	10	11	10	6	2	52
Yes comorbidity	9	7	14	21	9	2	62
Total	22	17	25	31	15	4	114

$N = 127$; Chi-Square findings were not significant pre-treatment ($n = 126$) or post-treatment ($n = 114$)

the clinician rating of the CGI by both the OCD only diagnosis and the OCD diagnosis plus comorbidity.

Discussion

The current investigation adds to the literature, as it examined family-based CBT vs. family-based relaxation therapy on secondary outcomes of non-OCD symptoms among children with early-onset OCD (ages 5–8 years). These findings show that FB-CBT significantly reduced symptoms of comorbid anxiety on the SCARED-R and internalizing on the CBCL (≥ 6 yo. version) than FB-RT condition. That is, FB-CBT was significantly more effective in lowering acute comorbid internalizing symptoms (non-OCD) in early-onset OCD from a clinical range to a sub-clinical range, whereas FB-RT did not. Interestingly, the CBCL did not show significant differences on externalizing symptoms from pre- to post-treatment in either condition.

Comorbid Psychiatric Symptoms

This sample of children with early-onset OCD exhibited high rates of comorbidity, with more than half of the sample affected by at least one other comorbid diagnosis and some meeting diagnostic criteria for up to six comorbid diagnoses. Additionally, comorbid internalizing disorders were identified as more common (71.7%) than comorbid externalizing disorders (22.0%). Despite their young age, the rates of comorbidity (e.g., anxiety disorders and disruptive behavioral disorders) were similar to those seen documented in the literature in older children with OCD (e.g., [12, 16, 47]), with the exception of depressive disorders. This type of presentation is observed in other samples of early-onset OCD (e.g., [23, 48]) and consistent with general developmental trends [49] and the literature on juvenile-onset OCD, where age of onset of comorbid depressive disorders often occurs in older children [14]. Alternatively, the higher prevalence of depressive symptoms could be due in part to a delay in the identification and/or treatment of OCD in adolescent samples [8], and thus the experience of greater symptomatology and

functional impairment causing an increase in depressive symptoms.

Clinical Severity

The clinician rating of OCD illness severity on the CGI showed significantly greater improvements in FB-CBT condition compared to FB-RT condition, whereby illness severity declined from pre-treatment to post-treatment. However, we do not know if the clinicians' rating was reduced due to a decrease in OCD symptoms and/or impairment, a decrease in comorbidity symptoms and/or impairment, or both. Surprisingly, a significant association was not observed pre-treatment or post-treatment on the clinician rated CGI when comparing children with OCD alone vs. children with OCD and comorbid psychiatric diagnoses.

Treatment for OCD Comorbidity

This study has identified downstream effects of FB-CBT on secondary acute treatment outcomes (non-OCD symptoms) among children with early-onset OCD, particularly for internalizing comorbidity. This finding is similar to what Lewin et al. [22] found in their treatment study of children with early-onset OCD and secondary outcomes of anxiety symptoms, as well as studies on secondary outcomes among samples of juvenile-onset OCD [26, 27]. It is possible that the underlying processes and mechanisms of CBT EX/RP treatment in particular, and, in early-onset OCD, FB-CBT specifically, extend beyond the primary target of OCD to secondary acute outcomes, particularly when the comorbid symptoms are internalizing symptoms. This is important given the high rate of psychiatric comorbidity identified in the early-onset OCD population and suggests that FB-CBT has the potential to target together both primary OCD and secondary psychiatric conditions. Towards this end, identifying the underlying processes and mechanisms of FB-CBT would help guide treatment and further investigation.

Exposure and response prevention is considered the main "active" ingredient and primary mechanism in CBT for OCD as well as in CBT for other anxiety disorders [50]. The focus on EX/RP practice in FB-CBT condition may have therefore led parents and children to generalize the strategies being learned in the context of OCD and apply them to other anxiety symptoms. The more general anxiety reduction strategies provided in FB-RT, perhaps because of the absence of exposure practice, did not have the same effect on comorbid anxiety.

The processes (possible mediators) of FB-CBT are also important to mention, as they assist in the delivery of the "active ingredient" of treatment. The processes of FB-CBT include all of the components of treatment that were tailored for children in this age range, including the aforementioned developmental, cognitive, and socioemotional characteristics, as well as parental participation. Parental participation during treatment is particularly important, as parents were instructed on the effects of accommodation as well as the acknowledgment of their ability to tolerate distress. The comparison condition, FB-RT, incorporated similar components of treatment (i.e., parents' expertise in coaching stress management, parent and child affective education, and relaxation training); however, these components did not bolster the active ingredient when compared to FB-CBT.

When considering the significant effects that were seen in the FB-CBT condition vs. the FB-RT condition on reduced anxiety and internalizing symptom, it is important to note that significant change was not observed on externalizing symptoms and problems for either condition, even with the parent-training component. This is of interest since externalizing disorders (i.e., ADHD and ODD) made up the second largest comorbid group (almost 25%) in this early-onset OCD sample [51]. A decrease in statistical means from pre- to post-treatment, however, was seen in each condition on externalizing symptoms and problems (see Table 3 for Means and SD). Interestingly, CBCL means at pre-treatment for externalizing disorders did not meet clinically relevant levels (T Score ≥ 64) for either conditions, FB-CBT: $M = 57.47$; $SD = 13.39$ and FB-RT: $M = 50.42$; $SD = 9.17$. This lack of generalization may be due to the attention given to behavioral parent training within the context of internalizing symptoms (e.g., praise and rewards for participating in exposure, removal of attention when protesting participating in exposure practice), instead of a broader focus on other elements of parent training within the context of externalizing symptomatology (e.g., rewards for overall behavior, modeling, and attention). While research documents the relation between OCD and anxiety disorders [12], there is no indication whether OCD and externalizing symptoms would be reduced utilizing EX/RP (FB-CBT), particularly what processes (possible mediators) would extend the treatment to externalizing outcomes.

There are several limitations to the current study, which must be taken into consideration when interpreting the results. First, these data were collected as part of a larger study and were not obtained to answer the proposed questions in the current study. As such, this study was not tailored to directly reduce comorbid psychiatric conditions among early-onset OCD populations nor designed to measure post-treatment outcomes on all identified pre-treatment comorbidities.

Secondly, study findings would be stronger if another measure assessing psychiatric diagnoses (e.g., KSADS) was employed at the end of acute treatment thus providing a paired sampling of comorbid diagnoses for each child. However, the measures used to assess acute outcomes on comorbid symptoms are reliable and valid and provide

useful information on the matrix of symptoms documented as frequently co-occurring in OCD samples. Moreover, the limits of categorical as opposed to continuous measures of psychopathology have been described and chronicled elsewhere [e.g. NIHM Research Domain Criteria (RDoC)].

A third limitation is the exclusion of previously diagnosed psychiatric diagnoses (e.g., other primary or co-primary psychiatric disorders, thought disorder or psychosis, conduct disorder, concurrent psychotherapy) that were considered "exclusionary criteria" for the parent study and, as a result, limited the findings for the current study. However, even with the detailed list of exclusionary diagnoses, the sample population showed considerable undiagnosed comorbidity at pre-treatment. Moreover, the question of interest here had to do with whether treatment for primary OCD would have secondary effects on comorbid symptoms, and thus the sampling frame was appropriate to address this specific question even if it limited our capacity to comment on these effects in a more diagnostically diverse sample.

Finally, despite guided efforts on enrollment strategies, the recruitment of diverse socioeconomic and racial and ethnic minority families and youth in this study was limited, similar to that of the broader OCD literature. This is a significant study weakness and leaves findings non-generalizable to the greater population, including the broad range of ethnic and racial groups [52].

Although research on the treatment of children with early-onset OCD is itself limited, even less is known about the effects of OCD treatment on comorbid psychiatric conditions that have been commonly identified in this population. Further investigation is necessary to both explore the direct effect of FB-CBT on comorbid proximal and distal outcomes, as well as explore symptom presentation with a dimensional focus. This may encourage the modification of current treatments to encompass both OCD and presenting comorbidities, thus acknowledging underlying mechanisms and processes and utilizing a dimensional approach to assessment and treatment. This may also introduce new research better aimed at understanding the underlying mechanisms and/or processes of OCD treatment and its comorbidities and encompassing elements that extend EX/RP not only to internalizing symptoms but to externalizing symptoms, as well.

Summary

This study investigated the differential effects of FB-CBT vs. FB-RT on acute secondary outcomes of non-OCD symptoms in a sample of children with early-onset OCD. Our findings suggest that FB-CBT significantly reduced symptoms of comorbid anxiety on the SCARED-R and internalizing symptoms on the CBCL (≥ 6 yo. version) more than the FB-RT condition. Given the association between OCD, anxiety disorders, and internalizing symptoms, the use of EX/RP in FB-CBT may have generalized to non-OCD anxiety symptoms. No significant effects were seen on the CBCL's (≥ 6 yo. version) externalizing subscale. These limited findings may be due in part to the pre-treatment CBCL's sub-clinical level of externalizing symptoms recorded for both conditions in this sample (and exclusionary criteria), thus not signaling the same degree of symptoms and clinician and parent focus as the CBCL's (≥ 6 yo. version) internalizing subscale. It also may be that behavioral parent training taught in the context of OCD symptoms, does not generalize to non-OCD behavioral issues. Significant differences were seen on the CGI from pre- to post-treatment, where symptom severity in the FB-CBT condition showed greater reductions than in the FB-RT condition; however, this may due to a change in OCD severity alone, OCD comorbid symptom severity, or both. There were no observed significant effects on the CGI from pre- to post-treatment when comparing OCD alone vs. OCD with comorbidities. Study findings, while taken from a longitudinal design, warrant further investigation directly on the treatment of OCD comorbidity in children with early-onset OCD, including a focus on mechanisms and processes of OCD treatment with a consideration of symptoms in a dimensional approach.

References

1. Walitza S, Wendland J, Gruenblatt E, Warnke A, Sontag T, Tucha O et al (2010) Genetics of early-onset obsessive–compulsive disorder. Eur Child Adolesc Psychiatry 19(3):227–235
2. Aptera A, Fallon T, King R, Ratzoni G, Zohar A, Binder M et al (1996) Obsessive–compulsive characteristics: from symptoms to syndrome. J Am Acad Child Adolesc Psychiatry 35(7):907–912
3. Rapoport J, Inoff-Germain G, Weissman M, Greenwald S, Narrow W, Jensen P et al (2000) Childhood obsessive–compulsive disorder in the NIMH MECA Study: Parent versus child identification of cases. J Anxiety Disord 14(6):535–548
4. Thomsen PH (2013) Obsessive–compulsive disorders. Eur Child Adolesc Psychiatry 22(1):23–28
5. Hollingsworth C, Tanguay P, Grossman L, Pabst P (1980) Long-term outcome of obsessive–compulsive disorder in childhood. J Am Acad Child Adolesc Psychiatry 19:134–144
6. Piacentini J, Peris TS, Bergman RL, Chang S, Jaffer M (2007) Functional impairment in childhood OCD: development and psychometrics properties of the child Obsessive–compulsive impact Scale–Revised (COIS-R). J Clin Child Adolesc Psychol 36:645–653
7. Steketee G (1997) Disability and family burden in obsessive compulsive disorder. Can J Psychiatry 42(9):919–928
8. The American Academy of Child and Adolescent Psychiatry (2012) Practice parameters for the assessment and treatment of children and adolescents with obsessive. J Am Acad Child Adolesc Psychiatry 51(1):98–113

9. Koran L (1999) Obsessive–compulsive and related disorders in adults: a comprehensive clinical guide. Cambridge University Press, Cambridge
10. Cederlof M, Lichtenstein P, Larsson H, Boman M, Rück C, Landén M et al (2015) Obsessive–compulsive disorder, psychosis, and bipolarity: a longitudinal cohort and multigenerational family study. Schizophr Bull 41(5):1076–1083
11. de Mathis MA, Diniz J, Hounie A, Shavitt R, Fossaluza V, Ferrao Y et al (2013) Trajectory in obsessive–compulsive disorder comorbidities. Eur Neuropsychopharmacol 23(7):594–601
12. Storch EA, Merlo LJ, Larson MJ, Geffken GR, Lehmkuhl HD, Jacob ML et al (2008) Impact of comorbidity on cognitive behavioral therapy response in pediatric obsessive–compulsive disorder. J Am Acad Child Adolesc Psychiatry 47:583–590
13. Farrell L, Waters A, Milliner E, Ollendick T (2012) Comorbidity and treatment response in pediatric obsessive–compulsive disorder: a pilot study of group cognitive-behavioral treatment. Psychiatry Res 199:115–123
14. Geller D, Bilderman J, Griffin S, Jones J, Lefkowitz T (1996) Comorbidity of Juvenile obsessive–compulsive disorder with disruptive behavior disorders. J Am Acad Child Adolesc Psychiatry 35:1637–1646
15. Swedo SE, Rapoport JL, Leonard H, Lenane M, Cheslow D (1989) Obsessive compulsive disorder in children and adolescent: clinical phenomenology of 70 consecutive cases. Arch Gen Psychiatry 46:335–341
16. Masi G, Millepiedi S, Mucci M, Bertini N, Pfanner C, Arcangeli F (2006) Comorbidity of obsessive–compulsive disorder and attention-deficit/hyperactivity disorder in referred children and adolescents. Compr Psychiatry 47(1):42–47
17. Peris T, Rozenman M, Bergman L, Chang S, O'Neill J, Piacentinin J (2017) Developmental and clinical predictors of comorbidity for youth with obsessive compulsive disorder. J Psychiatr Res 93:72–78
18. Torp N, Dahl K, Skarphedinsson G, Compton S, Thomsen P, Weidle B et al (2015) Predictors associated with improved cognitive-behavioral therapy outcome in pediatric obsessive–compulsive disorder. J Am Acad Child Adolesc Psychiatry 54(3):200–207
19. de Mathis M, Diniz J, Shavitt R, Torres A, Ferrao Y, Ferrao Y et al (2009) Early onset obsessive–compulsive disorder with and without tics. CNS Spectr 14(7):362–370
20. Garcia AM, Freeman JB, Himle MB, Berman N, Ogata A, Ng J et al (2009) Phenomenology of early childhood onset obsessive compulsive disorder. J Psychopathol Behav Assess 31(2):104–111
21. Hemmings S, Kinnear C, Lochner C, Niehaus D, Knowles J, Moolman-Smook J et al (2004) Early-versus late-onset obsessive–compulsive disorder: Investigating genetic and clinical correlates. Psychiatry Res 128:175–182
22. Lewin AB, Park J, Jones A, Crawford E, De Nadai A, Menzel J et al (2014) Family-based exposure and response prevention therapy for preschool-aged children with obsessive–compulsive disorder: a pilot randomized controlled trial. Behav Res Ther 30:30–38
23. Selles R, Storch E, Lewin A (2014) Variations in symptom prevalence and clinical correlates in younger versus older youth with obsessive–compulsive disorder. Child Psychiatry Hum Dev 45(6):666–674
24. Franklin M, Sapyta J, Freeman J, Khanna M, Compton S, Almirall D et al (2011) Cognitive behavioral therapy augmentation of pharmacotherapy in pediatric obsessive–compulsive disorder: the Pediatric OCD Treatment Study II (POTS II) randomized controlled trial. JAMA Psychiatry 306(11):1224–1232
25. Freeman J, Sapyta J, Garcia A, Compton S, Khanna M, Flessner C et al (2014) Family-based treatment of early childhood obsessive–compulsive disorder: the pediatric obsessive–compulsive disorder treatment study for young children (POTS Jr)—a randomized clinical trial. JAMA Psychiatry 71(6):689–698
26. Conelea C, Selles R, Benito K, Walther M, Machan J, Garcia et al (2017) Secondary outcomes from the pediatric obsessive compulsive disorder treatment study II. J Psychiatr Res 92:94–100
27. Sánchez-Meca J, Rosa-Alcázar A, Iniesta-Sepúlveda M (2014) Differential efficacy of cognitive-behavioral therapy and pharmacological treatments for pediatric obsessive–compulsive disorder: a meta-analysis. J Anxiety Disord 28:31–44
28. Freeman J, Garcia A, Benito K, Conelea C, Sapyta J, Khanna M et al (2012) The pediatric obsessive compulsive disorder treatment study for young children (POTS JR): developmental considerations in the rationale, design, and methods. J Obsess Compuls Rel 1:294–300
29. Scahill L, Riddle MA, McSwiggin-Hardin M, Ort SI, King RA, Goodman WK et al (1997) Children's Yale-brown obsessive compulsive scale: reliability and validity. J Am Acad Child Adolesc Psychiatry 36(6):844–852
30. Conners C, March J (1996) The Conners-March Developmental Questionnaire. Multi-Health Systems, Toronto
31. Cook N, Freeman J, Garcia A, Sapyta J, Franklin, M (2015) Assessment of obsessive compulsive disorder in young children: psychometric properties of the children's Yale-brown obsessive compulsive scale. J Psychopathol Behav Assess 37(3):432–441
32. March J, Leonard H (1998) Obsessive–compulsive disorder in children and adolescents. In: Swinson RP, Antony MM, Rachman S, Richter MA eds. Obsessive–compulsive disorder: theory, research, and treatment. Guilford Press, New York, NY
33. Guy W, ECDEU Assessment Manual for Psychopharmacology–Revised (1976) Rockville, MD: US Dept of Health, Education, and welfare; Public Health Service; Alcohol, Drug Abuse, Mental Health Administration; National Institute of Mental Health, Psychopharmacology Research Branch, Division of Extramural Research
34. Garvey MA, Perlmutter SJ, Allen AJ, Hamburger S, Lougee L, Leonard HL et al (1999) A pilot study of penicillin prophylaxis for neuropsychiatric exacerbations triggered by streptococcal infections. Biol Psychiatr 45(12):1564–1571
35. Perlmutter SJ, Leitman SF, Garvey MA, Hamburger S, Feldman E, Leonard HL, Swedo, SE (1999) Therapeutic plasma exchange and intravenous immunoglobulin for obsessive–compulsive disorder and tic disorders in childhood. Lancet 354(9185):1153–1158
36. Chambers WJ, Puig-Antich J, Hirsch M, Paez P, Ambrosini P, Tabrizi MA et al (1985) The assessment of affective disorders in children and adolescents by semistructured interview: test–retest reliability of the schedule for affective disorders and schizophrenia for school-age children, present episode version. Arch Gen Psychiatry 42(7):696–702
37. Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P et al (1997) Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry 36(7):980–988
38. Hirshfeld-Becker D, Biederman J (2002) Rationale and principles for early intervention with young children at risk for anxiety disorders. Clin Child Fam Psychol Rev 5(3):161–172
39. Youngstrom EA, Gracious B, Danielson CK, Findling RL, Calabrese J (2003) Toward an integration of parent and clinician report on the Young Mania Rating Scale. J Affect Disord 77(2):179–190
40. Achenbach T, Rescorla L (2000) Manual for ASEBA preschool forms & profiles. University of Vermont, Research Center for Children, Youth & Families, Burlington, VT
41. Birmaher B, Brent DA, Chiappetta L, Bridge J, Monga S, Baugher M (1999) Psychometric properties of the screen for child anxiety related emotional disorders (SCARED): a replication study. J Am Acad Child Adolesc Psychiatry 38(10):1230–1236

42. Muris P, Merckelbach H, van Brakel A, Mayer B (1999) The revised version of the screen for child anxiety related emotional disorders (SCARED–R): first evidence for its reliability and validity in a clinical sample. Br J Clin Psychol 40:35–44
43. Allison PD, (2012) Handling missing data by maximum likelihood. Statistics and data analysis, SAS Global Forum: pp 1–21
44. Little RJA (1988) A test of missing completely at random for multivariate data with missing values. J Am Stat Assoc 83:1198–1202
45. Enders CK (2001) A primer on maximum likelihood algorithms available for use with missing data. Struct Equ Model 8:128–141
46. Scheffer J (2002) Dealing with missing data. Res Lett Inf Math Sci 3:153–160
47. Alvarenga PG, Cesar R, Leckman J, Moriyama T, Torres A, Bloch M et al, (2015) Obsessive–compulsive symptom dimensions in a population-based, cross-sectional sample of school-aged children. J Psychiatr Res 62:108–114
48. Lewin AB, Piacentini J, De Nadai A, Jones A, Peris T, Geffken G et al (2014) Defining clinical severity in pediatric obsessive–compulsive disorder. Psychol Assess 26(2):679–684
49. Costello EJ, Mustillo S, Erkanli A, Keeler G, Angold A (2003) Prevalence and development of psychiatric disorders in childhood and adolescence. Arch Gen Psychiatry 60:837–844
50. Hudson JL, Kendall P (2002) Showing you can do it: homework in therapy for children and adolescents with anxiety disorders. Psychotherapy in Practice 58:525–534
51. Skriner LC, Freeman J, Garcia A, Benito K, Sapyta J, Franklin, M (2016) Characteristics of young children with obsessive–compulsive disorder: baseline features from the POTS Jr. sample. Child Psychiatry Hum Dev 47(1):83–93
52. Williams M, Powers M, Yeo-Gin Y, Foa E (2010) Minority participation in randomized controlled trials for obsessive–compulsive disorder. J Anxiety Disord 24(2):171–177

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