

Evidence-Based Treatment for Pediatric Obsessive-Compulsive Disorder

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ABSTRACT

Obsessive-compulsive disorder (OCD) is marked by incessant distressing thoughts or images (obsessions) and/or overt or covert behaviors (or mental rituals) aimed to reduce anxiety (compulsions). The disorder affects 1-2% of children and adults, with up to 80% of adults reporting symptom onset prior to the age of 18 years. Without appropriate intervention, symptoms tend to run a chronic course from childhood into adulthood. Obsessive-compulsive disorder contributes to considerable impairment across multiple domains of functioning, and as a result calls for effective and efficient treatment. To date, both psychological and pharmacological interventions have shown efficacy for pediatric OCD although there are associated advantages and disadvantages that must be considered in treatment planning. The intent of this review is to discuss the current state of literature regarding treatment for pediatric OCD, highlight efficient and cost-effective means of reducing impairment, and conclude with directions for future study.

Obsessive-compulsive disorder (OCD) is an impairing anxiety disorder which afflicts approximately 1-2% of youth and adults worldwide (1-3). The disorder is marked by distressing and uncontrollable thoughts or images (obsessions) and/or overt (i.e., washing, ordering) or covert (i.e., praying, counting) behaviors aimed to reduce distress (compulsions). Obsessive-compulsive symptoms are chronic in nature, and when present during childhood interfere considerably with a child's psychosocial development across social, family, and academic domains (4-7). If left inadequately treated, clinically significant obsessive-compulsive symptoms are likely to persist into adulthood and cause future impairment (8). Taken together, this information demonstrates the need for appropriate treatment for children with OCD to curtail the negative developmental trajectory that distinguishes OCD from other anxiety disorders (9).

Traditionally, many clinicians have conceptualized the etiology and treatment of adult and pediatric OCD through a psychodynamic perspective, viewing the obsession and compulsions as a complex set of neuroses arising from intrapsychic conflict (10, 11). Unfortunately, treatments based on this premise are not empirically supported in reducing obsessive-compulsive symptoms and have little face validity in understanding etiological factors or symptom maintenance. Due to the prevalence and precarious nature of OCD, mental health providers have begun to move towards evidence-based intervention modalities for the treatment of OCD, including serotonin reuptake inhibitors (SRI) and cognitive behavioral therapy (CBT) (10). Notably, the limited treatment dissemination may contribute to a number of risks (e.g., medication side effects) and in missing an opportunity to intervene during a developmentally critical time period (12). Many youth with OCD are being prescribed antipsychotic or benzodiazepine medications in the absence of efficacy data. Such

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widespread prescription practices are conducted in the absence of supporting pediatric data and the possibility of significant adverse metabolic and cardiovascular effects. Indeed, youth taking an atypical antipsychotic medication had an average weight increase of 8.5kg over 10 weeks (13). Thus, lower-risk alternatives should be considered prior to prescription of such medications in children (14). Second, inadequate treatment of OCD symptoms during childhood have been associated with numerous psychosocial sequelae, such as problematic family relations, social dysfunction, and academic distress (4-7), which together disrupt normative development. Third, unresolved OCD symptoms tend to be chronic in nature, result in higher rates of reported unemployment, interpersonal conflict, sleep problems, and chronic distress and impairment in adulthood when compared to non-OCD anxiety disorders (9). Thus, early effective intervention is crucial to improving a child's quality of life and preventing future impairment. Although such treatments are available, information regarding their implementation is not widely disseminated. With these points in mind, the text that follows reviews evidence-based practice for the treatment of pediatric OCD, highlights the intricacies of tailoring treatment to address developmental needs and psychological comorbidity of children, and also discusses the future of treatment for this tenacious disorder.

PHENOMENOLOGY OF PEDIATRIC OBSESSIVE-COMPULSIVE DISORDER

Like adults, youth with OCD experience obsessions that center upon themes of contamination, symmetry and precision, religiosity, lucky or unlucky numbers, and a marked preoccupation with inappropriate sexual or aggressive thoughts (15-17). Compulsions related to these common themes frequently present as cleaning or decontamination rituals, reassurance seeking, praying, touching or tapping, counting, behaviors that prevent the potential for a child to do harm to self or others, hoarding, or more general routinized behaviors. Although symptoms presentation in children is generally similar to that of adults, developmental differences do exist. Such differences include children endorsing more vague obsessions (particularly in younger children, 18), simplified content of obsessions (e.g., sexual or aggressive obsessions), increased reassurance-seeking and family involvement in rituals (19, 20), and more rituals focused on achieving a "just right" feeling (21, 22). Unfortunately, it appears that children and adolescents, like many adults

(23), experience a significant delay between symptom onset and appropriate clinical assessment/intervention (22). This may be related to a lack of knowledge/awareness of the disorder by the parent, limited clinician expertise in OCD, and/or lack of available appropriate treatment resources, the latter two issues having been cited as particular issues in Israel (22). Without intervention, OCD is likely to run a chronic course (8), increasing risk for social, academic and overall functional impairment (4). Fortunately, available treatments yield robust effects, with less than half of those treated with psychotherapy, pharmacotherapy, or a combination of both meeting diagnostic threshold at treatment follow-up (4, 24).

TREATMENT

Psychopharmacology. Serotonin reuptake inhibitors have been demonstrated to be effective for both pediatric and adult OCD (25-28). While numerous SRI medications have been examined in youth with OCD, the United States Food and Drug Administration has only given approvals for clomipramine (ages 10 up), sertraline (ages 6 and up), paroxetine (ages 6 and up), fluoxetine (ages 7 and up), and fluvoxamine (ages 8 and up). Clomipramine, sertraline, paroxetine, fluoxetine, and fluvoxamine have consistently demonstrated efficacy in attenuating OCD symptoms (26, 29-35) with case reports in children as young as 3.5 years of age (36). Clomipramine, once the first-line pharmacological treatment for OCD (37), has demonstrated superiority to placebo with statistical separation at 5-6 weeks (38). Sertraline (26, 31) and fluoxetine (30), similarly, have demonstrated superior efficacy to placebo in reducing OCD symptoms and overall impairment. In addition, sertraline appears to have enhanced effects when used in combination with CBT (26) leading to the suggestion of combined CBT and SRI therapy for the most severe cases. Paroxetine has demonstrated superior treatment response rates compared to placebo (64.9% v. 41.2%), but is unfortunately associated with mild to moderate side effects resulting in treatment discontinuation (34) and the nonlinear pharmacokinetics can complicate dosing in children. Finally, fluvoxamine (32) appears to be only marginally more efficacious in symptom reduction than placebo.

Unfortunately, treatment with pharmacotherapy alone rarely achieves standards of clinical remission (8, 14, 26, 28). In fact, Geller et al. (29) showed that although statistically superior to placebo, the overall difference in reduction between active treatment and placebo in the Children's Yale-Brown Obsessive Compulsive Scale (39) was marginal

(only 6 points on the 40 point scale). In addition to the concern that many youth will remain symptomatic following an adequate medication course, many SRIs are associated with adverse events which may lead to treatment discontinuation (31, 34, 36) and some families do not find SRI therapy an acceptable intervention (40). In addition, there are few SRI maintenance trials and – overall – there is limited information regarding durability of treatment gains once medications are discontinued in children with OCD. Results from numerous controlled trials in adults do suggest, however, that it is in the best interest of individuals treated with pharmacological interventions alone not to discontinue treatment as recurrence of symptoms is likely (41). Finally, there is concern regarding the risk of “suicidality” (suicidal thoughts and behavior) and behavioral activation in children and adolescents during treatment with antidepressants (see 42 for a comprehensive review). In sum, although pharmacotherapy presents as an efficacious and widely disseminated treatment for pediatric OCD, there are limitations including the presence of side effects (34), incomplete treatment response, potential for increased suicidality and behavioral activation (42), and recurrence of symptoms once active treatment ends (41).

Cognitive-behavioral therapy. Cognitive-behavioral therapy with exposure and response prevention is an empirically-supported treatment premised on classical and operant conditioning theories. In OCD, previously neutral stimuli become associated with aversive properties (i.e., anxiety, distress), which cause the individual to engage in compulsions to alleviate this distress. Compulsions, however, only temporarily reduce distress, causing the individual to repetitively engage in ritualistic behaviors. Exposure and response prevention is a central component of CBT which requires the individual to confront the anxiety-inducing thought or stimulus without engaging in compulsions. Distress associated with the stimulus eventually habituates over time with repeated exposures without ritual engagement (43).

Pragmatically, CBT for OCD is a multi-component treatment conducted in a sequential manner. First, an individual is provided with psychoeducation regarding the nature of OCD, including the neurobiological, cognitive, and behavioral underpinnings, and the typical treatment course. Second, a rank-ordered hierarchy is created delineating the degree of distress exposure to anxiety-inducing stimuli without ritual engagement would elicit. Treatment begins with exposure to lower-anxiety stimuli together with refraining from ritual engagement, and gradually progresses to exposure to

more anxiety-provoking stimuli. As previously described, the exposure involves having the individual confront the feared situation or focus on the anxiety-inducing thought, without engaging in compulsive behaviors. Individuals remain focused or engaged in the feared situation until habituation (i.e., reduction in anxiety to negligible levels) occurs. A single exposure is typically repeated until it no longer produces significant distress. Following successful completion of an exposure (or situation on the hierarchy), treatment progresses to more difficult exposures in a gradual manner through the hierarchy (44).

Based on available empirical data and consideration of the risk/benefit profile of SRI therapy, practice guidelines recommend CBT as the first line treatment for children and adolescents with mild to moderate obsessive-compulsive symptom severity. For those youngsters with more severe symptoms, practice parameters recommend CBT in conjunction with a trial of an SRI (38).

From an outcome standpoint, CBT has consistently shown impressive results in youth with OCD in both efficacy (i.e., controlled clinical trials) (45, 46) and effectiveness research (i.e., analysis of CBT approaches outside of clinical trials) (47, 48). Two separate meta-analyses of randomized-controlled trials comparing the efficacy of CBT to pharmacotherapy and/or control conditions indicated superiority of CBT to pharmacotherapy and control comparisons in reducing obsessive-compulsive symptom severity in youth (25, 49). A large multi-site study compared the efficacy of CBT alone, sertraline alone, CBT and sertraline combined, and pill placebo in the reduction of obsessive-compulsive symptom severity in youth with OCD. Although results suggest that combined treatment was superior to CBT alone, this difference was not statistically significant on some outcomes (e.g., remission). In addition, CBT alone showed a significantly larger treatment effect (overall effect $d = .97$; site effect $d = .51-1.6$) than sertraline alone (overall effect $d = .67$; site effect $d = .53-.80$). However, it is relevant to note that a site effect in terms of CBT efficacy was observed with one site performing significantly better than another ($d = 1.6$ versus $.51$) suggesting caution when interpreting study results.

In addition to these robust empirical findings, effectiveness of CBT outside of the research setting has been well-demonstrated. For example, two open trials of CBT suggest 79-80% response rates (and 45-54% symptom reduction) (47, 48). Similarly, a Norwegian outpatient clinic implementing a combination of individual and family-based CBT demonstrated a large treatment effect ($d = 3.49$), with youth experiencing an average of 60.6%

reduction in symptom severity over the course of 12 sessions (51). These data corroborate the author's clinical experiences at three specialty programs for cognitive-behavioral treatment of pediatric OCD.

Rates of remission following CBT range from 40-85% (46), and have been maintained up to 7 years following treatment (45, 46). Although the utility of maintenance therapy has not been empirically evaluated, clinical experience suggests that some children will experience symptom relapse. Accordingly, booster sessions may be one method of reducing relapse and maintaining treatment gains.

ENHANCING TREATMENT OUTCOMES

Despite their efficacy (25, 49), a significant portion of children with OCD do not respond to pharmacotherapy (~50%;(51)) or CBT (30%) (5, 26) and partial response is common. Effects are likely to be enhanced when treatments are tailored to: 1) fit the developmental needs of the child, 2) address the manner in which the family system may contribute to obsessive-compulsive symptoms, and 3) address comorbid conditions that may interfere with treatment (52). Next, we discuss the manner in which various treatment strategies have been developed to address these issues.

Family-based CBT. Many children lack the insight into the irrationality of their obsessions either due to their cognitive development level or as a function of the disorder (53-55). This lack of insight likely reduces motivation to engage in therapeutic tasks, attenuating treatment response (56, 57). In order to address this lack of insight and motivation, families are often included in the treatment of youth with OCD for multiple reasons. First, parents can help the child to generalize skills developed in session in real world settings. Second, a child's parents can increase a child's awareness of his/her OCD symptoms. Third, parents can help to motivate that child through contingencies to enhance the child's effort to confront symptoms adaptively. Lastly, by involving a family in treatment for youth with OCD, the manner in which the family system maintains a child's symptoms can be addressed (58).

Empirical trials of family-based CBT for youth with OCD have demonstrated its superiority to relaxation training (56) and waitlist control. Group or individual formats have been associated with significant remission rates and maintenance of treatment gains at an 18-month follow-up (45). Similarly, intensive (daily for 3 weeks) and weekly (once per week for 14 weeks) family-based CBT have also revealed significant rates of remission;

75% of intensive and 50% of weekly participants achieved remission, and were able to maintain gains at a 3-month follow-up (57). Finally, it has been suggested as an efficacious treatment for youth who only partially-responded to trials of pharmacological interventions (47). As a result, family-based CBT presents as an effective intervention for youth with OCD which can be implemented in an efficient (group or intensive formats) manner.

Comorbidity. Similar to adults, approximately 75% of youth with OCD experience a comorbid psychiatric condition, with comorbid anxiety, depressive, and externalizing disorders among the most prevalent (27, 59-61). As the number of comorbid conditions increases, not only does response to CBT or SRI medication tend to decrease, but risk of relapse increases (27, 61). Disruptive behavior disorders (DBD) and Tourette Syndrome are disorders frequently diagnosed in children with OCD, and as a result their impact on OCD treatment has been widely examined.

Disruptive behavior disorders, such as oppositional defiant disorder and conduct disorder are among the most common comorbid disorders associated with pediatric OCD (62). Obsessive-compulsive disorder with a comorbid DBD is associated with greater OCD symptom severity and impairment, as well as greater overall anxiety and internalizing problems than those without a DBD (63). The presence of DBDs has been found to attenuate response to pharmacological (27) and psychosocial interventions (61). Anecdotally, the presence of rage or aggressive behaviors has been noted among youth with OCD. Unfortunately, "rage attacks" among youth with OCD are poorly studied. A recent study suggests that youth with OCD who present with rage attacks versus those without have increased OCD symptom severity and are more likely to report sexual, religious and aggressive obsessions and increased checking rituals (64). The presence of OCD may predispose some youth to have rage attacks, perhaps due to exposure to obsessional triggers or limited family accommodation of symptoms (19, 64). For these cases, parent-training approaches which introduce contingencies for non-compliance with therapeutic or parental commands have shown to reduce OCD-related impairment in youth (19, 46, 57).

Tics are common among youth with pediatric onset OCD (69, 70), with approximately 16% of children and adolescents with OCD exhibiting tics at some point (26, 27, 67). Similarly, 50% of children with Tourette Syndrome/Chronic Tic Disorder (TS/CTD) meet diagnostic criteria for OCD at some point during their development (68).

Given this significant overlap, OCD may have a different clinical presentation when TS/CTD is also present particularly in the presence of motoric compulsions and tics, complicating differential diagnosis (69). Some clinicians suggest that examining the relationship between the behavior and purpose (e.g., non-specific or anxiety-relieving) aids in this distinction. The presence of comorbid tics may attenuate pharmacological treatment response in pediatric OCD (67), but not CBT (67, 70). Notably, albeit a preliminary study, the presence of a tic disorder did not predispose youth with OCD to greater risk of rage attacks (64). Having a comorbid diagnosis of major depressive disorder (MDD) may attenuate treatment response as it may affect habituation to exposures (60, 71). For such cases, sequential treatment of MDD prior to OCD through the use of CBT or SRIs may enhance the effects of CBT for OCD. Attention-deficit hyperactivity disorder has also been found to attenuate CBT response, as this condition may interfere with a child's ability to focus on therapeutic strategies, and execute exposures independently (59, 72). Comorbid anxiety disorders have no impact on treatment response in OCD (67, 73).

Overall, comorbidity is a common feature in pediatric OCD, affecting up to 75% of children which may affect treatment outcome if not properly considered and addressed within the treatment plan (27, 59-61). In addition to the psychosocial intervention strategies previously mentioned, there are pharmacological strategies to address comorbidities associated with pediatric OCD. As this is beyond the scope of the current review, however, we direct the reader to the following articles for more information on this topic (22, 27, 51, 74).

Flexible treatment modalities. Unfortunately, access to evidence-based psychotherapy for OCD is limited (75, 76), particularly for youth. In general, the dissemination of CBT for pediatric OCD is particularly problematic in Israel in that programs continue to train clinicians in psychodynamic approaches, rather than CBT, resulting in a shortage of available clinicians (76). In addition, there are many nuances involved in tailoring the treatment to match the clinical characteristics of the affected child. This predicament may be particularly relevant in Israel, as CBT has only recently begun to be recognized as an effective treatment for OCD (10, 77). As a result of limited training and treatment dissemination, many clinicians may rely on pharmacotherapy alone or with non-evidence-based psychotherapy given its accessibility.

Since treatment with pharmacotherapy does not have the same access issues as in psychotherapy (i.e., locat-

ing a CBT provider), a recent study in the United States examined the additive effects of CBT to ongoing pharmacotherapy (78). The study examined three modes of treatment: CBT provided by trained psychologists in conjunction with continued SRI treatment; a diluted form of CBT (encouraged the use of CBT strategies rather than implementing strategies in session) conducted by the prescribing psychiatrist with ongoing SRI treatment; and SRI treatment alone. Although results have yet to be published, this design highlights the potential of CBT dissemination through psychiatrists in a manner that decreases both time and financial burden on the family.

Intensive treatment. Intensive treatment serves as a treatment option which not only benefits more severe cases in which symptoms are pervasive and impairing, or when insight and motivation are low, but is also an option when typical treatment formats are not available (i.e., geographical barriers) (2, 79). Cognitive-behavioral therapy is quite flexible in terms of the frequency in which sessions are held. In standard CBT for OCD, 60-minute sessions are held once per week for 13-20 weeks (38). Intensive CBT, however, consists of sessions 3-5 times per week for typically 3-5 weeks. Numerous studies have demonstrated the efficacy of intensive CBT for children with OCD (47, 57, 80, 81).

FUTURE DIRECTIONS

D-Cycloserine. Research on the neural circuitry underlying fear extinction has led to the examination of d-cycloserine (DCS), a partial agonist at the NMDA receptor in the amygdala, as a method of enhancing CBT outcome. Among adult OCD, preliminary results have supported the use of DCS to augment exposure therapy (e.g., 82, 83). Storch and colleagues (84) recently examined the impact of DCS administration in conjunction with weekly CBT compared to placebo augmentation in youth with OCD. Compared to the CBT+Placebo group, youth in the CBT+DCS arm showed small-to-moderate treatment effects ($d=.31$ to $.47$ on primary outcomes). DCS was safe and well tolerated.

Treatment augmentation. Unfortunately, many youth suffer from treatment resistant OCD. Treatment resistant OCD is defined as failing adequate trials of either CBT (which is typically defined as a minimum of 12 sessions of CBT, including psychoeducation, exposure and response prevention, and discussions of relapse prevention), or failure to respond to two different SRIs (a trial of an adequate dose for at least 10 weeks, depending on

the medication) (85). For this subgroup of youth with OCD, use of an atypical antipsychotic has been used in an off-label fashion to augment SRI monotherapy (86, 87). Other medication augmentation strategies such as benzodiazepines and mood stabilizers have been used in an off-label manner but do not have empirical support in pediatric OCD (85). Psychotherapeutic strategies, such as tailoring treatments to address psychological comorbidity (as previously described), sequential treatment of comorbid disorders prior to OCD treatment, intensive treatment schedules, and home-based psychotherapies have also been suggested as means of augmenting treatment for treatment resistant pediatric OCD but also require empirical evaluation (85).

Telehealth. As discussed, CBT is a flexible treatment modality which can be tailored to address individual needs. A way in which this flexibility has been demonstrated and enhanced is its implementation via teletherapy. Teletherapy is a treatment conducted via webcam (either on a computer, tablet, or smartphone) in real time, in the contexts in which the symptoms occur. Theory suggests that treatment effects may be enhanced if treatment occurs in the same environment as the obsessional triggers. For many children, these triggers are present in less sterile environments than the clinic, such as at school or at home. Storch et al. (88) examined the efficacy of teletherapy for children and adolescents with OCD compared to 4-week waitlist control. Sessions were held for 60 minutes twice a week for 2 weeks, then weekly over the course of 10 weeks. A significant reduction in OCD symptoms was found at termination (56.1%), and gains were maintained over a 3-month follow-up. Although this mode of treatment may have limitations in regard to the types of exposures which can be conducted and negative impact on the therapeutic alliance, limitations may be balanced by the generalizability of skills from session to home, and the increased access to gold-standard treatment.

CONCLUSION

Obsessive-compulsive disorder is associated with significant impairment in childhood which extends into adulthood without adequate treatment. Due to the critical nature of pediatric OCD, appropriate and timely intervention is necessary. Research to date has highlighted the intricacies of treating youth with OCD, and in response has developed effective and efficient modes of intervention. Pharmacological interventions demonstrate adequate results in reducing symptom impairment (25-28), yet it

is unclear if these gains remain once active treatment is discontinued (41). Similarly, alternative theoretical interventions have yet to demonstrate efficacy in randomized controlled trials. Cognitive-behavioral therapy, however, poses as an optimal treatment option as it has demonstrated robust effects in time-limited settings (25, 38, 49), and maintenance of gains following treatment discontinuation (45, 46). Further, innovative treatments (e.g., DCS, telehealth) not only help to enhance CBT efficacy, but also aid in the dissemination of the gold-standard treatment for youth with OCD (82, 84, 88). It is with great hope that the current review highlights evidence-based interventions for treating pediatric OCD to further disseminate information and improve child quality of life.

References

1. Douglass HM, Moffitt TE, Dar R, McGee R, Silva P. Obsessive-compulsive disorder in a birth cohort of 18-year-olds: Prevalence and predictors. *J Am Acad Child Adolesc Psychiatry* 1995;34:1424-1431.
2. Zohar AH. The epidemiology of obsessive-compulsive disorder in children and adolescents. *Child Adolesc Psychiatr Clin North Am* 1999; 8:445-460.
3. Zohar AH, Ratzoni G, Pauls DL, Apter A, Bleich A, Kron S, et al. An epidemiological study of obsessive-compulsive disorder and related disorders in Israeli adolescents. *J Am Acad Child Adolesc Psychiatry* 1992;31:1057-1061.
4. Stewart SE, Geller DA, Jenike MA, Pauls D, Shaw D, Faraone SV. Long-term outcome of pediatric obsessive compulsive disorder: A meta-analysis and qualitative review of literature. *Acta Psychiatr Scand* 2004;110:4-13.
5. Piacentini J, Bergman RL, Keller M, McCracken J. Functional impairment in children and adolescents with obsessive-compulsive disorder. *J Child Adolesc Psychopharmacology* 2003;13: 61-69.
6. Storch EA, Ledley DR, Lewin AB, Murphy TK, Johns NB, Goodman WK, et al. Peer victimization in children with obsessive-compulsive disorder: Relations with symptoms of psychopathology. *J Clin Child Adolesc Psychology* 2006;35:446-455.
7. Rufer M, Hand I, Alsleben H, Braatz A, Ortman J, Katenkamp B, et al. Long-term course and outcome of obsessive-compulsive patients after cognitive-behavioral therapy in combination with either fluvoxamine or placebo: A 7-year follow-up of a randomized double-blind trial. *Eur Arch Psy Clin N* 2005;255:121-128.
8. Bloch MH, Craiglow BG, Landeros-Weisenberger A, Dombrowski PA, Panza KE, Peterson BS, et al. Predictors of early adult outcomes in pediatric-onset obsessive-compulsive disorder. *Pediatrics* 2009;124:1085-1093.
9. Barlow DH. Anxiety and its disorders: The nature and treatment of anxiety and panic. New York: Guilford, 2002.
10. Zohar J, Hermesh H. Editorial: Obsessive-compulsive disorder. *Isr J Psychiatry Relat Sci* 2008;45:149-150.
11. Fenichel O. The psychoanalytic theory of neurosis. New York, N.Y.: WW Norton, 1945.
12. Piacentini J, Bergman RL, Keller M, McCracken J. Functional impairment in children and adolescents with obsessive-compulsive disorder. *J Child Adolesc Psychopharmacol* 2003;13 Suppl 1:S61-S69.
13. Correll CU, Manu P, Olshanskiy V, Napolitano B, Kane JM, Malhotra AK. Cardiometabolic risk of second-generation antipsychotic medications during first-time use in children and adolescents. *JAMA* 2009;302:1765-1773.

14. Lewin AB, Storch EA, Storch HD. Risks from antipsychotic medications in children and adolescents. *JAMA* 2010;303:729-730.
15. Masi G, Millepiedi S, Mucci M, Bertini N, Milantoni L, Arcangeli F. A naturalistic study of referred children and adolescents with obsessive-compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 2005;44:673-681.
16. Swedo SE, Rapoport JL, Leonard H, Lenane M, Cheslow D. Obsessive-compulsive disorder in children and adolescents. Clinical phenomenology of 70 consecutive cases. *Arch Gen Psychiatry* 1989;46:335-341.
17. Gallant J, Storch EA, Merlo LJ, Ricketts ED, Geffken GR, Goodman WK, et al. Convergent and discriminant validity of the Children's Yale-Brown Obsessive Compulsive Scale-Symptom Checklist. *J Anxiety Dis* 2008 ;22:1369-1376.
18. Flessner CA, Allgair A, Garcia A, Freeman J, Sapyta J, Franklin ME, et al. The impact of neuropsychological functioning on treatment outcome in pediatric obsessive-compulsive disorder. *Depress Anxiety* 2009;27:365-371.
19. Storch EA, Geffken GR, Merlo LJ, Jacob ML, Murphy TK, Goodman WK, et al. Family accommodation in pediatric obsessive-compulsive disorder. *J Clin Child Adolesc Psychology* 2007;36:207-216.
20. Peris TS, Bergman RL, Langley A, Chang S, McCracken JT, Piacentini J. Correlates of accommodation of pediatric obsessive-compulsive disorder: Parent, child and family characteristics. *J Am Acad Child Adolesc Psychiatry* 2008;47:481-482.
21. Rettew D, Swedo S, Leonard H, Lenane M. Obsessions and compulsions across time in 79 children and adolescents with obsessive-compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 1992;31:1050-1056.
22. Mancuso E, Faro A, Joshi G, Geller DA. Treatment of pediatric obsessive-compulsive disorder: A review. *J Child Adolesc Psychopharmacology* 2010;20:299-308.
23. Blanco C, Olfson M, Stein D, Simpson HB, Gameroff M, Narrow W. Treatment of obsessive-compulsive disorder by U.S. Psychiatrists. *J Clin Psychiatry*. 2006;67:946-951.
24. Micali N, Heyman I, Perez M, Hilton K, Nakatani E, Turner C, et al. Long-term outcomes of obsessive-compulsive disorder: Follow-up of 142 children and adolescents. *Br J Psychiat* 2010;197:128-134.
25. Abramowitz JS, Whiteside SP, Deacon BJ. The effectiveness of treatment for pediatric obsessive-compulsive disorder: A meta-analysis. *Behav Ther* 2005;36:55-63.
26. Pediatric OCD Treatment Study (POTS) Team. Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: The Pediatric OCD Treatment Study (POTS) randomized controlled trial. *JAMA* 2004;292:1969-1976.
27. Geller DA, Biederman J, Stewart SE, Mullin B, Farrell C, Wagner KD, et al. Impact of comorbidity on treatment response to paroxetine in pediatric obsessive-compulsive disorder: Is the use of exclusion criteria empirically supported in randomized clinical trials? *J Child Adolesc Psychopharmacology* 2003;13 (Suppl 1):S19-S29.
28. Foa EB, Liebowitz MR, Kozak MJ, Davies S, Campeas R, Franklin ME, et al. Randomized, placebo-controlled trial of exposure and ritual prevention, clomipramine, and their combination in the treatment of obsessive-compulsive disorder. *Am J Psychiatry* 2005;162:151-161.
29. Geller DA, Hoog SL, Heiligenstein JH, Ricardi RK, Tamura R, Kluszynski S, et al. Fluoxetine treatment for obsessive-compulsive disorder in children and adolescents: A placebo-controlled clinical trial. *J Am Acad Child Adolesc Psychiatry* 2003;40:773-779.
30. Liebowitz MR, Turner SM, Piacentini J, Beidel DC, Clarvit SR, Davies SO, et al. Fluoxetine in children and adolescents with OCD: A placebo-controlled trial. *J Acad Child Adolesc Psychiatry* 2002;41:1431-1438.
31. March JS, Biederman J, Wolkow R, Safferman A, Mardekian J, Cook E, et al. Sertraline in children and adolescents with obsessive-compulsive disorder: A multicenter randomized controlled trial. *JAMA* 1998;280:1752-1756.
32. Riddle MA, Reeve EA, Yaryura-Tobias JA, Yang HM, Claghorn JL, Gaffney G, et al. Fluvoxamine for children and adolescents with Obsessive-Compulsive Disorder: A randomized, controlled, multicenter trial. *J Acad Child Adolesc Psychiatry* 2001;40:222-229.
33. Masi G, Millepiedi S, Perugi G, Pfanner C, Berloff S, Pari C, et al. Pharmacotherapy in paediatric obsessive-compulsive disorder: A naturalistic, retrospective study. *CNS Drugs* 2009;23:241-252.
34. Geller DA, Wagner KD, Emslie G, Murphy T, Carpenter DJ, Wetherhold E, et al. Paroxetine treatment in children and adolescents with obsessive-compulsive disorder: A randomized, multicenter, double-blind, placebo-controlled trial. *J Am Acad Child Adolesc Psychiatry* 2004;43:1387-1396.
35. Birmaher B, Axelson DA, Monk K, Kalas C, Clark DB, Ehmann M, et al. Fluoxetine for the treatment of childhood anxiety disorders. *J Acad Child Adolesc Psychiatry* 2003;42:415-423.
36. Coskun M, Zoroglu S. Efficacy and safety of fluoxetine in preschool children with obsessive-compulsive disorder. *J Child Adolesc Psychopharmacology* 2009;19:297-300.
37. March JS, Ollendick T. Integrated psychosocial and pharmacological treatment. Phobic and anxiety disorders in children and adolescents: A clinician's guide to effective psychosocial and pharmacological interventions. New York, N.Y.: Oxford University, 2004; pp. 141-172.
38. AACAP. Practice parameters for the assessment and treatment of children and adolescents with obsessive-compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 1998;37:27S-45S.
39. Scahill L, Riddle MA, McSwiggin-Hardin M, Ort SI, King RA, Goodman WK, et al. Children's Yale-Brown obsessive compulsive scale: Reliability and validity. *J Acad Child Adolesc Psychiatry* 1997;36:844-852.
40. Stevens J, Wang W, Fan L, Edwards MC, Campo JV, Gardner W. Parental attitudes toward children's use of antidepressants and psychotherapy. *J Child Adolesc Psychopharmacol* 2009;19:289-296.
41. Declodt EH, Stein DJ. Current trends in drug treatment of obsessive-compulsive disorder. *Neuropsychiatr Dis Treat* 2010;6:233-242.
42. Reid JM, Storch EA, Murphy TK, Bodzin D, Mutch PJ, Lehmkuhl H, et al. Development and psychometric evaluation of the treatment-emergent activation and suicidality assessment profile. *Child Youth Care Forum* 2010;39:113-124.
43. Bouton ME. Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. *Psychol Bull* 1993;114:80-99.
44. March JS, Franklin M, Nelson A, Foa E. Cognitive-behavioral psychotherapy for pediatric obsessive-compulsive disorder. *J Clin Child Psychol* 2001;30:8-18.
45. O'Leary EM, Barrett P, Fjermestad KW. Cognitive-behavioral family treatment for childhood obsessive-compulsive disorder: A 7-year follow-up study. *J Anxiety Dis* 2009;23:973-978.
46. Barrett P, Healy-Farrell L, March JS. Cognitive-behavioral family treatment of childhood obsessive-compulsive disorder: Long-term follow-up and predictors of outcome. *J Am Acad Child Adolesc Psychiatry* 2004;43:46-62.
47. Storch EA, Lehmkuhl HD, Ricketts E, Geffken GR, Marien W, Murphy TK. An open trial of intensive family based cognitive-behavioral therapy in youth with obsessive-compulsive disorder who are medication partial responders or nonresponders. *J Clin Child Adolesc Psychol* 2010;39:260-268.
48. Piacentini J, Bergman RL, Jacobs C, McCracken JT, Kretchman J. Open trial of cognitive behavior therapy for childhood obsessive-compulsive disorder. *J Anxiety Dis* 2002;16:207-219.
49. Watson HJ, Rees CS. Meta-analysis of randomized, controlled treatment trials for pediatric obsessive-compulsive disorder. *J Child Psychol Psychiatry* 2008;49:489-498.
50. Valderhaug R, Larsson B, Gotestam KG, Piacentini J. An open clinical trial of cognitive-behaviour therapy in children and adolescents with obsessive-compulsive disorder administered in regular outpatient clinics. *Behav Res Ther* 2007;45:577-589.

51. Geller DA, Biederman J, Stewart SE, Mullin B, Martin A, Spencer T, et al. Which SSRI? A meta-analysis of pharmacotherapy trials in pediatric obsessive-compulsive disorder. *Am J Psychiatry* 2003;160:1919-1928.
52. Lewin AB, Piacentini J. Evidence-based assessment of child obsessive compulsive disorder: Recommendations for clinical practice and treatment research. *Child Youth Care Forum* 2010;39:73-89.
53. Lewin AB, Bergman RL, Peris TS, Chang S, McCracken JT, Piacentini J. Correlates of insight among youth with obsessive-compulsive disorder. *J Child Psychology Psychiatry* 2010;51:603-611.
54. Lewin AB, Caporino N, Murphy TK, Geffken GR, Storch EA. Understudied clinical dimensions in pediatric obsessive compulsive disorder. *Child Psychiatry Hum Dev* 2010 ;41:675-691.
55. Storch EA, Milsom VA, Merlo LJ, Larson M, Geffken GR, Jacob ML, et al. Insight in pediatric obsessive-compulsive disorder: associations with clinical presentation. *Psychiatry Res* 2008;160:212-220.
56. Freeman JB, Garcia AM, Coyne L, Ale C, Przeworski A, Himle M, et al. Early childhood OCD: Preliminary findings from a family-based cognitive-behavioral approach. *J Am Acad Child Adolesc Psychiatry* 2008;47:593-602.
57. Storch EA, Geffken GR, Merlo LJ, Mann G, Duke D, Munson M, et al. Family-based cognitive-behavioral therapy for pediatric obsessive-compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 2007;46:469-478.
58. Merlo LJ, Lehmkuhl HD, Geffken GR, Storch EA. Decreased family accommodation associated with improved therapy outcome in pediatric obsessive-compulsive disorder. *J Consult Clinical Psychology* 2009;77:355-360.
59. Rapee RM. The influence of comorbidity on treatment outcome for children and adolescents with anxiety disorders. *Behav Res Ther* 2003;41:105-112.
60. Steketee G. Effects of axis I and II comorbidity on behavior therapy outcome for obsessive-compulsive disorder and agoraphobia. *Compr Psychiat* 2001;42:76-86.
61. Storch EA, Merlo LJ, Larson MJ, Geffken GR, Lehmkuhl HD, Jacob ML, et al. Impact of comorbidity on cognitive-behavioral therapy response in pediatric obsessive-compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 2008;47:583-592.
62. Geller DA, Biederman J, Griffin S, Jones J, Lefkowitz TR. Comorbidity of juvenile obsessive-compulsive disorder with disruptive behavior disorders. *J Acad Child Adolesc Psychiatry* 1996;35:1637-1646.
63. Storch EA, Lewin AB, Geffken GR, Morgan JR, Murphy TK. The role of comorbid disruptive behavior in the clinical expression of pediatric obsessive-compulsive disorder. *Behav Res Ther* 2010; 48: 1204-1210.
64. Storch EA, Jones A, Lewin AB, Mutch J, Murphy TK. Rage and obsessive-compulsive disorder. *Minerva Psichiatrica* 2011;52:89-95.
65. Geller D, Biederman J, Jones J, Park K, Schwartz S, Shapiro S, et al. Is juvenile obsessive-compulsive disorder a developmental subtype of the disorder? A review of the pediatric literature. *J Acad Child Adolesc Psychiatry* 1998;37:420-427.
66. Geller DA, Biederman J, Faraone S, Agranat A, Cradock K, Hagermoser L, et al. Developmental aspects of obsessive compulsive disorder: findings in children, adolescents, and adults. *J Nervous Mental Disease* 2001;189:471-477.
67. March JS, Franklin ME, Leonard H, Garcia A, Moore P, Freeman J, et al. Tics moderate treatment outcome with sertraline but not cognitive-behavior therapy in pediatric obsessive-compulsive disorder. *Biol Psychiatry* 2007;61:344-347.
68. Leckman JF, Grice DE, Barr LC, de Vries AL, Martin C, Cohen DJ, et al. Tic-related vs. non-tic-related obsessive compulsive disorder. *Anxiety* 1994;1:208-215.
69. Goodman WK, Storch EA, Geffken GR, Murphy TK. Obsessive-compulsive disorder in Tourette syndrome. *J Child Neurology* 2006;21:704-714.
70. Himle JA, Fischer DJ, Van Etten ML, Janeck AS, Hanna GL. Group behavioral therapy for adolescents with tic-related and non-tic-related obsessive-compulsive disorder. *Depress Anxiety* 2003;17:73-77.
71. Abramowitz JS. Treatment of obsessive-compulsive disorder in patients who have comorbid major depression. *J Clin Psychol* 2004;60:1133-1141.
72. Olley A, Malhi G, Sachdev P. Memory and executive functioning in obsessive-compulsive disorder: A selective review. *J Affective Dis* 2007;104:15-23.
73. Storch EA, Bjorgvinsson T, Riemann B, Lewin AB, Morales MJ, Murphy TK. Factors associated with poor response in cognitive-behavioral therapy for pediatric obsessive-compulsive disorder. *Bulletin of the Menninger Clinic* 2010;74:167-185.
74. Murphy TK, Bengtson MA, Soto O, Edge PJ, Sajid MW, Shapira N, et al. Case series on the use of aripiprazole for Tourette syndrome. *Int J Neuropsychoph* 2005;8:489-490.
75. Foa EB, Steketee G. Behavioral treatment of phobics and obsessive-compulsives. In: Jacobson NS, editor. *Psychotherapists in clinical practice: Cognitive and behavioral perspectives*. New York: Guilford, 1987: pp. 78-120.
76. Abramowitz MZ, Greenberg D, Levav I. Editorial: Treatment gap in mental health care. *Isr J Psychiatry Relat Sci* 2008;45:80-82.
77. Lev-Ran S. Points to ponder regarding contemporary psychiatric training in Israel. *Isr J Psychiatry Relat Sci* 2007;44:187-193.
78. Freeman JB, Choate-Summers ML, Garcia AM, Moore PS, Sapyta JJ, Khanna MS, et al. The Pediatric Obsessive-Compulsive Disorder Treatment Study II: Rationale, design and methods. *Child Adolesc Psychiatry Mental Health* 2009;3:4.
79. Lewin AB, Storch EA, Adkins J, Murphy TK, Geffken GR. Intensive cognitive behavioral therapy for pediatric obsessive compulsive disorder: A treatment protocol for mental health providers. *Psychol Serv* 2005;2:91-104.
80. Abramowitz JS, Foa EB, Franklin ME. Exposure and ritual prevention for obsessive-compulsive disorder: effects of intensive versus twice-weekly sessions. *J Consult Clin Psychol* 2003;71:394-398.
81. Bjorgvinsson TP, Wetterneck CTP, Powell DMP, Chasson GSM, Webb SAP, Hart JM, et al. Treatment outcome for adolescent obsessive-compulsive disorder in a specialized hospital setting. *J Psychiatric Practice* 2008;14:137-145.
82. Wilhelm S, Buhlmann U, Tolin DF, Meunier SA, Pearson GD, Reese HE, et al. Augmentation of behavior therapy with D-cycloserine for obsessive-compulsive disorder. *Am J Psychiatry* 2008;165:335-341; quiz 409.
83. Kushner MG, Kim SW, Donahue C, Thuras P, Adson D, Kotlyar M, et al. D-cycloserine augmented exposure therapy for obsessive-compulsive disorder. *Biol Psychiatry* 2007;62:835-838.
84. Storch EA, Murphy TK, Goodman WK, Geffken GR, Lewin AB, Henin A, et al. A preliminary study of D-cycloserine augmentation of cognitive-behavioral therapy in pediatric obsessive-compulsive disorder. *Biol Psychiatry* 2010; 68: 1073-1076.
85. Krebs G, Heyman I. Treatment-resistant obsessive-compulsive disorder in young people: Assessment and treatment strategies. *Child Adolesc Mental Health* 2010;15:2-11.
86. Storch EA, Lehmkuhl H, Geffken GR, Touchton A, Murphy TK. Aripiprazole augmentation of incomplete treatment response in an adolescent male with obsessive-compulsive disorder. *Depress Anxiety* 2008;25:172-174.
87. Masi G, Pfanner C, Millepiedi S, Berloff S. Aripiprazole augmentation in 39 adolescents with medication-resistant obsessive-compulsive disorder. *J Clinical Psychopharmacology* 2010;30:688-693.
88. Storch EA, Caporino N, Morgan JR, Lewin AB, Rojas A, Brauer L, et al. Preliminary efficacy of web-camera delivered cognitive-behavioral therapy for youth with obsessive-compulsive disorder. *Psychiatry Res* 2011; 189:407-412.