ORIGINAL PAPER

Does D-Cycloserine Augmentation of CBT Improve Therapeutic Homework Compliance for Pediatric Obsessive–Compulsive Disorder?

Jennifer M. Park · Brent J. Small · Daniel A. Geller · Tanya K. Murphy · Adam B. Lewin · Eric A. Storch

© Springer Science+Business Media New York 2013

Abstract Clinical studies in adults and children with obsessive-compulsive disorder (OCD) have shown that D-cycloserine (DCS) can improve treatment response by enhancing fear extinction learning during exposure-based psychotherapy. Some have hypothesized that improved treatment response is a function of increased compliance and engagement in therapeutic homework tasks, a core component of behavioral treatment. The present study examined the relationship between DCS augmented cognitive-behavioral therapy (CBT) and homework compliance in a double-blind, placebo controlled trial with 30 vouth with OCD. All children received 10 CBT sessions, the last seven of which included exposure and response prevention paired with DCS or placebo dosed 1 h before the session started. Results suggested that DCS augmented CBT did not predict improved homework compliance over the course of treatment, relative to the placebo augmented CBT group. However, when groups were collapsed, homework compliance was directly associated with treatment outcome. These findings suggest that while DCS may

J. M. Park (🖂)

Department of Psychology, University of South Florida, 4202 E Fowler Ave, PCD 4118G, Tampa, FL 33611, USA e-mail: jmpark@mail.usf.edu

B. J. Small School of Aging Studies, University of South Florida, Tampa, FL, USA

D. A. Geller Department of Pediatric Psychopharmacology, Massachusetts General Hospital, Boston, MA, USA

T. K. Murphy \cdot A. B. Lewin \cdot E. A. Storch Departments of Pediatrics and Psychiatry, University of South Florida, St Petersburg, FL, USA not increase homework compliance over time, more generally, homework compliance is an integral part of pediatric OCD treatment outcome.

Keywords Obsessive–compulsive disorder · D-Cycloserine · Exposure and response prevention · Homework compliance · Children

Introduction

Obsessive–compulsive disorder (OCD) is a chronic and disabling neuropsychiatric disorder that is characterized by the presence of recurrent, distressing, and disabling obsessions and/or compulsions (American Psychiatric Association 2000). Obsessive–compulsive disorder tends to have its onset during childhood or adolescence (Berg et al. 1989), has a lifetime prevalence of 1–2 % (Douglass et al. 1995; Zohar 1999), and is associated with marked impairments in psychosocial, academic, and family functioning (Lack et al. 2009; Piacentini et al. 2003). Additionally, pediatric OCD is often accompanied by comorbid conditions including tic, anxiety, mood and behavioral disorders, which may further complicate course of illness and treatment (Geller et al. 1998, 2000; Storch et al. 2008).

Two modalities of treatment, cognitive behavioral therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs), have demonstrated efficacy for the treatment of pediatric OCD in a number of randomized-controlled trials (RCTs; e.g., Abramowitz et al. 2005; Barrett et al. 2004; Storch et al. 2007a, b; POTS 2004). A current meta-analysis of RCTs of SSRIs and CBT for pediatric OCD found that both treatment modalities were efficacious (Watson and Rees 2008) with the effect size for CBT (d = 1.45) somewhat larger than for SSRIs (d = 0.48). Based on this

literature, practice parameters suggest the use of CBT alone for mild and moderate cases, and multimodal treatment for severe cases or those who fail to respond to behavioral intervention (AACAP 2012).

A critical component of CBT for OCD is exposure and response prevention (E/RP). In E/RP sessions, fear extinction is facilitated through systematic and repeated exposures to feared stimuli in the absence of compulsion engagement. According to learning theory, extinction refers to breaking the contingency between behavior and consequences for that behavior. In fear learning, extinction involves breaking the relationship between the feared situation and perceived consequence, perhaps via the formation of new associations that compete with the original aversive associations (e.g., Davis et al. 2000; Falls and Davis 1995). Despite the efficacy of CBT with E/RP, exposure exercises are anxiety provoking and time intensive; some patients consider E/RP to be aversive and refuse to participate in treatment and/or eventually drop out of treatment (Schruers et al. 2005; Storch et al. 2007a, b). Therefore, the success of CBT relies heavily on the individual's willingness to engage in the exposures both during and outside of sessions.

To address the need for improved treatment outcome and patient refusal and dropout during treatment, attention has been given to augmenting CBT with D-cycloserine (DCS) as an adjunctive medication that is believed to facilitate fear extinction during exposures (e.g., Abramowitz and Deacon 2010; Abramowits et al. 2009; Hofmann et al. 2006; Norberg et al. 2008). D-Cycloserine is a partial agonist that acts on the strychnine-insensitive glycine-recognition site of the *N*-methyl-D-aspartate (NMDA) glutamatergic receptor complex. NMDA antagonists are known to block fear extinction learning; conversely, NMDA agonists have enhanced fear extinction learning in both animals and adults (e.g., Guastella et al. 2008; Hofmann et al. 2006; Ledgerwood et al. 2003; Walker et al. 2002).

Several studies have supported DCS augmentation of exposure-based psychotherapy with a putative mechanism of enhancing fear extinction learning during exposure sessions for adults with acrophobia (Ressler et al. 2004), social phobia (Guastella et al. 2008; Hofmann et al. 2006) and panic disorder (Otto et al. 2010). There are three published studies regarding DCS augmented E/RP in adult OCD (Kushner et al. 2007; Storch et al. 2007c; Wilhelm et al. 2008) and one in pediatric OCD (Storch et al. 2010a, b). All studies were randomized, double-blind, and placebo-controlled. Kushner et al. (2007) found that those who received 125 mg of DCS 2 h before E/RP had significantly lower levels of obsession-related distress after 4 E/RP sessions relative to those who received placebo. The DCS + E/RP group reached a decrease of more than 50 %reduction of subjective units of distress scale two sessions more quickly than those in the placebo group. Wilhelm et al. (2008) found that those who received 100 mg of DCS 1 h prior to each E/RP session had significantly lower OCD severity scores than the placebo group (Cohen's d = 0.63) after five exposure sessions relative to those in the placebo group, suggesting that DCS significantly increased the pace of symptom reduction in those with OCD (Chasson et al. 2010). Storch et al. (2007a, b, c) (n = 24) did not find significant differences in OCD severity at post-treatment or follow up between the DCS + E/RP and placebo + E/RP group. Both groups improved significantly from pre- to post-treatment. Null findings were likely due to methodological differences as patients were administered 250 mg of DCS 4 h prior to 12 E/RP sessions versus 1–2 h at smaller doses for fewer E/RP sessions in past studies.

Currently, there is only one published study on the effect of DCS as an adjunct to CBT in children with OCD. Storch et al. (2010a, b) conducted a pilot randomized, doubleblind, placebo-controlled DCS + E/RP treatment trial on 30 children and adolescents (ages 8-17 years) with a primary diagnosis of OCD. Both the placebo + E/RP and DCS + E/RP groups improved significantly from pre- to post-treatment. At post-treatment, significant differences and large effect sizes were found on the Clinical Global Impressions-Severity scale (CGI-Severity; National Institute of Mental Health 1985), which is a measure of global functioning severity, between the DCS + E/RP and placebo + E/RP groups (p < 0.05, Cohen's d = 0.91).Additionally, at post-treatment, differences between the two groups approached significance (p = 0.08) and produced moderate effect sizes (Cohen's d = 0.67) on the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS; Scahill et al. 1997), favoring the DCS + ERP group. Group by time interactions produced small to moderate effect sizes in favor of the DCS + E/RP group on the CY-BOCS (Cohen's d = 0.31) and CGI-Severity (Cohen's d = 0.47), indicating that DCS + E/RP may positively enhance E/RP in children with OCD.

Increasing evidence supports DCS as an adjunct for exposure sessions in CBT. Improved treatment response may be hypothesized to be a function of increased compliance and engagement in therapeutic homework tasks. This may be because as DCS facilitates fear extinction during exposure sessions, the enhanced associative learning makes practicing exposures independently outside of session less aversive and easier to complete, which in turn is associated with compounded extinction learning and generalization of gains. To date, however, there is no information regarding the relationship between DCS and homework compliance. From a clinical standpoint, homework assignments are considered an integral component of CBT, regardless of diagnosis, to achieve a meaningful outcome (e.g., Abramowitz et al. 2002; Shelton and Levy

1979). Practicing exposures outside of session is critical as repeated exposures to feared stimuli lead towards habituation; in other words, the more that an exposure is practiced, the more quickly the patient will habituate to the anxiety-provoking situation. Additionally, practicing E/RP tasks outside of session often result in generalization, where patients experience decreased anxiety when confronted with previously anxiety-provoking tasks, due to prior success with E/RP and habituation. Given this, E/RP sessions typically end with assigning the patient homework based on session content that lasts up to 60 min per day. Between sessions, individuals are instructed to practice E/RP tasks and cognitive strategies used during therapy up to 60 min a day to enhance generalization. As each session builds upon the exposures that were practiced between sessions, lack of adherence to homework tasks can impede treatment progress.

A number of studies have examined the role of psychotherapeutic homework compliance among varied adult anxiety disorders, outside the context of DCS augmentation. The adult anxiety literature on the association between homework compliance and treatment outcome has produced inconsistent results, as some trials show strong associations between homework compliance and treatment outcome (Edelman and Chambless 1993; Schmidt et al. 2000) while others show a weak relationship (Leung and Heimberg 1996; Woody and Adessky 2002). The only published study to examine the relationship between homework compliance and treatment outcome in anxious children and adolescents found no significant association between the two constructs (Hughes and Kendall 2007).

There is limited empirical research specifically examining homework compliance and treatment outcome in OCD (Abramowitz et al. 2002; De Araujo et al. 1996; Lax et al. 1992; O'Sullivan et al. 1991; Simpson et al. 2011). Amongst adult OCD studies, O'Sullivan et al. (1991) found that treatment compliance significantly predicted treatment outcome at 6-year follow up. Abramowitz et al. (2002) reported similar results where general CBT compliance (which comprised of understanding of treatment rationale, in-session compliance and homework compliance) was associated with treatment response. De Araujo et al. (1996) identified homework compliance during the first week of treatment to be the best predictor of treatment outcome. Most recently, Simpson et al. (2011) found that homework compliance, as well as early homework adherence (sessions 5-9) significantly predicted lower OCD severity at post-treatment. In contrast, Lax et al. (1992) found no relationship between E/RP treatment compliance and treatment outcome; however, these results may be due to lack of variance within the sample, as the group had generally high rates of compliance throughout homework compliance throughout treatment was associated with higher post-treatment anxiety symptoms in individuals with OCD or panic disorder with agoraphobia. On balance, this effect was small and although there was a considerable amount of variance in the homework compliance, in general homework compliance was low. Thus, it is possible that if overall homework compliance in the sample were higher, the effect may not have been produced. Overall, the OCD literature suggests that homework compliance is an important aspect of treatment outcome; however, this has not yet been examined in the pediatric OCD population. In the context of E/RP augmented with DCS, the effect

the study. Woods et al. (2002) reported that higher

of DCS on homework compliance is unknown. D-Cycloserine may contribute to improved homework adherence due to the enhanced facilitation of extinction learning during the therapy sessions. Previously mentioned studies have shown that DCS administration is associated with improved treatment outcomes (e.g., Storch et al. 2010b; Wilhelm et al. 2008), which theoretically may make individuals more likely to engage in CBT homework between sessions. Should this relationship exist, it may provide an added mechanism to explain how DCS translates into improved treatment outcome. With this in mind, the primary aim of this study is to examine whether DCS combined with E/RP would be related to improved homework compliance relative to placebo augmentation of E/RP in pediatric OCD. It is hypothesized that the DCS combined with E/RP group will be associated with greater homework compliance ratings than the placebo arm. We also examined the extent to which baseline clinical variables, such as OCD severity, internalizing symptoms, externalizing symptoms, and depressive symptoms, predicted homework compliance across the sample.

Method

Participants

Youth participated in an NIH-funded study examining DCS augmentation of CBT in children and adolescents with OCD (Storch et al. 2010b). Data were collected at two study sites: the outpatient psychiatric clinics at University of Florida (n = 20) and Massachusetts General Hospital (n = 10). Participants were included in the study if they had a primary diagnosis of OCD, a Children's Yale-Brown Obsessive–Compulsive Scale (CY-BOCS) ≥ 16 (Scahill et al. 1997), no comorbid bipolar disorder, psychotic disorder, mental retardation, autism spectrum disorder, or substance abuse/dependence. Participants were also included if they were English speaking and stable on

psychotropic medication for at least 12 weeks (if applicable). Participants with only hoarding symptoms were excluded. Epilepsy, renal insufficiency, pregnancy or generally poor physical health was also exclusionary.

Procedures

All research procedures were reviewed and approved by the corresponding institutional review boards, and all parents and children provided written informed consent and assent prior to involvement in the treatment protocol. An OCD diagnosis was ascertained before treatment through a clinical evaluation with an experienced psychiatrist or psychologist and confirmed through the Anxiety Disorders Interview Schedule for DSM-IV for Children: Parent Version (ADIS-P; Silverman and Albano 1996) by a trained independent evaluator. The same independent evaluator administered the baseline, mid- and post-treatment CY-BOCS ratings thereafter. The Child Behavior Checklist (CBCL; Achenbach 1994) and Child Depression Inventory-Short Form (CDI-SF; Kovacs 1992) were completed at baseline and post-treatment by the parent and child respectively. Parent reports were collected from the primary caretaking parent. Patients received ten weekly 60-minute treatment sessions. At the beginning of each session, therapists reviewed homework from the past week with the patient and completed the homework compliance rating scale.

Physical examinations and laboratory tests (e.g., urine pregnancy and toxicology tests, blood count) were administered at screening. Participants were then randomized via computer, and clinicians, raters, and patients were blinded to medication status. D-Cycloserine/placebo administrations were given by a research coordinator 1 h prior to sessions 4 through 10. Dosing was based according to weight; children who weighed between 25-45 kg were given 25 mg of DCS or placebo and children weighing \geq 45 were given 50 mg of DCS or placebo (2 capsules were administered). Dosages used were derived from findings from previous adult studies that indicated that approximately 0.7 mg/kg was the most effective (Hofmann et al. 2006; Otto et al. 2010; Ressler et al. 2004; Wilhelm et al. 2008). Time of dosing was determined based off of previous studies, which noted that with a 10-h half life, 50 mg of DCS is estimated to reach peak cerebrospinal fluid levels within 1-2 h of administration (Hofmann et al. 2006; Nair et al.1956; Ressler et al. 2004). Prior studies have also suggested that the intended of effects of DCS on fear extinction is seen only when administered in acute, isolated doses, as opposed to daily chronic doses (Davis et al. 2005; Parnas et al. 2005; Ressler et al. 2004; Quartermain et al. 1994); therefore DCS was administered on a weekly, rather than a daily basis.

Measures

Anxiety Disorders Interview Schedule for DSM-IV–Parent Version (ADIS-/P)

The ADIS-P (Silverman and Albano 1996) assesses current episodes of Axis I disorders and provides differential diagnosis based on DSM-IV-TR criteria (American Psychiatric Association 2000). The ADIS-C/P has consistently demonstrated strong psychometric properties, including test–retest reliability, inter-rater reliability, and concurrent validity (Silverman and Albano 1996; Silverman et al. 2001; Wood et al. 2002). This measure was completed at screening, before baseline.

Children's Yale-Brown Obsessive–Compulsive Scale (CY-BOCS)

The CY-BOCS (Scahill et al. 1997) is a 10-item semistructured clinician-administered measure of current obsession and compulsion severity. The CY-BOCS has demonstrated good psychometric properties (e.g. inter-rater reliability, internal consistency, test-retest reliability, discriminant validity, convergent validity; (Scahill et al. 1997; Storch et al. 2004).

Child Behavior Checklist (CBCL)

The CBCL (Achenbach 1994) is a widely used parent-rated questionnaire that assesses the intensity and frequency of behavioral and emotional problems exhibited by children within the past 6 months. Composite scores for externalizing (e.g., inattentiveness, aggression) and internalizing (e.g. anxiety, depression) symptoms are provided by this measure. The CBCL has exhibited good reliability, internal consistency and discriminant validity.

Children's Depression Inventory-Short Form (CDI-SF)

The CDI-SF (Kovacs 1992) is a 10-item self-report form that assesses the presence of depressive symptoms within the past 2 weeks. Responses range from not present (0) to severe (3). The CDI-SF is based on the full 27-item version and has demonstrated good internal consistency and is strongly correlated with the full version (r = 0.89).

Clinical Global Impressions–Severity (CGI-Severity)

The CGI-Severity (National Institute of Mental Health 1985) is a clinician-rated scale of global OCD severity rated on a 7-point Likert scale from 0 (no illness) to 6 (extremely severe). The CGI-Severity has been widely

used in treatment studies and has demonstrated sound psychometric properties including convergent validity with the CY-BOCS and treatment sensitivity (Storch et al. 2007a, b; Storch et al. 2010a).

Homework Compliance

Homework compliance was assessed weekly by therapists at sessions 2-10 to measure the quantity and quality of homework compliance. Homework compliance ratings were obtained during the session following the homework assignment in question and were based on parent and child's report of the extent to which the assignment was completed. Clinicians asked general prompts regarding homework compliance (i.e., how did your homework go this week?) at the beginning of each session and could ask follow-up questions as needed. Ratings were determined based on the difficulty of exposures completed, amount of habituation experienced during the exposure, the deliberateness of the exposure (accidental exposures to feared stimuli was not considered when completing the homework compliance rating), and the clinician's judgment. The rating scale was based on a 7-point Likert scale ranging from 0 ("did not complete any assigned homework") to 6 ("completed all homework and made efforts above and beyond assignments"). The homework compliance ratings are modeled off the CGI-Severity scores; ratings for the homework compliance have similar anchors and scoring processes as the CGI-Severity, providing face validity for the homework compliance ratings.

Statistical Analysis

To examine whether group assignment (DCS or placebo) would be related to changes in homework compliance, a random effects model was employed (Littell et al. 2006; Singer and Willett 2003). The model included a within subjects effect of time, a between subjects effect of treatment group and a treatment group \times time interaction. The presence of a statistically significant interaction would indicate suggest that changes in homework compliance varied as a function of treatment group. Power analyses demonstrated that given a sample of N = 30, we will have a power of .80 to detect 'medium' sized (f = 0.18) interaction effects.

To examine whether internalizing symptoms (CBCL), externalizing symptoms (CBCL), depressive symptoms (CDI-SF) and baseline OCD symptom severity (CY-BOCS) were predictors of homework compliance, four linear regression analyses were conducted. Similar to the mediation analyses above, homework compliance scores were averaged across all time points.

Results

Sample Characteristics

The sample consisted of 30 youth outpatients (37 % female) diagnosed with primary OCD. Fifteen participants (50 %) were randomized into the DCS condition, while the remaining 15 received placebo. Ages of participants ranged from 8 to 17 years (M = 12.2, SD = 2.8 years). In terms of race and ethnicity, 97 % were Caucasian (N = 29), 3 % were Hispanic (N = 1). Twenty-two participants (73 %) had one or more comorbid disorder and 15 participants (50 %) were on concomitant psychotropic medication.

Relationship Between Group Assignment and Homework Compliance Over Time

Homework compliance was moderately and significantly correlated with the post-treatment CGI-Severity (r = -0.67) and the post-treatment CY-BOCS total score (r = -0.65). The mean homework compliance score at the first E/RP session (session 4) was 4.68 (SD = 0.82) for the DCS group, and 4.02 (SD = 0.90) for the placebo group (see Table 1 for homework compliance means and SD for sessions 4–10). A significant main effect for group (Est = -1.02; SE = 0.37; p = 0.008) was identified, with the placebo group scoring approximately one point lower than the DCS group at the first E/RP session. The main effects of time (Est. = -0.07, SE = 0.13, p = 0.57) and the group x time interaction (Est = 0.06; SE = 0.08; p = 0.49) were not statistically significant.

The next set of analyses examined changes in CY-BOCS scores as a function of homework compliance ratings. The mean CY-BOCS score across groups at baseline was 25.1 (SD = 4.16). A statistically significant homework compliance x time interaction (Est = -1.54, SE = 0.54, p = 0.006) was identified and indicated that as mean

Table 1 Mean scores and (SD) on homework compliance

	()	1
Sessions	DCS $(n = 15)$	Placebo $(n = 15)$
4	4.68 (0.82)	4.02 (0.90)
5	4.33 (1.8)	3.67 (1.23)
6	5.07 (1.1)	3.80 (1.32)
7	4.80 (1.15)	3.93 (1.03)
8	4.60 (1.24)	3.87 (1.56)
9	5.00 (0.47)	3.67 (1.35)
10	4.40 (1.17)	4.21 (1.42)

DCS D-cycloserine

Homework compliance scores range from 0 (did not complete any assigned homework) to 6 (completed all homework and made efforts above and beyond assignments)

homework compliance increased by one point, CY-BOCS scores decreased 1.54 points for each assessed time point. The main effects of group (Est = -0.46, SE = 1.25, p = 0.72) and time (Est = -1.38, SE = 2.39, p = 0.57) were not significant.

Predictors of Homework Compliance

Externalizing symptoms significantly and inversely predicted homework compliance (b = -0.36, t(29) = -2.05, $p \le 0.05$), while baseline OCD severity approached significance (b = -0.35, t(29) = -1.99, p = 0.06). Internalizing and depressive symptoms did not predict homework compliance (b = -0.07, t(29) = -0.36, p = 0.72; b = -0.14, t(29) = -0.75, p = 0.46).

Discussion

The present study examined the relationship between DCS group status and homework compliance. Results revealed that DCS group status was not associated with improved homework compliance over the course of treatment. Rather, homework compliance was statistically higher for the DCS group at the point of randomization and these differences persisted across treatment. These findings may perhaps be because the DCS group had slightly less severe, albeit not significant, baseline OCD severity than the placebo group. Overall, the results suggest that DCS group status does not impact homework compliance; therefore, the mechanism in which DCS improves treatment outcome may occur primarily through augmented fear extinction during within session exposures.

Consistent with previous adult OCD research (Abramowitz et al. 2002; De Araujo et al. 1996; Simpson et al. 2011), homework compliance inversely predicted posttreatment OCD severity when the sample was collapsed. That is, the more the child engaged in homework exposures (e.g., exposures that lead to habituation), the more the child was rated to have improved at both mid- and post-treatment time points. Additionally, homework compliance at randomization predicted later compliance, suggesting that those who were doing the E/RP homework initially, continued to do so throughout the treatment. Taken together, these findings suggest that good homework compliance is essential for treatment success and that initial levels of compliance provide a good indicator of the degree of homework compliance to be expected throughout treatment.

Because the quality and quantity of homework compliance does not tend to change over time, it is important that patients and their families exhibit good homework compliance from the beginning of treatment. Clinicians should emphasize the importance of homework compliance early on, discuss the nature of homework (e.g., what homework will consist of), agree upon homework exposures and goals, explain implementation of exposures, and stress the necessity of frequent exposure exercises between sessions. Even though homework compliance is unlikely to change over time (i.e., those who were non compliant with homework at early sessions, were likely to be non compliant with homework at later sessions), homework compliance should be assessed at every session as more challenging exposures may be associated with differential compliance. As treatment expectancies (i.e., the individual's expectancy that he/she will benefit from the treatment) are associated with early homework compliance (Lewin et al. 2011), active efforts should also be made to increase treatment expectation. Expectations can be improved via proper psychoeducation (e.g., the therapist successfully relays the message to the patient that he/she should expect to benefit from the treatment; Bednar 1970) or with the individual's successful engagement and experience with therapeutic skills learned in session (Newman and Fisher 2010). These data also speak to the role of motivation in exposure-based CBT; those who are more motivated during therapy may be more engaged and compliant during exposure sessions and while completing homework tasks, while those who were less motivated may exert substantially less effort throughout treatment. As motivation is a predictor of treatment response (Vogel et al. 2006), assessing the patient's motivation during the first few sessions can provide important information regarding treatment prognosis. When issues regarding motivation and treatment compliance are noted, clinicians should intervene promptly. Motivational interviewing strategies such as decisional balancing (i.e., weighing out the good and less good aspects of their behavior to promote change) and eliciting change talk (i.e., having the patient come up with ways their lives will change if the behavior changes) can be included in sessions where individuals show low motivation or poor homework compliance at treatment onset, so as to address these issues directly and early on (Merlo et al. 2010; Simpson et al. 2008).

Regarding clinical predictors of homework compliance, externalizing symptoms and increased baseline OCD severity were negatively associated with homework compliance but depressive and internalizing symptoms were not. Children with increased externalizing symptoms may resist completing exposures for homework by refusing to comply with homework or not completing exposures to habituation. Additionally, parents with children exhibiting externalizing symptoms may engage in family accommodation (i.e., modify activities due to child's obsessive– compulsive symptoms, participate in child's rituals), to avoid temper tantrums or arguments (Storch et al. 2007a, b). This may explain why those with comorbid disruptive behavior disorders show attenuated treatment outcome (Storch et al. 2008). Regarding baseline OCD severity, those with more severe obsessive–compulsive symptoms may find exposures too challenging or anxiety provoking and thus may not be able to complete homework exposures properly. In such cases, a sequential treatment approach involving pharmacotherapy prior to CBT may reduce baseline levels of distress to facilitate E/RP treatment engagement.

This study is the first to examine the relationship between DCS and homework compliance and also adds to the literature on homework compliance in pediatric anxiety disorders. However, this study has several limitations that warrant comment. First, the sample size is modest and may not be generalizable to the pediatric OCD population; therefore, replication of this study in a larger sample is required. Second, although therapists carefully assessed homework compliance at the beginning of each session using all available information and their judgment, a oneitem measure of homework compliance may not have captured all the nuances of homework compliance. Therefore, ratings may have been constrained by the nature in which the questions were asked, making homework compliance ratings susceptible to floor and ceiling effects and difficult to measure any potential for change. Additionally, as the two groups were participating in a treatment study, motivation may have been high, which may have also resulted in ceiling effects in homework compliance ratings. On balance, the homework compliance measure was significantly negatively correlated with the CY-BOCS and CGI-Severity post-treatment scores, indicating that greater homework compliance was associated with decreased OCD symptoms and global severity. Third, there was no independent verification of homework compliance. A clinical synthesis of all available information was utilized to determine the level of homework compliance; however, while reporting homework compliance, the parent and/or child may have felt susceptible to demand characteristics and presented a more favorable representation of homework completion. Additionally, homework compliance ratings were not checked for inter-rater reliability. Thus, it may be possible that therapists did not rate homework compliance in a standardized manner. Finally, other salient variables that may have affected the levels of homework compliance and/or improvements in OCD severity throughout treatment, such as motivation or insight, were not assessed in the present study.

Overall, this study provides important information for the anxiety homework compliance literature. First, homework compliance is an important component of E/RP for children and adolescents with OCD as increased homework compliance predicts better treatment outcome. Second, obtaining homework compliance early on in treatment is essential as homework compliance may be unlikely to change over time and provides the clinician with data about the degree of homework compliance to expect throughout the treatment course. On balance, homework compliance should be thoroughly assessed throughout treatment (e.g., gather daily ratings of compliance from parents and children) and reasons and barriers for homework non-compliance (e.g., time constraints, fear of completing exposures, misunderstanding homework assignments) should be promptly investigated and addressed. Finally, due to the importance of early homework compliance in treatment outcome, future research should confirm our findings involving externalizing symptoms and baseline OCD severity, and examine other possible predictors of decreased homework compliance (e.g., motivation, insight, age, family factors, etc.). Such information will foster the development of interventional approaches to target these variables so to increase homework compliance prior to the start of treatment.

Acknowledgments This work was supported by grants to the last author from the National Institutes of Health (MH076775; L40 MH081950-02) and National Alliance for Research on Schizophrenia and Affective Disorders (Robidoux Foundation Young Investigator Award). The authors would like to acknowledge the contributions of the following individuals: Michael Bengtson, M.D., Alex De Nadai, Alyssa Faro, Gary Geffken, Ph.D., Wayne K. Goodman, M.D., Aude Henin, Ph.D., Marni Jacob, Mark Lewis, Ph.D., Elizabeth Mancuso, Jamie Micco, Ph.D., Emily Ricketts, Susan Sprich, Ph.D., Sabine Wilhelm, Ph.D., and Mark Yang, Ph.D.

References

- Abramowits, J. S., Taylor, S., & McKay, D. (2009). Obsessive– compulsive disorder. *Lancet*, 374, 491–499.
- Abramowitz, J. S., & Deacon, B. (2010). Anxiety and its disorders: Implications for pharmacotherapy. *Clinical Psychology: Science* and Practice, 17, 105–106.
- Abramowitz, J. S., Franklin, M. E., Zoellner, L. A., & DiBernardo, C. L. (2002). Treatment compliance and outcome in obsessive– compulsive disorder. *Behavior Modification*, 26, 447–463.
- Abramowitz, J. S., Whiteside, S. P., & Deacon, B. J. (2005). The effectiveness of treatment for pediatric obsessive–compulsive disorder: A meta-analysis. *Behavior Therapy*, 36, 55–63.
- Achenbach, T. M. (1994). Child behavior checklist and related instruments. In M. E. Marush (Ed.), *The use of psychological testing for treatment planning and outcome* (pp. 517–549). Hillsdale: Lawrence Eribaum Associates, Inc.
- American Academy of Child and Adolescent Psychiatry. (2012). Practice parameter for the assessment and treatment of children and adolescents with obsessive–compulsive disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, 51(1), 98–113. doi:10.1016/j.jaac.2011.09.019.
- American Psychiatric Association. (2000). Diagnostic and statistical manual of mental disorders (DSM-IV-TR). Washington, DC: American Psychiatric Association.
- Barrett, P., Healy-Farrell, L., & March, J. S. (2004). Cognitivebehavioral family treatment of childhood obsessive-compulsive

disorder: A controlled trial. *Journal of the American Academy of Child and Adolescent Psychiatry*, 43, 46–62. doi:10.1097/00004583-200401000-00014.

- Bedner, R. L. (1970). Persuability and the power of belief. Personnel and Guidance Journal, 48, 647–652.
- Berg, C. Z., Rapoport, J. L., Whitaker, A., Davies, M., Leonard, H., Swedo, S. E., et al. (1989). Childhood obsessive–compulsive disorder: A two-year prospective follow-up of a community sample. *Journal of the American Academy of Child and Adolescent Psychiatry*, 28, 528–533. doi:10.1097/00004583-198907000-00010.
- Chasson, G. S., Buhlmann, U., Tolin, D. F., Rao, S. R., Reese, H. E., Rowley, T., et al. (2010). Need for speed: Evaluating slopes of OCD recovery in behavior therapy enhanced with d-cycloserine. *Behaviour Research and Therapy*, 48, 675–679. doi:10.1016/ j.brat.2010.03.007.
- Davis, M., Falls, W. A., & Gewirtz, J. (2000). Neural systems involved in fear inhibition: Extinction and conditioned inhibition. In M. Myslobodsky & I. Weiner (Eds.), *Contemporary issues in modeling psychopathology* (pp. 113–142). Boston: Kluwer Academic.
- Davis, M., Meyers, K. M., Ressler, K. J., & Rothbaum, B. O. (2005). Facilitation of extinction of conditioned fear by D-cycloserine. *Current Directions in Psychological Science*, 14, 214–219.
- De Araujo, L. A., Ito, L. M., & Marks, I. M. (1996). Early compliance and other factors predicting outcome of exposure for obsessive– compulsive disorder. *British Journal of Psychiatry*, 169(6), 747–752.
- Douglass, H. M., Moffitt, T. E., Dar, R., McGee, R., & Silva, P. (1995). Obsessive–compulsive disorder in a birth cohort of 18-year-olds: Prevalence and predictors. *Journal of the American Academy of Child and Adolescent Psychiatry*, 34, 1424–1431. doi:10.1097/ 00004583-199511000-00008.
- Edelman, R. E., & Chambless, D. L. (1993). Compliance during sessions and homework in exposure-based treatment of agoraphobia. *Behaviour Research and Therapy*, 31, 767–773.
- Falls, W. A., & Davis, M. (1995). Behavioral and physiological analysis of fear inhibition. In M. J. Friedman, D. S. Charney, & A. Y. Deutch (Eds.), *Neurological and clinical consequences of stress: From normal adaptation to PTSD* (pp. 177–202). Philadelphia: Lippencott-Raven.
- Geller, D. A., Biederman, J., Faraone, S. V., Frazier, J., Coffey, B. J., Kim, G., et al. (2000). Clinical correlates of obsessive–compulsive disorder in children and adolescents referred to specialized and non-specialized clinical settings. *Depression and Anxiety*, *11*, 163–168. doi:10.1002/1520-6394(2000)11:4<163:AID-DA3 >3.0.CO;2-3.
- Geller, D. A., Biederman, J., Jones, J., Shapiro, S., Schwartz, S., & Park, K. S. (1998). Obsessive–compulsive disorder in children and adolescents: A review. *Harvard Review of Psychiatry*, 5, 260–273.
- Guastella, A. J., Richardson, R., Lovibond, P. F., Rapee, R. M., Gaston, J. E., Mitchell, P., & Dadds, M. R. (2008). A randomized controlled trial of D-cycloserine enhancement of exposure therapy for social anxiety disorder. *Biological Psychiatry*, 63, 544–549. doi:10.1016/j.biopsych.2007.11.011.
- Hofmann, S. G., Meuret, A. E., Smits, J. A., Simon, N. M., Pollack, M. H., Eisenmenger, K., et al. (2006). Augmentation of exposure therapy with D-cycloserine for social anxiety disorder. *Archives of General Psychiatry*, 63, 298–304. doi:10.1001/ archpsyc.63.3.298.
- Hughes, A. A. & Kendall, P. C. (2007). Prediction of cognitive behavior treatment outcome for children with anxiety disorders: Therapeutic relationship and homework compliance. *Behavioural and Cognitive Psychotherapy*, 35, 487–494. doi:10.1017/ S1352465807003761.

- Kovacs, M. (1992). The children's depression inventory (CDI). *Psychopharmacology Bulletin*, 21, 995–998.
- Kushner, M. G., Kim, S. W., Donahue, C., Thuras, P., Adson, D., Kotlyar, M., et al. (2007). D-Cycloserine augmented exposure therapy for obsessive–compulsive disorder. *Biological Psychiatry*, 62(8), 835–838. doi:10.1016/j.biopsych.2006.12.020.
- Lack, C. W., Storch, E. A., Keeley, M. L., Geffken, G. R., Ricketts, E. D., Murphy, T. K., et al. (2009). Quality of life in children and adolescents with obsessive–compulsive disorder: Base rates, parent-child agreement, and clinical correlates. *Social Psychiatry and Psychiatric Epidemiology*, 44, 935–942. doi:10.1007/s00127-009-0013-9.
- Lax, R., Basoglu, M., & Marks, I. M. (1992). Expectancy and compliance as predictors of outcome in obsessive–compulsive disorder. *Behavioral Psychotherapy*, 20, 257–266.
- Ledgerwood, L., Richardson, R., & Cranney, J. (2003). Effects of D-cycloserine on extinction of conditioned freezing. *Behavioral Neuroscience*, 117, 341–349.
- Leung, A. W., & Heimberg, R. G. (1996). Homework compliance, perceptions of control, and outcome of cognitive-behavioral treatment of social phobia. *Behaviour Research and Therapy*, 34, 423–432.
- Lewin, A. L., Peris, T. S., Bergman, L., McCracken, J. T., & Piacentini, J. (2011). The role of treatment expectancy in youth receiving exposure-based CBT for obsessive-compulsive disorder. *Behaviour Research and Therapy*, 49, 536–543. doi: 10.1016/j.brat.2011.06.001.
- Littell, R. C., Milliken, G. A., Stroup, W. W., Wolfinger, R. D., & Schabenberger, O. (2006). SAS for mixed models (2nd ed.). Cary, NC: SAS Press.
- Merlo, L. J., Storch, E. A., Lehmkuhl, H. D., Jacob, M. L., Murphy, T. K., Goodman, W. K., et al. (2010). Cognitive behavioral therapy plus motivational interviewing improves outcome for pediatric obsessive–compulsive disorder: A preliminary study. *Cognitive Behaviour Therapy*, 39, 24–27. doi:10.1080/1650607090 2831773.
- Nair, K. S., Epstein, I. G., Baron, H., & Mulinos, M. G. (1956). Absorption, distribution and excretion of cycloserine in man. *Antibiotics Annals*, 3, 136–140.
- National Institute of Mental Health. (1985). Clinical Global Impressions. *Psychopharmacology Bulletin*, 21, 839–843.
- Newman, M. G., & Fisher, A. J. (2010). Expectancy/credibility change as a mediator for cognitive behavioral therapy for generalized anxiety disorder: Mechanism of action or proxy for symptom change? *International Journal of Cognitive Therapy*, 3, 245–261.
- Norberg, M. M., Krystal, J. H., & Tolin, D. F. (2008). A meta-analysis of d-cyloserine and the facilitation of fear extinction and exposure therapy. *Biological Psychiatry*, 63, 1118–1126.
- O'Sullivan, G., Noshirvani, H., Marks, I., Monteiro, W., & Lelliott, P. (1991). Six-year follow-up after exposure and clomipramine therapy for obsessive–compulsive disorder. *Journal of Clinical Psychiatry*, 52, 150–155.
- Otto, M. W., Tolin, D. F., Simon, N. M., Pearlson, G. D., Basden, S., Meunier, S. A., et al. (2010). Efficacy of d-cycloserine for enhancing response to cognitive-behavior therapy for panic disorder. *Biological Psychiatry*, 67, 365–370. doi:10.1016/j.biopsych.2009.07.036.
- Parnas, A. S., Weber, M., & Richardson, R. (2005). Effects of multiple exposures to D-cycloserine on extinction of conditioned fear in rats. *Neurobiology of Learning and Memory*, 84, 224–231.
- Piacentini, J., Bergman, R. L., Keller, M., & McCracken, J. (2003). Functional impairment in children and adolescents with obsessive–compulsive disorder. *Journal of Child and Adolescent Psychopharmacology*, *13*(Suppl 1), S61–S69. doi:10.1089/ 104454603322126359.

- POTS. (2004). Cognitive-behavior thearpy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder. *Journal of the American Medical Association*, 292, 1969–1976.
- Quartermain, D., Mower, J., Rafferty, M. F., Herting, R. L., & Lanthorn, T. H. (1994). Acute but not chronic activation of the NMDA0coupled glycine receptor with D-cycloserine facilitates learning and retention. *European Journal of Pharmacology*, 157, 7–12.
- Ressler, K. J., Rothbaum, B. O., Tannenbaum, L., Anderson, P., Graap, K., Zimand, E., et al. (2004). Cognitive enhancers as adjuncts to psychotherapy: Use of D-cycloserine in phobic individuals to facilitate extinction of fear. *Archives of General Psychiatry*, 61, 1136–1144. doi:10.1001/archpsyc.61.11.1136.
- Scahill, L., Riddle, M. A., McSwiggin-Hardin, M., Ort, S. I., King, R. A., Goodman, W. K., et al. (1997). Children's Yale-Brown obsessive–compulsive scale: Reliability and validity. *Journal of the American Academy of Child and Adolescent Psychiatry*, 36, 844–852.
- Schmidt, N. B., & Woolaway-Bickel, K. (2000). The effects of treatment compliance on outcome in cognitive-behavioral therapy for panic disorder: Quality versus quantity. *Journal of Consulting and Clinical Psychology*, 68, 13–18.
- Schruers, K., Koning, K., Luermans, J., Haack, M. J., & Griez, E. (2005). Obsessive–compulsive disorder: A critical review of therapeutic perspectives. *Acta Psychiatra Scandinavica*, 111, 261–271. doi:10.1111/j.1600-0447.2004.00502.x.
- Shelton, J. L., & Levy, R. (1979). Home practice activities and compliance: Two sources of error variance in behavioral research. *Journal of Applied Behavior Analysis*, 12, 324.
- Silverman, W. K., & Albano, A. M. (1996). The Anxiety Disorders Interview Schedule for DSM-IV—Child and parent versions. San Antonio: Psychological Corporation.
- Silverman, W. K., Saavedra, L. M., & Pina, A. A. (2001). Test-retest reliability of anxiety symptoms and diagnoses with the Anxiety Disorders Interview Schedule for DSM-IV: Child and parent versions. Journal of the American Academy of Child and Adolescent Psychiatry, 40, 937–944. doi:10.1097/00004583-200108000-00016.
- Simpson, H. B., Maher, M. J., Wang, Y., Bao, Y., Foa, E. B., & Franklin, M. (2011). Patient adherence predicts outcome from cognitive behavioral therapy in obsessive–compulsive disorder. *Journal of Consulting and Clinical Psychology*, 79, 247–252. doi:10.1037/a0022659.
- Simpson, H. B., Zuckoff, A., Page, J. R., Franklin, M. E., & Foa, E. B. (2008). Adding motivatinoal interviewing to exposure and ritual prevention for obsessive–compulsive disorder: An open pilot trial. *Cognitive Behaviour Therapy*, 37, 38–49. doi:10.1080/ 16506070701743252.
- Singer, J. D., & Willett, J. B. (2003). Applied longitudinal data analysis: Modeling change and event occurrence. New York, NY: Oxford University Press.
- Storch, E. A., Geffken, G. R., Merlo, L. J., Jacob, M. L., Murphy, T. K., Goodman, W. K., et al. (2007a). Family accommodation in pediatric obsessive–compulsive disorder. *Journal of Clinical Child and Adolescent Psychology*, *36*, 207–216. doi:10.1080/15374410701277929.
- Storch, E. A., Geffken, G. R., Merlo, L. J., Mann, G., Duke, D., Munson, M., et al. (2007b). Family-based cognitive-behavioral therapy for pediatric obsessive–compulsive disorder: Comparison of intensive and weekly approaches. *Journal of the American Academy of Child and Adolescent Psychiatry*, 46, 469–478. doi:10.1097/chi.0b013e31803062e7.

- Storch, E. A., Lewin, A. B., De Nadai, A. S., & Murphy, T. K. (2010a). Defining treatment response and remission in obsessive-compulsive disorder: A signal detection analysis of the Children's Yale-Brown obsessive-compulsive scale. *Journal of the American Academy of Child and Adolescent Psychiatry*, 49, 708–717. doi:10.1016/j.jaac.2010.04.005.
- Storch, E. A., Merlo, L. J., Bengtson, M., Murphy, T. K., Lewis, M. H., Yang, M. C., et al. (2007c). D-Cycloserine does not enhance exposure-response prevention therapy in obsessive–compulsive disorder. *International Clinical Psychopharmacology*, 22, 230–237. doi:10.1097/YIC.0b013e32819f8480.
- Storch, E. A., Merlo, L. J., Larson, M. J., Geffken, G. R., Lehmkuhl, H. D., Jacob, M. L., et al. (2008). Impact of comorbidity on cognitive-behavioral therapy response in pediatric obsessive– compulsive disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, 47, 583–592. doi:10.1097/CHI. 0b013e31816774b1.
- Storch, E. A., Murphy, T. K., Geffken, G. R., Soto, O., Sajid, M., Allen, P., et al. (2004). Psychometric evaluation of the children's Yale-Brown obsessive–compulsive scale. *Psychiatry Research*, 129, 91–98. doi:10.1016/j.psychres.2004.06.009.
- Storch, E. A., Murphy, T. K., Goodman, W. K., Geffken, G. R., Lewin, A. B., Henin, A., et al. (2010b). A preliminary study of Dcycloserine augmentation of cognitive-behavioral therapy in pediatric obsessive–compulsive disorder. *Biological Psychiatry*, 68, 1073–1076. doi:10.1016/j.biopsych.2010.07.015.
- Vogel, P. A., Hansen, B., Stiles, T. C., & Gotestam, K. G. (2006). Treatment motivation, treatment expectancy, and helping alliance as predictors of outcome in cognitive behavioral treatment of OCD. Journal of Behavior Therapy and Experimental Psychiatry, 37, 247–255. doi:10.1016/j.jbtep.2005.12.001.
- Walker, D. L., Ressler, K. J., Lu, K. T., & Davis, M. (2002). Facilitation of conditioned fear extinction by systemic administration or intra-amygdala infusions of D-cycloserine as assessed with fear-potentiated startle in rats. *Journal of Neuroscience*, 22, 2343–2351.
- Watson, H. J., & Rees, C. S. (2008). Meta-analysis of randomized, controlled treatment trials for pediatric obsessive–compulsive disorder. *Journal of Child Psychology and Psychiatry*, 49, 489–498. doi:10.1111/j.1469-7610.2007.01875.x.
- Wilhelm, S., Buhlmann, U., Tolin, D. F., Meunier, S. A., Pearlson, G. D., & Rauch, S. L. (2008). Augmentation of behavior therapy with D-cycloserine for obsessive–compulsive disorder. *American Journal of Psychiatry*, 165, 335–341. doi:10.1176/appi.ajp.2007. 07050776. quiz 409.
- Wood, J. J., Piacentini, J. C., Bergman, R. L., McCracken, J., & Barrios, V. (2002). Concurrent validity of the anxiety disorders section of the Anxiety Disorders Interview Schedule for DSM-IV: Child and parent versions. *Journal of Clinical Child* and Adolescent Psychology, 31, 335–342.
- Woods, C. M., Chambless, D. L., & Steketee, G. (2002). Homework compliance and behavior therapy outcome for panic with agrophobia and obsessive–compulsive disorder. *Cognitive Behaviour Therapy*, 31, 88–95.
- Woody, S. R., & Adessky, R. S. (2002). Therapeutic alliance, group cohesion, and homework compliance during cognitive-behavioral group treatment of social phobia. *Behavior Therapy*, 33, 5–27.
- Zohar, A. H. (1999). The epidemiology of obsessive-compulsive disorder in children and adolescents. *Child and Adolescent Psychiatric Clinics of North America*, 8, 445–460.