Published in final edited form as:

Depress Anxiety. 2016 March ; 33(3): 229–237. doi:10.1002/da.22468.

Fear Conditioning and Extinction in Youth with Obsessive Compulsive Disorder

Joseph F. McGuire, Ph.D.¹, Scott P. Orr, Ph.D.², Monica S. Wu, M.A.^{3,4}, Adam B. Lewin, Ph.D.^{3,4,5,6}, Brent J. Small, Ph.D.⁷, Vicky Phares, Ph.D.³, Tanya K. Murphy, M.D.^{4,5,6}, Sabine Wilhelm, Ph.D.², Daniel S. Pine, M.D.⁸, Daniel Geller, M.D.², and Eric A. Storch, Ph.D.^{3,4,5,6,9,10}

¹Semel Institute of Neuroscience and Human Behavior, University of California Los Angeles

²Massachusetts General Hospital and Harvard Medical School

³Department of Psychology, University of South Florida

⁴Department of Pediatrics, University of South Florida

⁵Departments of Psychiatry and Behavioral Neuroscience, University of South Florida

⁶All Children's Hospital, Johns Hopkins Medicine

⁷School of Aging Studies, University of South Florida

⁸National Institute of Mental Health

⁹Rogers Behavioral Health – Tampa Bay

¹⁰Department of Health Policy and Management, University of South Florida

Abstract

Background—Fear acquisition and extinction are central constructs in the cognitive-behavioral model of obsessive-compulsive disorder (OCD), which underlies exposure-based cognitive-behavioral therapy (CBT). Youth with OCD may have impairments in fear acquisition and extinction that carry treatment implications. We examined these processes using a differential conditioning procedure.

Methods—Forty-one youth (19 OCD, 22 community comparisons) completed a battery of clinical interviews, rating scales, and a differential conditioning task that included habituation, acquisition, and extinction phases. Skin conductance response (SCR) served as the primary dependent measure.

Results—During habituation, no difference between groups was observed. During acquisition, differential fear conditioning was observed across participants as evidenced by larger SCRs to the CS+ compared to CS−; there were no between-group differences. Across participants, the number

Corresponding Author: Joseph F. McGuire, Ph.D., Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles, 760 Westwood Plaza, 48-228B, Los Angeles, CA, 90095. Phone: 310-794-5609, Fax: 310-206-4446, jfmcguire@mednet.ucla.edu.

Financial Disclosures

Ms. Wu, and Drs. McGuire, Small, Phares, and Pine report no potential conflicts of interest.

and frequency of OCD symptoms and anxiety severity was associated with greater reactivity to stimuli during acquisition. During extinction, a three-way interaction and follow-up tests revealed that youth with OCD showed a different pattern of SCR extinction compared to the community comparison group.

Conclusions—Youth with OCD exhibit a different pattern of fear extinction relative to community comparisons. This may be attributed to impaired inhibitory learning and contingency awareness in extinction. Findings suggest the potential benefit of utilizing inhibitory-learning principles in CBT for youth with OCD, and/or augmentative retraining interventions prior to CBT to reduce threat bias and improve contingency detection.

Keywords

Fear conditioning; extinction; skin conductance; inhibitory learning; obsessive compulsive disorder; children

Introduction

Obsessive-compulsive disorder (OCD) is characterized by the presence of obsessions and/or compulsions that affect approximately 1–2% of the population,^[1] with a majority of individuals reporting symptom onset during childhood.^[2] Youth with OCD experience functional impairment,^[3] and impaired quality of life.^[4] Although multiple factors have been implicated in the etiology of OCD,^[5] the cognitive-behavioral model^[6] underlies the front-line treatment, viz., exposure-based cognitive-behavioral therapy.^[7]

In the cognitive-behavioral model, the mechanisms of fear acquisition and extinction play an important role in symptom development, maintenance and treatment of OCD. Conditioned fear occurs when an emotionally neutral stimulus (conditioned stimulus, CS) is paired with an aversive unconditioned stimulus (US). Although not a conventional US like a shock, obsessions are purported to serve as the US in OCD (e.g., fear that a door handle is contaminated and that contact will cause severe illness/death). Subsequent exposures to the CS become capable of producing a conditioned response (CR) such as fear/distress. Some individuals with OCD generalize these learned associations to other stimuli creating a "chain of contagion".^[8] Thus, these individuals have difficulty discriminating between perceived and actually dangerous stimuli. Extinction is a learning process whereby the response to the CS declines through repeated exposure in the absence of the feared outcome (e.g., illness/death) and/or engagement in safety behaviors (e.g., avoidance, compulsive rituals). This process does not eradicate the initial CS-US association, but rather forms a new CS-no US association that inhibits the existing dysfunctional CS-US association.^[9] Over repeated exposures to the CS, the original fear/distress response (CR) becomes inhibited.^[9]

Despite the presumed central role in OCD, limited empirical data on conditioned fear acquisition and extinction derive primarily from adults with other anxiety disorders.^[10–13] Only two studies of adults with OCD have examined fear learning using Pavlovian fear conditioning tasks and skin conductance responses (SCRs).^[14, 15] Nanbu and colleagues^[14] used a classical conditioning task, and found no significant difference between adults with OCD and healthy controls. Meanwhile, Milad and colleagues^[15] used a differential

conditioning task and found no significant difference in either fear acquisition or extinction learning between adults with OCD and healthy controls. However, Milad and colleagues^[15] did observe impaired extinction recall in adults with OCD, compared to healthy controls. Despite methodological differences, findings collectively suggest that adults with OCD demonstrate comparable differential fear conditioning and extinction learning relative to community comparisons.^[14, 15] Age differences have been found for both differential fear conditioning^[16–18] and the neurobiology underlying fear acquisition and extinction between youth and adults.^[16, 19] Moreover, there are considerable phenomenological distinctions between adults and youth with OCD that limit the generalization of findings.^[20]

To date, there has been no published examination of conditioned fear acquisition and extinction in youth with OCD compared to community comparisons. Notably, a few studies have compared fear conditioning in youth with anxiety disorders and community comparisons.^[21–27] Findings suggest that fear conditioning produces comparable differential fear learning in anxious and non-anxious youth during acquisition; however, results for extinction are less definitive. Some evidence suggests that anxious youth exhibit resistance to within-session extinction,^[21–23, 25] and/or show larger CRs to stimuli after extinction.^[23, 25, 26] Conversely, other findings suggest that there is no significant difference in extinction,^[19, 27] with both anxious and non-anxious youth exhibiting comparable extinction of the CR.^[24] These inconsistencies may be attributable to differences in sample characteristics, conditioning procedures, outcome measures, and unconditioned stimuli.^[19]

Even though a fear conditioning model may not account for the entire phenomenology of OCD (e.g., not-just-right experiences, disgust),^[28, 29] understanding fear conditioning in youth with OCD is clinically relevant. First, as OCD typically onsets in childhood,^[2] examining fear acquisition and extinction processes closer to symptom onset may help to identify whether impairments in these processes contribute to OCD phenomenology. Second, a considerable portion of youth with OCD exhibit inadequate or incomplete response to CBT. In the Pediatric OCD Treatment Study, up to 25% of youth did not respond to exposure-based CBT and 60% of youth remained symptomatic after treatment.^[30] Given the central role that fear conditioning concepts are accorded in CBT, a better understanding of these mechanisms may improve treatment outcome. For example, it may be that youth with OCD who demonstrate typical fear acquisition and extinction will benefit from standard CBT approaches. However, youth who show impaired extinction might benefit from augmentative interventions to retrain attention/cognitive/threat biases before initiating CBT to achieve optimal benefit,^[31, 32] or CBT approaches that emphasize engagement of specific brain regions implicated in extinction among youth.^[16] Finally, improved understanding of conditioned fear in OCD may help to guide future research.

The present study examined fear conditioning and extinction in youth with OCD and healthy community comparisons (CC) using a differential conditioning task. We tested two primary hypotheses. First, we hypothesized that youth with OCD would exhibit poorer extinction of a fear-conditioned SCR compared to CC. Second, given prior associations between lower OCD severity and improved CBT outcomes,^[33–35] we hypothesized that greater OCD severity would be associated with poorer fear extinction. Finally, we examined the

associations between anxiety severity and anxiety sensitivity to determine whether deficits in extinction were related to co-occurring anxiety symptoms.

Methods

Participants

Participants were recruited through a southeastern OCD specialty clinic and the surrounding community using flyers posted in community locations and by word-of-mouth. Interested participants completed a phone screen interview with the first author to determine possible eligibility. Inclusion criteria for OCD participants were: a primary diagnosis of OCD based on a clinical interview, 7–17 years of age, and English speaking. Exclusion criteria for youth with OCD included: the presence of autism spectrum disorder, mental retardation, psychosis, bipolar disorder, posttraumatic stress disorder, conduct disorder, or schizophrenia. Psychiatric medication was permissible and no participant had any medication changes reported within eight weeks prior to participation. Inclusion criteria for CC included: the absence of any psychiatric disorder other than specific phobia as determined by a clinical interview, 7–17 years of age, and English speaking.

A total of 57 participants underwent differential fear conditioning. Seven participants (4 OCD, 3 CC) discontinued the study during the acquisition phase, with 50 participants completing the entire fear conditioning procedure. Several participants' data were excluded from analyses due to unreliable recording of SC activity ($n=4$) and small mean SCRs to the US ($n=4$). Data from 1 OCD participant was excluded due to missing parent and self-report measures. The final sample consisted of 41 youth (19 OCD, 22 CC) between 8 and 17 years of age. There were no significant differences in demographic characteristics between the original and final sample.

Measures

Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version (KSADS-PL)—The KSADS-PL is a clinician-administered interview for DSM-IV childhood disorders that has demonstrated excellent reliability and validity.^[36] The rates of OCD, anxiety disorders, and other comorbid conditions are reported in Table 1.

Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS)—The CY-BOCS is a clinician-administered measure that is the gold-standard metric of obsessive-compulsive symptom severity in youth.^[37] The CY-BOCS consists of a symptom checklist and 10 severity items that are summed for a total severity score. The CY-BOCS has demonstrated strong psychometric properties.^[37, 38]

Obsessive-Compulsive Inventory-Child Version (OCI-CV)—The OCI-CV is a 21-item child-report measure that assesses the presence and frequency of OCD symptoms. Items rated on 3-point scale, and are summed to yield a total score.^[39] The OCI-CV has good reliability and validity among youth with OCD.^[39, 40]

Multidimensional Anxiety Scale for Children (MASC)—The MASC is a 39-item child-report questionnaire that assesses anxiety severity.^[41] Items are rated on a 4-point scale and summed to produce a total score that is adjusted for age and gender (T-score). The MASC has good reliability and validity in youth.^[41]

Anxiety Sensitivity Index-3 (ASI-3)—The ASI-3 is an 18-item patient-rated measure that assessed beliefs about the feared consequences of symptoms associated with anxious arousal.^[42] Items are summed to produce a total anxiety sensitivity score. The ASI-3 has good reliability and validity.^[42]

Fear Conditioning Task—A differential fear conditioning procedure was administered, whereby a 95 decibel scream and fearful facial expression (US) was paired with a neutral female face (CS+) but not with a second neutral female face (CS−). During a habituation phase, participants passively viewed 4 presentations each of the to-be CS+ and CS− without the US. The stimulus presentation order was held constant to minimize procedural variability. During the acquisition phase, the CS+ female face was paired with the US for 8 of 10 presentations; the CS− female face was never paired with the US. The US duration was 3 seconds; its onset immediately followed the offset of the CS+. During the extinction phase, there were 8 presentations each of the CS+ and CS− in the absence of the US. These stimuli and US have been used in studies of children with anxiety disorders^[16, 24] and healthy comparisons.^[17] Skin conductance response served as the primary dependent measure of fear acquisition and extinction, with larger SCR values suggesting greater fear.

Procedure

All study procedures were approved by the local institutional review board. After written parental consent and child assent were obtained, parents and youth completed the KSADS-PL to determine eligibility and the CY-BOCS. Next, youth completed the OCI-CV, MASC, and ASI-3. Afterward, youth completed the fear conditioning task. Participants were informed that they could discontinue participation at anytime. Youth and families were collectively compensated \$30.

Data Analysis

The SCR score for each CS presentation was calculated by subtracting the average SC level during the 2-second interval immediately preceding CS onset from the peak SC level during the 8-second CS interval. For the UCR, a SCR score for each US presentation was calculated by subtracting the average SC level during the last 2 seconds of the CS interval from the peak SC level during the 5-second interval following US onset. In order to address skewness in the SCR distribution, a square-root transformation was applied to the absolute values of all SCRs prior to analysis. If a SCR was negative, the minus sign was replaced following the square-root transformation. SCR values were evaluated to determine potential measurement failure and/or that there was an appropriately large average response to the US (SCR $\geq .50$ μ S). Trial-block scores were created by calculating the average SCR to successive blocks of 2 trials of the same trial type. This produced 2 blocks each for the CS+ and CS− for the habituation phase, 5 blocks for the acquisition phase, and 4 blocks for the extinction phase. Consistent with previous work,^[11, 24] a repeated-measures analysis of variance (ANOVA)

was conducted with diagnostic group (OCD, CC) as a between-group factor, stimulus type (CS+, CS-) as a within-group factor, and trial block as the repeated measure for each phase. Independent sample t-tests were used to compare orienting responses (the first presentations of the CS+ and CS-) between groups and averaged unconditioned response to the US across trials. Additionally, the unconditioned response to the US was compared between groups using a repeated-measure ANOVA. For all repeated-measure ANOVAs, significance levels reflect the Greenhouse-Geisser correction for sphericity. Because age may influence fear acquisition and extinction,^[18] analyses were reexamined using only those participants matched for gender and age within two years ($n=38$, 19 OCD, 19 CC). There were no substantive differences in findings, with the noted exception of the three-way interaction in the extinction phase that reached statistical significance and is reported below. Pearson correlations examined associations between clinical characteristics and the average SCR for the CS+, CS-, and their differential score (difference between the CS+ and CS-) within each phase. Given the preliminary nature of fear conditioning analyses among youth with OCD, statistical significance was set at $p=.05$ for all analyses.^[27]

Results

Participants

Comparisons of sample characteristics are presented in Table 1. Although the groups did not differ in age or gender, there was a non-significant trend towards fewer Caucasians among community comparisons. Youth with OCD were more likely to be taking a serotonin reuptake inhibitor (SRI) medication compared to community comparisons ($p<.001$), with no significant difference found for other psychiatric medication types.

Habituation phase and orienting response

There was no significant group difference in the SC orienting response magnitudes, i.e., SCRs to the first CS+ presentation ($t_{39}=.34$, $p=.74$, $d=.11$) or the first CS- presentation ($t_{39}=.21$, $p=.84$, $d=.05$). Table 2 provides results from repeated-measures ANOVA for the habituation phase. There was a main effect for trial block that approached significance and reflected larger SCRs to the first trial block, compared to the second trial block. Additionally, there was a significant stimulus $\times$ trial block interaction. This interaction reflects a greater decrease in SCR magnitude for the CS+ from trial block 1 to trial block 2. Given that the CS+ was always the first stimulus presented, it was not surprising that there would be a larger initial SCR and larger subsequent decreases in SCR as participants habituated to its novelty.

Acquisition phase

As seen in Table 2, there was a significant stimulus main effect that reflected robust differential conditioning as indicated by larger SCR to the CS+, compared to CS-. There was also a significant main effect for trial block suggesting that SCR magnitudes differed across trials. There was no significant group difference between youth with OCD ($M=.53$, $SD=.26$) and the CC group ($M=.42$, $SD=.19$, $\eta^2_p=.06$). There was a significant stimulus $\times$ trial block interaction reflecting differing SCR magnitudes to the CS+ and CS- in later relative to earlier trial blocks.

No significant difference was found in the average SCR magnitude to the US between the OCD and CC groups for CS+ trials paired with the US ($t_{39}=.74$, $p=.46$, $d=.24$). Although there was a significant main effect for trial block ($F=6.46$, $p<.001$, $\eta^2_p=.14$), the main effect for group ($F<1$, ns) and the group $\times$ trial block interaction ($F<1$, ns) were not significant.

Extinction Phase

As seen in Table 2, there was a significant stimulus main effect, with the CS+ ($M=.49$, $SD=.29$) producing larger SCRs, compared to the CS- ($M=.40$, $SD=.25$). The group $\times$ stimulus $\times$ trial block interaction approached significance; this interaction reached significance when the analysis included only the age-and-gender matched samples ($n=38$; $F=2.72$, $p=.05$, $\eta^2_p=.07$). When the OCD and CC groups were examined separately, different group patterns emerged (see Table 3).

For community comparisons, a differential SCR to the CS+ and CS- was observed throughout extinction as evidenced by a stimulus main effect. For youth with OCD, a significant stimulus $\times$ trial block interaction was observed suggesting that the differential SCR to CS+ and CS- trials varied across extinction. As can be seen in Figure 1, youth with OCD exhibited initially larger SCRs to the CS- during extinction, which diminished to a comparable level to that of the CC group at the end of extinction. Curiously, youth with OCD exhibited smaller SCRs to the CS+ during initial extinction trial blocks, but produced an increasingly large SCR over successive trials that persisted through the end of the extinction phase.

Correlations for Acquisition, Extinction, and Differential SCR

During acquisition, there was a moderate positive association between SCR magnitude to both the CS+ and CS- with the MASC total score, and a similar association observed between the CS+ and OCI-CV total score (see Table 4). During early extinction, there were moderate negative associations between the differential SCR and CY-BOCS severity score and ASI-3 score. No other associations were significant.

Discussion

To our knowledge, this is the first examination of differential fear conditioning in youth with OCD. Similar to adult studies,^[14, 15] we found that there was no significant difference between youth with OCD and the CC sample in the acquisition of a fear-conditioned SCR. Interestingly, youth with OCD did exhibit a different pattern of SCRs during extinction than that shown by the CC group. Specifically, community comparisons retained a differential SCR to the CS+ and CS- throughout extinction. Although the persistence of a differential SCR throughout extinction is not always found among healthy CC participants,^[11, 19] it is consistent with self-report ratings from studies that have used the same conditioning task.^[24] In contrast, youth with OCD showed a reversal of SCRs to the CS+ and CS- during early extinction followed by increased reactivity to the CS+ and decreased reactivity to the CS- over later extinction trials. The persistence of differential fear conditioning throughout extinction in both groups suggest that youth, compared to adults, may have greater difficulty inhibiting conditioned fear. Notably, the ability to inhibit conditioned fear appeared to be

weaker among youth with OCD as evidenced by their larger differential SCR in late extinction. Similar to other fear-based psychopathological conditions such as anxiety disorders,^[10, 43] this finding suggests that inhibitory learning deficits play a central role in extinction for youth with OCD. While initial CBT models emphasized within-and-between session habituation as the central mechanism for CBT,^[44] within- and between-session habituation in CBT has not been found to predict treatment outcome for youth with OCD.^[45, 46] Given the inhibitory learning impairments noted above, inhibitory learning may be a key therapeutic component for future CBT protocols for youth with OCD to improve treatment outcomes.^[47, 48]

Along with inhibitory learning impairments in late extinction, youth with OCD displayed an initial reversal of SCRs to the CS+ and CS- during early extinction, i.e., increased reactivity to the CS-. A similar reversal has been observed in other studies of youth and attributed to an anticipated reversal of the CS-US contingency in the absence of a clear threat cue.^[18] Youth with OCD may show a threat-related bias in an ambiguous context when the association between a CS and US is unclear and a new threat may be anticipated. It is also possible that youth with OCD are delayed in their recognition of a shift in association between the CS+ and US, which is eventually corrected with further non-reinforced trial presentations. Given that the ability to correctly detect new associations plays an important role in updating fear memories during extinction, this impaired recognition may serve as a harbinger of diminished extinction in CBT, and/or may reflect a biological marker for OCD symptom persistence into adulthood. Indeed, youth with fear-based psychopathology who fail to develop more complex fear learning capabilities (e.g., fear extinction, discrimination) may have a higher risk of symptom persistence into adulthood.^[49]

Across participants, anxiety severity was associated with larger SCRs to both the CS+ and CS- during the acquisition phase. Similarly, the number and frequency of OCD symptoms was associated with larger SCRs to the CS+. Given their similar magnitude, this provides empirical support for the relationship between anxiety and OCD phenomenology with greater reactivity during fear conditioning. As there have been inconsistent findings regarding fear acquisition differences between diagnostic groups, this suggests that dimensional factors may be contributing to fear conditioning across youth. Additionally, greater OCD severity was associated with smaller differential SCR scores during early extinction. A smaller differential SCR suggests that the youth responded similarly to the fear and safety cues during early extinction. While this may be partially attributed to greater difficulty discriminating between feared stimuli among younger children,^[17, 18] it seems more likely attributable to impaired inhibitory learning deficits and diminished contingency awareness, i.e., the ability to correctly recognize contingencies. The magnitude of differential SCR was negatively associated with OCD severity, one of the few replicated predictors of poor CBT response,^[33, 34] suggesting a possible link between impaired inhibitory learning, contingency awareness, and diminished CBT response.

Interestingly, youth with higher anxiety sensitivity scores also showed poorer discrimination of the CS+ and CS- during early extinction. Anxiety sensitivity is an important construct in adults with OCD and is associated with symptoms,^[50] severity,^[51] and impairment.^[52] Based on these findings, youth with greater anxiety sensitivity may be more prone to

developing learned fear associations, and/or have difficulty distinguishing between threatening and non-threatening stimuli due to anxious arousal. Given that increased anxiety sensitivity is a consequence of anxious arousal and the current study elicited anxious arousal via an aversive US, increased anxiety sensitivity may serve as a partial explanation for the reported findings. Prior associations observed in adults with OCD^[50, 51] and findings from the current study suggest that there is likely an overlap between anxiety sensitivity and OCD severity that warrants further examination.

Several limitations to the reported work should be considered. First, although similar to adult OCD studies,^[15] the reported study had a small sample that included youth on psychotropic medications. Given that psychotropic medications might be expected to reduce SCR values,^[53] results that trended towards statistical significance may emerge as more robust in a larger and/or unmedicated sample. Second, the significance value was set at $p=.05$ for all analyses. Although possibly impacting statistical significance, this would not have impacted the magnitude of effect sizes. Third, this study measured anxiety sensitivity using the ASI-3 to facilitate comparability with prior adult OCD research. Findings may differ from those that would be obtained using another anxiety sensitivity measure (e.g., Child Anxiety Sensitivity Index). Finally, the magnitude of conditioning can be influenced by study specific methodology.^[19] Thus, findings from the present study may be limited to our conditioning procedure and sample characteristics.

Conclusions

Youth with OCD exhibit normal acquisition but impaired extinction of a fear-conditioned SCR. This pattern is suggestive of impairments in inhibitory learning and contingency awareness. Additionally, both anxiety severity and OCD symptoms were associated with greater overall reactivity, but not differential responding during fear conditioning. Furthermore, both greater OCD symptom severity and anxiety sensitivity were associated with poorer discrimination between the CS+ and CS– in early extinction. These findings highlight several possible directions for future OCD research. First, given variable findings in prior conditioning studies of youth with anxiety disorders,^[27] replication and extension of these findings is warranted. In doing so, it may be useful to capture a trial-by-trial US expectancy rating to assess youth's explicit contingency awareness and recognition of impaired fear extinction. Second, it would be informative to further examine the role of anxiety sensitivity in OCD. Although briefly examined in adults with OCD^[42] and included in the current study, its investigation in youth and role in treatment is largely unknown. It may be that greater anxiety sensitivity is associated with diminished contingency awareness due to threat anticipation. Third, given the poorer discrimination of the CS+ and CS– during the contingency shift in early extinction, the use of attention/cognitive/threat bias modification protocols may be of benefit prior to CBT in order to improve threat and contingency recognition. Although attention/cognitive/threat bias modification protocols have been found to provide some benefit as stand-alone interventions,^[54] they may be of greater benefit when used to precede and/or augment CBT.^[31, 32] Additionally, there is a growing body of evidence that highlights the importance of inhibitory learning in exposure therapy.^[47] Although predominantly focused on adults with anxiety disorders,^[47] the

incorporation of inhibitory-learning based CBT may prove beneficial in reducing inhibitory deficits and thereby maximize the therapeutic benefit for youth with OCD.^[48]

Acknowledgments

Support for this article comes in part from the National Institute of Mental Health (NIMH) of the National Institutes of Health (NIH) as a research supplement to promote diversity in health-related research to award R01MH093381 to Dr. Storch (R01MH093381-02S1). Dr. Pine is supported by the NIMH Intramural Research Program. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIMH or NIH.

Dr. Orr reports having received research funding from the National Institutes of Health/National Institute of Mental Health (NIH/NIMH), Department of Defense, and Department of Veterans Affairs.

Dr. Lewin has received research support from the International OCD Foundation (IOCDF), All Children's Hospital, Joseph Drown Foundation, and National Alliance for Research on Schizophrenia and Depression (NARSAD), has an agreement for a publishing honorarium from Springer Publishing, speakers honorarium from the Tourette Syndrome Association (TSA), reviewer honorarium from Children's Tumor Foundation, Oxford Press, University of Central Oklahoma, travel support from the American Psychological Association (APA), Rogers Memorial Hospital, NIMH, the Society for Clinical Child and Adolescent Psychology (SCCAP) and American Academy of Child and Adolescent Psychiatry (AACAP), Tourette Syndrome Association and consulting fees from Prophase LLC. He is on the Scientific Advisory Board for the IOCDF.

Dr. Murphy receives or has received research funding from the Florida Agency for Healthcare Administration, AstraZeneca Research & Development, Brain and Behavior Research Foundation, the Center for Disease Control and Prevention, F. Hoffmann-La Roche Ltd., Indevus Pharmaceuticals, IOCDF, National Institutes of Health/National Institute of Mental Health (NIH/NIMH), Otsuka Pharmaceuticals, Pfizer, Inc., Psyadon Pharmaceuticals, Inc, and Shire Pharmaceuticals. She has received travel support from the TSA and honoraria from grand rounds/CME lectures.

Dr. Wilhelm reports receiving support in the form of free medication and matching placebo from Forest Laboratories for clinical trials funded by the NIH and receiving book royalties from Guilford Publications, New Harbinger Publications, and Oxford University Press. She also receives support in the form of speaking honoraria from academic institutions, the NIMH, International Obsessive Compulsive Disorder Foundation, Tourette Syndrome Association, Springer SBM LLC, Association for Behavioral and Cognitive Therapies, and the Mayo Foundation for Medical Education and Research. Dr. Wilhelm also receives salary support from Novartis.

Dr. Geller has received support from the NIH, the IOCDF, the TSA, AACAP and Eli Lilly, Pfizer, Otsuka and Forest Pharmaceuticals.

Dr. Storch has received support from the NIH, CDCP, Agency for Healthcare Research and Quality, IOCDF, TSA, and Janssen Scientific Affairs. He receives textbook royalties from Springer publishers, American Psychological Association, Lawrence Erlbaum and Wiley-Blackwell. Dr. Storch has been an educational consultant for Rogers Memorial Hospital. He is a consultant for Prophase, Inc. and CroNos, Inc., and is on the Speaker's Bureau and Scientific Advisory Board for the IOCDF. He receives research support from the All Children's Hospital Guild Endowed Chair.

References

1. Ruscio AM, Stein DJ, Chiu WT, Kessler RC. The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication. *Mol Psychiatry*. 2010; 15(1):53–63. [PubMed: 18725912]
2. Nestadt G, Samuels J, Riddle M, et al. A family study of obsessive-compulsive disorder. *Arch Gen Psychiatry*. 2000; 57(4):358–363. [PubMed: 10768697]
3. Piacentini J, Peris TS, Bergman RL, et al. Functional impairment in childhood OCD: development and psychometrics properties of the Child Obsessive-Compulsive Impact Scale-Revised (COIS-R). *J Child Adolesc Psychol*. 2007; 36(4):645–653.
4. Lack CW, Storch EA, Keeley ML, et al. Quality of life in children and adolescents with obsessive-compulsive disorder: base rates, parent-child agreement, and clinical correlates. *Soc Psychiatry Psychiatr Epidemiol*. 2009; 44(11):935–942. [PubMed: 19255701]

5. McGuire JF, Lewin AB, Horng B, et al. The nature, assessment, and treatment of obsessive-compulsive disorder. *Postgrad Med*. 2012; 124(1):152–165. [PubMed: 22314125]
6. Abramowitz JS, Taylor S, McKay D. Obsessive-compulsive disorder. *Lancet*. 2009; 374(9688):491–499. [PubMed: 19665647]
7. Geller DA, March J. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Obsessive-Compulsive Disorder. *J Am Acad Child Adolesc Psychiatry*. 2012; 51(1):98–113. [PubMed: 22176943]
8. Tolin DF, Worhunsky P, Maltby N. Sympathetic magic in contamination-related OCD. *J Behav Ther Exp Psychiatry*. 2004; 35(2):193–205. [PubMed: 15210379]
9. Myers KM, Davis M. Mechanisms of fear extinction. *Mol Psychiatry*. 2007; 12(2):120–150. [PubMed: 17160066]
10. Lissek S, Powers AS, McClure EB, et al. Classical fear conditioning in the anxiety disorders: a meta-analysis. *Behav Res Ther*. 2005; 43(11):1391–1424. [PubMed: 15885654]
11. Orr SP, Metzger LJ, Lasko NB, et al. De novo conditioning in trauma-exposed individuals with and without posttraumatic stress disorder. *J Abnormal Psychol*. 2000; 109(2):290–298.
12. Michael T, Blechert J, Vriends N, et al. Fear conditioning in panic disorder: Enhanced resistance to extinction. *J Abnormal Psychol*. 2007; 116(3):612–617.
13. Pitman RK, Orr SP. Test of the conditioning model of neurosis: differential aversive conditioning of angry and neutral facial expressions in anxiety disorder patients. *J Abnormal Psychol*. 1986; 95(3):208–213.
14. Nanbu M, Kurayama T, Nakazawa K, et al. Impaired P50 suppression in fear extinction in obsessive-compulsive disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2010; 34(2):317–322. [PubMed: 20035817]
15. Milad MR, Furtak SC, Greenberg JL, et al. Deficits in conditioned fear extinction in obsessive-compulsive disorder and neurobiological changes in the fear circuit. *JAMA Psychiatry*. 2013; 70(6):608–618. [PubMed: 23740049]
16. Lau JY, Britton JC, Nelson EE, et al. Distinct neural signatures of threat learning in adolescents and adults. *Proc Natl Acad Sci U S A*. 2011; 108(11):4500–4505. [PubMed: 21368210]
17. Glenn CR, Klein DN, Lissek S, et al. The development of fear learning and generalization in 8–13 year-olds. *Dev Psychobiol*. 2012; 54(7):675–684. [PubMed: 22072276]
18. Jovanovic T, Nylocks KM, Gamwell KL, et al. Development of fear acquisition and extinction in children: Effects of age and anxiety. *Neurobiol Learn Mem*. 2014; 113:135–142. [PubMed: 24183838]
19. Shechner T, Hong M, Britton JC, et al. Fear conditioning and extinction across development: evidence from human studies and animal models. *Biol Psychol*. 2014; 100:1–12. [PubMed: 24746848]
20. Farrell L, Barrett P, Piacentini J. Obsessive-Compulsive Disorder Across the Developmental Trajectory: Clinical Correlates in Children, Adolescents and Adults. *Behaviour Change*. 2006; 23(2):103–120.
21. Pliszka SR, Hatch JP, Borcharding SH, Rogeness GA. Classical conditioning in children with attention deficit hyperactivity disorder (ADHD) and anxiety disorders: a test of Quay's model. *J Abnorm Child Psychol*. 1993; 21(4):411–423. [PubMed: 8408987]
22. Liberman LC, Lipp OV, Spence SH, March S. Evidence for retarded extinction of aversive learning in anxious children. *Behav Res Ther*. 2006; 44(10):1491–1502. [PubMed: 16360117]
23. Craske MG, Waters AM, Bergman RL, et al. Is aversive learning a marker of risk for anxiety disorders in children? *Behav Res Ther*. 2008; 46(8):954–967. [PubMed: 18539262]
24. Lau JYF, Lissek S, Nelson EE, et al. Fear conditioning in adolescents with anxiety disorders: Results from a novel experimental paradigm. *J Am Acad Child Adolesc Psychiatry*. 2008; 47(1):94–102. [PubMed: 18174830]
25. Waters AM, Henry J, Neumann DL. Aversive Pavlovian conditioning in childhood anxiety disorders: Impaired response inhibition and resistance to extinction. *J Abnormal Psychol*. 2009; 118(2):311–321.
26. Britton JC, Grillon C, Lissek S, et al. Response to learned threat: An fMRI study in adolescent and adult anxiety. *Am J Psychiatry*. 2013; 170(10):1195–1204. [PubMed: 23929092]

27. Shechner T, Britton JC, Ronkin EG, et al. Fear Conditioning and Extinction in Anxious and Nonanxious Youth and Adults: Examining a Novel Developmentally Appropriate Fear-Conditioning Task. *Depress Anxiety*. 2015; 32(4):277–288. [PubMed: 25427438]
28. Olatunji BO, Tart CD, Ciesielski BG, et al. Specificity of disgust vulnerability in the distinction and treatment of OCD. *J Psychiatr Res*. 2011; 45(9):1236–1242. [PubMed: 21353249]
29. Coles ME, Heimberg RG, Frost RO, Steketee G. Not just right experiences and obsessive-compulsive features: Experimental and self-monitoring perspectives. *Behav Res Ther*. 2005; 43(2): 153–167. [PubMed: 15629747]
30. Pediatric OCD Treatment Study (POTS). 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(16):1969–1976. [PubMed: 15507582]
31. Riemann BC, Kuckertz JM, Rozenman M, et al. Augmentation of youth cognitive behavioral and pharmacological interventions with attention modification: A preliminary investigation. *Depress Anxiety*. 2013; 30(9):822–828. [PubMed: 23658147]
32. Shechner T, Rimon-Chakir A, Britton JC, et al. Attention bias modification treatment augmenting effects on cognitive behavioral therapy in children with anxiety: randomized controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2014; 53(1):61–71. [PubMed: 24342386]
33. Garcia AM, Sapyta JJ, Moore PS, et al. Predictors and moderators of treatment outcome in the Pediatric Obsessive Compulsive Treatment Study (POTS I). *J Am Acad Child Adolesc Psychiatry*. 2010; 49(10):1024–1033. [PubMed: 20855047]
34. Ginsburg GS, Kingery JN, Drake KL, Grados MA. Predictors of treatment response in pediatric obsessive-compulsive disorder. *J Am Acad Child Adolesc Psychiatry*. 2008; 47(8):868–878. [PubMed: 18596553]
35. Rudy BM, Lewin AB, Geffken GR, et al. Predictors of treatment response to intensive cognitive-behavioral therapy for pediatric obsessive-compulsive disorder. *Psychiatry Res*. 2014; 220(1–2): 433–440. [PubMed: 25193378]
36. Kaufman J, Birmaher B, Brent D, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry*. 1997; 36(7):980–988. [PubMed: 9204677]
37. Scahill L, Riddle MA, McSwiggin-Hardin M, et al. Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. *J Am Acad Child Adolesc Psychiatry*. 1997; 36(6):844–852. [PubMed: 9183141]
38. Lewin AB, Piacentini J, De Nadai AS, et al. Defining clinical severity in pediatric obsessive-compulsive disorder. *Psychol Assessment*. 2014; 26(2):679–684.
39. Foa EB, Coles M, Huppert JD, et al. Development and validation of a child version of the Obsessive Compulsive Inventory. *Behav Ther*. 2010; 41(1):121–132. [PubMed: 20171333]
40. Jones AM, De Nadai AS, Arnold EB, et al. Psychometric properties of the obsessive compulsive inventory: child version in children and adolescents with obsessive-compulsive disorder. *Child Psych & Hum Dev*. 2013; 44(1):137–151.
41. March JS, Parker JD, Sullivan K, et al. The Multidimensional Anxiety Scale for Children (MASC): factor structure, reliability, and validity. *J Am Acad Child Adolesc Psychiatry*. 1997; 36(4):554–565. [PubMed: 9100431]
42. Taylor S, Zvolensky MJ, Cox BJ, et al. Robust dimensions of anxiety sensitivity: development and initial validation of the Anxiety Sensitivity Index-3. *Psychol Assessment*. 2007; 19(2):176–188.
43. Craske MG, Rauch SL, Ursano R, et al. What is anxiety disorder? *Depress Anxiety*. 2009; 26(12): 1066–1085. [PubMed: 19957279]
44. Foa EB, Kozak MJ. Emotional processing of fear: exposure to corrective information. *Psychol Bulletin*. 1986; 99(1):20–35.
45. Kircanski K, Peris TS. Exposure and response prevention process predicts treatment outcome in youth with OCD. *J Abnorm Child Psychol*. 2014; 43(3):543–552.
46. Kircanski K, Wu M, Piacentini J. Reduction of subjective distress in CBT for childhood OCD: Nature of change, predictors, and relation to treatment outcome. *J Anxiety Disord*. 2014; 28(2): 125–132. [PubMed: 23774008]

47. Craske MG, Liao B, Brown L, Vervliet B. Role of inhibition in exposure therapy. *J Exp Psychopathol.* 2012; 3(3):322–345.
48. Craske MG, Treanor M, Conway CC, et al. Maximizing exposure therapy: An inhibitory learning approach. *Behav Res Ther.* 2014; 58:10–23. [PubMed: 24864005]
49. Britton JC, Lissek S, Grillon C, et al. Development of anxiety: the role of threat appraisal and fear learning. *Depress Anxiety.* 2011; 28(1):5–17. [PubMed: 20734364]
50. Wheaton MG, Mahaffey B, Timpano KR, et al. The relationship between anxiety sensitivity and obsessive-compulsive symptom dimensions. *J Behav Ther Exp Psychiatry.* 2012; 43(3):891–896. [PubMed: 22321579]
51. Calamari JE, Rector NA, Woodard JL, et al. Anxiety Sensitivity and Obsessive—Compulsive Disorder. *Assessment.* 2008; 15(3):351–363. [PubMed: 18310595]
52. Storch EA, Wu MS, Small BJ, et al. Mediators and moderators of functional impairment in adults with obsessive-compulsive disorder. *Compr Psychiatry.* 2014; 55(3):489–496. [PubMed: 24342055]
53. Boucsein W, Fowles DC, Grimnes S, et al. Publication recommendations for electrodermal measurements. *Psychophysiology.* 2012; 49(8):1017–1034. [PubMed: 22680988]
54. Salemink E, Wolters L, de Haan E. Augmentation of Treatment As Usual with online Cognitive Bias Modification of Interpretation training in adolescents with Obsessive Compulsive Disorder: A pilot study. *J Behav Ther Exp Psychiatry.* 2015; 49(Pt A):112–119. [PubMed: 25724385]

Figure 1.
Skin Conductance Responses During Habituation, Acquisition, and Extinction Phases for Youth with OCD (n=19) and Community Control Youth (n=22)

Table 1

Characteristics for Youth with OCD and Community Comparisons (N = 41)

	OCD Group (n = 19)	Community Comparison Group (n = 22)		
	N (%)	N (%)	χ^2	p
Male Participants	10 (53%)	10 (45%)	0.21	.65
Race/Ethnicity				
White/Caucasian	18 (95%)	16 (73%)	3.49	.06
Non-Hispanic	17 (89%)	21 (95%)	0.54	.46
Psychiatric Diagnoses				
OCD	19 (100%)	0 (0%)	41.00	< .01
Any Anxiety Disorder ^a	6 (32%)	6 (27%)	0.09	.76
Attention Deficit Hyperactivity Disorder	2 (11%)	0 (0%)	2.44	0.12
Depressive Disorders	1 (5%)	0 (0%)	1.19	0.28
Chronic Tic Disorder	2 (11%)	0 (0%)	2.44	0.12
Disruptive Behavior Disorder	1 (5%)	0 (0%)	1.19	0.28
Psychiatric Medication				
SRI	8 (42%)	0 (0%)	11.51	< .01
Antipsychotic	2 (11%)	0 (0%)	2.44	.12
Stimulant	2 (11%)	0 (0%)	2.44	.12
Benzodiazepine	1 (5%)	0 (0%)	1.19	.28
	Mean (SD)	Mean (SD)	t	p
Age	13.26 (3.07)	12.59 (2.24)	0.81	.43
CY-BOCS Total Score	23.42 (6.31)	0.00 (0.00)	16.18	< .01
OCI-CV Total Score ^b	14.33 (7.78)	9.32 (4.59)	2.41	.02
MASC Total T-Score ^c	55.53 (17.07)	50.56 (8.58)	1.03	.31
ASI-3 Total Score ^d	12.60 (11.98)	9.55 (7.56)	0.88	.39

Note. OCD = Obsessive-Compulsive Disorder; SRI = Serotonin Reuptake Inhibitor; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; OCI-CV = Obsessive Compulsive Inventory-Child Version; MASC = Multidimensional Anxiety Scale for Children; ASI-3 = Anxiety Sensitivity Index-3rd Edition.

^aAny Anxiety Disorder = Specific Phobia, Social Anxiety Disorder, Generalized Anxiety Disorder, Separation Anxiety Disorder, or Anxiety Disorder - Not Otherwise Specified. Community Controls only had Specific Phobias.

^b1 participant did not complete the OCI-CV.

^c2 participants did not complete the MASC.

^d4 participants did not complete the ASI-3.

Table 2

ANOVA Results for Comparisons of SC Responses for All Three Phases (N = 41)

Habituation Phase	F	p	η^2_p
Group	< 1.00	NS	.01
Stimulus	< 1.00	NS	< .01
Trial Block	3.84	.06	.09
Stimulus $\times$ Trial Block	9.19	.004	.19
Group $\times$ Stimulus	1.34	.26	.03
Group $\times$ Trial Block	< 1.00	NS	.02
Group $\times$ Stimulus $\times$ Trial Block	< 1.00	NS	< .01
Acquisition Phase	F	p	η^2_p
Group	2.59	.12	.06
Stimulus	9.80	.003	.20
Trial Block	5.60	.002	.13
Stimulus $\times$ Trial Block	6.18	< .001	.14
Group $\times$ Stimulus	< 1.00	NS	.01
Group $\times$ Trial Block	1.87	.14	.05
Group $\times$ Stimulus $\times$ Trial Block	1.25	.29	.03
Extinction Phase	F	p	η^2_p
Group	1.48	.23	.04
Stimulus	4.49	.04	.10
Trial Block	1.66	.19	.04
Stimulus $\times$ Trial Block	2.26	.09	.06
Group $\times$ Stimulus	1.24	.27	.03
Group $\times$ Trial Block	< 1.00	NS	.02
Group $\times$ Stimulus $\times$ Trial Block	2.54	.06	.06

Note. NS = Not significant.

Table 3

Skin Conductance Response Separated by Diagnostic Group during Extinction Phase

Youth with OCD (<i>n</i> = 19)	F	<i>p</i>	η^2_p
Stimulus	< 1.00	NS	.03
Trial Block	1.15	.34	.06
Stimulus $\times$ Trial Block	4.34	.01	.19
Community Comparisons (<i>n</i> = 22)	F	<i>p</i>	η^2_p
Stimulus	4.94	.04	.19
Trial Block	1.22	.31	.06
Stimulus $\times$ Trial Block	< 1.00	NS	< .01

Correlations between Clinical Characteristics and Acquisition, Extinction and Differential SCR across Participants (N = 41)

Table 4

Clinical Characteristic	ACQUISITION			EARLY EXTINCTION			LATE EXTINCTION		
	CS+	CS-	DIFF	CS+	CS-	DIFF	CS+	CS-	DIFF
CY-BOCS Total Score	0.19	0.17	0.05	-0.09	0.19	-0.33*	0.15	0.14	-0.03
OCL-CV Total Score	0.34*	0.28	0.12	0.02	0.15	-0.17	0.06	0.08	0.07
MASC Total T-Score	0.36*	0.41**	0.02	0.12	0.24	-0.18	0.25	0.19	-0.03
ASI-3 Total Score	0.29	0.09	0.23	-0.17	0.23	-0.46**	-0.07	-0.18	-0.18

* $p < .05$,** $p < .01$,

Note. CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; OCL-CV = Obsessive Compulsive Inventory-Child Version; MASC = Multidimensional Anxiety Scale for Children; ASI-3 = Anxiety Sensitivity Index-3rd Edition;