Enhancing treatment outcome for youth with OCD and anxiety

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UCLA Semel Institute for Neuroscience and Human Behavior
## Disclosures

<table>
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<tr>
<th>Source</th>
<th>Research Funding</th>
<th>Advisor/Consultant</th>
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Evidence supports the efficacy of:

- Psychosocial interventions (e.g., CBT)
- Pharmacologic interventions (e.g., SSRIs)
- Combined Approaches

Newer data provides varying levels of support for additional treatment approaches:

- Cognitive Bias Modification (CBM)
- Mindfulness-based approaches
- Neuromodulation enhancers (e.g., DCS)
Child/Adol Anxiety Multimodal Treatment Study (CAMS)

Cooperative agreement (U01) funded by NIMH

Multi-site RCT across six sites:
- Columbia (Albano), Duke (March), Johns Hopkins (Walkup), Temple (Kendall), UCLA (Piacentini), Pittsburgh (Birmaher)

488 children (aged 7-17) with Separation (SAD), Social (SoP), or Generalized anxiety disorder (GAD)

Comparing the relative efficacy of:
- Cognitive behavior therapy (CBT)
- Sertraline (SRT) and
- CBT+SRT (COMB)
- Pill placebo (PBO)
CAMS Acute Outcomes

COMB > CBT = SRT > PBO

Walkup et al., 2008; Ginsburg et al., 2010
CAMS Remission at 6 Mo Followup

Wks 12 & 36: Comb>CBT=SRT

Piacentini et al., 2014
CAMELS: CAMS Long-Term Outcomes

- Five year study examining symptom and service use outcomes
- Participants evaluated twice annually
- At first FU:
  - M age 17.7 yrs, 56% female
  - M 6 yrs since CAMS post-tx
- ~ 65% participation rate
CAMELS: 6yr FU Remission Rates

NO DIFFERENCE IN REMISSION RATE BY CAMS TREATMENT GROUP

Ginsburg et al., 2014
COMB > CBT = SER > PBO

Effect Size
CBT = .98
Comb = 1.46

POTS Team, 2004
UCLA Family CBT Study

ITT: 57% vs. 27%
p<.05%

TC: 68% vs. 35%
p<.05%

Piacentini et al., 2011
Change in CYBOCS

\[ t = 2.25; \ p < .05 \]
## Child OCD Treatment Meta-analysis

<table>
<thead>
<tr>
<th></th>
<th>CBT</th>
<th>SSRi</th>
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<tr>
<td>Tx Efficacy</td>
<td>1.21</td>
<td>0.50</td>
</tr>
<tr>
<td>Tx Response</td>
<td>3.93</td>
<td>1.80</td>
</tr>
<tr>
<td>Remission</td>
<td>5.40</td>
<td>2.06</td>
</tr>
<tr>
<td>NNT</td>
<td>3</td>
<td>5</td>
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**CBT Moderators:** Comorbid anxiety, amt of therapist contact, lower attrition associated with greater efficacy

**SSRI Moderators:** Methodologic rigor associated with poorer efficacy

McGuire et al., 2015
Remission in Child OCD CBT Trials

POTS and UCLA

(CY-BOCS < 10)

Piacentini et al., 2011; POTS Team, 2004
POTS: Non Remitters

Symptomatic:
- Combo 46%
- CBT 61%
- SSRI 79%

POTS Team, 2004
Summary

- CBT and medication both lead to improvement
- COMB offers additional benefit for anxiety, and possibly OCD
- Response rates higher than remission rates
- At 5 year follow-up, half of CAMS youth in remission
- Treatments lead to short-term *improvement* but half of treated youth do not remit and many relapse over follow-up.
- Initial treatment response provides some protection against future anxiety disorder, but this effect was small.
- Treatment type unrelated to long-term outcomes.
Glass Half-Full or Half-Empty

We Are Here
We Need to Fill the Glass

Evidence-based psychotherapy for anxiety/OCD can:

• provide significant symptom reduction to a majority of patients
• provide significant symptom relief to a minority of patients
• long-term relief to approximately half of patients

Child mental health has not achieved the “curative therapeutics” nor personalized care characteristic of so many other areas of medicine
Strive for Prevention and Cures

- Develop new treatments based on discoveries in genomics, neuroscience, and behavioral science
- Develop ways to tailor existing and new interventions to optimize outcomes
- Test interventions for effectiveness in community practice settings
Demonstrate that the intervention exerts some measurable effect on a hypothesized “target” or mechanism of action

• Intervention used as manipulation to engage (or affect) the target rather than as a clinical intervention

Once target is “engaged” then examine how changes in the target impact clinical outcome.

• Validation of the hypothesized mechanism of action
Engagement Phase Targets
Higher baseline treatment expectations associated with more robust outcomes for medical, psychiatric, and psychological interventions

- **Adult anxiety** (Chambless et al., 1997; Westra et al., 2007)
- **Adult depression** (Krell, Leuchter et al., 2004; Papakostis et al., 2009)
- **Pediatric depression** (Curry et al., 2006)
- **Adult and pediatric chronic pain** (Goossens et al., 2005; Liossi et al., 2007; Smeets et al., 2008)
- **Medical procedures** (Flood et al., 1993; Henn et al., 2007)
Assessed at pre-treatment following the treatment reveal:

“How sure are you that doing the behavior therapy will help your / your child’s / this child’s obsessive compulsive symptoms”

Lewin et al, 2008
### Treatment Expectancy and Outcome

#### BASELINE EXPECTANCY RATINGS

<table>
<thead>
<tr>
<th>WEEK 14</th>
<th>PARENT</th>
<th>CHILD</th>
<th>THERAPIST</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGI-Improvement</td>
<td>-.10</td>
<td>-.52***</td>
<td>-.42***</td>
</tr>
<tr>
<td>CGI-Severity</td>
<td>-.20</td>
<td>-.37***</td>
<td>-.29***</td>
</tr>
<tr>
<td>ΔCYBOCS (%)</td>
<td>-.17</td>
<td>-.38***</td>
<td>-.44***</td>
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Lewin et al, 2008
Mechanism of Action

• Positive treatment expectations correlate with subsequent homework compliance as early as the third week of treatment.

• Relationship considerably more robust for child and therapist than for parents. Not surprising given that focus of work is on child.

• Suggests possible mechanism for expectancy: higher expectations lead to greater treatment engagement and compliance and better outcome.

• Important given the potentially aversive nature of exposure.

<table>
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<tr>
<th>HOMEWORK COMPLIANCE</th>
<th>BASELINE EXPECTANCY RATINGS</th>
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<tr>
<td></td>
<td>PARENT</td>
</tr>
<tr>
<td>Week 3</td>
<td>.21</td>
</tr>
<tr>
<td>Week 4</td>
<td>.14</td>
</tr>
<tr>
<td>Week 8</td>
<td>.01</td>
</tr>
<tr>
<td>Week 14</td>
<td>.44**</td>
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Positive expectations may be enhanced by:

• Effective psychoeducation with emphasis on treatment model and course

• Early efforts to instill sense of trust and efficacy in therapist

**Fire Drill Analogy.** The fire alarm is scary sounding to get your attention and make you leave the school building in case there’s a fire. But sometimes the alarm goes off when there’s no fire (a false alarm). It still sounds scary, even though there’s no real danger. Anxiety is like a false fire alarm. It makes you scared even when there’s no real danger. In treatment you will learn how to ignore your anxiety false alarm so it doesn’t bother you anymore.
Psychoeducation

Prevalence
• Common Disorder (0.5 - 2%)

Neurobiological Framework
• “Asthma” analogy

Ethological Perspective
• Anxiety as “False Alarm”

Present Treatment Model
Psychoeducation

Ethological Perspective

Anxiety has been conserved as an evolutionary trait across species because it serves a protective function.
Ethological Perspective:
Anxiety as an adaptive advantage

Early Caveman Game:
Kiss the Mammoth and Run
Step One in Treatment

False Alarm or Real Fear

Is this my OCD talking or real danger?
Intervention Phase Targets
Exposure is the Key Ingredient in CBT for OCD and Anxiety

Abramowitz, 1996; Kendall et al., 2005; Peris et al., 2014; Stanley & Turner, 1995
Traditional Conceptualization of Exposure

- **HABITUATION** = Repeated exposure to a feared stimulus leads to learning that the stimulus is no longer relevant and a decrease in response strength.

- Habituation, or corrective learning, requires initial activation of fear (IFA) during the exposure task.

- Corrective learning requires Habituation to occur both **WITHIN** and **BETWEEN** exposure sessions.

- **FEAR REDUCTION, VIA HABITUATION, IS PRIMARY DRIVER OF TREATMENT PLANNING AND EVALUATION**

Foa & Kozak, 1986; Foa & McNally, 1996 Groves & Thompson, 1970
Within Session Fear Habituation

![Graph showing SUDS (subjective units of distress) over time. The graph depicts a curve that rises to a peak at around time 6 and then declines, indicating habituation to a fear stimulus.]
Between Session Fear Habituation

The graph shows the SUDS (Subjective Units of Distress) over time. The SUDS scale ranges from 0 to 10, with higher numbers indicating greater distress. The graph indicates a decrease in SUDS over time, with some fluctuations. The Y-axis represents SUDS, and the X-axis represents time.
Rethinking Exposure!

Invited Essay

Optimizing inhibitory learning during exposure therapy

Michelle G. Craske*, Katharina Kircanski, Moriel Zelikowsky, Jayson Mystkowski, Najwa Chowdhury, Aaron Baker

Department of Psychology, 1285 Franz Hall, Box 951563, Los Angeles, CA 90095-1563, USA

Received 3 August 2007; received in revised form 29 September 2007; accepted 2 October 2007
Fear Reduction vs Expectancy Violation

- Mixed evidence that initial levels of distress (IFA) during exposure therapy predict clinical outcomes.
- Little evidence that habituation within sessions predicts outcomes.
- Little evidence that final fear ratings predict outcomes.
- Learning is context dependent – Habituation in one setting does not always transfer to other settings.
- Fear reduction is NOT COMMENSURATE with Fear learning.

Craske et al., 2008; Baker et al., 2010; Kircanski et al., 2012
Exposure in Children/Adolescents

Evidence base smaller and less consistent for youth

- Between session decreases in self-reported distress not linked to post-treatment SUDS for youth with OCD.
- Peak anxiety ratings averaged across exposure sessions do not predict treatment outcome for non-OCD anxiety.
- Duration of exposure unrelated to outcome in pediatric OCD.

Knox, Albano, & Barlow, 1996; Hedtke et al., 2009; Benito et al., 2012; Peris et al., 2015
Fear extinction involves formation of inhibitory associations rather than erasure of fear associations.

Strength of Inhibitory Learning independent of fear reduction during extinction and more dependent on factors such as CONTEXT and TIME.

This suggests an increased focus on FEAR TOLERANCE rather than FEAR REDUCTION during exposure.

Craske et al., 2008
Another way to look at this:

- Maximize the discrepancy between feared and real outcomes.
- Violate fear-triggered expectations of negative outcomes.
Maximizing Inhibitory Learning

- Sustained fear arousal and tolerance not fear reduction
- Maximize mismatch with expectations
- Greater variability and unpredictability of exposure
- De-contextualize exposure
- Multiple fear triggers
- Greater temporal spacing
- Wean safety signals and behaviors
Exposure – The Hard *Most Effective* Way?

Professor Jones and his controversial technique of simultaneously confronting the fear of heights, snakes, and the dark
• Lag Analysis used to examine directionality and sequencing of potential mediators on outcome.

• Youth coping in session did not predict better outcome

• Therapist extensiveness (pushing exposures) predicted better outcome

• Sustained exposures led to acute increase in anxiety but better overall outcome

• Results consistent with Craske et al. (2008) recommendations
Therapeutic Relationship

- Better therapeutic relationship at Week 6 predicted better outcome for CAMS CBT, but not COMB or SRT.

- Youth generally reported positive relationships with providers, and relationships increased following exposure tasks

Cummings et al. 2014, JCCP
Helpful Therapist Behaviors

Collaborative approach to treatment
  • Patient should know what he/she is doing and why

More time doing more extensive exposures
  • As treatment progresses, don’t be afraid to push

For younger patients anyway, make treatment fun!

Balance long-term outcome with short-term anxiety
  • Too much cognitive and coping interventions may attenuate benefits of exposure
Cognitive Intervention

(What are implications of changing views on exposure for CT)
Reasoning with our Fear Circuitry

Professor Weg and his controversial technique of simultaneously confronting the fear of heights, snakes, and the dark.

What we say to dogs
Okay, Ginger! I've had it!
You stay out of the garbage!
Understand, Ginger? Stay out of the garbage, or else!

What they hear
blah blah GINGER blah
blah blah GINGER blah
blah blah GINGER blah
blah blah GINGER blah
In line with desire to emphasize fear tolerance over fear reduction, techniques to challenge or change anxious thoughts may not be as helpful as previously thought.

Coping thoughts may serve to distract patients from exposure task or serve as safety signals.

Coping thoughts ("this isn’t dangerous") may lead to acute reduction of anxiety but interfere with long-term habituation of fear.

Cognitive Interventions

Craske et al., 2008; Kircanski et al., 2012
Coping thoughts may be used initially to facilitate difficult exposures but then neutralized as the exposure progresses – “remember when I said touching that toilet was safe, now I’m not sure”

• Affect labeling may be useful “I feel frightened right now”

• Imaginal exposure – alone or in conjunction with in vivo exposure – to enhance focus on catastrophic outcome may also be helpful

Abramowitz, 1996; raske et al., 2008; Kircanski et al., 2012
Biological Targets
Glutamatergic Hypothesis of OCD

- Glutamate is the principal excitatory neurotransmitter in the adult brain.
- Glutamate acts on NMDA receptor “Coincidence Detector, associative learning”
- Limited evidence, albeit mixed for altered glutamate levels in adult and child OCD.
- OCD ↔ disruption of glutamate neurotransmission in CSTC circuits.

Rosenberg & Keshavan, 1998; Pittenger & Bloch, 2012
Examine effects of CBT on regional metabolite levels
  • Compare pre- and post-CBT levels
  • Brain bases of CBT

Regional metabolite levels as predictors of CBT response
  • Correlate pre-CBT levels with post-CBT response
  • Clinical relevance; inform “personalized medicine”
Magnetic Resonance Spectroscopic Imaging (MRSI)

MRSI provides a measure of metabolite concentrations in discrete brain areas.

These metabolite levels are thought to indicate neuronal integrity and function.

SLAB: select multi-voxel array voxel size <1 cc; scan ~10 min
Study Method

OCD Group
- Randomized to 12 wks CBT or 8 wks WL
- CBT Group: MRSI scan pre- and post-CBT
- WL Group: scanned pre- and post-WL, then provided with CBT and scanned post-CBT
- Treatment responders followed for 3 mos

Controls
- Scanned at Wks 0 & 8
Glu Changes Pre-Post CBT

Cingulate Glutamate decreases following CBT but not WL

**Pre-Post CBT or Waitlist**

**Pre-Post CBT Entire Sample**
Baseline Glu Predicts CBT Response

92% response rate for Lo BL Glu group vs. 57% for Hi group.

Higher baseline Glu predicts smaller CYBOCS change

Baseline Glu 31% lower for CBT Responders vs Nonresponder
Clinical Implications

Augmenting CBT with glutamatergic modulators (to reduce high glutamate levels) in some patients may improve CBT outcomes.

- **D-cycloserine**: Accelerates extinction learning in rodents; partial support for use in adult and child OCD
- **N-acetyl-cysteine (NAC)**: OTC supplement used as SSRI augmenter; Trichotillomania efficacy
- **Riluzole**: FDA-approved for ALS, open and RCT evidence, side effect concerns
- **Memantine**: FDA-approved for Alzheimers, open and single-blind evidence in OCD and ASD
Family-Based Targets
Family Accommodation

Definition

The process by which family members assist or participate in rituals

Examples

• Buying soap, doing extra loads of laundry
• Excusing the child from chores or homework
• Answering questions/providing reassurance
• Dressing/undressing
Family Accommodation of Adult OCD

Calvocoressi et al. (1995; 1999)
• High rates of family accommodation
• Associated with increased family distress

Amir et al. (2000)
• Modification of family routine linked with maternal depression
• Refusal to accommodate linked to parental anxiety
• Accommodation not linked to severity of child’s OCD
# Family Accommodation of Child OCD

## Family participation in OCD

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<tr>
<th>Activity</th>
<th>Weekly</th>
<th>Daily</th>
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<tbody>
<tr>
<td>reassure patient</td>
<td>97 %</td>
<td>56 %</td>
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<tr>
<td>participate in rituals</td>
<td>66 %</td>
<td>46 %</td>
</tr>
<tr>
<td>assist in avoidance</td>
<td>78 %</td>
<td>22 %</td>
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## Consequences of not participating

<table>
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<th>Consequence</th>
<th>Weekly</th>
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<tbody>
<tr>
<td>pt becomes distressed/anxious</td>
<td>80 %</td>
</tr>
<tr>
<td>pt becomes angry/abusive</td>
<td>55 %</td>
</tr>
<tr>
<td>rituals increase</td>
<td>63 %</td>
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## Modification of Routine

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<th>Routine</th>
<th>Percentage</th>
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<tr>
<td>family routines</td>
<td>65 %</td>
</tr>
<tr>
<td>work routines</td>
<td>43 %</td>
</tr>
<tr>
<td>leisure routines</td>
<td>50 %</td>
</tr>
<tr>
<td>assuming child’s responsibilities</td>
<td>48 %</td>
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*Peris et al., 2007*

N = 65
62% Male
M age = 12.3 yrs
Parental OCD associated with:

• Higher total accommodation score
• More frequent modification of family routines
• Greater parental distress when accommodating
• More negative child consequences when not accommodating

Child behavior problems associated with:

• More frequent modification of family routines
• More negative child consequences when not accommodating

Peris et al., 2007
Greater Family Cohesion associated with:

- Fewer negative consequences when not accommodating
- Lower levels of parental distress when accommodating

Greater Family Conflict associated with:

- Increased distress when accommodating
- More negative child consequences when not accommodating

Peris et al., 2007
Family Context of Childhood OCD

Asking families of OCD children – especially distressed families - to resist accommodating child symptoms likely to lead to:

- Emotional distress on part of family
- Negative reaction on part of child
Implications for Treatment

• Setting limits in OCD youngsters with comorbid behavior problems needs to be done carefully

• Treatment response may be facilitated by:
  • Lessening family conflict
  • Enhancing family relations
  • Strengthening family organization

• Parental OCD symptoms may need to be addressed:
  • Associated with less family organization
  • More negative consequences of OCD limit setting
  • Greater distress when limit setting
Goals of Family Intervention

• Reduce level of conflict and feelings of anger, blame, guilt
• Enhance family problem solving
• Facilitate disengagement from child’s OCD symptoms
• Rebuild normal (OCD-free) family interaction patterns
• Foster environment conducive to maintaining treatment gains
Predictors of Worse CBT Response

Child/Adolescent Studies

- More severe OCD
- Poorer psychosocial functioning
- More externalizing symptoms
- Family factors
  - Family History of OCD
  - Overall family dysfunction
  - Parental blame/criticism
  - Poorer family cohesion
  - Higher family conflict

Barrett et al. (2005); Piacentini et al. (2002); Peris et al. (in press); Mars Garcia, 2010
Child OCD CBT Response

Worse response associated with:

- Higher parental blame, $t = 3.12, p < .01$
- Greater family conflict, $t = 2.44, p < .05$
- Lower family cohesion, $t = -4.36, p < .001$

Peris et al., JCCP, 2012
## CBT Response by Family Risk Status

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<th>Family Risk Status</th>
<th>Response Rate</th>
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<tr>
<td>0</td>
<td>92.9%</td>
</tr>
<tr>
<td>1</td>
<td>80.0%</td>
</tr>
<tr>
<td>2</td>
<td>60.0%</td>
</tr>
<tr>
<td>3</td>
<td>14.3%</td>
</tr>
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\[ X^2 (3, 41) = 14.33, p = .002 \]

Peris et al., 2012
Positive Family Interaction Therapy

Six-session family adjunct to standard CBT for high-risk families

- Psychoeducation
- Self-Efficacy
- Affect Regulation
- Parenting Skills
- Family Dynamics

Peris & Piacentini, 2014
Affect Regulation

- Monitor and label emotions
- Learn to tolerate distress
- Increasing parents’ understanding of/ability to model good emotion management
Family-Enhanced vs. Standard CBT for OCD Youth in High Risk Families

Peris et al., 2013

$d = .65$
Technological Enhancements
OC-Go Treatment App

HIPAA-compliant web-based clinician portal and patient-side mobile application designed to increase patient adherence CBT for OCD

Clinicians create and push tailored assignments to patients on their mobile devices

Patients complete between-session assignments with increased fidelity

Searchable clinician-sourced library of exposures, multimedia assignments, and assessments

Supported by Pettit Foundation (Piacentini) and NIMH R42 Grant (Tuerk, Piacentini)
Assignment Builder allows clinicians to sequence and present treatment exercises including psychoeducation, assessments, exposures, and anxiety management techniques quickly and easily.
OC-Go Treatment App

Figure 2. Individual Screen shots of an assignment to address a child’s unrealistic compulsions regarding neatness and school performance.
UCLA Child OCD, Anxiety and Tic Disorders Program

- R. Lindsey Bergman, Ph.D.
- Susanna Chang, Ph.D.
- Tara Peris, Ph.D.
- Michelle Rozenman, Ph.D.
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- IOCDF (Piacentini, Peris, Rozeman, Nurmi)
- NARSAD (Lewin, Peris)
- TSA (Piacentini, Nurmi, McGuire, Ricketts)
- TLC (Piacentini, Peris)
- Friends of Semel Award (Lewin, Peris, Rozenman)
- Pettit Foundation
UCLA Center for Child Anxiety Resilience Education and Support

Supporting the development of resilient, emotionally healthy children through training, research, and community outreach to foster early recognition of childhood anxiety and support families in accessing resources to build family strengths and resilience.

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QUESTIONS