Cognitive Control Targets for the Treatment of Obsessive Compulsive Disorder in Young Children

NCT06102941

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Background

Study Purpose and Rationale:
Cognitive behavioral therapy (CBT) with exposure and response prevention (EXRP) is highly effective for children with Obsessive-Compulsive Disorder (OCD), yet not all children will fully remit. For treatment to be effective, patients must deliberately engage with distressing, obsessive thoughts (exposures) while resisting the compulsive urge to "neutralize" distress with compulsive rituals (response prevention). EXRP efficacy therefore depends on a patient's capacity to actively engage top-down cognitive control to flexibly adapt and regulate their thinking and behavior. Thus, enhancing cognitive control capacity has the potential to reduce OCD symptoms and improve EXRP response in children.

Within the NIMH RDoC framework, Cognitive Systems are responsible for various processes, including cognitive control, that can be examined across units of analysis (e.g., behavior, brain circuits, self-report). These systems are broadly supported by the interplay between the default mode network (DMN) and several task control (TC) circuits, e.g., cingulo-opercular network (CON). Theoretical models and emerging evidence suggest alterations in the development of cognitive control in children with OCD, including altered neural response during cognitive control tasks and resting state functional connectivity (RSFC). Critically, it is also found that the functioning of TC networks and DMN can predict EXRP response.

In this clinical trial, cognitive training (CT) will be utilized to engage and improve cognitive control functioning in children with OCD with the goal of alleviating symptoms and augmenting EXRP. Improved capacity for cognitive control should increase patients' ability to resolve interference between fearful avoidance and exposures to fear-triggers. Thus, CT will be utilized prior to EXRP to enhance behavioral and neural capacity for cognitive control.

A proof-of-concept study (R61 phase) will first be conducted to determine if CT enhances cognitive control behavioral performance (target engagement) in 60 children (8.00–12.99 years old) with OCD sampled from the general community and affiliated clinics. Children will receive 4 weeks of an at-home computerized cognitive training program (AKL-T01) delivered on iPad.

AKL-T01 is available via prescription from Akili Interactive under the name "EndeavorRx" and is currently FDA-authorized for pediatric ADHD. AKL-T01 CT games train multiple elements of cognitive control (e.g., cognitive interference, response inhibition, working memory); improvements have been shown to transfer to non-trained cognitive tasks. AKL-T01 shows good tolerability/acceptability, being rated as fun and engaging, but has yet to be tested in OCD.

Study Design:
This is an NIMH-funded clinical trial (1R61MH129544-01A1) of cognitive training in children with OCD. The clinical trial is registered on ClinicalTrials.gov (NCT06102941).

Participants (*N*=60 children aged 8.00–12.99 years with OCD) will be sampled from the general community and affiliated clinics.

Participants will receive 4 weeks of an at-home computerized CT program (AKL-T01) delivered on iPad (25-min/day, 5 days/week). All children will receive active treatment (no randomization). An iPad will be provided to the participant if the family does not have one for the child's regular at-home use. Adherence to AKL-T01 will be monitored remotely and, if no game play is detected for several days, parent(s)/guardian(s) can be contacted to ensure compliance.

Participants will complete the NIH Toolbox at baseline, mid (2-weeks from CT initiation), and post (4-weeks from CT initiation). Cognitive control behavior will be indexed by NIH Toolbox Fluid Cognition Composite.

Participants will complete MRI scans at baseline and post. Resting state functional connectivity between TC networks and the DMN will be explored as a potential mechanism of action.

Participants will be offered up to 12 sessions of gold-standard CBT/EXRP, generally completed over ~16 weeks, provided by study clinicians at no cost to the child or their family (or community referrals) after study completion.

Statistical Procedures:
Overview: All diagnostics and analyses will be performed in R. Before any statistical technique is applied, we will examine the primary variables using descriptive statistics. Any outlier values will be excluded, and data transformations will be applied if necessary. All statistical models will be reported with 95% confidence intervals and standardized effect sizes to guide future studies.

Target Engagement: The primary clinical trial outcome is NIH Toolbox Fluid Cognition Composite age-normed T-scores pre-CT (Week 0), mid-CT (Week 2), and post-CT (Week 4). We hypothesize that CT will significantly improve NIH Toolbox Fluid Cognition Composite scores.

We will examine a linear mixed effect (LME; R lme4 package) model with Fluid Cognition Composite scores as the outcome, assessment timepoint (W0, W2, W4), age, and sex as fixed effects, and a random effect for participant. Our main outcome of interest is a significant effect of time indicating within-person increases in cognitive performance.

For ClinicalTrials.gov reporting, we will present the mean and standard deviation of NIH Toolbox Fluid Cognition Composite age-normed T-scores at each assessment and paired-test statistics comparing baseline vs. mid-CT and baseline vs. post-CT.

Dosing: We hypothesize that more CT will predict greater improvement in Fluid Cognition Composite scores. Results of the LME model above will be further parsed to examine differences in Fluid Cognition Composite scores between Week 2 and Week 4. We can

also probe this in an LME model examining W2 and W4 scores as repeated-measures outcomes, controlling for baseline scores; a significant effect of timepoint would directly compare change at W2 vs. W4. We will finally explore adherence via the Akili remote monitoring. Specifically, we will examine amount of training (number of sessions, total minutes played, max difficulty level achieved) as a predictor of Week 4 Fluid Cognition Composite scores controlling for baseline scores in a linear regression. Furthermore, we will examine patterns of adherence over the 4 weeks to examine if adherence wanes over time.

Exploratory: We will explore how CT modulates DMN-TC connectivity. LME models will be used to examine within-person change in resting-state functional connectivity (RSFC) pre- to post-CT. Specifically, network-to-network average connectivity (Fisher r-to-z transformed Pearson's correlations) between the DMN and CON, FPN, and DAN respectively will be examined as outcomes in separate LME models, with assessment timepoint (pre-, post- CT), age, and sex as fixed effects, and a random effect for participant. Our outcome of interest is a significant effect of time indicating within-person change in RSFC. Using a parallel LME model in AFNI (3dLME), we will further explore voxel-wise connectivity from the ventromedial prefrontal cortex – a key DMN node.

Power Analysis: We aim to recruit N=70 participants with OCD to achieve a final sample of N=60 allowing for ~15% attrition/data loss. A paired t-test with N=60 would yield 80% power for a minimal detectable effect size of Cohen's $d>.32$ (at $p<.05$ testing the one-sided hypothesis of W4>W0 improvement). Thus, we are powered to detect a small-to-medium effect size. In mediation analyses, assuming an association between independent variable and mediator of standardized regression $\beta>0.30$, we would anticipate >80% power to identify a minimal detectable mediation effect of $\beta>.38$.

Recruitment and Consent

Recruitment:

Describe plans for screening and/or determining eligibility of prospective participants:

Phone Pre-Screening. Prospective participants and their parent/guardian will be screened using an IRB-approved phone screen. Staff will follow an IRB-approved phone screen consent script template. Prior to beginning the phone screen, the parent/guardian will be asked to provide verbal consent to the maintenance of their phone screen data in the study database, even if it is later determined that the child is not eligible for the study. Families will also be asked if they consent to be recontacted for future studies. Phone screen information can be destroyed upon participant request. Regardless of study participation, the information from phone screens will be entered into a password-protected database. An MRI infosheet can be provided to families for additional information about scanning.

Research staff will document verbal consent from the parent/caregiver on REDCap.

Participants who are likely eligible for the study based on the phone screen will be invited to provide consent and assent for study participation.

Note: Several inclusion criteria can be determined fully via the phone screen (prior to assent, e.g., age). Several criteria assessed on the phone screen will require confirmation at the screening assessment after assent/consent (e.g., phone screening may indicate a likely OCD diagnosis to be confirmed via K-SADS after assent). Potential MRI contraindications are assessed on the phone screen. Certain items are automatic exclusions for the MRI portion of the study (e.g., pacemakers, braces), whereas others may require additional confirmation (e.g., dental retainer or metal crowns, bone pin/screw). Parents who endorsed their child having any ASD symptoms on the phone screen will be asked to complete the social communication questionnaire (SCQ) after consent to further assess ASD symptoms (A score of >= 15 is consistent with a diagnosis of ASD and thus will be exclusionary under the pervasive developmental disorder criterion). If a participant has an SCQ score between 11-14, study clinicians will review the case during consensus meetings. Depending on the answers endorsed, if symptoms cannot be better explained by OCD as determined by clinicians during consensus meetings, a participant may be excluded for ASD.

Describe how participants will be recruited:
The study will recruit pediatric participants through methods such as referrals, online (e.g. websites, advertising), flyers, word of mouth, presentations, newsletters, email, or community outreach events. These methods may be used for any of the recruitment settings listed below. All recruitment materials are intended to inform parents/guardians of our study and do not directly address children. Despite precautionary measures enacted to deter children from responding to our postings, if a child does respond to a social media posting, study staff will ask to speak with their guardian regarding their participation in the study; the parent then may contact us.

Paid services: BuildClinical will be engaged to enhance the range and representativeness of recruitment efforts. These services will be provided our IRB-approved recruitment materials and help facilitate outreach via social media, community organizations, parent-teacher groups, clinicians, guidance counselors, etc.

Clinics and Private Practices: Participants may be recruited through local private practices and clinics such as the Morgan Stanley Children's Hospital (CHONY), Columbia University Center for Anxiety and Related Disorders (CUCARD), and the New York-Presbyterian Ambulatory Care Network. Clinicians will be provided info about the study, as well as the flyer and a letter for families who express interest in our research. These community clinicians will initially approach parents or guardians to ascertain their interest in our protocol.

Advocacy and Support Groups: Participants may be recruited through patient advocacy and support groups, such as the International OCD Foundation (IOCDF).

Social Media: Participants may be recruited via ads and posts on social media platforms like Facebook, Instagram, X, Google, Nextdoor, Reddit, etc. A description of this study will

be posted on related social media pages or groups, such as Dr. Marsh's Cognitive Development and Neuroimaging Lab, parenting groups in New York City, and other pages relevant to OCD and anxiety disorders.

RecruitMe: Participants will be recruited through Columbia University's RecruitMe, an online tool to connect potential research participants with researchers conducting relevant studies.

ResearchMatch: Participants may be recruited through ResearchMatch, a nonprofit program funded by the NIH to connect potential research participants with researchers conducting relevant studies.

Libraries, community centers or other community settings: Participants may be recruited from the community through our recruitment methods mentioned above. Such settings include Columbia affiliated spaces, local laundromats, grocery stores, cafes, libraries, and community centers.

Informed Consent Process:
Describe how participants' written consent will be obtained:
Trained research staff (B.A.-level or higher) will obtain written assent from child participants and written consent from a parent/legal guardian providing permission for their child to participate in the study. The assent/consent process will be conducted after the phone pre-screen but before any other part of the study is conducted. HIPAA authorization is contained within the IRB-approved assent/consent forms.

Typically, families will complete the assent/consent discussion via HIPAA-compliant videoconferencing or telephone meeting and families will sign forms remotely by providing a certified e-signature via REDCap. If these processes are conducted in person, forms may be signed on paper, scanned, and stored in REDCap.

The research staff who obtains assent/consent will explain the protocol and associated risks in language that is appropriate to the prospective participant's developmental level. The trained member of the research team will review the study objectives and procedures with the family. The research staff can also ensure that the family understands that information collected as part of this study may be used in the future to answer other research questions not specified in this protocol as we learn more about the diagnoses and neurobiological mechanisms of interest. The assent/consent forms will clearly state that the family may stop participation at any time without penalty. The research staff will answer any questions that the family may have.

As part of the assent/consent process, the study team will seek permission to record diagnostic assessments (clinical interviews) and CBT to obtain reliability/fidelity. Not all visits will be recorded; this will be determined by the needs of the study. Participants may opt out of the recordings during the assent/consent process and still remain eligible for the rest of the study.

Study Procedures

Overview. Participants will complete four study visits detailed below (screening, baseline, mid-training, post-training) as well as cognitive training at home. After the study, participants will have the option to complete CBT for OCD. Remote contact with the family during and between study visits will occur via institutional email, HIPAA-compliant videoconferencing, telephone, text (e.g. SimpleText and Google Voice) or HIPAA-compliant phone systems (e.g., Doximity). Families can be sent a REDCap link to complete questionnaires before or during each study visit. Upon parent/guardian request, an absence note can be provided to the family to explain that they are attending a research visit (during school/work hours).
Assessment measures are detailed below along with a Schedule of Events table.

Eligibility. Participants will be eligible for the study if they meet the inclusion criteria and do not meet any exclusion criteria.

Inclusion Criteria

1. Age 8–12 years at the time of consent (i.e., 8.00–12.99 years)
2. DSM-5 diagnosis of OCD as their psychiatric principal problem. They must have clinically significant symptoms (C-YBOCS ≥ 16)
3. Not on psychotropic medication (either treatment-naïve or free of psychotropic medication for at least one month) or on stable medication regime for ADHD or OCD (e.g., stimulants or SSRIs, respectively), and not receiving current psychotherapy for OCD
4. Ability to tolerate a treatment-free period (i.e. not initiating exposure therapy for OCD during the Akili phase of the study)
5. Capacity to provide written informed assent by the participants and permission by the parent/guardian

Exclusion Criteria

1. DSM-5 current major depressive disorder,
2. DSM-5 current or lifetime diagnosis of PTSD, substance/alcohol abuse, psychotic disorder, bipolar disorder, eating disorder, pervasive developmental disorder**
3. Current or lifetime history of a major medical or neurological problem (e.g., unstable hypertension, seizure disorder, major head trauma)
4. Active suicidal ideation with some intent to act
5. Presence of metallic device (ferromagnetic implants or dental braces)***
6. Females who are pregnant or nursing
7. Wechsler Abbreviated Scale of Intelligence II Full-scale IQ <80

***Note: Anxiety disorders (i.e., generalized anxiety, panic disorder, social anxiety, and specific phobia, and separation anxiety), attention-deficit hyperactivity disorder, and tic disorders will be permitted as long as OCD is the principal problem as defined above. Pervasive developmental disorder includes ASD diagnosis.*

***Note: Participants with MRI contraindications or otherwise unwilling or unable to complete MRI (e.g., severe claustrophobia) will be permitted to participate and complete all procedures, except for MRI procedures.

Assessment Measures

Questionnaires

- Pubertal Development Scale: child-report of **Tanner** stage (2-5 mins)
- Edinburgh **Handedness** Inventory: child-report preference for left/right hand (2-5 mins)
- Temperament in Middle Childhood Questionnaire (**TMCQ**): parent-report of child temperament, including Inhibitory Control and Attention Focusing. (5-10 mins)
- Behavior Rating Inventory of Executive Function (**BRIEF**): parent-report of child executive functions at home. (5-15 mins)
- K-SADS Family History Screen (**FHS**): parent-report of family psychiatric disorders. (5-15 mins)
- Demographics form: family report of sociodemographic characteristics (5 min)
- Obsessive Compulsive Inventory (**OCI**): child-report of OCD symptoms. (5-15 mins)
- Children's Depression Inventory (**CDI**): child-report of depression symptoms. (5-15 min)
- Screen for Child Anxiety Related Disorders (**SCARED**): child and parent report of child anxiety symptoms (generalized, separation, panic, social phobia) (5-15 mins)
- **Conners**-3: parent-report of child ADHD symptoms. (10-25 mins)
- **Screen-Q**: parent-report of child screen exposure including access, frequency, content, and parent-child interaction (co-viewing) (5-15 mins)
- Family Accommodation Scale (**FAS**): parent-report of parental accommodation of OCD symptoms. (5-15 mins)
- Akili Acceptability: brief child-report of experience with CT at home (5 min)
- ZMBBI Metal Screen: ZMBBI provides and requires a comprehensive safety screening for contraindications before MRI. (5-15 mins)
- Social Communication Questionnaire (SCQ): self-report on 40 questions for Autism Spectrum Disorder (ASD) screening (5-10 mins). A total score of >= 15 has been indicative of ASD and thus will be exclusionary.

Clinical Assessments

- Child Yale-Brown Obsessive-Compulsive Scale, Present and Lifetime version (**C-YBOCS-PL**): semi-structured interview of OCD severity. It will be used to establish OCD as a diagnosis and rate OCD severity. (30-60 mins)
- The Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version (**K-SADS-PL**): validated semi-structured clinical interview designed to assess lifetime history of mental disorders. (45-90 mins)
- Children's Global Assessment Scale (**CGAS**): brief clinician rating of general functioning. (1 min)
- The Clinical Global Impression of Severity/Improvement Scale (**CGI**): brief clinician rating of illness severity. (1 min)
- The NIMH Global Obsessive Compulsive Scale (**GOCS**): brief clinician rating of overall OCD severity from 1 (minimal symptoms) to 15 (very severe). (1 min)

- Columbia-Suicide Severity Rating Scale (**C-SSRS**): semi-structured clinician rating of suicide ideation, suicidal behavior, suicide attempts. (5-15 mins)
- Patient Ex/Rp Adherence Scale (**PEAS**): brief clinician rating of a child's completion of exposure therapy techniques between sessions (1 min).

Cognitive Testing

- Wechsler Abbreviated Scale of Intelligence (**WASI-II**): This estimates Full Scale IQ with excellent reliability and validity for ages 6-90. Two sub-tests will be administered: Vocabulary and Matrix Reasoning. (20-30 mins)
- NIH Toolbox Cognition Battery (**NIHTB-CB**): This battery tests multiple well-validated indices related to cognitive control capacity in children. Children will complete five standardized, validated tasks on an iPad: (1) Flanker inhibitory control and attention task, (2) Dimensional Change Card Sort test of set-shifting function, (3) List Sorting Working Memory Test, (4) Pattern Comparison Processing Speed Test, and (5) Picture Sequence Memory. Sample demonstrations of the tasks can be found here: http://www.healthmeasures.net/explore-measurement-systems/nih-toolbox/intro-to-nihtoolbox/cognition. The Toolbox also generates a standardized Fluid Cognition Composite score from these five tests (30-45 mins)

Schedule of Events

	Assessment	Screening	Baseline	Mid-CT	Post-CT	CBT
	MRI Scan		**Child**		**Child**	
Surveys	Tanner		**Child**			
	Handedness		**Child**			
	TMCQ		**Parent**			
	BRIEF		**Parent**			
	K-SADS FHS		**Parent**			
	Demographics		**Child/Parent**			
	OCI		**Child**		**Child**	
	CDI	**Child**			**Child**	
	SCARED		**Child/Parent**		**Child/Parent**	
	Conners		**Parent**		**Parent**	
	ScreenQ		**Parent**		**Parent**	
	FAS		**Parent**		**Parent**	
	Akili accept.			**Child**	**Child**	
	SCQ *	**Parent**				
	ZMBBI Screen	**Parent**	**Parent**		**Parent**	
Cognitive Tasks	NIH Toolbox		**RA**	**RA**	**RA**	
	WASI	**RA**				
Clinical Interview	K-SADS	**IE**				
	C-YBOCS	**IE**			**IE**	**IE**
	CSSRS	**IE**			**IE**	**IE**
	GOCS	**IE**			**IE**	**IE**
	CGI	**IE**			**IE**	**IE**
	PEAS					**IE**

Note: Within a given visit, assessments may be conducted in any order. Tasks and interviews administered by RA=Research Assistant or IE=Independent Evaluator

*** 4 SCQ items are included on the phone screen; if any items are endorsed, then the full measure will be completed at the screening assessment.**

Schedule of Research Visits

Screening Assessment

Families will complete initial diagnostic assessment and questionnaires to confirm eligibility and determine baseline clinical status. The visit will ideally be completed in one day but may be spread out over the course of multiple days to accommodate participant schedules. The clinical interviews can take approximately 4-5 hours, though the duration of the interviews varies based on symptoms endorsed by the participant. This visit can be conducted remotely or in-person. An eligibility checklist will be signed by a study MPI, PhD-level, or LMSW-level staff. This assessment may be paused or ended if a likely or definitive exclusion is identified. In that circumstance, staff will complete the C-SSRS before ending the visit to ensure assessment of participant safety.

Final diagnoses will be confirmed through a consensus meeting with a clinically licensed member of the team. Upon request, diagnostic results can be provided to families by a clinically licensed member of the study staff after completion of the diagnostic evaluation. If a participant is not eligible, community resources/referrals can be provided, if appropriate. Results regarding eligibility can be communicated by study coordinators and/or clinically licensed study staff via email and/or over the phone.

If the participant requests a full day study visit to complete their screening assessments and baseline assessments, we may initiate baseline assessments once eligibility is tentatively confirmed via the C-YBOCS to reduce participant time burden. In these full day visits, a meal may be provided for the participant and guardian(s). The family will have the option to choose their meal from a menu offered by one of the vendors at the CU Zuckerman Institute, so they are able to decide their item based on their dietary restrictions. The items will total up to $35.

Additionally, depending on scheduling and logistics, participants may complete the baseline self-report CDI during the screening assessment visit (post-consent). As the CDI assesses suicidal ideation, having this information prior to the baseline assessment's clinical interview can help guide the clinician's approach and risk evaluation with the participant.

Baseline Assessment

Eligible participants can proceed to the baseline study visit, including an MRI scan, NIH Toolbox, and questionnaires. During the MRI, the participant will be instructed to lie as still as possible within the magnet for approximately 60-70 minutes to acquire structural and functional MRI scans. All precautions and protections will be given to the participant to ensure that they are as safe and comfortable as possible. The participant will be given a squeeze ball to request to terminate the scan at any time. All of the MRI procedures will be conducted on the 3-Tesla MRI scanner at ZMBBI. The participant will have the option to undergo training for the MRI in an MRI simulator prior to scanning. If the study team determines that the participant is unsuitable for the MRI scan (e.g., due to claustrophobia

or an inability to remain still), the MRI portion of the study may be omitted for that participant.

Cognitive Control Training (CT)
Following completion of baseline assessments, eligible children will receive 4 weeks of cognitive training with AKL-T01 (from Akili Interactive). Participants will be instructed to use AKL-T01 at home for 25 minutes per day, 5 days per week with an iPad provided if needed. Note that, study staff will retain access to the iPad "Find my" device function but that this will only be used in the case that a family loses the device.

Adherence to training can be monitored electronically by study staff using an Akili-provided dashboard. Parents can be contacted if several days have elapsed without game play. The AKL-T01 training can generate automatic reminders to parents.

Mid-CT Assessment
Participants will be asked to return for a visit approximately 2 weeks after initiating the Cognitive Training to complete the NIH Toolbox.

Post-CT Assessment
Approximately 4 weeks after initiating at-home cognitive training, participants will be asked to return for a post-Training visit, including the NIH Toolbox and MRI. The MRI protocols will be the same as the baseline assessment.

Post-Research Study Participation: Cognitive Behavioral Therapy/Exposure and Response Prevention (CBT/EXRP) for OCD
After completing research procedures, participants will be offered no-cost CBT/EXRP for OCD or community referrals. The CBT/EXRP provided will focus on treating clinically significant OCD symptoms that remain after research participation, i.e., as of the Post-CT assessment. If a participant does not exhibit clinically significant OCD symptoms after the research protocol, community referrals will be offered. If the participant would like to complete OCD treatment with our team, they will be offered up to 12 sessions of manualized CBT/EXRP, generally completed over ~16 weeks. Participants must opt-in to treatment within 6-8 weeks after being enrolled into the study, after which point community referrals can be provided. If participants elect for optional CBT/EXRP, the C-YBOCS will be administered to measure symptom severity post-CBT. The CGI will be completed at all CBT sessions. The C-SSRS will be administered as needed given identified risk at prior clinical evaluations. The PEAS will be administered at CBT sessions after initiation of between-session exposures (i.e., homework).

Early Discontinuation
Participants who experience significant clinical worsening (e.g., worsening of OCD) or adverse effects sufficient to require removal from the study (e.g., new onset major medical problems) can be referred for appropriate clinical care by the research staff. The study clinicians can review the clinical assessments and questionnaires to assess clinical worsening. If the family is unable to complete the at-home cognitive training regimen (25-

min/day, 5 days/week), study staff may discontinue their research participation. If a participant withdraws from the study (for any reason), staff will work with the family to return the study-provided iPad as needed (e.g., by providing the family a pre-paid return shipping box).

Risks, Benefits & Monitoring

Potential Risks:

There are several risks associated with this study. Although they are believed to be no more than minimal, these risks are taken very seriously; we have carefully considered their occurrence and potential impact and take several steps to minimize them.

(i) Psychological Distress. As in all psychological and psychiatric survey research, there is a risk that some of the questions asked may lead participants to experience psychological distress. Participants will be informed of such during the consent procedures. In the event that participants experience discomfort when completing the interviews/self-report measures/tasks, they can refuse: (a) to answer any questions and/or (b) to complete any tasks that make them uncomfortable. Further, all participants may choose to discontinue an assessment session at any time, or, if they wish, to withdraw from the study. This will be explained in the informed consent form as well as reiterated orally prior to the onset of the assessment.

(ii) Privacy. Another potential risk is a breach of confidentiality. To protect against the loss of confidentiality, all study materials will be kept on secure, encrypted servers. Additionally, paper materials will be locked in a separate file, coded by a unique study code number (with names and other personal identifying information kept separately). All data will be de-identified prior to securely sending to the investigator team.

(iii) Magnetic Resonance Imaging. The FDA has deemed MRI scanning on a Siemens 3-Tesla MRI scanner at ZMBBI to be classified as a non-significant risk. We run the scanner at a level called ‘Normal Mode.’ With this level, all scans remain within the FDA’s safe operational limits and as a result, the FDA considers this mode of operation for our scanner to be a non-significant risk. All available precautions and protections will be given to the participant to ensure that they are as safe and comfortable as possible. Some participants may report feeling uncomfortable or nervous while in the scanner. Additionally, participants may feel uncomfortable during the scan due to the small space. The participant will be given a squeeze ball to alert staff of any issues; the scan can be terminated at any time upon participant request.

Although scans from this study will be used only for research purposes, the T1 and T2 anatomical images from each participant’s first MRI (pre-CT) will be sent to a radiologist to be examined for evidence of any incidental structural findings within two weeks of the scan visit. The study team will provide approved MRI findings letters indicating the results of the radiologist report to the participant. The PIs will be available to discuss findings with families as needed.

(iv) Delay to treatment: As with any study that involves a treatment-free period, there is a risk that symptoms will worsen over time, as they might in a non-research environment. If a participant's symptoms worsen and/or there is a concern for safety (e.g., suicidality), the participant may be withdrawn from the study and referrals to external standard care may be provided.

(v) Data sharing with the NIMH Data Archive (NDA): every effort will be made to ensure the confidentiality of these data, however, there is a potential risk of identification.

Potential Benefits:
This research study is not designed to directly benefit the participant. The knowledge to be gained may impact our understanding of OCD and methods of treatment.

Alternatives:
The study poses no greater than minimal risk.

Currently, CBT/EXRP and serotonin reuptake inhibitor medication are considered the first line treatments for OCD. However, pharmacotherapies have relatively modest effects in OCD. CBT/EXRP treatment is the mainstay of the treatment for OCD. Yet, CBT/EXRP alone results in response rates of anywhere between 60% and 80%, and fear of non-adherence to EXRP is hypothesized to contribute to the lack of EXRP efficacy across age groups.

Data and Safety Monitoring:
Members of the research team involved in data and safety monitoring have all been trained in confidentiality protection and complete all required CITI and HIPAA trainings. Data will only be collected via secure, compliant methods (e.g., institutional REDCap). To ensure confidentiality, links between ID code and PHI will be kept only in secure databases with access restricted only to study staff.

Any protocol deviations, adverse events, or unanticipated problems will be logged within the project REDCap with forms adapted from NIH templates. The study PIs will review and sign off on any of these events. The study team will report all serious adverse events and unanticipated problems to the IRB and sponsor, as needed per Columbia University and NIMH policy.

Study staff will monitor and help ensure timely completion of study records and appropriate source documentation, updating of regulatory documentation, and fulfilling reporting requirements to the Sponsor, including timely submission of information for annual reports.

Clinically licensed members of the research team will be responsible for monitoring the clinical safety of all research participants.

Subjects

Describe and justify reimbursement/compensation:

Participants will be compensated with gift cards through Amazon, Trucentive, or other similar services. Gift cards will be given or sent securely via email to the caregiver(s) for their child's participation.

Total compensation is up to $400.

1. Screening visit compensation = $75
2. Baseline visit compensation = $125 ($100 for MRI and cognitive testing; $25 for travel). If the child is ineligible or does not complete MRI, they will be compensated $75 ($50 for cognitive testing and $25 for travel)
3. Mid-CT (wk2) visit compensation = $75 ($50 for cognitive testing and $25 for travel)
4. Post-CT (wk4) visit compensation = $125 ($100 for MRI, cognitive testing, and clinical assessment; $25 for travel). If the child is ineligible or does not complete MRI, they will be compensated $75 ($50 for cognitive testing, and clinical assessment; $25 for travel).

Note: If the participant comes in for a full day visit, a meal will be provided for the participant and their family for up to $35.

Suicide Risk Management Plan

Overview: Potential suicide risk will be assessed during the initial screening visit and follow-up evaluations. This risk may be identified during the C-SSRS interview and/or via self-report on the CDI. Additionally, for participants who complete CBT after cognitive training, the C-SSRS will be administered as needed given identified risk at prior clinical evaluations.

Emergency contacts. Families will provide an emergency contact outside of the parent/guardian. If the parent/guardian is not reachable during an emergency, study staff will contact the alternate emergency contact. Staff will ascertain the family's home location on the demographics form and best contact phone number during phone screen. The clinical interviewer will confirm that this is the location that the participant is currently at during any remote assessment.

Indication of Potential Suicide Risk: [1] if a participant endorses C-SSRS Ideation item 4 (intent to act) or item 5 (plan), within the last month and/or [2] if a participant endorses a 2 ("I think about killing myself but would not do it") or a 3 ("I want to kill myself") on CDI item #9, the following steps will be initiated:

Suicide Risk Follow-Up: If potential suicide risk is ascertained during an ongoing interview, the clinical interviewer will conduct these steps. If risk is reported on the CDI self-report only, a study clinician will contact the family within 48 hours to conduct a risk assessment.

1. The clinical interviewer will assess imminent risk (i.e., risk for suicide in the next 24-48 hours). If participant is deemed at imminent risk, the clinical interviewer will speak with the child's parent/guardian to engage appropriate intervention (e.g., taking child to ED, calling 911, etc.).

2. The clinical interviewer will create a Stanley-Brown Safety Plan with the participant, as appropriate. This information will be entered into REDCap and, upon completion, immediately emailed to the participant and their parent/guardian.
3. The clinical interviewer will relay the results of the risk assessment to the parent/guardian and discuss recommendations (e.g. treatment referrals, coping skills) related to the child's safety, as appropriate.
4. The study staff will document the encounter in REDCap, which will include both risk assessment details as well as associated steps to mitigate risk.

* If risk is ascertained on the C-SSRS at the screening assessment, the remainder of the study procedures can be discontinued as the child will not be eligible for the study. Referrals for clinical care in the community can be provided via email.