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STUDY INFORMATION

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  Resurgence as Choice: Basic and Clinical Studies
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1.0 Research Design

1.1 Purpose/Specific Aims

Destructive behavior within intellectual disability. About 4 million people in the U.S. have an intellectual disability, and 12.5% (½ million) display destructive behavior, such as aggression and self-injurious behavior (SIB).[1] The risk for destructive behavior increases with intellectual-disability severity, communication deficits, and co-occurring autism spectrum disorder.[2] Severe destructive behavior is a primary reason for institutionalization. In 1994, the annual costs of destructive behavior exceeded $3.5 billion in the U.S., and the costs are considerably higher today.[3] SIB produces health complications, including soft-tissue damage, blindness, self-amputation of body parts, fractures, brain trauma, and even death.[4] Individuals with aggressive behavior are at increased risk for institutionalization, social isolation, physical restraint, over-use of medication, denial of services, and physical abuse.

Functional analysis and treatment of destructive behavior. The assessment of aberrant behavior has traditionally been based on its structural characteristics and the extent to which certain responses co-occur (e.g., peculiar vocal, social, and motor responses lead to the diagnosis of autism). Another approach to assessing aberrant behavior is by its function (i.e., the behavior's effect on the environment). Other fields of science have long understood the importance of analyzing both the structure and function of dynamic entities, and recently behavior analysts have increasingly assessed destructive behavior both in terms of its structural characteristics (e.g., aggression, SIB) and its function. For example, a boy with autism might display SIB because when he does, others do not approach or interact with him. In this case, the function of SIB would be to avoid or escape social interaction. Functional analysis, as a specific method for analyzing, understanding, and developing treatments for destructive behavior, began in 1982 with the publication of the seminal paper by Iwata and colleagues.[6] This method consisted of a control condition (play) and three test conditions (attention, demand, and alone) designed to test the prevailing behavioral hypotheses regarding SIB articulated by Carr.[7] These three hypotheses were that SIB was maintained by (a) positive reinforcement in the form of contingent attention; (b) negative reinforcement in the form of escape from or avoidance of nonpreferred tasks; and/or (c) automatic reinforcement (e.g., reinforced by the sensory stimulation automatically produced by the response).

Functional analysis has become the predominant method of prescribing effective behavioral treatments for persons with intellectual disability who display severe destructive behavior.[8] Numerous investigations directly comparing function- and non-function-based treatments have consistently produced results favoring the function-based approach.[9,10] In addition, results of large-scale, meta analyses and epidemiological studies indicate that, across studies, behavioral treatments were more effective when they were based on a prior functional analysis.[12,13,14]

Functional communication training. Perhaps the most important asset of functional-analysis methods has been the systematic identification of the reinforcer (i.e., reward that maintains behavior in the environment) for destructive behavior, which allows the behavior analyst to decrease destructive behavior and replace it with more prosocial behavior.[15] One such treatment that is inexorably linked to

functional analysis is differential reinforcement of alternative behavior (DRA). DRA is often prescribed when a functional analysis indicates that destructive behavior is reinforced by socially mediated consequences.[16-24] With DRA, the social consequence (e.g., attention, toys, breaks from instructions) that heretofore reinforced destructive behavior is delivered contingent on an appropriate communication response, while destructive behavior is on extinction (i.e., reinforcers are no longer provided). For example, if a functional analysis shows that aggression is reinforced by escape from demands, DRA would typically involve (a) teaching the child to access breaks from demands via a functional communication response (FCR; e.g., saying, "Break, please") and (b) placing destructive behavior on extinction (i.e., continuing with scheduled demands independent of destructive behavior). In large studies and reviews, investigators have cited DRA as the most commonly implemented, effective treatment for destructive behavior that is based on the results of a functional analysis.[17-21]

Limitations of DRA. Although highly effective, DRA has a number of limitations[17-21] that compromise its effectiveness when implemented by caregivers in the natural environment. In the latter stages of DRA, caregivers are trained to implement treatment, and it is critical that they do so with high procedural integrity (e.g., 90% accuracy), which is more likely if the intervention is practical and compatible with their daily routine. Researchers have identified two important practical limitations of DRA that can interfere with accurate caregiver implementation, namely that treated individuals request reinforcement via the FCR (a) at exceedingly high rates (e.g., request to escape every adult directive) or (b) when it is difficult for the caregiver to deliver reinforcement (e.g., requesting attention when a parent is changing an infant sibling). Our research team and others have used reinforcer-schedule thinning procedures to address these limitations and improve the practicality of DRA.[21,23] Reinforcer schedule thinning involves progressively and systematically reducing the amount of reinforcers available during treatment sessions. This process is conducted in order to prepare the treatment to be practically used when reinforcers cannot always be feasibly delivered. Unfortunately, in the first large study on reinforcer-schedule thinning, we found that DRA was ineffective in 14 of 25 applications when schedule thinning reached a practical endpoint.[21] In most cases, it was necessary to add a more restrictive and intrusive punishment component to DRA in order to thin the schedule and also maintain low rates of destructive behavior. A recent replication of this large study reported somewhat more favorable outcomes, but DRA plus schedule thinning still only maintained a 90% reduction from baseline in 11 of 23 applications (48%).[23] In addition, other recent studies have found that when participants treated with DRA were subsequently exposed to extinction of the FCR (or thin reinforcement schedules), treatment relapse often occurred in the form of resurgence of destructive behavior.[24-26] Similarly, in the first large scale study examining the prevalence of resurgence during schedule thinning, we found that resurgence occurred in 19 out of 25 applications or 76%.[27] Collectively, the limitations stated above are evidence for continued refinement to DRA procedures to increase efficacy. In the same way, it is imperative that we develop more durable procedures that will reduce the likelihood of resurgence (i.e., relapse of destructive behavior). These limitations of DRA are actually predicted by a quantitative model derived from behavioral momentum theory. Behavioral momentum theory is a quantitative theory that predicts that DRA, as it is typically implemented, actually promotes resurgence and resistance to extinction for destructive behavior when the FCR is exposed to extinction or thin reinforcement schedules. More importantly, behavioral momentum theory provides clear quantitative guidance on how DRA procedures might be altered in order to mitigate or prevent treatment relapse.[28] Several lines of research have used behavioral momentum theory as a guide to develop more efficacious DRA procedures. Unfortunately, recent developments suggest that behavioral momentum theory may not

accurately predict resurgence, and the core concepts may be flawed.[31,32]Accordingly, Resurgence as Choice Theory provides an alternative avenue as a quantitative model that provides more accurate predictions of resurgence during extinction challenges (i.e., reinforcers are no longer provided for appropriate behavior) and reinforcement schedule thinning (i.e., fewer reinforcers are available for appropriate behavior).[31,32]

The following specific aims relate to only those clinical studies that will be conducted at Children's Specialized Hospital–Rutgers University Center for Autism Research and Services (CSH–RUCARES) and at the Douglas Developmental Disabilities Center (DDDC), both of which are Rutgers University research and training sites owned by Rutgers University. Other specific aims from the grant application pertain to studies involving nonhuman animal subjects, which will be conducted solely at Utah State University.

Specific Aim 1: Identify the optimal duration of treatment with DRA. We will compare short, moderate, and extended durations of treatment with DRA to identify the optimal duration of treatment to reduce the extent of relapse of destructive behavior. We will demonstrate that the degree of relapse may depend on the length of treatment with DRA.

Specific Aim 2: Demonstrate the benefits of DRA treatments with empirically informed schedule thinning progressions. We will use measurements of destructive behavior, appropriate behavior, and reinforcer deliveries during each treatment session to inform the number of reinforcers that will be available during upcoming treatment sessions, informed by both the Resurgence as Choice (RaC) Theory and on the results of a coordinated study with nonhuman animals. We will demonstrate that this schedule thinning progression is efficacious at maintaining an 85% reduction in problem behavior (i.e., relative to baseline) during each treatment session.

A. Objectives

Severe problem behavior (e.g., self-injurious behavior, aggression) of children with intellectual disabilities is prevalent, potentially dangerous, and negatively impacts social integration and quality of life.[33, 34] Function-based differential reinforcement of alternative behavior (DRA) interventions reduce such behavior effectively,[21,35,36] but treatment relapse often occurs when a caregiver does not deliver reinforcement for the alternative behavior (e.g., caregiver is busy with an infant sibling). Such relapse is known as resurgence. Resurgence is typically studied in a three-phase experiment: (a) reinforcement is delivered exclusively for the target response in the Phase 1 baseline; (b) reinforcement is delivered exclusively for an appropriate alternative response in the Phase 2 treatment; and (c) all reinforcer deliveries cease in the Phase 3 extinction challenge, which serves as the resurgence test and simulates a lapse in treatment implementation by caregivers. Resurgence as Choice (RaC) is a quantitative theory of resurgence built from two fundamental and well-established principles of reinforcement: (a) individuals allocate proportionally more responding to responses that produce proportionally more reinforcement (i.e., the matching law); and (b) the value of reinforcement decreases over time, typically by a hyperbolic-decay function (e.g., delay discounting). Nevin et al [37] attempted to apply the matching law early on to the phenomenon of response persistence, which is related closely to resurgence, but failed largely because the matching law typically applies to multiple, concurrently available reinforcers. Researchers typically evaluate response persistence and resurgence when reinforcers are unavailable

(e.g., during extinction). Nevin developed behavioral momentum theory (BMT) as a result, which accounts for response persistence and resurgence in some situations but not in others.[31,32] Our preliminary data suggest that RaC better describes resurgence by adding the principle of reinforcement-value decay using a mathematical formula to account for reinforcement history. Reinforcement-value decay quantitatively accounts for dynamically changing reinforcement conditions, including when all reinforcement ceases during the resurgence test. RaC combines these two well-established principles into a mathematical model that appears to account for resurgence in situations in which BMT has failed. Moreover, RaC is a more general model of resurgence that makes predictions about variables not accounted for by BMT (e.g., response effort; reinforcer quality). In addition, it does so more parsimoniously, with fewer free parameters. Our overarching hypothesis is that RaC-informed differential reinforcement treatments, relative to BMT, will be less susceptible to resurgence of problem behavior: (a) during periods when reinforcers are unavailable during the resurgence test; (b) when reinforcer availability diminishes during reinforcement schedule thinning; and (c) when other response or reinforcement parameters change, such as increases in response effort.

1.2 Research Significance

Resurgence as Choice theory is based on two well-developed concepts: (a) Individuals allocate proportionally more behavior towards responses that proportionally produce more reinforcement, and (b) the value of different experiences with reinforcers decreases over time. The theory is relatively more parsimonious than behavioral momentum theory and provides more general predictions than behavioral momentum theory.[32] In essence, the theory is grounded in the notion that relapse of behavior is governed by the same processes that underlie choice behavior (e.g., destructive behavior and appropriate communicative responses).[32]The two predictions that are most relevant to our project are (a) resurgence of destructive behavior will decrease with increased DRA treatment duration, and (b) reinforcement schedule thinning show included slow, small decreases in reward deliveries (smaller than those previously reported in the literature). Accordingly, our project will examine the effects of different durations of DRA on resurgence and the effects of adjusting the schedule of reinforcement for each session to include slow and small decreases to avoid resurgence. Findings from this project could have vast clinical implications in that we will demonstrate that time in treatment affects relapse and that schedule thinning can be accomplished without recurrence of destructive behavior.

1.3 Research Design and Methods

A. Research Procedures

General methods common to Experiments 1 and 2. Potential subjects will receive treatment 3 to 6 hours a day, 5 days a week for about 8-16 weeks depending on the subject's availability. If Experiment 1 is successful at reducing destructive behavior to a desirable level with DRA at a dense schedule, we may conduct Experiment 2 with the same subjects. However, each experiment tof the project is independent of the other experiment, and no experiment is required before conducting the other experiment. We may assign subjects to experiments of the project via randomization procedures. Assessment and treatment will be conducted initially in treatment rooms with adjacent observation windows to allow unobtrusive measurement of behavior. Some treatment rooms will have padded walls and floors, which will be used, when necessary, to maintain patient and staff safety. Therapists will conduct multiple sessions daily with each child. We will use controlled, single-case experimental designs (e.g., multielement, reversal) to conduct analyses and

test clinical hypotheses for each child in which subjects serve as his/her own control. We will interpret assessment and treatment results for each child using structured, visual inspection criteria developed and refined by our research team, which have demonstrated reliability, validity, and power to detect differences between test and control conditions with individual children (within-subject; each child serves as his/her own control).[38,39] A large amount of our methodology will be performed as our standard-of-care procedures in a severe behavior program.

Children referred to the Severe Behavior program engage in severe destructive behavior such as aggression, property destruction, or self-injurious behavior for several different reasons. That is, their destructive behavior may be evoked (or triggered) by commonly occurring situations such as having a preferred toy or snack removed, being asked to do schoolwork or chores or having a caregiver too busy to pay attention to them at the moment. The research activities will not introduce any new triggers other than those that maintain destructive behavior in the natural environment. For example, in the course of the research, we may determine (using functional analysis methods) that a child's aggression is maintained by escape from non-preferred tasks, and we will present these work tasks throughout the study. We will present these tasks in order to teach the child to ask for a break instead of engaging in aggression, and in order to determine whether the use of a multiple schedule (signals for periods in which the child will be given a break if (s)he asks and periods when (s)he needs to do her work) will mitigate relapse of aggression during common treatment challenges. While none of the research procedures will expose children to evocative situations that do not occur in their natural (home or school) environment, there is still the likelihood that we will see temporary increases in destructive behavior during (a) assessment (i.e., functional analysis), (b) when increasing the amount of time that the child needs to wait or work without getting his or her way (i.e., schedule thinning), and (c) during treatment challenges (i.e., tests for resurgence). The following procedures are in place to minimize risk to subjects. All therapists participating in the study will receive formal training on how to appropriately and safely block problem behavior in a manner that minimizes risks of harm. For example, if a child engages in self-injurious behavior in the form of hand-to-head hitting, therapists working with the child will stay within arms reach of the child at all times and carry small pads which can be used to reduce the impact of the self-injurious behavior. If the child's problem behavior appears to escalate to unsafe levels, the session will be ended and clinically-approved measures will be taken to ensure the safety of the child.

Experiment 1: Clinical study on treatment duration.

Our preliminary data[40] suggest that DRA treatments for destructive behavior like those described below consistently produce at least 85% reduction in baseline rates of destructive behavior after 1-4 DRA sessions. Based on these results, we will set the length of our short-duration condition to approximately 4 sessions. RaC predicts that this short duration of DRA will produce high magnitudes of resurgence during a resurgence test but less resurgence than predicted by BMT. We will compare this short-duration condition with a moderate-duration condition (i.e., approximately 8 sessions of DRA) and an extended-duration condition (i.e., approximately 32 sessions of DRA). RaC predicts that, relative to the short-duration condition, the moderate-duration condition will reduce resurgence only slightly, but the extended-duration condition will reduce resurgence considerably. Each of three durations of DRA (i.e., short, moderate, and extended) will

consist of three phases, a baseline phase, a treatment phase (i.e., DRA), and an extinction phase (i.e., resurgence test). We will conduct this progression of phases three times per participant (i.e., one progression for each duration of DRA), with each progression occurring in a novel stimulus context (i.e., three contexts per participant assigned to conditions randomly), to minimize carryover effects.

Baseline- and DRA-progressive-interval assessment. We will conduct a brief, progressive-interval assessment (PIA) to identify a sufficiently dense schedule of reinforcement for use in subsequent baseline and DRA sessions. The assessment will be identical to the functional-analysis condition with the highest rates of destructive behavior (e.g., the attention condition of the functional analysis for attention-reinforced destructive behavior) with the following exceptions: (a) initially, destructive behavior will be reinforced on a dense schedule of reinforcement, (b) periods of nonreinforcement will begin and increase after every two reinforcer deliveries, and (c) the assessment will end after two reinforcement deliveries corresponding to a nonreinforcement period of 180 s or if untoward effects are observed (i.e., a burst of destructive behavior or negative emotional responding). We will use the results of the PIA to select a dense schedule of reinforcement that does not produce bursts of destructive behavior nor negative vocalizations for use in the baseline and DRA phases.

Stimulus contexts. Reinforcement effects tend to be specific to the stimulus context in which reinforcement is delivered.[41] Therefore, we will compare the effects of different durations of DRA (i.e., short, moderate, and extended) in equivalent but distinct stimulus contexts. We will correlate each stimulus context with a color, counterbalanced across participants and DRA durations. For example, we will use a blue overhead light, blue alternative communication card, and blue therapist clothing in one progression (e.g., short-DRA duration). We will correlate another progression (e.g., moderate-DRA duration) with yellow, and the final progression (e.g., extended-DRA duration) with red.

Baseline. The baselines will be identical to the functional-analysis condition associated with the highest levels of destructive behavior (e.g., the attention condition for attention-reinforced destructive behavior), except that we will reinforce problem behavior according to a dense, intermittent schedule of reinforcement, using the schedule identified from the PIA. To obtain stable rates of destructive behavior across the baseline conditions, data collection will continue for at least five sessions in each condition once the data in each condition meet the following stability criteria: (a) the standard deviation of the last five sessions is less than 50% of its mean (e.g., M = 2, SD ≤ 0.8) and (b) the baseline trend is flat (slope ≤ |.05|) or trending upward.

DRA Training. Once the above stability criteria have been met, DRA training will begin in a separate stimulus context (e.g., in a room without an overhead light, with a white alternative communication card and white therapist clothing). In most cases, exchanging a card with a picture of the child consuming the reinforcer (e.g., attention) will be used as the functional (alternative) communication response (FCR) because it can be effectively prompted using gentle physical guidance regardless of the child's functioning level (but other response options, such as card touches or vocal responses, may be used). Reinforcers for the alternative behavior are those functional reinforcers identified in the functional analysis (i.e., the consequence that maintains problem behavior in the natural environment, and the same reinforcer used in baseline). For example, the reinforcer for a child with escape-maintained problem behavior would be a break from academic, pre-academic,

household, or daily living tasks, whereas the reinforcer for a child with attention-maintained problem behavior would be access to attention (e.g., playing, chatting) from an adult, and the reinforcer for a child with problem behavior maintained by access to tangibles will be a specific toy or food. DRA training will be identical to baseline, except that the therapist will (a) not provide reinforcement for destructive behavior (extinction) and (b) use gentle physical guidance to prompt the FCR, increasing the delay to physical guidance as the child learns the FCR while displaying little or no destructive behavior.

Training will vary across participants depending on the functional reinforcer identified in the functional analysis assessment that precedes all research procedures. The appropriate functional communication response for a participant will be determined by the doctoral-level case manager based on functioning level and existing communication repertoire. For participants for whom the functional reinforcer (that is, the consequence that maintains problem behavior in the home or school) is identified as attention, pretraining will involve the following steps. First, the therapist will provide approximately 1 minute of high-quality attention (e.g., chatting, playing, tickles). Second, the therapist will briefly remove attention (i.e., pretend to read a book or magazine or do some work). Third, a second therapist will prompt the functional communication response. The prompt might be hand-over-hand guidance if the child is being taught to use a card exchange as a functional communication response for attention. The prompt might be a point prompt (pointing to the card) if the child is being taught to use a card touch as the functional communication response for attention. The prompt might be a vocal model prompt (e.g., “say ‘play with me’) if the child is being taught to use a vocal functional communication response for attention. Fourth, as soon as the participant responds to the prompt by emitting the functional communication response, the therapist will again provide high-quality attention. In initial sessions (a session consists of ten trials in which attention is removed, a prompt is given, and attention is returned), the child will be prompted immediately after attention is removed (i.e., a 0-second prompt delay). The prompt delay will be increased systematically across sessions (i.e., from 0-s delay to 2-s delay after 2 consecutive sessions with 80% or above prompted or independent responding) according to the following progression: 0-s, 2-s, 5-s, 10-s. Training will continue until the participant is responding independently (i.e., without a prompt) for 80% of trials in two consecutive sessions.

For participants for whom the functional reinforcer (that is, the consequence that maintains problem behavior in the home or school) is identified as tangible, pretraining will involve the following steps. First, the therapist will provide approximately 1 minute of access to the specific toy or food. Second, the therapist will briefly remove the toy or food. Third, a second therapist will prompt the functional communication response. The prompt might be hand-over-hand guidance if the child is being taught to use a card exchange as a functional communication response for the toy or food. The prompt might be a point prompt (pointing to the card) if the child is being taught to use a card touch as the functional communication response for the toy or food. The prompt might be a vocal model prompt (e.g., “say ‘toy please’”) if the child is being taught to use a vocal functional communication response for the toy or food. Fourth, as soon as the participant responds to the prompt by emitting the functional communication response, the therapist will again provide the toy or food for the child to play with or consume. In initial sessions (a session consists of ten trials in which the toy or food is removed, a prompt is given, and the toy or food is returned), the child will be prompted immediately after the toy or food is removed (i.e., a 0-second prompt delay). The prompt delay will

be increased systematically across sessions (i.e., from 0-s delay to 2-s delay after 2 consecutive sessions with 80% or above prompted or independent responding) according to the following progression: 0-s, 2-s, 5-s, 10-s. Training will continue until the participant is responding independently (i.e., without a prompt) for 80% of trials in two consecutive sessions.

For participants for whom the functional reinforcer (that is, the consequence that maintains problem behavior in the home or school) is identified as escape, pretraining will involve the following steps. First, the therapist will provide approximately 1 minute of break time (i.e., the child is not required to do schoolwork, housework, pre-academic tasks, activities of daily living, etc. Second, the therapist will briefly present instructions to do tasks using a tell-show-do procedure (i.e., giving an instruction, modeling completion of the task, and prompting the child to complete the task). Third, a second therapist will prompt the functional communication response. The prompt might be hand-over-hand guidance if the child is being taught to use a card exchange as a functional communication response for escape from demands. The prompt might be a point prompt (pointing to the card) if the child is being taught to use a card touch as the functional communication response for escape from demands. The prompt might be a vocal model prompt (e.g., "say 'break please'") if the child is being taught to use a vocal functional communication response for escape from demands. Fourth, as soon as the participant responds to the prompt by emitting the functional communication response, the therapist will remove all instructions and demand materials. In initial sessions (a session consists of ten trials in which the toy or food is removed, a prompt is given, and escape from demands is provided), the child will be prompted immediately the therapist begins delivering instructions (i.e., a 0-second prompt delay). The prompt delay will be increased systematically across sessions (e.g., from 0-s delay to 2-s delay after 2 consecutive sessions with 80% or above prompted or independent responding) according to the following progression: 0-s, 2-s, 5-s, 10-s. Training will continue until the participant is responding independently (i.e., without a prompt) for 80% of trials in two consecutive sessions.

DRA. During DRA, each therapist will (a) discontinue reinforcement for destructive behavior (extinction) and (b) use a dense, intermittent schedule of reinforcement for independent (not guided) FCRs. The number of DRA sessions will depend on the current DRA-duration condition (i.e., short = approximately 4, 10-min sessions, moderate = approximately 8, 10-min sessions, or extended = approximately 32, 10-min sessions). Following each duration of DRA, participants will begin the resurgence test.

Resurgence Test. Next, we will discontinue reinforcement (i.e., program extinction) for the alternative response (i.e., the FCR), while problem behavior continues to go unreinforced. This condition will mimic lapses in the integrity with which caregivers often implement treatment in the home, school, or community settings. This phase will continue until the rate of destructive behavior is approximately 90% lower than its baseline mean for two consecutive sessions. We expect large differences in resurgence of destructive behavior between the extended-DRA condition and the short-DRA condition and a small-to-nonsignificant effect for the other paired comparisons (i.e., short vs. moderate and moderate vs. extended).

Experiment 2: Clinical study on schedule thinning.

We will develop and then assess an alternative schedule-thinning progression for use with children receiving DRA for destructive behavior that we predict to greatly reduce or prevent resurgence of destructive behavior during schedule thinning. One advantage of RaC over BMT is that with RaC we can update our prediction model dynamically after each session during schedule thinning. The prediction of RaC regarding how many reinforcers should be programmed for the next session would change as a result of this recent episode of responding (or lack thereof). We will use this feature of RaC to guide schedule thinning in our test group. The control group will be based on typical responding during reinforcer-schedule thinning observed in the published literature, much of which is based on research from our own clinic (see below). Thus, we do not intend to enroll participants prospectively into the control group. Baseline, DRA training, DRA, and stimulus context. Baseline, DRA training, and DRA procedures will be identical to those conducted in Experiment 1 except that destructive behavior and the alternative response (i.e., the FCR) will be reinforced on a continuous (or near-continuous) schedule in baseline and DRA sessions, respectively. DRA training will be conducted in a manner identical to the procedures used in Experiment 1. The baseline and DRA sessions will continue until the stability criteria specified for Experiment 1 are met. All sessions will be conducted within one stimulus context, as described above.

DRA schedule thinning. Following an initial demonstration of the efficacy of DRA in which the participant is taught the FCR to access the reinforcer maintaining problem behavior, we will initiate DRA schedule thinning by introducing and then systematically lengthening periods of time in which that reinforcer is unavailable. Periods in which the reinforcer is available and unavailable will be signaled using strategies most relevant to the child's treatment and skill-level, such as different colored stimuli (e.g., green and red wristbands), the presentation and absence of work materials, or the presentation and absence of the communication materials. For schedule-thinning steps, we will use the quantitative models of RaC Theory and the results of a corresponding study with nonhuman animals to dynamically adjust each upcoming schedule-thinning step. We will use additional teaching procedures (e.g., prompting, blocking) as necessary to facilitate schedule thinning, as we would clinically. DRA schedule thinning will continue until the stability criteria specified for Experiment 1 are met under terminal schedules that are similar to those found within our control group. We will then compare these data to a control group consisting of the published data depicted in Briggs et al.[27] and reviewed by Saini et al.[42] We will compare our results from the test group in the current study to the published data to determine whether RaC-informed schedule thinning substantially reduced resurgence compared to traditional schedule-thinning methods published in the literature.

B. Data Points

Dependent variables and measurement. The primary dependent measure will be the rate of destructive behavior (aggression, property destruction, self-injurious behavior) assessed via direct observation. Aggression will be defined as forceful pushing or striking others with body parts (e.g., pushing, hitting, kicking, head-butting), hitting others with objects or throwing objects at others, pinching, scratching, or biting. Property destruction will be defined as forceful banging, throwing, overturning, tearing or climbing on objects not made for that purpose. Self-Injurious Behavior will be defined as forceful striking, scratching, rubbing, poking or biting ones own body parts such that

repetition of the behavior has or will cause bodily injury (e.g., head punching or banging, eye-poking). Observation, blinding, reliability, and validity of dependent and procedural-integrity measures. Trained observers will collect data on child destructive behavior and therapist implementation of the assessment and treatment protocols to assess procedural integrity using BDataPro®[42], software developed in our lab. A second observer will score at least one third of sessions independently to assess data accuracy (reliability). The second data collector will be blind to the research questions and hypotheses for one half (17%) of these sessions. For at least one third of sessions, observers will collect procedural-integrity data to determine whether the assessment and treatment protocols are implemented as planned. That is, we will collect data on whether therapists correctly implemented the planned antecedents, prompts, and consequences for each target response. We will then transform the data into a percentage-correct measure by dividing the number of correct therapist responses by the number of opportunities for a correct response. (reliability).

The reliability of direct-observation measures is typically established through measurement of interobserver agreement. To calculate interobserver agreement, sessions will be partitioned into successive, 10-s intervals (e.g., Seconds 0-9, 10-19, 20-29). In each 10-s interval, we will determine whether the observers agreed or disagreed on the frequency of each target behavior. An exact agreement will be defined as both observers recording the same frequency of a target behavior in a given 10-s interval. We then calculate the percentage of exact agreements per session. Interobserver agreement in our program averages above 90%, and observers undergo retraining if agreement levels fall below 80% on any dependent measure for 3 consecutive sessions. We recently completed the first calibration study to determine the accuracy of continuous recording of direct-observation measures of behavior.[43] In this study, five novice and five experienced observers recorded response samples on laptop computers with a priori determined response rates ranging from 0 to 8 responses per minute, which covered the range of 90% of the data sets published in the Journal of Applied Behavior Analysis, the flagship journal of applied behavior analysis. Results showed that the experienced observers recorded rates that were accurate to within ± 0.2 responses per minute (M = ± 0.12). Observers for this project will be comparably experienced and accurate. In addition to its accuracy, direct-observation measures have several advantages over other assessments (e.g., rating scales) in terms of validity. Because target behaviors are directly measured, issues related to construct and predictive validity are not relevant (i.e., no need to predict or estimate a criterion variable when it is measured directly). Instead, direct-observation measures are judged primarily in terms of their face validity (e.g., Does the operational definition of aggression match the everyday meaning of the term?) and content validity (e.g., Do the topographies of destructive behavior measured in this project adequately cover the ones included in prior investigations?).[44] We developed the current definitions of destructive behavior based on recommendations of an NIH consensus conference[45] and subsequent reviews of the literature.[15]

C. Study Duration

We will conduct routine-clinical and study-specific procedures with each participant approximately 3 to 6 hours per day for approximately 5 days per week for about 8-16 weeks. We expect the study-specific procedures to last approximately 3 weeks during each participant's clinical admission. Therapists will conduct approximately 15 to 30 sessions daily per participant.

D. Endpoints

The primary endpoint for Study 1 will be a rate of destructive behavior that is approximately 90% lower than the baseline mean for two consecutive sessions. The primary endpoint for Study 2 will be stable responding (standard deviation not exceeding 50% of the mean), under a terminal schedule that is similar to those found within our control group.

1.4 Preliminary Data

Our preliminary data[40] suggest that DRA treatments for problem behavior like those described below consistently produce at least an 85% reduction in baseline rates of problem behavior after 1 to 4 DRA sessions. Based on these results, we will set the length of our short-duration condition to 4 sessions. RaC predicts that this short duration of DRA will produce high magnitudes of resurgence during a resurgence test, but less resurgence than predicted by BMT. We will compare this short-duration condition with a moderate duration condition (i.e., 8 sessions of DRA), and an extended-duration condition (i.e., 32 sessions of DRA). RaC predicts that, relative to the short-duration condition, the moderate-duration condition will reduce resurgence only slightly, but the extended-duration condition will reduce resurgence considerably.

1.5 Sample Size Justification

With a minimum expected reduction in the per-case prevalence of 50% across 12 participants, we estimate a power of 0.89 with alpha=0.05. In addition, on a per-schedule-step basis, the power increases to 0.98 with alpha=0.05. We will assess the adequacy of RaC and BMT in describing the data.

1.6 Study Variables

A. Independent Variables, Interventions, or Predictor Variables

Study 1.

Extended DRA. This intervention involves conducting DRA treatment for approximately 32 sessions.

Moderate DRA. This intervention involves conducting DRA treatment for approximately 8 sessions.

Short DRA. This intervention involves conducting DRA treatment for approximately 4 sessions.

Study 2.
RaC-Informed Schedule Thinning. For schedule-thinning steps, we will use the quantitative models of RaC Theory and the results of a corresponding study with nonhuman animals to dynamically adjust each upcoming schedule-thinning step. We will use additional teaching procedures (e.g., prompting, blocking) as necessary to facilitate schedule thinning, as we would clinically.

Traditional Schedule Thinning. We will look to the published literature to identify studies in which schedule-thinning was conducted arbitrarily (i.e., not in accordance with the predictions of RaC).

B. Dependent Variables or Outcome Measures

Study 1.

Rate of destructive behavior during the Resurgence Test following Extended DRA. We will collect continuous, direct-observation measures of destructive behavior throughout all phases of the study.

Rate of destructive behavior during the Resurgence Test following Moderate DRA. We will collect continuous, direct-observation measures of destructive behavior throughout all phases of the study.

Rate of destructive behavior during the Resurgence Test following Short DRA. We will collect continuous, direct-observation measures of destructive behavior throughout all phases of the study.

Study 2.

Rate of destructive behavior during RaC-informed Schedule Thinning. We will collect continuous, direct-observation measures of destructive behavior throughout all phases of the study.

Rate of destructive behavior during Traditional Schedule Thinning. We will collect continuous, direct-observation measures of destructive behavior throughout all phases of the study.

1.7 Drugs/Devices/Biologics

Not Applicable

A. Drug/Device Accountability and Storage Methods

Not Applicable

1.8 Specimen Collection

A. Primary Specimen Collection

Not Applicable

- **Types of Specimens**: Not Applicable
- **Annotation**: Not Applicable
- **Transport**: Not Applicable
- **Processing**: Not Applicable
- **Storage**: Not Applicable
- **Disposition**: Not Applicable

B. Secondary Specimen Collection

Not Applicable

- **Types of Specimens**: Not Applicable
- **Annotation**: Not Applicable
- **Transport**: Not Applicable
- **Storage**: Not Applicable
- **Disposition**: Not Applicable

1.9 Data Collection

A. Primary Data Collection

- **Location**: We will conduct the study within the Severe Behavior Program at CSH–RUCARES. We will conduct initial assessment and treatment in rooms with an adjacent observation window for unobtrusive measurement of behavior. We plan for almost all rooms to contain padded walls and floors to maintain patient and staff safety.

  We will also conduct the study within research rooms of the DDDC. We will conduct the study within rooms with an adjacent observation window for unobtrusive measurement of behavior. All research rooms contain padded walls and floors and are approximately 3 meters by 2 meters.

- **Process of Data Collection**: Trained observers will use laptop computers with BDataPro® software developed in our lab to score frequency of participant destructive behavior and caregiver or therapist behavior. We will define destructive behavior as pushing, pinching, scratching, kicking, or biting others; hitting others with body parts or objects; banging, throwing, overturning, or tearing objects; climbing on objects not made for that purpose; striking, scratching, rubbing, poking or biting self, such that repetition has or will cause injury (e.g., eye-poking). We will convert destructive-behavior frequency to a rate by dividing the number of destructive responses in a session by the session duration in minutes. We will assess procedural integrity by scoring whether therapists correctly implemented the planned antecedents, prompts, and consequences for target responses. We will convert correct antecedents, prompts, and consequences to a percentage after dividing the number of correct responses by the number of correct-response opportunities.
- **Timing and Frequency**: We will collect data continuously during 5- or 10-min sessions during the majority of each participant's appointment (e.g., spending 2.75 hr of a 3-hr appointment in-session).
- **Procedures for Audio/Visual Recording**: We will video-record most sessions of the research for later data collection (e.g., collecting reliability or treatment-integrity data).
- **Study Instruments**: Our study does not use formal research instruments (e.g., questionnaires) but instead relies on observational data collection. See below for more information.
- **Ethnographic Studies, Interviews, Or Observation**: Trained observers will collect data using a specialized data-collection program developed and recently validated by our research group [42] A second independent observer will score at least one third of sessions to assess data accuracy (i.e., reliability). For at least half of sessions in which reliability data are collected (17%), the second data collector will be blind to the experimental conditions and study hypotheses. The reliability of direct-observation measures is typically established by measuring interobserver agreement, which involves comparing the exact number of target behaviors scored in each 10-s observation interval and dividing the number of exact agreement intervals by the total number of intervals and multiplying by 100 to determine a percentage. We will then use structured visual inspection to analyze each caregiver's single-case data sets for both experiments. Members of our research group developed these visual-inspection procedures, which have been validated and are highly reliable. [38,39]

- **Subject Identifiers**: When recording observational data with BDataPro, the program will record the patient's name and the date/time of data collection. When depicting these data in graphical form or in presentation/publication, we will assign the subject a pseudonym. We will retain this pseudonym key on a secure network drive within a password-protected spreadsheet available only to the study personnel.

B. Secondary Data Collection

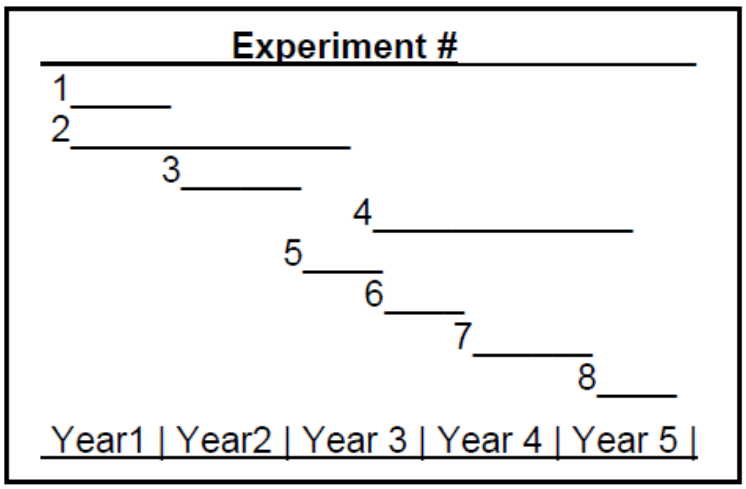
Not Applicable

- **Type of Records**: Not Applicable
- **Location**: Not Applicable
- **Inclusion/Exclusion**: Not Applicable
- **Data Abstraction Form(s):** Not Applicable

1.10 Timetable/Schedule of Events

Dr. Shahan (Utah State University) will coordinate the project and meet with the clinical team (Greer and Fisher) via teleconference monthly and in person twice yearly. Such meetings will ensure the methods and analyses of the clinical studies are informed by incoming results from the animal studies and that the animal studies remain clinically relevant based on incoming clinical data. We will adjust studies in both domains as needed to meet these goals.

If the first animal experiment conducted at Utah State University (Experiment 1 in the grant and figure below) shows that cycles of on/off DRA reduce resurgence in animals, we will examine this procedure in the clinic in a subsequent project period. Should Study 2 of the present application (Exp. 4 in the grant and figure below) find that the RaC-informed, schedule-thinning procedure is more effective than the standard procedure in the clinic, a new R01 will propose a randomized clinical trial. If differences in response effort or reinforcer quality in Exp. 6 and 8 (animal studies conducted at Utah State) impact resurgence in animals as predicted, later experiments will examine such effects in the clinic. If increases in alternative-response effort produce resurgence as predicted in Exp. 7, we will later conduct an experiment (akin to Study 2 / Exp. 4) in the clinic in which a RaC-informed effort increasing procedure is developed to minimize resurgence. Future animal studies could examine how other factors common with DRA in the clinic impact resurgence. RaC makes specific predictions about how punishment, changes in motivating operations, and training of multiple alternative responses affect resurgence. Finally, should RaC poorly describe the data from the present project, we will work to refine the theory. We are confident a matching-law based approach to DRA and resurgence has considerable merit, but RaC is currently based on specific assumptions about how changing reinforcement conditions affect the value of the target and alternative behaviors (e.g., hyperbolic decay via the temporal weighting rule). Although these assumptions work well with existing data, data from this project will be critical for assessing these assumptions further and, if needed, refining them to improve predictions about how to reduce resurgence in the clinic.



2.0 Project Management

2.1 Research Staff and Qualifications

Dr. Greer is the director of the Severe Behavior Program at CSH–RUCARES, assistant director of RUCARES, and an assistant professor of Pediatrics at Rutgers. Previously, Dr. Greer was the associate director of the Severe Behavior Program in the Center for Autism Spectrum Disorders and an assistant professor at the UNMC. Dr. Greer received his Ph.D. in behavioral psychology from the University of Kansas in 2013. He later completed a postdoctoral fellowship at the UNMC's Munroe-Meyer Institute under the direction of Dr. Wayne Fisher. He has served on the Board of Editors for the Journal of Applied Behavior Analysis and currently serves as an associate editor for Behavioral Development. Dr. Greer is the 2013 recipient of the Baer, Wolf, and Risley Outstanding Graduate Student Award, and he received the National Institutes of Health's Loan Repayment Program Award in 2016.

Dr. Fisher is the Henry Rutgers Endowed Professor of Pediatrics, RWJMS and the director of Rutgers Center for Autism Research, Education and Services (RUCARES). He is a board-certified behavior analyst at the doctoral level, and a licensed psychologist. Previously, Dr. Fisher was the H.B. Munroe professor of behavioral research in the UNMC's Munroe-Meyer Institute and the Department of Pediatrics. During this time he was also is the director of the Center for Autism Spectrum Disorders at the Munroe-Meyer Institute. Prior to his time at the Munroe-Meyer Institute, he was a professor of psychiatry at Johns Hopkins University School of Medicine and served as executive director of the Neurobehavioral Programs at the Kennedy Krieger Institute and the Marcus Behavior Center at the Marcus Institute, where he built clinical-research programs in autism and developmental disabilities with national reputations for excellence. Dr. Fisher's methodologically sophisticated research has focused on several intersecting lines including preference, choice, and the assessment and treatment of autism and severe behavior disorders. His research has been notable for the creative use of concurrent schedules of reinforcement, which have become commonplace in clinical research primarily

due to his influence. He has published over 180 peer-reviewed papers in over 35 different behavioral and medical journals, including: Journal of Applied Behavior Analysis, Psychological Reports, American Journal on Developmental and Developmental Disabilities, Pediatrics, Journal of Developmental and Behavioral Pediatrics, and The Lancet. Dr. Fisher has had near-continuous federal grant support for his research for 19 years. He is a past Editor-in-Chief and past Associate Editor of the Journal of Applied Behavior Analysis, a past president of the Society for the Experimental Analysis of Behavior, a fellow in the Association for Behavior Analysis International (ABAI) and a recipient of the Bush Leadership Award, the American Psychological Association's (APA; Division 25) Award for Outstanding Contributions to Applied Behavioral Research, the UNMC Distinguished Scientist Award, the University of Nebraska system-wide Award for Outstanding Research and Creative Activity, and the Society for the Experimental Analysis of Behavior's Don Hake Translational Research Award.

2.2 Research Staff Training

The principal investigator, secondary investigator, and key personnel will meet with research staff at least 2 hours per week to review research data and protocols. Postdoctoral personnel will train and supervise research assistants and monitor data collection and protocol implementation. Postdoctoral personnel will meet daily with the clinical-research team and observe protocol implementation daily for 1 hour per participant.

The investigators will train all staff to implement assaultive-behavior-management procedures to criterion and maintain criterion levels of clinical performance. Staff will receive periodic retraining and investigators will collect data on participant and team physical status and behavior during all procedures to monitor for safety and treatment fidelity. The principal investigator and coinvestigators will approve, oversee, and monitor the assaultive-behavior-management procedures and accompanying participant and team data and problem solve about participants or situations that are associated with increased injury or that teams report are more problematic than usual. The principal investigator and co-investigators will be on-call throughout the day to provide support in difficult situations.

Examples of components that the principal investigator and co-investigators will monitor are correct context and color, scheduling and implementing the DRA components in the correct order and duration, ensuring that participant responding meets the stability criterion before a phase change, and implementing schedule thinning procedure correctly. In our routine clinical practice, one full-time psychologist or doctoral-level behavior analyst will supervise the treatment of three to five children with severe destructive behavior simultaneously. Supervisors will maintain this small caseload because patients will typically receive treatment for 3 to 6 hours per day, 5 days per week and will have severe and complex destructive behavior. For the current project, the principal investigator and co-investigators will maintain a similar caseload to provide the level of supervision necessary to ensure that the clinical-research team manages the participants using appropriate and safe assaultive-behavior-management procedures; follows research protocols with high procedural integrity; collects reliable data; and accurately analyzes, graphs, and interprets the data. As indicated above, the research team will meet daily to review participant data. Based on our clinical experience,

the principal investigator and co-investigators often review data, observe sessions, and problem solve with the team multiple times per day.

2.3 Resources Available

CSH–RUCARES includes an indoor playroom, multiple self-contained therapy rooms, some of which are equipped with one-way observation windows and padded floors and walls. The clinic is fully equipped with furniture, office equipment, computers, digital audio-visual recording equipment, and support staff. The clinic has multiple faculty members, administrative staff, and enough therapists to maintain a staff-to-client ratio equal to or greater than 2:1. Therapists have training ranging from the baccalaureate to postdoctoral level. All staff are trained in CPR and safe management of assaultive behavior.

Children treated by the clinic spend up to 6 hours per day in behavior-therapy sessions. Based on the needs of each child, the child's treatment team develops a program to increase functional communication, social, and daily living skills and decrease challenging behavior. The faculty in the clinic supervise therapy sessions and the therapeutic milieu. Therapists collect and graph direct-observation data on target skills and behaviors. Each faculty member and therapist has a laptop computer capable of analyzing and graphing data. The therapists graph session-by-session data, and the therapist and faculty review and analyze the data throughout the day. The treatment team uses these data to systematically guide assessment and evaluate and refine treatment development. The team systematically evaluates treatment components using single-case experimental designs; they refine or replace ineffective components until discharge goals are achieved. Each child's progress receives peer review multiple times per week by senior behavior analysts and staff.

The research will also be conducted in one or two research rooms in a self-contained area of the DDDC. These rooms are equipped with an adjacent observation window for unobtrusive measurement of behavior by caregivers/research assistants. All research rooms contain padded walls and floors and are approximately 3 meters by 2 meters.

2.4 Research Sites

CSH–RUCARES
888 Easton Avenue
Somerset, New Jersey 08873

Douglass Developmental Disabilities Center
151 Ryders Lane
New Brunswick, New Jersey 08901-8557

3.0 Multi-Center Research

N/A

4.0 Subject Considerations

4.1 Subject Selection and Enrollment Considerations

A. Method to Identify Potential Subjects

Potential subjects will be identified within the patient population of the clinic on the basis of meeting the inclusion criteria below.

B. Recruitment Details

The clinical team will recruit subjects from the clinical population of children receiving treatment for severe problem behavior. The team will approach the caregivers of children who meet the inclusion criteria below early on in their admission and will conduct the process of consent with caregivers who express interest in having their children participate in the study.

C. Subject Screening

Members of the research team involved in clinical care of the patients will evaluate each patient consecutively admitted to the program for participation in the research based on an interdisciplinary- evaluation and functional-analysis results. We will consider any patient who meets the inclusion criteria eligible for participation.

Inclusion criteria.

(a) males and females between the ages of 3 and 17;
(b) problem behavior (e.g., aggression, property destruction, self-injurious behavior) that has been the focus of outpatient behavioral and pharmacological treatment but continues to occur, on average, more than once per hour;
(c) problem behavior reinforced by social consequences (i.e., significantly higher and stable rates of the behavior in one or more social test conditions of a functional analysis [e.g., attention, escape] relative to the control condition [play] and the test condition for automatic reinforcement [alone or ignore]);
(d) IQ and adaptive behavior scores between 35 and 70 (i.e., mild to moderate intellectual disability);
(e) on a stable psychoactive drug regimen (or drug free) for at least 10 half-lives of each medication with no anticipated changes;
(f) stable educational plan and placement, with no anticipated changes during the study.

Exclusion criteria.

(a) children not meeting the inclusion criteria above;
(b) children currently receiving intensive (i.e., 15 or more hours per week), function-based, behavioral treatment for their problem behavior through the school or another program;
(c) DSM-V diagnosis of Rett syndrome or other degenerative conditions (e.g., inborn error of metabolism);
(d) presence of a comorbid health condition (e.g., blindness) or major mental disorder (e.g., bipolar disorder) that would interfere with participation in the study (e.g., requiring frequent hospitalizations);
(e) children with self-injurious behavior who, based on the results of the risk assessment, cannot be exposed to baseline conditions without placing them at risk of serious or permanent harm (e.g., detached retinas);

(f) children requiring changes in drug treatment (but such children will be invited to participate after they meet the above criteria for a stable drug regimen).

4.2 Secondary Subjects

Not Applicable

4.3 Number of Subjects

A. Total Number of Subjects

We conservatively estimate at least 60% of patients receiving clinical treatment in our program will meet the inclusion criteria. During the project, we will recruit 22 (12 for study 1 and 10 for Study 2) and retain 20 children with severe destructive behavior. We expect 10% attrition.

B. Total Number of Subjects If Multicenter Study

Not Applicable

C. Feasibility

We will recruit 22 and retain 20 children with severe destructive behavior from the Severe Behavior Program. We will recruit 12 and retain 11 children for Study 1, and we will recruit 10 and retain 9 children for Study 2. We conservatively estimate at least 60% of patients will meet the criteria (n = 45 per year available; eight per year needed, maximum). The research team will communicate the recruitment plan to all case managers in the Severe Behavior Program so that case managers can recommend relevant participants. The principal investigator and research staff will meet to discuss recruitment status and resolve any issues related to recruitment.

Additionally, the DDDC has 10 classes with a class size between 5 and 8 patients. Thus, the DDDC has between 50 and 80 patients at a given time. The majority of patients have a diagnosis of ASD, and a large minority of patients are reported to display destructive behavior. We expect that roughly 5-10 patients will be appropriate for the study, and recruitment is deemed feasible.

4.4 Consent Procedures

A. Consent Process

- **Location of Consent Process**
  The consent process will take place in a private area such as a conference room to allow the caregivers to reflect on their child's participation in the study in a quiet environment. The consent process may also take place remotely via telephone or video conference (e.g., Zoom) for caregivers who do not attend appointments in person. Consent forms will be physically sent home to caregivers to obtain signatures if the consent process does not occur in person.
- **Ongoing Consent**
  Not Applicable
- **Individual Roles for Researchers Involved in Consent**
  Primary or secondary investigators or participating personnel who are credentialed as Board Certified Behavior Analysts will provide caregivers with an overview of the study and the consent process. These investigators will ask questions to ensure that the caregivers

understand the documents presented to them and will refer any of their concerns to the primary investigator. Providers at the DDDC who are aware of the inclusion criteria for this protocol will identify potential participants from their site; however, only the research team from CSH–RUCARES listed on this IRB will approach caregivers regarding participation and conduct consent with these caregivers.

- **Consent Discussion Duration**
  Parents/guardians will be allowed as much time as they would like to review the research procedures that we plan to implement and will be encouraged to take the information home to make their decisions.
- **Coercion or Undue Influence**
  We will provide the option for caregivers to include family, friends, an advocate, or other confidants.
- **Subject Understanding**
  Investigators will question the caregivers about each section of the consent form to ensure that they understand. In addition, we will offer to read the consent to the caregivers.

B. Waiver or Alteration of Consent Process

- **Waiver or Alteration Details**
  We are requesting the omission of the assent portion of the consent document. Assent is being waived because the capability of these children (taking into account the ages, maturity, and psychological state of the children involved) is so limited that they cannot reasonably be consulted. Thus, we will not obtain assent from any subjects. A majority will be diagnosed with autism and/or developmental disability and all of our patients engage in high levels of destructive behavior (e.g., aggression, self-injury, and property destruction). Thus, the children are typically incapable of providing assent to participate in treatment or research procedures. In situations in which we have had typically developing children over the age of 7 as patients at UNMC, it was often still the case that these children are unable to make informed decisions regarding the assessment and treatment of their destructive behavior. We will conduct the process of consent with the children's caregivers. The children's caregivers will be fully informed of the procedure, risks, and benefits. The caregivers have full rights to remove their child from the study at any time. If the child's problem behavior appears to escalate to unsafe levels, the session will be ended and clinically approved measures will be implemented to ensure the safety of the child.

- **Destruction of Identifiers**
  We will obtain parental permission for each participant in the study. We will collect the following subject identifiers in association with the research data: Name, all elements of dates (except year) related to an individual (e.g., birth, admission, discharge, medical record numbers, and full-face photographic images). A unique subject identifying code will be used to link data to these identifiers. Subject names will be converted to initials during the subject's participation. Following completion, pseudonyms will be assigned to subjects and the pseudonym identifier will be encrypted on the server. The justification for recording these specific subject identifiers is to schedule appointments and follow up with subjects. Subject identifiers will be maintained for a minimum of six years, at which point they will be destroyed with the help of the Rutgers IT department. All electronic data (e.g., session data) will be stored on the encrypted server

and any hard copy data will be stored in the client's long-term file located in a locked cabinet in a locked office. After six years, the IT department will assist with data destruction. During the course of the study, we may record sessions for data-collection purposes for children whose caregivers. These videos will be recorded through a webcam directly into an encrypted computer and stored on the encrypted network drive or encrypted hard drive. We will delete these videos six years from the collection date or earlier (if no additional data collection is required)

- **Use of Deception/Concealment**
  Not Applicable
  a. **Minimal Risk Justification**
     Not Applicable
  b. **Alternatives**
     Not Applicable
  c. **Subject Debriefing**
     Not Applicable

C. Documentation of Consent

- **Documenting Consent**
  At the end of the process of consent, the study representative conducting the process of consent will ask the caregiver if they would like their child to participate in the study, and if so, they will be asked to sign the consent form. If the consent process occurs remotely, a physical copy of the consent form will be sent to the caregiver's home, and they will be asked to return it signed if they would like their child to participate in the study. A copy of the signed consent form will be given to the parent or legal guardian, a copy will be scanned into the child's medical record, and a copy will be kept securely (i.e., in a locked cabinet behind a locked door) by a primary or secondary investigator. The consent process (including people present, time, date, length of the consent process, questions asked, and answers provided) will be documented in narrative form in a progress note which is part of the child's medical record.
- **Waiver of Documentation Of Consent (i.e., will not obtain subject's signature)**
  Not Applicable

4.5 Special Consent/Populations

A. Minors-Subjects Who Are Not Yet Adults

- **Parental Permission**
  Parental permission in the form of parent/legal guardian consent will be the primary form of consent obtained in the study.
- **Non-Parental Permission**
  Only parents and legal guardians will be authorized to provide consent for participation in the study.
- **Assent Process**
  We will not obtain assent from any subjects. A majority will be diagnosed with autism and/or developmental disability and all of our patients engage in high levels of destructive behavior

(e.g., aggression, self-injury, and property destruction). Thus, the children are typically incapable of providing assent to participate in treatment or research procedures. In situations in which we have had typically developing children over the age of 7 as patients at UNMC, it was often still the case that these children are unable to make informed decisions regarding the assessment and treatment of their destructive behavior. We will conduct the process of consent with the children's caregivers. The children's caregivers will be fully informed of the procedure, risks, and benefits. The caregivers have full rights to remove their child from the study at any time. If the child's problem behavior appears to escalate to unsafe levels, the session will be ended and clinically approved measures will be implemented to ensure the safety of the child.

- **Documentation of Assent**
  Not Applicable
- **Reaching Age of Majority During Study**
  Not Applicable

B. Wards of the State

Not Applicable

- **Research Outside of NJ Involving Minors**
  Not Applicable

C. Non-English-Speaking Subjects

Non-English speaking subjects will be enrolled in the study.

- **Process for Non-English-Speaking Subjects**
  - If we encounter a non-English speaking family, we will request to use the short-form process as per the eIRB policies. We will use a qualified or certified translator to translate the study title into the consenting caregiver's native language (e.g., Italian), provide the translator's qualifications, and submit the materials to the IRB for review. We will then follow the respective short-form policies to use a qualified translator and witness during the consent process with the study personnel and family. Because we anticipate frequent opportunities to serve Spanish-speaking patients, we have submitted Spanish translation of the IRB long form for the IRB's consideration. For these Spanish-speaking families, we will use the translated long form. For all other non-English speaking families, we will continue to leverage the short-form process. Additionally, we will include an interpreter to conduct the consent process and use such translation services to provide at least weekly updates on the subject's participation. Contact information for translation services will be made available to the caregivers such that the caregivers can ask questions or refer concerns at any point during the study. The caregivers will be told to take as much time as needed with the investigators and translator and will be asked questions about each section of the consent form to ensure that they understand.
- **Short Form Consent for Non-English Speakers**
  Yes (see above). We anticipate frequent opportunities to serve Arabic-speaking families and have therefore included an Arabic short form for consent.

D. Adults Unable to Consent / Cognitively Impaired Adults (for interventional studies)

Not Applicable

- **NJ Law-Assessment of Regaining the Capacity to Consent**
  Not Applicable
- **Capacity to Consent**
  Not Applicable
  a. **NJ Law-Selecting A Witness**
     Not Applicable
  b. **Removing a Subject**
     Not Applicable

4.6 Economic Burden and/or Compensation for Subjects

A. Expenses

Many of the procedures are clinically indicated and represent the standard of care. Procedures that fall in this category will be billed to the participants' health insurance. There are no other financial obligations that the subject will incur as a result of participating in the study.

B. Compensation/Incentives

No compensation or incentives will be provided.

C. Compensation Documentation

Not Applicable.

4.7 Risks of Harm/Potential for Benefits to Subjects

A. Description of Risks of Harm to Subjects

- **Reasonably Foreseeable Risks of Harm**
  There is a potential for child and therapist injury as a result of the child's problem behavior. Problem behavior such as aggression, property destruction, or self-injury may be occasioned by presenting difficult demands, restricting access to preferred items, or activities or restricting access to adult attention. All therapists participating in the study will have received formal training on how to appropriately and safely block problem behavior in a manner that minimizes these risks. If the child engages in problem behavior that may result in injury to the therapist, the therapist will have the option to wear protective equipment during the assessment (e.g., arm guards, chest and shoulder pads, etc.). If the child's problem behavior appears to escalate to unsafe levels, the session will be ended and clinically approved measures will be implemented to ensure the safety of the child. There is also a risk of loss of confidentiality. We will minimize this risk by using only Rutgers-approved storage solutions to maintain protected health information.
- **Risk of Harm from an Intervention on a Subject with an Existing Condition**
  Not applicable
- **Other Foreseeable Risks of Harm**
  There is also a risk of loss of confidentiality. The loss of confidentiality is unlikely due to the use of a secured network hard drive to store all personal identifiers.
- **Observation and Sensitive Information**

All observation procedures conducted as part of the study are identical to the observation procedures routinely experienced by patients, and are therefore part of the standard of care.

B. Procedures which Risk Harm to Embryo, Fetus, and/or Pregnant Subjects
Not applicable

C. Risks of Harm to Non-Subjects
Therapists participating in therapy may be exposed to the same risks of bodily harm that they would otherwise experience as part of participating in treatment for a child's severe problem behavior.

D. Assessment of Social Behavior Considerations
Not Applicable

E. Minimizing Risks of Harm
If the child has self-injurious behavior, the initial exam includes an assessment to determine the potential health risks associated with this behavior. In our previous program at the Munroe-Meyer Institute, we excluded approximately 5% of children admitted to the Severe Behavior Program from research participation who had such dangerous forms of self-injurious behavior that it would be unsafe to allow the behavior to occur while attempting to complete a functional analysis. The clinical supervisors in the Severe Behavior Program will closely monitor individuals admitted to the program who display self-injurious behavior to ensure that the tissue damage produced during assessment and treatment sessions is not serious, permanent, or even significantly worse than what typically occurs in the natural environment. The clinical team will terminate sessions and block self-injurious behavior or prevent it with protective equipment if the behavior results in reddening, bruising, or bleeding, or if the patient directs the self-injurious behavior toward delicate organs (e.g., the eyes). If the clinical team observes soft-tissue symptoms, they will closely monitor the symptoms and document them in medical progress notes until the symptoms resolve. If symptoms persist or if they are serious and acute, the patient will be seen by a physician or taken to the Emergency Room.

- **Certificate of Confidentiality**
  A Certificate of Confidentiality has been obtained from the NIH. All NIH-funded studies are automatically issued a Certificate of Confidentiality
- **Provisions to Protect the Privacy Interests of Subjects**
  The team will collect the minimum amount of personal information required to conduct effective assessment and treatment of the subject, consistent with clinical practice. No more personal information than would be obtained as part of routine treatment for severe problem behavior will be obtained from subjects in this study or their caregivers.

F. Potential Benefits to Subjects
Participants may receive treatment services for their destructive behavior and be taught replacement behaviors based on the results of the functional analyses. A reduction in destructive behavior may be a result of basing treatment on the functional analyses.

5.0 Special Considerations

5.1 Health Insurance Portability and Accountability Act (HIPAA)

We will be obtaining, creating, and using individually identifiable health information associated with a HIPAA-covered component or entity in the research

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5.2 Family Educational Rights and Privacy Act (FERPA)
No student records will be accessed for research purposes.

5.3 NJ Access to Medical Research Act (Surrogate Consent)
Not Applicable

5.4 General Data Protection Regulation (GDPR)
Not Applicable

5.5 Code of Federal Regulations Title 45 Part 46 (Vulnerable Populations)

A. Special Populations

- Children:

The purpose of this checklist is to provide support for IRB members or the Designated Reviewer following the WORKSHEET: Criteria for Approval (HRP-314) when research involves children as subjects. This checklist must be used for all reviews (initial, continuing, modification, review by the convened IRB, and review using the expedited procedure.)

- For initial review using the expedited procedure and modifications and continuing reviews where the determinations relevant to this checklist made on the previous review have changed, the Designated Reviewer completes this checklist to document determinations required by the regulations along with protocol specific findings justifying those determinations. The Designated Reviewer attaches this checklist to "Submit Non-Committee Review" activity. The IRB Office retains this checklist in the protocol file.
- For initial review using the convened IRB and for modifications and continuing reviews where the determinations relevant to this checklist made on the previous review have changed, one of the following two options may be used:
  1. The convened IRB completes the corresponding section of the meeting minutes to document determinations required by the regulations along with protocol specific findings justifying those determinations, in which case this checklist does not need to be completed or retained.
  2. The convened IRB completes this checklist to document determinations required by the regulations along with protocol specific findings justifying those determinations and the IRB Office uploads this checklist in the "Submit Committee Review" activity and retains this checklist in the protocol file.

Use a separate checklist for each child determination for a study.

1	The research meets all of the following: (Check if **"Yes".** All must be checked)			
☒	The research falls into one of the following categories of research involving children[i]: (Check box that is true)			
	☐ Section 2 Criteria	☒ Section 3 Criteria	☐ Section 4 Criteria	☐ Section 5 Criteria
☒	Adequate provisions are made for soliciting the permission of parents or guardians[ii]. **(**Complete Section 7**)**			
☒	Adequate provisions are made for soliciting the assent of the children. **(**Complete Section 12**)**			
☒	One of the following is true: **(Check the one that is true)** ☒ The research falls into Section 2 or 3 **or** does **NOT** involve wards of the state or any other agency, institution, or entity ☐ The research falls into Section 4 or 5 **and** involves wards of the state or any other agency, institution, or entity **(Complete Section 6)**			
2	**Research involving children under 21 CFR §50.51/45 CFR §46.404** (Check if **"Yes".** All must be checked)			

☐	No greater than Minimal Risk to children is presented. *Provide protocol specific findings justifying this determination:*
Return to Section 1.	
3	**Research involving children under 21 CFR §50.52/45 CFR §46.405** (Check if **"Yes".** All must be checked)
☒	The research involves greater than Minimal Risk to subjects. *Provide protocol specific findings justifying this determination:* **There is a potential for child, therapist, and parent/caregiver injury as a result of the child's problem behavior. Problem behavior such as aggression, property destruction, or self-injury may be occasioned by presenting difficult demands, restricting access to preferred items, or activities or restricting access to caregiver attention. The risks may be greater during the extinction challenge/relapse test. All therapists participating in the study have received formal training on how to appropriately and safely block problem behavior in a manner that minimizes these risks. If the child engages in problem behavior that may result in injury to the therapist, the therapist will have the option to wear protective equipment during the assessment (e.g., arm guards, chest and shoulder pads, etc.). If the child engages in problem behavior that may result in injury to the caregiver, the caregiver will have the option for a therapist to come in and assist them or to terminate the session. If the child's problem behavior appears to escalate to unsafe levels, the session will be ended and clinically-approved measures will be implemented to ensure the safety of the child. There is also a risk of loss of confidentiality. The loss of confidentiality is unlikely due to the use of a secured network hard drive to store all personal identifiers.**
☒	The research presents the prospect of direct benefit to the individual subjects. *Provide protocol specific findings justifying this determination:* **Participants may receive treatment services for their destructive behavior and be taught replacement behaviors based on the results of the functional analyses. A reduction in destructive behavior may be a result of basing treatment on the functional analyses.**
☒	One of the following is true**. (Check box that is true**) ☒ The risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject. ☐ The risk to children is presented by a monitoring procedure that is likely to contribute to the subject's well-being. *Provide protocol specific findings justifying this determination:* **By programming for common treatment challenges (e.g., extinction challenge/relapse test), the clinical team will be able to identify scenarios in which children are likely to engage in increased problem behavior after treatment, and may be able to use this information to (a) provide additional treatment, (b) adjust or modify the treatment, and/or (c) provide caregiver education that may reduce the likelihood of problem behavior recurring at unmanageable levels in the natural environment.**
☒	The risk is justified by the anticipated benefit to the subjects. *Provide protocol specific findings justifying this determination:* **Children participating in the study are referred for treatment because they engage in severe and unmanageable problem behavior. Participants in the study will have the functions of their behavior assessed, and have a function-based treatment (FCT) applied to reduce their problem behavior. Participants in the study will be taught to engage in socially appropriate communication to access what they want, which has been demonstrated to reduce problem behavior maintained by escape from demands and access to attention and tangible items.**

☒	The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches. *Provide protocol specific findings justifying this determination:* **Participants in the study will receive a similar treatment to individuals in our clinic who do not participate. That is, all the procedures of the study are identical to clinical practice except for the extinction challenge/relapse test, which is conducted solely for research purposes. Therefore, the anticipated benefit-risk ratio is similar to that presented by alternative approaches.**
Return to Section 1.	
4	**Research involving children under 21 CFR §50.53/45 CFR §46.406** (Check if **"Yes".** All must be checked)
☐	The research involves greater than Minimal Risk to children presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject. *Provide protocol specific findings justifying this determination:*
☐	The risk represents a minor increase over Minimal Risk. ("Minor increase over Minimal Risk" *means*, though the risks are greater than minimal, they do not exceed the socially acceptable risks for children with the condition or disorder under study.[iii]) *Provide protocol specific findings justifying this determination:*
☐	The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations. *Provide protocol specific findings justifying this determination:*
☐	The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition. *Provide protocol specific findings justifying this determination:*
Return to Section 1.	
5	**Not otherwise approvable research involving children under 21 CFR §50.54/45 CFR §46.407** (Check if **"Yes".** All must be checked)
☐	The research does not meet the requirements of Sections 2, 3, or 4 *Provide protocol specific findings justifying this determination:*
☐	The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children. *Provide protocol specific findings justifying this determination:*
Return to Section 1.	
6	**Research involving wards of the state or any other agency, institution, or entity under 45 CFR §46.409** (Check if **"Yes".** All must be checked)
☐	One of the following is true: **(Check box that is true**) ☐ The research is related to their status as wards. ☐ The research is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards. *Provide protocol specific findings justifying this determination:*
☐	An advocate will be appointed for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis for research approved under §46.406 or §46.407. *Provide protocol specific findings justifying this determination:*

☐	The advocate will have the background and experience to act in, and will agree to act in, the best interests of the child for the duration of the child's participation in the research. *Provide protocol specific findings justifying this determination:*
☐	The advocate is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization. *Provide protocol specific findings justifying this determination:*
Return to Section 1.	

7	**Adequate provisions for soliciting the permission of parents or guardians** (Check if **"Yes".** All must be checked)
☒	**One of the following is true: (Check box that is true)** ☐ **Permission is to be obtained from both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.** ☒ **Permission of one parent is sufficient even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child. (Cannot be selected for Section 4 or 5 criteria)** ☐ Parental permission is waived under criteria in Section 8 ☐ Parental permission is waived under criteria in Section 9 ☐ Parental permission is waived under criteria in Section 10
Return to Section 1.	

8	**Waiver of Parental Permission under 45 CFR §46.408(c)** (Check if **"Yes".** All must be checked)
☐	The research is not FDA-regulated.
☐	The research does not involve non-viable neonates.
☐	The research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects. *Provide protocol specific findings justifying this determination:*
☐	An appropriate mechanism for protecting the children who will participate as subjects in the research is substituted. *Provide protocol specific findings justifying this determination:*
☐	The waiver is not inconsistent with Federal, State, or local law. *Provide protocol specific findings justifying this determination:*
Return to Section 1.	

9	**Waiver of Parental Permission under 45 CFR §46.408(c)/45 CFR §46.116(d)/45 CFR §46.116(f)** (Check if **"Yes".** All must be checked)
☐	The research is not FDA-regulated.
☐	The research does not involve non-viable neonates.
☐	The research involves no more than Minimal Risk to the subjects. *Provide protocol specific findings justifying this determination:*
☐	The waiver or alteration will not adversely affect the rights and welfare of the subjects. *Provide protocol specific findings justifying this determination:*
☐	The research could not practicably be carried out without the waiver or alteration *Provide protocol specific findings justifying this determination:*

☐	Whenever appropriate, the subjects will be provided with additional pertinent information after participation. *Provide protocol specific findings justifying this determination:*
☐	If the research involves using identifiable private information or identifiable biospecimens, the research could NOT practicably be carried out without using such information or biospecimens in an identifiable format. **(N/A if research is subject to Pre-2018 Requirements OR if research does not use identifiable private information or biospecimens)** ☐ **N/A** Provide protocol specific findings justifying this determination:
☐	Waiver of consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens cannot be granted for those who refused to provide broad consent. **(N/A if research is subject to Pre-2018 Requirements OR broad consent not used for the research)** ☐ **N/A**
☐	Alteration of the consent process can only omit or alter the basic and/or additional elements of consent[1]. **(N/A if research is subject to Pre-2018 Requirements OR if waiving informed consent)** ☐ **N/A**
Return to Section 1.	

10	**Waiver of Parental Permission under FDA Guidance "IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects"[iv]** (Check if "**Yes**." All must be checked.)
☐	The research **IS** FDA-regulated.
☐	The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(i)) to the subjects. *Provide protocol specific findings justifying this determination:*
☐	The waiver or alteration will not adversely affect the rights and welfare of the subjects. *Provide protocol specific findings justifying this determination:*
☐	The clinical investigation could not practicably be carried out without the waiver or alteration. *Provide protocol specific findings justifying this determination:*
☐	Whenever appropriate, the subjects will be provided with additional pertinent information after participation. *Provide protocol specific findings justifying this determination:*
Return to Section 1.	

11	**Waiver of Parental Permission under 45 CFR §46.408(c)/45 CFR §46.116(c) (Check if "Yes". All must be checked)**
☐	The research is not FDA-regulated.
☐	The research does not involve non-viable neonates.
☐	The research or demonstration project is to be conducted by or subject to the approval of state or local government officials. *Provide protocol specific findings justifying this determination:*

[1] An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent set forth in 45 CFR 46.116(b) and (c). An IRB may not omit or alter any of the requirements described in 45 CFR 46.116(a). If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under 45 CFR 46.116(d).

☐	The research or demonstration project is designed to study, evaluate, or otherwise examine one or more of the following: **(Check boxes that are true)** ☐ Public benefit or service programs. ☐ Procedures for obtaining benefits or services under those programs. ☐ Possible changes in or alternatives to those programs or procedures. ☐ Possible changes in methods or levels of payment for benefits or services under those programs. *Provide protocol specific findings justifying this determination:*
☐	The research could not practicably be carried out without the waiver or alteration. *Provide protocol specific findings justifying this determination:*

Return to Section 1.

12 Adequate provisions to solicit the assent of children (Check if **"Yes".** All must be checked)

☒	Assent will be obtained from: **(Check box that is true)** ☐ All children. **(**Complete Section 14**)** ☒ None of the children. **(**Complete Section 13**)** ☐ Some children. **(Complete** Section 13 **and** Section 14**. The protocol needs to describe which children will not be asked for assent)**

Return to Section 1.

13 Reason why assent is not necessary 45 CFR §46.408(a)/21 CFR §50.55(c) (Check if **"Yes".** All must be checked)

☒	One or more of the following are true. **(Check all boxes that are true.)** ☒ The capability of these children (taking into account the ages, maturity, and psychological state of the children involved) is so limited that they cannot reasonably be consulted. ☐ The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research ☐ Assent is waived under Section 15 criteria ☐ Assent is waived under Section 16 criteria

Return to Section 1.

14 Documentation of assent (Check if **"Yes".** All must be checked)

☐	If **"Yes"**, specify the process for documentation: ☐ Investigator will document assent in the consent signature block. ☐ Other **(NOTE: The protocol needs to describe the process of assent documentation)**

Return to Section 1.

15 Waiver of child assent under 45 CFR §46.408(a)/45 CFR §46.116(c)/21 CFR §50.55(d) (Check if **"Yes".** All must be checked)

☐	The research involves no more than Minimal Risk to the subjects.
☐	The waiver or alteration will not adversely affect the rights and welfare of the subjects.
☐	The research could not practicably be carried out without the waiver or alteration
☐	Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

☐	If the research involves using identifiable private information or identifiable biospecimens, the research could NOT practicably be carried out without using such information or biospecimens in an identifiable format. **(N/A if research is FDA regulated, is subject to Pre-2018 Requirements OR if does not use identifiable private information or biospecimens)** ☐ **N/A**
Return to Section 1.	

16	**Waiver of Child Assent under 45 CFR §46.408(a)/45 CFR §46.116(d)** (Check if **"Yes".** All must be checked)
☐	The research is not FDA-regulated.
☐	The research or demonstration project is to be conducted by or subject to the approval of state or local government officials
☐	The research or demonstration project is designed to study, evaluate, or otherwise examine one or more of the following: **(Check all boxes that are true. At least one must be checked.)** ☐ Public benefit or service programs. ☐ Procedures for obtaining benefits or services under those programs. ☐ Possible changes in or alternatives to those programs or procedures. ☐ Possible changes in methods or levels of payment for benefits or services under those programs.
☐	The research could not practicably be carried out without the waiver or alteration.
Return to Section 1.	

6.0 Data Management Plan

6.1 Data Analysis

The site PI and treatment team will meet on a daily basis to review the data and the safety of participants. The investigators will graph and analyze the data for all participants at least daily.

6.2 Data Security

Only members of the CSH–RUCARES research team listed on this protocol will collect and analyze data for this study. That is, these team members will conduct sessions with all patients, even those at DDDC, and collect data using BDataPro on encrypted CSH laptops. These data will be electronic. BDataPro data and video recordings will be saved to the encrypted C:/ drives of these laptops and then transferred to a secure server at Children's Specialized Hospital or to a secure cloud server (e.g., OneDrive for Business, Box Enterprise). These data will then be deleted from the laptop's C:/ drive following the transfer in accordance with ITS procedures. The following subject identifiers will be recorded in association with the research data: Name, all elements of dates (except year) related to an individual (e.g., birth, admission, discharge, medical record numbers, and full-face photographic images). A unique subject identifying code will be used to link data to these identifiers. Subject names will be converted to initials during the subject's participation. Following completion, pseudonyms will be assigned to subjects and the pseudonym identifier will be encrypted on the server. The justification for recording these specific subject identifiers is to schedule appointments and follow up with subjects. Subject identifiers will be maintained for a minimum of six years. All electronic data (e.g., session data) will be stored on the encrypted server and any hard copy data will be stored in the client's long-term file located in a locked cabinet in a locked office. After six years, the IT department will assist with data destruction. During the course of the study, we may record sessions for data-collection purposes for children whose caregivers. These videos will be recorded through a webcam directly into an encrypted

computer and stored on the encrypted network drive or encrypted hard drive. We will delete these videos six years from the collection date or earlier (if no additional data collection is required). Research data that contain subject identifiers will not be disclosed to outside researchers who are uninvolved with the study, or to any commercial sponsor, contract research organization, or external organization or entity. Provisions in place to protect the subject's privacy include ensuring that only personnel listed on the IRB application are present during the consent process, ensuring that the fewest number of individuals possible are aware of the subject's participation in research, and ensuring that research activities are performed in as private a place as possible.

6.3 Data and Safety Monitoring

A. Data/Safety Monitoring Plan

The investigators will ensure compliance with the current Guideline for Good Clinical Practice from the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use.[47] All study personnel will complete the Collaborative Institutional Training Initiative (CITI) Human Subjects Research and Good Clinical Practice courses offered online by the CITI Program. Investigators will submit annual reports to the IRB that provide information about informed consent, accrual, results, withdrawals, non-compliance, complaints and unexpected problems, as well as a risk and benefit assessment.

We will interview the primary caregiver(s) to determine how often and under what conditions the participant's destructive behavior results in physical harm to self or others. We will use this information to ensure that no participant is exposed to more risk during participation in this project than in the natural environment. We will always block or use protective equipment (e.g., arm splints) to prevent self-injurious behavior or aggression directed toward vulnerable organs (e.g., eye-gouging). Potentially harmful effects of severe head banging (e.g., detached retinas, concussions) will be mitigated by conducting sessions in a well- padded therapy room or, if necessary, having the individual wear a padded helmet. We will terminate sessions if self-injurious behavior results in reddening of the skin or frank bleeding. Further occurrences of self-injurious behavior will be blocked or prevented with protective equipment until the tissue has fully healed or the child has been examined by a nurse or physician and medically cleared to continue participation. In the Severe Behavior Program, we will routinely collect data on all adverse events (e.g., patient-to-patient aggression, staff or patient injuries), regardless of severity level. If we observe soft-tissue symptoms, they will be monitored daily and documented with images in medical progress notes until the symptoms resolve. If symptoms persist or are serious and acute, we will have a physician evaluate the child if one is immediately available, or if not, we will bring the child to a local emergency room. All adverse events will be reviewed during monthly meetings. Additionally, any unexpected or serious adverse event will be reported to the IRB, and we will respond to the adverse event as advised by the IRB. The emergence of unexpected or serious adverse events related to this study may result in removal of the participant from the study.

B. Data/Safety Monitoring Board Details

One of the postdoctoral fellows on this project will serve as the data coordinator and track the IRB application, and ensure that study personnel are using only the latest version of the protocol. In addition, this postdoctoral fellow will conduct an annual audit to ensure compliance with all IRB policies and procedures, including review of consent forms to make certain that consent forms are up to date and

are properly signed and dated. The postdoctoral fellow will report the results of the annual audit to the investigators. If corrective actions are required following the audit, the investigators and data coordinator will work with the IRB to develop correction and prevention plans. In addition, we may conduct audits on a more frequent basis if suggested by the IRB.

6.4 Reporting Results

A. Individual Subjects' Results
The results of the study for an individual participant will be shared with the parent/legal guardian of the participant at their request. The general result of all clinical procedures (i.e., not specifically those procedures conducted for the purposes of this research study) will be shared with parties for which releases of information are obtained (e.g., primary care physicians, teachers).

B. Aggregate Results
All informed consent documents will include a specific statement informing the participants that we will share the study results on ClinicalTrials.gov. We will use this website in addition to dissemination of our work through peer-reviewed publications and presentations at professional conferences.

C. Professional Reporting
We will present papers and posters by the end of the first year and throughout the entire five-year project. We will present our data at regional and national conferences hosted by organizations such as the Association for Behavior Analysis International, the Society for the Quantitative Analyses of Behavior, the Association of Professional Behavior Analysts, and the Association for Psychological Science. Beginning in the second year, we will begin publishing preliminary outcomes. We will submit papers for publication in flagship journals for behavior-analytic research, such as the Journal of the Experimental Analysis of Behavior and the Journal of Applied Behavior Analysis. In the fourth year, we will begin to summarize the findings across the larger number of accrued subjects, and we will submit these findings for publication.

D. Clinical Trials Registration, Results Reporting and Consent Posting
The research qualifies as a clinical trial that must comply with the federal requirement for public registration, results reporting and consent posting at its conclusion.

6.5 Secondary Use of the Data

N/A

7.0 Research Repositories – Specimens and/or Data

After information that could identify each participant has been removed, de-identified data collected for this research may be used by or distributed to investigators for other research without obtaining additional consent. For example, de-identified graphs of a participant's responding during the study might be re-analyzed as part of a secondary study evaluating different outcome variables.

8.0 Approvals/Authorizations

We are uploading non-Rutgers IRB approval (University of Nebraska Medical Center) and a letter of approval of an exception to allow newly recruited faculty to submit IRB applications as PIs prior to their official start dates.

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[i] "Children" are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.
[ii] "Guardian" means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.
[iii] Wendler D. "What is a "minor" increase over minimal risk?" *J Pediatr;* 01-Nov-2005; 147(5): 575-8.
[iv] https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM566948.pdf.