Virtual-reality and Emotion Regulation in Violence-Exposed youth (VERVE)

NCT05022550

Version date: 9/19/25

Protocol Title

Long Title: Virtual-reality and Emotion Regulation in Violence-Exposed youth (VERVE)

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Project Summary

The goal of this proposal is to determine the feasibility of a novel virtual-reality-based biofeedback (VR-B) treatment among youth highly vulnerable to difficulties in emotion regulation. Biofeedback, which involves the provision of real-time information about physiology, is a well-studied approach to enhancing self-regulatory ability, with potential promise for alleviating mental health problems. In children (as well as adults), biofeedback may be ideally facilitated through video game environments, which offer engaging, immersive, yet dynamic environments that can be changed in real-time. Video games are enormously popular with youth and may represent an important avenue for treatment in adolescent populations. The current proposal aims to evaluate a novel virtual-reality-based video game treatment for emotional dysregulation for youth currently under the supervision of the juvenile justice system. Exposure to risk factors known to promote impaired self-regulation, such as child maltreatment, is nearly endemic in this population. Indeed, 'delinquent' youth (i.e., youth in contact with the justice system) are considerably more likely to meet diagnostic criteria for a range of disorders centrally involving dysregulation of affect or arousal, such as posttraumatic stress disorder, anxiety, depression, oppositional defiant disorder, and many others. Relatedly, This pilot study will: 1) evaluate the feasibility of applying a VR-B treatment for these adolescents, 2) identify potential changes in physiological signaling (e.g., heart rate, skin conductance) across treatment sessions, 3) identify potential changes in self-regulatory ability or symptom severity across treatment sessions.

Background and Significance

A legacy of research demonstrates that youth who experience early life adversity (e.g., violence, maltreatment) are at dramatically higher risk of engaging in delinquent and criminal behavior across the lifespan (Bowlby, 1944; Kerig & Becker, 2012). Indeed, roughly 90% of juvenile offenders in the U.S. report exposure to at least one traumatic event (e.g., domestic violence), with multiple exposures typical (Fox et al., 2015). Childhood trauma exposure may be the single most potent risk factor for future psychopathology, and indeed, nearly 80% of justice-involved youth meet diagnostic criteria for at least one psychiatric disorder. Though justice-involved youth exhibit elevated rates of all psychiatric problems, these youth are particularly likely to experience a constellation of disorders clinically rooted in difficulty regulating emotion and bodily arousal in response to psychosocial stress. Common therapeutic frameworks (e.g., cognitive behavioral therapy) specifically target self-regulation through didactic skills training. In theory, practicing these skills may effect change in the brain-body systems underlying regulation, facilitating greater stress tolerance. However, evidence supporting the practical effectiveness these self-regulation treatment components is limited at best. The broader benefits of mental health treatments for disorders of dysregulation (e.g., PTSD) are selectively distributed among youth, and often provide only temporary relief from

symptoms, Advances may come from blending knowledge of biological *and* behavioral systems underlying self-regulation, as well as using novel technological approaches to enhance engagement and improve accessibility for underserved populations, such as justice-involved youth (JIY). Indeed, despite pressing need, clear potential for benefit, and extensive theoretical justification, pediatric treatment development research rarely involves JIY, neglecting a mutually beneficial partnership between clinical scientists and children (and families) at critical risk. Contrary to this trend, the proposed work seeks to evaluate the fidelity, feasibility, tolerability, and potential clinical benefit of a novel treatment for dysregulation in partnership with area JIY and justice officials.

Biofeedback is a legacy, evidence-based mental health treatment wherein individuals are provided with real-time information about physiological arousal. This information enhances awareness of the somatic sensations of high arousal and can be used as the basis for conditioning behaviors that modulate those sensations. use acquired skills or conditioned behavior to control that arousal. Biofeedback treatment typically requires sustained attention to an information stream detailing one's own physiological activation, such as heart or respiration rates, electrocardiograms, electromyograms, or other numerical or graphical data. Consistent engagement may be difficult for adults, and extraordinarily challenging for children experiencing mental illness. This process could be considerably enhanced by translating biofeedback signals into engaging stimuli to be presented in a paradigm broadly acceptable (or even enjoyable) for youth. With these aims in mind, our team is continuing to develop a virtual-reality based biofeedback video game for dysregulated youth, including careful consideration of accessibility and portability in effort to benefit youth who are most at risk.

Video games are an ideal treatment vehicle for adolescents – nearly 97% of whom play video games on a regular basis – as well as an established avenue for training cognitive processes, such as effortful autonomic regulation. Davidson and colleagues recently demonstrated that a mobile game teaching focused attention on breathing enhanced functional connectivity in prefrontal regulatory circuits among adolescents. Biofeedback-based breath awareness is an efficacious technique for augmenting effortful autonomic regulation (Zafar et al., 2020). Regularized guided breathing treatment decreases autonomic reactivity to stress among adults with PTSD (Fonkoue et al., 2020). Notably, common approaches to biofeedback with heart rate or respiration make use of textual or abstract graphical feedback (e.g., sine waves, breaths per minute). Virtual reality allows biofeedback to be embedded in the characteristics of the environment itself, thereby sustaining attention and engagement, with proven benefits over traditional implementations (Blum et al., 2019). Indeed, VR-based applications are now widely used to great benefit for a variety of psychiatric disorders (Rizzo & Koenig, 2017). Furthermore, a recent systematic review of VR-based interventions in adolescents to reduce psychological distress found preliminary evidence within a small number randomized control trials (RCTs) and uncontrolled pilot studies that VR-based interventions report clinically significant reductions in psychological distress across youth with mental health disorder or histories of victimization (Kelson et al., 2021). Finally, its simplicity, versatility, and portability make VR-based treatment an ideal avenue for expanding mental

health treatments to underserved populations residing in impoverished or restricted environments.

For justice-involved youth, the limitations of current approaches are compounded by barriers of access, administration, and availability. First, JIY are nearly six-times more likely to live below the poverty line, a widely recognized practical obstacle to seeking and obtaining quality health services broadly, and mental health treatment specifically. Impoverished youth are considerably more likely to carry an undiagnosed mental illness through adulthood, a product of their diminished likelihood of encountering a clinically trained mental health professional. Second, and relatedly, there is currently a remarkable dearth of pediatric mental health clinicians, of whom only a small percentage are likely to possess the training and experience necessary to work with JIY, particularly in forensic settings. Assessment and treatment of mental health problems within the juvenile justice system, and specifically among detained youth, is uncommon due to the lack of professionals, as well as the funding to pay them. Third, chronically justice-involved youth may be considerably less likely to maintain the consistent, typically multi-month, individualized therapy schedule required by most treatment frameworks. Transitions between homes, schools, detention centers, court dates, parole and probation are extraordinarily common for JIY, and in combination make the provision of regular treatment extremely difficult.

Truly, the lack of current treatment approaches for pediatric mental health problems become acutely clear when examined among those at greatest risk, such as JIY. There is a clear need for novel advances in mental health treatment that build from multidisciplinary knowledge about the biobehavioral roots of mental illness, such as impairments in self-regulation. Yet, it is also critical that the development of such treatments consider issues of access and availability from the very beginning, such that the potential benefits can be equitably distributed to a broad population, while maintaining pediatric applicability. To that end, the current proposal aims to evaluate the feasibility of a novel, virtual-reality biofeedback video game.

PTSD is common in adolescence and causes significant suffering and burden throughout the lifespan. The incidence of PTSD rises markedly in adolescence, reaching a lifetime prevalence of 5% by age 18 and up to 40% in cases of sexual abuse and assault (Copeland et al., 2007). In addition to psychological suffering, PTSD is associated with lower academic achievement and increased incidence of depression, suicide attempts, and substance abuse into adulthood (Warshaw et al., 1993). Childhood trauma and PTSD also impose tremendous societal costs in terms of health care utilization and financial outlay. For example, the sequelae of childhood maltreatment, including PTSD, cost the United States an estimated $500 billion annually (Fang et al., 2012). These sobering statistics highlight the urgent need to uncover novel, evidence-based treatments to improve the well-being of afflicted youth. Unfortunately, current pharmacological approaches to youth PTSD show only minimal efficacy. Psychotherapy offers modest benefits, yet only for some, and only temporarily.

Advances may come from multidisciplinary efforts to evaluate and adapt current treatments. Many mental illnesses, including PTSD, are driven in part by difficulty self-regulating emotional and physical arousal. Biofeedback is an evidence-based mental health treatment involving provision of real-time information about physiological arousal. Individuals learn to recognize the bodily sensations of high arousal and use acquired skills or conditioned behavior to control that arousal. Yet this approach has historically been difficult for youth, as it requires sustained attention and engagement to the biofeedback signals. The current proposal aims to evaluate the feasibility of a novel virtual-reality-based video game biofeedback system.

Video games are an ideal treatment vehicle for adolescents – nearly 97% of whom play video games on a regular basis – as well as an established avenue for training cognitive processes, such as effortful autonomic regulation. Davidson and colleagues recently demonstrated that a mobile game teaching focused attention on breathing enhanced functional connectivity in prefrontal regulatory circuits among adolescents. Biofeedback-based breath awareness is an efficacious technique for augmenting effortful autonomic regulation (Zafar et al., 2020). Regularized guided breathing treatment decreases autonomic reactivity to stress among adults with PTSD (Fonkoue et al., 2020). Notably, common approaches to biofeedback with heart rate or respiration make use of textual or abstract graphical feedback (e.g., sine waves, breaths per minute). Virtual reality allows biofeedback to be embedded in the characteristics of the environment itself, thereby sustaining attention and engagement, with proven benefits over traditional implementations (Blum et al., 2019). Indeed, VR-based applications are now widely used to great benefit for a variety of psychiatric disorders (Rizzo & Koenig, 2017). This will be the first study to integrate these concepts – virtual reality and biofeedback – for the targeted treatment of adolescent PTSD and suicidal ideation.

Specific Aims

AIM 1: Evaluate the feasibility of a virtual reality treatment for youth
Hypothesis 1: Study youth receiving treatment with the virtual reality-based paradigm will qualitatively report the experience to be tolerable and positive with minimal discomfort.

AIM 2: Identify potential changes in physiological signaling (e.g., heart rate, skin conductance) across treatment sessions
Hypothesis 2: Youth receiving virtual reality biofeedback (VRB) treatment will exhibit physiological changes across sessions (e.g., increased heart rate variability or changes in skin conductance responses).

AIM 3: Identify potential changes in symptom severity across treatment sessions
Hypothesis 3: Youth receiving virtual reality biofeedback (VRB) treatment will show greater improvements in youth emotion regulation and reduced severity of mental health symptoms.

Research Design and Methods

Subject Population

Over approximately two years, we plan to enroll up to 135 youth under the age of 18 in residential placement pending resolution of delinquency proceedings in the Dane County Juvenile Court (Madison, WI). Each youth will be asked to complete up to six sessions of VR-B. The study will continue to enroll until up to 30 youth have completed 3 days of DEEP, and up to 30 youth have completed 3 days of DEEP-Challenge. Participants will be given the opportunity to complete DEEP-Challenge after completion of one session of standard DEEP.

1. **Inclusion Criteria (Youth Participants)**
    a. Youth between the ages of 13 and 17 at enrollment
    b. Availability of a caregiver to provide oral consent
    c. Able to provide assent/consent in English
    d. Visual acuity adequate to read text on a computer monitor
2. **Exclusion Criteria (Youth Participants)**
    a. Report of previous discomfort with immersive experiences, including virtual reality, 3D films, or similar media.
    b. Active psychosis or comparably impairing psychiatric condition

Residence facilities in the Dane County Juvenile Court Program (Dane County Juvenile Detention Center:210 Martin Luther King Jr Blvd, Madison, WI 53703; Dane County Juvenile Shelter Home: 2402 Atwood Ave, Madison, WI 53704) typically house approximately 15 youth per site at any time, with lengths of stay averaging approximately one week but up to 60 days. Due to the multi-session nature of this study, we plan to recruit and collect data at least once a day at one or both sites to have as many youths as possible complete all six sessions.

Recruitment Plan

Subject Identification. A staff member at the Dane County Juvenile Detention Center or Dane County Juvenile Shelter Home will identify potential participants from youth currently residing in their care that are available to participate and will assist in contacting the appropriate parent or legal guardian of youth and facilitating phone communication scheduling/transfer to a study staff member, who will ultimately be the one to complete parental oral consent via telephone. All youth residing at the detention center or shelter home will be invited to participate in the study, excluding those meeting exclusionary criteria (see above). To avoid coercion, all recruitment procedures emphasize that the choice to participate/not participate will not influence the outcome of adjudication proceedings or their duration (i.e., length of placement), any gain/loss of residence privileges, or any other disciplinary action. Additionally, we will explicitly review the confidentiality of data collected, specifically that

original subject data will *not* be shared with Dane County Juvenile Justice officials, will not be considered in adjudication proceedings, but will be de-identified and housed in secure, restricted access digital storage hosted by the BRAVE Research Center. Additionally, we will explicitly detail the legal protections afforded by the NIH Certificate of Confidentiality to be obtained for this research (as required).

Consent/Assent Process. Upon identification and facilitation by Detention Center staff, parents/guardians of candidate youth participants will be contacted by telephone by a study staff member to complete an oral informed consent procedure therefore parent/guardian consent documentation will not be obtained**.** This waiver of parental consent documentation is reasonable given the minimal risk nature of study activities. Further, participation in the planned study activities (i.e., virtual-reality video games) would not normally require written consent outside of a research setting. For example, in the community, participating in similar VR or video games would not require written parental consent (like surgeries or other high-risk procedures). However, we will still receive oral parental consent prior to participant enrollment and provide parents easy electronic access to the full Consent and HIPAA Authorization form located on our website.

During the oral consent process, study staff will first instruct parents on where and how to access the consent form in real time so they are able to look at the form during the conversation. This includes offering the parent a mailed paper copy of the consent form prior to completing oral consent, or a text/email with the link to the web-based consent form to open during the oral consent process. Study staff will then complete an informal review of the key components of the consent form, including a detailed description of the study and culminating with receiving and documenting oral consent. The consent form will provide all information regarding the basic procedures of the study, the voluntary nature of participation, potential risks and benefits associated with study participation, and the terms of confidentiality. As above, we will explicitly state that individual study data will only be accessible by the study team, and that neither the data nor the decision to participate will be considered elsewhere. Parents will then be asked whether they agree to allow their child to participate in the study. Following affirmation of oral consent, parents will be reminded of where they will always have access to the consent form for the reference going forward.

Exception for Parent Oral Consent. At the Dane County Juvenile Shelter Home (DCJSH), admission includes extensive background work on the youth and their family. For a small proportion of youth in their care, approximately 1 in every 4 youth, this process concludes an internal determination that the youth has "unavailable parents". This determination could be made for a variety of reasons: protection of the child's safety requires no parent contact, parent estrangement, parent mental incapacity, parent denial of contact, etc. Therefore, a waiver or parent/guardian consent for this subset of youth in the DCJSH is the most appropriate course of action under the general requirements (46.116) and the special provisions under the children's regulations, which allows for the absence of parent/guardian consent

in circumstances where such parent/guardian permission is not a reasonable requirement to protect subjects.

In accordance with Subpart D of the children's regulations (46.408(c)), requiring parental consent for youth determined to have "unavailable parents" by the DCJSH is not a reasonable requirement to protect this population. This waiver would *only* apply to youth with this specific determination and without such a requirement we would be unable to enroll these youth as it would either be impossible or unsafe (e.g., protection of the child's safety requires no parent contact, or parent estrangement, parent mental incapacity, and/or parent denial of contact result in an inability to make contact). As a substitute, appropriate mechanism for protecting this subset of children who will participate as subjects in the research, permission will be provided by the Director of the DCJSH or by the youth's social worker, both of whom have the full context of the youth's current mental and physical state and are able to make reasonable decisions in the best interest of the child. This protection plan will not involve LAR consent, rather their permission to allow for child participation would be a separate determination, documented in study records, and serve as added protection. The youth assent process, described below, remains unchanged for these youth.

Further, the waiver of parent/guardian consent is justified by:

i. This research involves no more than minimal risk to the subjects
    a. This study has already been determined to be of minimal risk. Participation in the planned study activities (i.e., virtual-reality video games) would not normally require written consent outside of a research setting. For example, in the community, participating in similar VR or video games would not require written parental consent (like surgeries or other high-risk procedures). Finally, questionnaires ask for information that would normally be provided at a doctors visit.
ii. The research could not practicably be carried out without the requested waiver or alteration
    a. This waiver would only apply to youth with this specific determination and without such a requirement we would be unable to enroll these youth as it would either be impossible or unsafe (e.g., protection of the child's safety requires no parent contact, or parent estrangement, parent mental incapacity, and/or parent denial of contact result in an inability to make contact)
iii. As the research involves using identifiable private information, the research could not practicably be carried out without using such information in an identifiable format
    a. The research needs to obtain measures of mental health symptoms and participant history within the juvenile justice system via online record review attached to their name in order to test efficacy of the intervention.
iv. The waiver or alteration will not adversely affect the rights and welfare of the subjects

a. As a substitute, appropriate mechanism for protecting this subset of children who will participate as subjects in the research, permission will be provided by the Director of the DCJSH or by the youth's social worker, both of whom have the full context of the youth's current mental and physical state and are able to make reasonable decisions in the best interest of the child. This protection plan will not involve LAR consent, rather their permission to allow for child participation would be a separate determination, documented in study records, and serve as added protection; and

v. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

Assent/Consent Procedures. Procedures for youth assent/consent will be implemented either individually or in small group sessions, depending on staff availability relative to the number of youth to be consented at a given time. While recruitment and referral may be assisted by Juvenile Court Program staff, all informed consent or assent from the youth will only be obtained by trained study staff members. Due to the elevated likelihood of reading impairment or illiteracy in this population, staff will orally 'walk through' the consent form to highlight basic study procedures, the voluntary nature of participation, potential risks and benefits associated with participation, and the terms of confidentiality. As in parental assent, we will attempt to minimize risk of coercion by emphasize that the choice to participate/not participate will not influence the outcome of adjudication proceedings or their duration (i.e., length of placement), any gain/loss of residence privileges, or any other disciplinary action. Additionally, we will explicitly review the confidentiality of data collected, specifically that individual subject data will *not* be shared with Dane County Juvenile Justice officials, will not be considered in adjudication proceedings, but will be de-identified and housed in secure, restricted access digital storage hosted by the BRAVE Research Center to be used for research purposes only. Additionally, we will explicitly detail the legal protections afforded by the NIH Certificate of Confidentiality to be obtained for this research (as required). To further ensure comprehension during consent, youth will be provided with an additional information sheet describing the study in simplified language. Candidate participants will also be given an information sheet during the process with simplified language to aid in comprehension and consent capacity. They will be informed that refusal to participate will not result in disciplinary action. Finally, potential participants will be encouraged to ask questions about the study before agreeing to participate. Youth that agree to participate will document their consent by providing their e-signature on a REDCap electronic consent form. The informed consent/assent process will be documented in each subject's research record.

Study Activities

Overview. After parent consent, and immediately following youth assent, all participants will be invited to engage in at least one 30-minute VR-B session, but may complete up to six total sessions (no more than one per day), depending on interest and availability. Before and

after the first session, participants will complete a set of online questionnaires (via REDCap survey on provided laptops). For participants that complete more than one session, questionnaires will only be completed at the end of each subsequent session.

In order to ensure privacy and confidentiality protections, all study activities detailed below will be completed in a private, closed-door room. Only research study staff will be in the room with the participants while completing activities, with corrections personnel wholly unable to read or hear survey responses or other conversations. Corrections personnel may need to enter the room under extenuating circumstances (e.g. logistics, emergencies, etc.), at which point all study activities will be paused or ended. Potentially sensitive subject information will be collected via online survey only, not by verbal interview, further reducing risk of corrections staff overhearing any information.

VR-B Sessions. We will have study staff set up in an available private room for 2-3 hours per day, multiple days per week. During those times, detention and shelter home staff will assist in directing youth that are interested in participating and that they have received oral parental consent for to our room.

The following data collection procedures will be utilized with all youth who are determined eligible for participation after the consent/assent procedures. During each session, youth will be asked to experience an immersive virtual-reality simulation. Youth will wear a lightweight, ultra-high-resolution, wireless, head-mounted display (Oculus Quest 2 Enterprise VR Headset, www.oculus.com). Each session will proceed through a series of four stages. First, participants will begin with a 5-min. acclimation period inside a demo VR environment. Second, baseline levels of physiological arousal will be captured over a 5 min. resting period where participants will be asked to sit quietly in a serene virtual environment. Third, youth will youth will progress through the DEEP VR experience for 15 minutes (see *Behavioral Task*). Finally, participants will complete a short series of online questionnaires and may be asked for feedback about the VR experience by study staff.

We will invite youth to complete additional VR-B sessions, though we will cap the number of sessions to six total, including baseline, and will not allow any participant to complete more than one session per day.

Questionnaires

All questionnaires used in this study are detailed in the table below but may not be administered directly in the order listed. Instruments will be administered via UW ICTR REDCap instance survey (see *Data and Record Keeping*) and are specified as to whether they are administered only before the baseline session, after each VR-B session, or both. None of the instruments outline below collect information on illegal behaviors or criminal activities (that are not already included in their institutional file) that could affect any part of their juvenile

criminal proceedings, and none of the data collected will be provided to Juvenile Court Program staff.

Instrument	Brief Description	Baseline	At Session
Child Behavior Checklist (CBCL)	Assesses a broad array of problem behaviors and symptoms in youth	X	
Childhood Trauma Questionnaire (CTQ)	Assesses history of childhood maltreatment experiences, including abuse and neglect	X	
Difficulty in Emotion Regulation Scale (DERS)	Assesses emotion regulation abilities	X	X
Gender and Orientation	Assesses gender, biological sex, and sexual orientation	X	
PROMIS-A	Assesses youth depressive symptoms	X	
PROMIS-D	Assesses youth anxiety symptoms	X	
Race and Ethnicity	Assesses race and ethnicity	X	
Child PTSD Symptom Scale (CPSS)	Assesses lifetime trauma experiences and severity of PTSD symptom severity	X	X
VR-B Engagement Survey	Assesses immersion, satisfaction, and boredom related to the VR treatment	X	X
VR-B DEEP Challenge Feedback	Collect participant feedback about the challenging aspects of the game		X*
*This feedback will only be collected after the first DEEP Challenge session, if a participant has opted-in to DEEP Challenge			

Alternative Administration. While all assessments are administered electronically, coded paper versions may be used in the event of electronic malfunction; no PHI will be recorded on paper administration of assessments.

VR-B DEEP Challenge Feedback: If a participant opts-in to a DEEP Challenge session, they will be briefly asked about their experience with the challenge version by a study staff member. This feedback will be noted and kept in a REDCap form.

Record Review

Record Review Forms. Depending on the accessibility and scope of records available to study staff, background information may be extracted from the available institutional files of each participant by trained study staff members. The Record Review form consists of items

measuring basic demographic information, criminal history data, trauma histories, and mental health variables.

A member of our study staff will work with the staff at the Dane County Juvenile Court Program facility to get electronic access to the Juvenile Wisconsin Circuit Court Access (CCAP) program to gather very basic demographics, the current offense that brings them to the facility, any prior dispositions in the system, and any indication of trauma and mental health history. According to the Detention Staff, online records may or may not include all of the information on the Record Review Sheet, in which case we are also able to review the paper intake information collected at the Detention Center for anything missing, which *may* have the information. Either way, we will collect only what is available. Electronic and paper review will always take place at the Detention Facility with direct permission and facilitation by a Detention Facility staff member. Access to electronic records will not be available to review on our personal or University devices at any time. The Record Review Sheet will be filled out and stored in a private REDCap project (ICTR instance), which is only accessible by study members currently approved on the IRB protocol. Access can only be granted by the PI or Point of Contacts for this study.

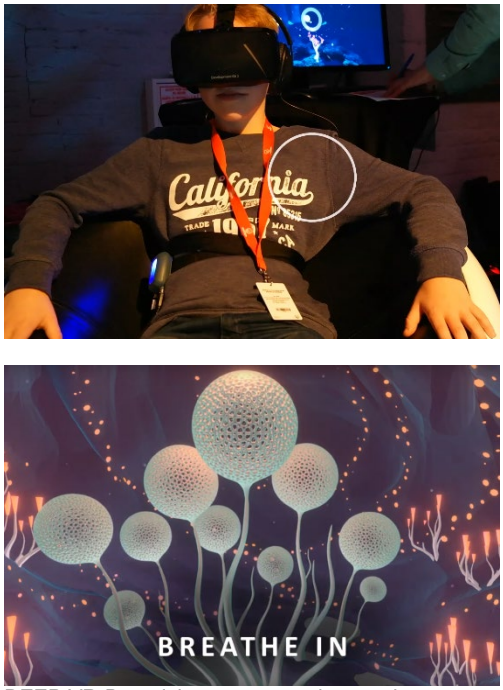
Behavioral Tasks

VR-B Session. At each session, youth will be asked to experience an immersive virtual-reality simulation while wearing a VR headset. Prior to VR, research staff will work with participants to affix electrodes to the fingers and abdomen to measure sweat levels and heart rate



Virtual outdoor scene

respectively and place two respiration belts around the upper waist (one that controls the VR-B task and one that collects respiration data). Each session will proceed through a series of three stages. First, to reduce potential bias due to the novelty of VR, before the very first session, participants will complete a 5-min. acclimation period inside a demo VR environment.



DEEP VR-B participant setup and example screenshot of respiratory biofeedback training in the VR environment.

Second, before every session, baseline levels of physiological arousal will be captured over a 5 min. resting period. Participants will be asked to sit quietly within a serene virtual outdoor scene.

Third, youth will progress through the DEEP VR experience for 15 minutes. Youth in the will receive explicit instructions to attempt to regulate their breathing, with visual feedback provided by expanding and contracting sea flora (see here for demonstration video). Physiological data will be recorded during baseline and VR stages using a wireless monitoring system (Mindware Mobile Recorder, Mindware Technologies Ltd., OH) and include electrocardiography for heart rate, galvanic skin response, and respiration.

DEEP VR is an immersive underwater experience where navigational movement is controlled by breathing via a stretch-sensor respiratory belt placed at the diaphragm. This sensor measures the expansion of the diaphragm associated with breathing, providing input to control in-game movement: the slower and deeper players breathe through their diaphragm, the better they can move around in the underwater world. Using this design, players are conditioned to regulate physiological arousal using diaphragmatic breathing – the facilitation of breath into the lungs from contraction of the diaphragm muscle rather than the rib cage. Biofeedback mechanics are applied in multiple ways. First, players receive feedback about stage of breathing through movement – inhalation is accompanied by an upward and forward force, which is strengthened by exhalation. Second, a circle in the center of the visual field expands and contracts with the breath cycle. Third, breathing is mirrored by changes in color, size, and movement of flora and fauna in the environment. An example participant setup and screenshot are provided in Figure 3.

If a participant successfully completes one VR-B session of DEEP VR, they will have the option to complete sessions 2-6 in a more challenging version of the task called DEEP Challenge. DEEP Challenge functions on the same biological principles and technology as DEEP VR, and only differs in the music and aesthetic presentation of obstacles. The DEEP Challenge environment is darker and feels deeper underwater than DEEP VR. This is done to increase physiological arousal of participants and more realistically mimic a situation where emotion regulation via deep breathing would provide optimal benefit. The setup of psychophysiology equipment and the mechanism controlling player movement is the exact same for both DEEP VR and DEEP Challenge. An example illustrating the difference between obstacles in DEEP VR and DEEP Challenge is provided in Figure 4.



Figure 4: A similar section of DEEP VR (left) compared to DEEP Challenge (right).

Payment of Research Subjects

Participants will be compensated under the following compensation scheme after each session that they complete. Payments will be made directly to the youth in the form of cash or a debit card, that will be stored with the youth's personal belongings and released to them at the time of release from the detention facility. In total, participants may receive $200 in total for completing up to six sessions.

Study Day 1	$30
Study Day 2	$30
Study Day 3	$30
Study Day 4	$35
Study Day 5	$35
Study Day 6	$40
Total	$200

Statistical Considerations

Analysis Plan.

AIM 1: Evaluate the feasibility of a virtual reality treatment for youth
Study youth receiving treatment with the virtual reality-based paradigm will provide qualitative and quantitative reports about their experience across each session. These will include questions about enjoyment or boredom with the task itself, comfort with the equipment, ease of navigation in the virtual environment, etc. These questions will be used to inform redesign of the VR simulation (DEEP VR) and inform future investigations at a larger scale.

AIM 2: Identify potential changes in physiological signaling (e.g., heart rate) across treatment sessions
We aim to identify whether physiological responses, including skin conductance and heart rate variability, exhibit change across session. We will compare physiological signaling between baseline and task-conditions as well as across study days. Additionally, we intend to evaluate how these physiological changes may be related to change in symptom severity or self-regulation. Exploratory analyses will investigate how these changes in physiology may be different in DEEP versus DEEP-Challenge sessions across time.

AIM 3: Identify potential changes in symptom severity across treatment sessions
We aim to identify whether changes in self-regulation or mental health symptom severity are evident pre- to post-treatment. Youth receiving virtual reality biofeedback (VRB) treatment will show greater improvements in emotion regulation and reduced severity of PTSD symptoms. Exploratory analyses will investigate whether symptoms changes may be different in related to participation in DEEP versus DEEP and DEEP-Challenge sessions across time.

Analytical Strategies. When appropriate, analyses described above will be conducted using linear mixed effects (LME) modeling and will include age and sex as covariates. In order to control for false positives and ensure conservative analytical approaches, we will utilize multiple comparison correction when applicable.

Supplemental Analyses. We may further explore secondary outcome variables, including but not limited to the following: PTSD severity, comorbid disorder diagnoses and symptom levels, trauma load, stressful life events, juvenile criminal justice involvement (past or pending charges, convictions, etc.) cognitive scores, pubertal stage, symptom/trauma scores, parent-child relationship quality, socioeconomic status.

Data and Record Keeping

Recruitment. Trained study team members will manage the overall recruitment and enrollment processes and will be assisted by Juvenile Court Program staff. Record of oral parental consent will be stored and managed in an individual ICTR-instanced REDCap project (hereafter, 'REDCap'), and only the study team members who are directly assisting with recruitment will have access to the Project. If the parent provides oral consent for their child to participate, we will also provide them with a copy of the consent form either electronically or in the mail. Subsequent youth assent/consent will be captured via electronic REDCap forms, including a typed e-signature. All recruitment and consent information will be stored in REDCap and associated with a randomly assigned study ID code.

Study Activities. All self-administered assessments will be collected and stored in REDCap using a lab-owned laptop. Any assessments completed on the laptop would be administered using REDCap and therefore data would not directly be stored on the device. Nevertheless, laptops will be password-protected and stored in a locked office in the Department of Psychiatry (UW-Psychiatry; Wisconsin Psychiatric Institutes & Clinics).

De-identified psychophysiological and behavioral task data will be stored in the lab's Wisc.edu Box folder. This Box folder is only accessible by study team members and will never store personally identifiable information. The raw data may be accessed, copied, and analyzed using the lab's private processing server. This server is only accessible from a private, internal network, through password-authorized secure channels.

Data Protection and Sharing Overview. All data collected during study activities will be linked only to subject ID numbers. Upon study completion, study data will be banked indefinitely for possible future research. Some study data may also be shared for future collaborative research projects. Physiological data may be shared with outside researchers for preprocessing. These collaborators will not receive any PHI during the data sharing process; only subject identification number and collection information will be included.

External Data Sharing. All data will be banked indefinitely for future research and sharing. Throughout the study, physiological or gameplay data may be shared with outside researchers for processing, and only study ID number will be shared with the samples.

Internal Data Sharing. If subjects participate in more than one study in the research lab, data may be shared across the studies. In other words, data may be included for analyses in multiple studies. When there is data sharing across protocols, the study team will assure that all study team members are added to any overlapping IRB protocols.

Data Safety and Monitoring Plan

Devices

None of the study devices used in the study are being investigated for safety or efficacy as part of this study. Therefore, we will not be reporting any results from study activities to the Federal Drug Administration (FDA). Below you will find a description of the various headsets that may be used to deliver the virtual environment.

Oculus Quest 2 Virtual Reality Headset. A lightweight, ultra-high-resolution, wireless head-mounted VR display (Facebook Technologies; Menlo Park, CA). This headset does not require an accompanying computer. This device does not have FDA status.

Risks and Anticipated Problems

Psychological distress. Many of our assessments and probe sensitive topics that may cause psychological distress or discomfort. All study team members who administer these assessments are extensively trained in working with adults and children within this vulnerable population. In addition, all participants are welcome to stop and start self-administered surveys in order to ensure comfortability and can arrange with a study team member to leave a survey incomplete if they do not feel comfortable finishing. However, a majority of our surveys are validated within this population and most participants are able to finish all assessments. Study team members are also trained on assuring ongoing consent and working with participants to solicit feedback, ask and answer questions, and assuage anxiety by several methods. Throughout the study, subjects will be able to talk with staff, and support will be provided to minimize distress and discomfort.

Virtual Reality Discomfort. In some individuals, exposure to immersive environments such as virtual reality or 3D films can cause symptoms akin to motion sickness, here referred to as 'simulation sickness'. Such symptoms most commonly include general discomfort, headache, nausea, and fatigue. These symptoms are thought to stem from incongruity between information provided by the vestibular system (awareness of orientation and movement) and visual systems (Golding, 2016). In VR, the visual system may register change in movement or orientation, while the vestibular system does not (due to the lack of physical movement). These symptoms are readily alleviated after exiting the virtual environment (e.g., removing the headset, leaving the theater).

Several steps will be taken to minimize the risk of VR discomfort in participants. First, participants will be warned about the potential for simulation (motion) sickness during the consent process. Second, several design aspects known to minimize simulation sickness will be incorporated (ARVI VR Inc., 2018). Participants will be seated during VR tasks and will engage in a simple 'warm-up' period to adjust to the VR environment. Furthermore, the DEEP VR task incorporates design concepts known to reduce risk of VR sickness. Specifically, the simulation does not involve sharp or sudden changes in orientation or movement.

Darker colors and smoothed textures are used in crafting the scenes. Finally, we will utilize cutting-edge VR hardware incorporating the latest advances in VR simulation, such as high screen refresh rate, which may also reduce likelihood of VR sickness (ARVI VR Inc., 2018)

The DEEP VR and DEEP Challenge environments involve dynamic underwater scenes that are designed to increase physiological arousal. Some participants may become overwhelmed or distressed in these VR environments, and all participants have the option to end the task immediately if they wish to stop.

Suicidality. Youth participants answer a question pertaining to suicide on the Child Behavior Checklist (CBCL). On the CBCL, endorsing suicidality is defined as responding "Somewhat or Sometimes True" or "Very True or Often True" to the question "I deliberately try to hurt of kill myself" within the timeframe "now or within the past six months." For any youth participant who endorses either or both of these items, we will inform the center staff indicating what they have endorsed suicidality, in the event that further actions may be deemed necessary by the medical staff.

Abuse/Neglect. If abuse or serious risk of abuse is verbally disclosed to a study staff during the session, this will be reported to the appropriate authorities, such as Child Protective Services (CPS), when deemed necessary by the Principal Investigator, based on mandated reporter laws. This includes any possible sexual abuse/assault, any physical abuse, or any situation in which the child is possibly in danger. Documentation regarding follow-up will be kept for clinical purposes (i.e. in instances where a clinician may desire documentation) but will *not* be kept for data analysis purposes. Any follow-up documentation sent to study staff regarding CPS follow-ups will also be retained as proof of the CPS phone call. All documents described in this section will be uploaded to a designated instrument in REDCap and carefully safeguarded. For this instrument, user permissions will be set so that only the PI and study staff can access it, no study staff can export any data from the instrument, and even de-identified data from this instrument will never be shared with researchers outside the necessary members of the study team. Caregivers/subjects are informed of reporting possibilities as part of the consent process and may decline to participate further.

Confidentiality. There is always a slight chance of breach of confidentiality, which could result in legal implications or stigmatization. Every effort will be made to protect the participants' confidentiality. A Certificate of Confidentiality will be obtained to further protect subject privacy. In order to minimize the risk of a breach of confidentiality, all subject data, including psychiatric diagnostic information, physiological data, and responses to non-clinical questionnaires, will be coded and identified by a subject number. Codes linking the subject ID to identifiable information will be stored only in REDCap or in a password protected key saved on our local departmental secure server. Electronic information is stored on a secure server or in REDCap, and it is accessible only to study team members using network credentials. Furthermore, user permissions in REDCap will be minimally allocated so that

study staff have access and appropriate permissions only to data that they need for their particular roles.

Research Involving Prisoners as Subjects. This research with youth detained by the State of Wisconsin falls under the regulations of Research Involving Prisoners as Subjects. This project represents research on innovative and accepted practices which has the intent and reasonable probability of improving health or well-being of the subjects, and all groups of participants enrolled in this project may benefit from the research. Virtual-reality biofeedback (VR-B) interventions have been previously been implemented in non-detained adolescent populations using the DEEP VR biofeedback game that already suggest meaningful clinical benefit (Bossenbroek et al., 2020; see review, Kelson et al., 2021; van Rooij et al., 2016). This research aims to expand this research and pilot program to a population of youth that may be great need of enhanced self-regulatory skills, especially while they are residing in structured and stressful environments like juvenile detention centers. Further, there is preliminary evidence that VR-B may be particularly beneficial and effective for youth with a history of interpersonal violence or other childhood victimization (Kelson et al., 2021). The rate of trauma and violence exposure in youth involved in the juvenile criminal justice system are astronomically higher than in a general community population (Bowlby, 1944; Fox et al., 2015; Kerig & Becker, 2012), making the Juvenile Court Program a particularly crucial and urgently in-need population for VR-B programs.

This pilot project proposes short VR-B sessions that may be completed between one and six times for feasibility of implementation in vulnerable populations and participation does not provide any benefits that would cloud a youth's ability to weigh the risks and benefits as this intervention is commensurate to television, computer, and video games that youth are generally knowledgeable about, and will be completed during recreational times in which youth have their choice of activities.

We have taken risk minimization actions to ensure the risks of this research with incarcerated youth are commensurate to research with non-incarcerated youth, in that no substantial additional risks are posed by participation within the Juvenile Court Program residency. First, we have ensured that no self-administered questionnaires probe violent behaviors or illegal activities or behaviors, and further that no responses or instruments will be provided back to staff in the Juvenile Court Program or any other juvenile criminal justice system court officer. These measures taken to ensure confidentiality minimize the risk of detrimental ripple effects on their current court involvement, and will be clearly communicated to the youth and parent. We have implemented the ability for youth to talk directly to study staff members, rather than requiring contact be through Juvenile Court Program staff, whenever we are in-person during their recreational times. Finally, the research itself is in very short sessions and are completed individually in a completely virtual environment that is monitored and can be terminated at any time by a study staff member without the need of Juvenile Court Program staff to monitor or intervene and likelihood of disciplinary action. We do not expect any care or follow-up examination of subjects will be needed after study participation is over, based on previous reported studies of similar interventions in youth populations. Any risks that were outlined in above sections apply equally to any population that participates in this

research, regardless of detention status, but are outweighed by the potential direct and indirect benefits.

The selection of subjects within the Juvenile Court Program is inherently fair and impartial, as all participants will take part in the VR-B session without a control group condition, selection of participants will not be impacted or intervened with arbitrarily by staff or other youth, and most (if not all) youth in the Juvenile Court Program will be eligible. For youth who are interested, we will provide them with youth-friendly language and information sheets, and full informed consent/assent will be done with a trained study staff member, in order to ensure full comprehension of the study.

Direct and Indirect Benefits

Direct Benefits. Youth receiving treatment with VR-biofeedback may potentially experience a reduction in symptom severity and enhanced self-regulatory ability. Further, these youth gain knowledge about the links between psychological distress and sensations of physiological arousal. Finally, families may find that completing questionnaires informative to understanding the nature of mental illness.

Indirect Benefits. By evaluating the feasibility of a novel therapeutic intervention for youth with emotion regulation difficulties, this study sets the stage for a larger investigation examining the neural and biological substrates of that treatment, as well as its broader efficacy with youth. The potential benefits for identifying novel, and more effective treatments outweigh any minimal risks associated with study procedures.

Monitoring Plan

Study Monitoring. Following every in-person participant interaction, study team members will fill out an internal monitoring survey in REDCap in order to track both potential problems for administrative purposes as well as reportable events. This will include participant complaints, withdrawals, adverse events, unanticipated problems, and protocol deviations. The study team will be directed to immediately email a study team leader for any issues warranting immediate attention. A study team leader will periodically review all monitoring surveys to identify and address any patterns of issues and also evaluate which events need to be reported to which monitoring bodies. All study team members will be periodically updated about trends by a study team leader and, if necessary, will be provided with appropriate additional training in the event of any repeating issues.

Study Withdrawal. A family may contact a study team member to withdraw some or all participation at any time while the study is ongoing either during in-person research sessions or coordinated through Juvenile Court Program. In this case, withdrawing means clearly stating that the subject is no longer participating in the study. Withdrawal may also

occur at any point before or during study activities, including during or in between visits. If withdrawal occurs during a visit, participants would immediately cease the study activity, receive payment for that visit, and be dismissed. The reason for withdrawal would be properly documented in the internal monitoring survey and reviewed by a study team leader. If withdrawal occurred between visits, all future study visits would be cancelled. In any case of withdrawal, the study team will retain all current recruitment and study data indefinitely, but no new data will be collected.

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