PROTOCOLS

#20206069 - Animal Assisted Intervention with Dogs for Children with Attention Deficit/Hyperactivity Disorder: Exploring Candidate Physiological Markers of Response to AAI

Protocol Information

Review Type	Status	Approval Date	Continuing Review Date
Expedited	**Approved**	**Oct 19, 2022**	--

Expiration Date	Initial Approval Date	Initial Review Type
Oct 18, 2025	**Oct 21, 2020**	**Expedited**

Feedback

Approval Comment

The IRB Approval Letter and any approved documentation (e.g. stamped consent forms) can be downloaded in the Attachments section of the protocol.

Protocol Renewal Form

Renewal Information

Protocol Type

Are you submitting a renewal for an IRB, sIRB, or hSCRO protocol?

IRB (UCI is the IRB of Record)

IRB Renewal Instructions

Timing of Submission

Exempt and Expedited IRB protocols must submit a short version of the renewal every three (3) years unless determined otherwise by the IRB. Investigators should plan ahead and submit 60 days prior to the study's expiration date.

Full Committee IRB protocols must submit a renewal at least annually (not more than 365 days). Investigators should plan ahead to meet required continuing review dates. For full committee review protocols, please submit 90 days prior to the expiration date to guard against a lapse in IRB approval.

Amendments at the Time of Renewal

Please refrain from making major changes during the renewal as this could result in a lapse of IRB approval.

Protocol Closure

To close out an approved protocol at the time of renewal, the transaction must be submitted as Request Close. If this option was not initially selected and closure is required, please Abandon the draft and start again. For more information, visit Post-Review Responsibilities and select the Protocol Renewal Tab.

Renewal Screener

Does any of the following apply to the currently approved protocol:

- **research involves Greater than Minimal Risk (Full Committee)**
- **research is subject to Food and Drug Administration (FDA) regulations**
  - **Involves a drug**
  - **A clinical investigation of a medical device**
- **research is funded/supported by the Department of Justice (DOJ)**
- **current approval period is 1 year or less**

Yes (Continuing Renewal Required)

Protocol Expiration

Protocol Expiration

Has IRB approval for this protocol expired or will it expire within 3 weeks?

No

Confirmation of Protocol

Protocol Changes

Are changes required to the protocol and/or supporting document(s)?

Yes, changes are required (complete the amendment form)

Study Team

Review the Study Team Section and consider whether anyone should be removed.

RP Heat Map

Are RP tracked outside the approved protocol, in accordance with the RP Heat Map?

Yes, RP are tracked on a Study Team Log or other comparable log

Financial Interests

Review the Study Team section and verify that the financial disclosures are accurate for each member.

See Conflict of Interest Oversight Committee (COIOC) for more details.

Yes, the financial interest disclosure for each member of the study team is accurate

Relying Non-UCI Entity (as applicable)

When UCI is the IRB of Record for a non-UCI entity (i.e., site or independent investigator), review the IRB Reliance section and remove any non-UCI entities (site or independent investigator) that are no longer *engaged* in research.

ClinicalTrials.gov Registration

Confirm that the response for ClinicalTrials.gov registration is accurate.

If the clinical trial is not registered, please specify why (skip question if not applicable):

Current Status

Accruals

Please mark the option that represents the current status of subject enrollments:

Enrollment ongoing - research procedures ongoing

Subject Enrollments

Please confirm the total number of subjects (i.e. individuals, specimens, records) approved by the UCI IRB in the Subject Populations section.

Indicate the number of new subjects enrolled since last IRB review:

22

Indicate the total number of subjects (including the number in the previous question) enrolled since initial UCI IRB approval:

22

Did the total number of subjects enrolled to date exceeds the total number approved by the IRB?

No

Indicate the total number of subjects enrolled per group since initial IRB approval:

Male (total)	Female (total)
20	2
Non-Binary (total)	Not Collected (total)
0	0
Adults (total)	Minor (total)
0	22

Multi-Center Studies: If known, indicate the total number of subjects enrolled at ALL sites to date:

n/a

Subject Withdrawals

Early Termination(s)

Did the Lead Researcher or a Co-Researcher remove any subject(s) from the study?

No

Voluntary Withdrawal(s)

Did any subject(s) voluntarily withdraw from the study?

No

Reportable Events

Reportable Events

Have there been any problems that required prompt reporting to the UCI IRB?

No problems that require reporting

Complaints

Have there been any complaints from UCI participants or others that required reporting to the UCI IRB?

No

Progress Report

UCI Progress

Please provide a detailed description of the progress of the study, including a brief summary of any interim findings or trends, and plans for the next approval period:

Initial participant recruitment and intervention was delayed by the pandemic, with the first eligibility visits starting in the fall of 2021. Recruitment, screening, eligibility visits, and intervention are presently ongoing. The targeted enrollment for this study is 48-52 participants, with 22 participants consented and found eligible for enrollment to date. A no-cost extension was filed with NIH, extending the research period to 8/31/2023 in an effort to complete recruitment of the targeted sample size indicated by power analysis. No data has been analyzed to date. Full enrollment is targeted for March of 2023, with intervention sessions ending by June, 2023. Data analysis, presentation and publication of findings are expect for Summer 2023.

Relying Entity Progress (as applicable)

If UCI is the IRB of Record for a non-UCI entity, provide a progress report for each relying entity (e.g., number of participants enrolled at the sub-site; data analysis performed, if any, etc):

N/A

Informed Consent

Confirm that there is no new information that raises concerns about the circumstances under which informed consent is being obtained:

No new information

Confirm that any new findings that have developed since the last continuing review, have been provided to enrolled subjects, as appropriate:
No new findings

Confirm that the research team is using the most recently approved version of the consent/assent document and that it contains the most accurate, up-to-date information about the research:
Yes

Confirm that all signed consent documents are on file and available for inspection:
Yes

Specify if any subjects were enrolled using a non-English consent document, information sheet, or script:
No

Given that some research studies have multiple consent/assent forms, please indicate which approved consent/assent forms should be reviewed by the IRB:
Review all consent/assent forms

Re-Consent Status

Are there approved Re-Consent Cover Memos on file?

IMPORTANT! To verify, review the 'Approved' documents in the Attachments section.
Yes

Is the re-consenting of participants complete?
Yes, all reconsenting is complete

REQUIRED! **Review and review the Attachments section to remove all re-consent cover memos that are no longer being used.**

Internal and External Audits

Internal Audit(s)

Have any internal (UCI/UCI Health) audits occurred since last IRB review?
No

External Audit(s)

Have any external (FDA/OHRP/Sponsor) audits occurred since last IRB review?
No

Risk and Safety Assessments

Relevant Recent Literature

During the past year has there been anything in relevant literature that the IRB should consider when reviewing this application for continuing approval?
No

Current Risk/Benefit Assessment

Has there been a change in risk/benefit?

Take into account the information gathered during the past year such as interim results, reportable events/problems, changes in scientific knowledge, and/or relevant regulatory actions regarding study-wide safety and/or efficacy (e.g., product recall). This assessment should be sufficiently detailed to assist the IRB in determining whether continuation of IRB approval is appropriate.

No

Data Safety Monitoring Board (DSMB)

Has there been any new DSMB findings relating to subject safety?

No new findings related to subject safety

Investigator's Brochure (IB)

For FDA regulated drug studies, enter the current version number and date of the Investigator's Brochure in the Supplemental Documents section.

End of renewal form!

IMPORTANT! Go to the next section to complete the amendment form.

Protocol Amendment Form

Amendment Instructions

Specify the type of submission:

AMENDMENT: IRB (UCI is the IRB of Record)

- **Complete the amendment form to describe the change(s) and to provide rationale for the change(s).**
- **After the amendment form is complete, review and revise the protocol, as necessary.**
- **Submit all new and/or revised supporting documents in the Attachments section near the end of the protocol.**
- **If the protocol is within 30 days of the expiration date, it is recommended that a renewal be included with the amendment. If Renew & Amend was not initially selected and a renewal is required, please Abandon the draft and start again.**
- **IMPORTANT! Please refrain from making major changes during a renewal as this could result in a lapse of approval.**

For more information, visit:

- **IRB Protocol Amendments**
- **hSCRO Protocol Amendments**

ATTENTION! Amendments are NOT required for the following determinations:

- **Non-Human Subjects Research (NHSR)**
- **Exempt Self-Determinations**

These amendments are to be tracked by the Lead Researcher independently. If the amendment changes the level of review to where IRB review is required, a new protocol must be submitted.

IRB Amendment

What type of changes are being proposed for this request?

Minor Revision(s)

Current Status of Enrollments:

Enrollment ongoing - research procedures ongoing

Number of subjects currently receiving active research intervention *or if on hold, the number of subjects who were receiving active intervention prior to the hold*.

8 subjects are actively engaged in research intervention at this time.

Re-consent

Are there approved Re-Consent Cover Memos on file?

IMPORTANT! To verify, review the 'Approved' documents in the Attachments section.

Yes

Is the reconsenting of participants complete?

Yes, all reconsenting is complete

REQUIRED! Review and review the Attachments section to remove all re-consent cover memos that are no longer being used.

Is there significant new information that would warrant notification or reconsenting of participants?

No

List of Protocol Changes

List all requested changes below and provide justification for the change, as applicable.

IMPORTANT! The list below must be complete / comprehensive of all changes as it will be reflected in the IRB Approval Letter. Failure to provide a complete list of changes will delay IRB approval.

Change in Consent

Provide the details and reason for the change in consent:

The approved consent form indicates participants will be paid by check but they will be paid in cash. The Informed Consent has been modified with tracked changes and will be attached.

Other Change(s)

Provide the details and reason for the other change(s):

The approved Protocol Narrative indicates participants will be paid by check but they will be paid in cash. The Protocol Narrative has been modified with tracked changes and will be attached.

Confirmation of Changes:

Check here to confirm that all changes to the protocol are listed above

End of amendment form!

Project Details

Specify the study title (this title should not exceed more than 100 words):

Animal Assisted Intervention with Dogs for Children with Attention Deficit/Hyperactivity Disorder: Exploring Candidate Physiological Markers of Response to AAI

Lead Researcher/Investigator:

Sabrina E Brierley Schuck

Enter the Lead Unit:

IR-7462 - PEDIATRICS (Lead Unit)

Project Screener

Submit a Human Subject Protocol for UCI Institutional Review Board (IRB) Review

Will this protocol be reviewed under a sIRB process?

No, there is no reliance involved. UCI serves as the IRB of record

Are the research procedures limited to the use/analysis of identifiable private information and/or identifiable biospecimens (no subject contact)?

No

Select the required level of review for this protocol:

Minimal Risk (Expedited)

Check all sites where UCI investigator(s) will conduct research activities (e.g., recruitment, informed consent, and research procedures including accessing identifiable, private information about participants):

UCI Facilities or Sites (e.g. school, hospital or clinics, etc.)

Provide a non-technical summary of the project that can be understood by IRB/hSCRO members with varied research backgrounds, including non-scientists and community members (this summary should not exceed more than 250 words):

Attention-Deficit/Hyperactivity Disorder (ADHD) is the most commonly occurring neurodevelopmental disorder in the US. Common treatments are stimulant medications and counseling but these practices are not always feasible or acceptable due to adverse side-effects, cost, and poor adherence. As such individuals remain at risk for poor outcomes. ADHD is considered to be a result of a disruption of select physiological systems and related under-arousal of parts of the brain involved in executive functioning (EF). Our previous research indicates that Animal Assisted Intervention (AAI) with dogs is effective for improving outcomes related to EF deficits (Schuck, et al., 2018a; 2018b). The mechanisms by which AAI improves outcomes for this group however, is not yet understood. These gaps in understanding hinder progress in the application of AAI, limiting the acceptability and availability of this integrative healthcare practice. We contend that dogs elicit physiological responses related to arousal of EF systems, thereby enhancing response to treatments. Furthermore, individual differences potentially mediate outcomes. This purpose of this research is to replicate our previous work(Schuck, Emmerson, Fine, & Lakes, 2015; Schuck et al., 2018a; 2018b), to determine if physiological responses to AAI change over time, and to ascertain if individual differences during AAI mediate findings. To explore these hypotheses our research procedures will include conducting an exploratory parallel-group randomized controlled clinical trial with 48 young children with ADHD, participating in intervention with/without AAI during which we will collect and analyze physiological measures (candidate salivary analytes and heart-rate-variability) thought to play an important role in AAI for children with ADHD.

Instructions

IRB Protocol Instructions

- **For research with a Master Protocol or with a detailed project proposal, specify this in the protocol and an abbreviated protocol will be generated.**
- **Submit all new and/or revised supporting documents in the Protocol Attachments section near the end of the protocol.**
- **The Lead Researcher (LR) is responsible for maintaining all supplemental documentation (as indicated in the form) in the research records. This documentation may be requested by Human Research Protections for quality assurance review.**

For regulatory or institutional guidance:

- **Visit Human Research Protections**
- **Contact the Human Research Protections staff**

For technical issues or questions:

- **Visit the Kuali Research Protocols (KRP) User Guide**
- **Contact Electronic Research Administration (ERA)**

Type of Research

The purpose, specific aims or objectives of the research is:

Social/Behavioral/Educational

The research protocol is:

Investigator-Initiated

Does the investigator-initiated study have any industry support?

No

Is this study an extension of a UCI IRB approved study (e.g., resubmission of ongoing exempt research; Open Label Extension) or is it otherwise related to a UCI IRB approved study?

No

Does this research meet the definition of a clinical trial that requires adherence to Clinicaltrials.gov?

Yes

If currently available, provide the CT.gov registration NCT # (**Enter 8-digit sequence of numbers only**):

NCT #05102344

Specify the rationale for Clinicaltrials.gov registration:

NIH-funded Clinical Trial

STOP! All clinical trials must be conducted under the auspices of an Organized Lead Unit (OLU). Please update. Go to Project Details and choose the appropriate OLU for the trial.

Level of Review

Minimal Risk - No more than minimal risk to subjects

Select the applicable category(ies):

3. Prospective collection of biological specimens for research purposes by noninvasive means

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves

6. Collection of data from voice, video, digital, or image recordings made for research purposes

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies

Study Funding

Select the funding source(s) (**check all that apply**):

Grant/Contract

Select the sponsor type(s) (**check all that apply**):

Health and Human Services (HHS) (includes National Institutes of Health (NIH)

List below all extramural proposals or awards that will support the study (if applicable):

IMPORTANT! Skip this table if extramural funding is not available.

Sponsor Name

NICHD

Title of Proposal/Award (if different from study title):

Animal Assisted Intervention with Dogs for Children with Attention Deficit/Hyperactivity Disorder; Exploring Candidate Physiological Markers of Response to AAI

Proposal or Award #:

5R21HD103422-02

Scientific/Scholarly Review

Is the research Sponsor-Initiated?

Yes

The proposed research qualifies as minimal risk research. The Department Chair, Division Chief, or Institute Director provides assurance that the research uses procedures consistent with sound research design, the study design can be reasonably expected to answer the proposed question, and the importance of the knowledge expected to result from the research is known.

Check here to confirm the above assurance

Potentially Hazardous Materials

If any of the following hazardous materials are involved in this research please check below:

N/A

Other UCI Committee Reviews

Check all ancillary committees that apply:

N/A

Study Team

Study Team:

- **List only study team members who are engaged in human subjects research below.**
    - **Administrative Contact (AC): Do not add ACs to the study team table. To add ACs, navigate to the Permissions tab on top-right-hand-side of form. All ACs must complete the requisite Human Research Protections CITI Training.**
- **Lead Researcher (LR): LRs must meet requirements specified on the Lead Researcher Eligibility page for study to be approved.**
    - **Select 'Oversight of Research' along with other applicable duties.**
    - **Select 'Full Access'.**
- **Faculty Sponsor (FS): FSs are required when the person serving the LR role is not qualified to serve as LR-- the FS must be eligible to be LR.**
    - **Select 'Oversight of Research' along with other applicable duties.**
    - **Select 'Full Access'.**
- **Co-Researcher (CR): CRs are faculty, staff, students and other academic appointees who the LR considers to be key personnel for conducting the research study. These individuals work closely with the LR to design, conduct, and/or report on the research.**
- **Research Personnel (RP): List RP as required per the Research Personnel Heat Map. For those RP who do not need to be listed on the protocol, they may be tracked by alternative methods, see below.**
- **IMPORTANT! Do NOT list non-UCI researchers below, in the Permissions tab at top or on the Study Team Tracking Log (or equivalent); instead, follow the Single IRB Reliance (sIRB) process.**
- **Collaborative Institutional Training Initiative (CITI) Human Research Protections Training Courses**
    - **Confirm CITI training is complete and current for all study team members.**
    - **Incomplete or expired CITI training will delay IRB approval.**
    - **For more information, visit HRP Training and Education.**

Researcher

Sabrina E Brierley Schuck

Training

Social/Behavioral Investigators - Refresher Course
03/02/22 - (no expiration)

Social/Behavioral Investigators - Basic Course
02/24/17 - 02/23/22
Expired

To promote the objectivity of the research, all researchers are required to disclose their **related disclosable financial interests**, per the IRB COI Policy. If you have any questions about the COI process in general, contact the COI team.

Each member of the study team for this protocol must be asked the following question to comply:

"Do you, your spouse/registered domestic partner, and dependent children have any disclosable financial interests* (i) that would reasonably appear to be affected by this research study; or (ii) in entities whose financial interests would reasonably appear to be affected by this research study?"

No

Degree

PhD

Position/Title

Assistant Professor

Department

IR-6125 - PEDIATRICS-DEVELOPMENTAL/BEHAVIORAL

Affiliation

UCI Faculty

Researcher Role

Lead Researcher

Permissions

Full Access

Duties

Oversight of Research
Screen/Recruit Subjects
Finalize Informed Consent
Access/Analyze Identifiable Information
Access/Analyze Identifiable Biospecimens

Specify relevant training and experience for the referenced duties/responsibilities:
All study team members will be certified in CITI and HIPPA compliance trainings. Those team members who will be handling saliva samples will also be certified and trained specifically in the collection, handling, coding/labeling and transport of saliva samples for the purpose of analysis of salivary analytes. All study personnel have been trained in all procedures involved with conducting psychosocial intervention groups and animal assisted intervention groups with children. Furthermore, prior to each treatment cohort, the study consultant, will provide a thorough review of the safe and effective protocol standards for working with therapy animals and children.

Are RP tracked outside the approved protocol, in accordance with the RP Heat Map?
Yes, RP are tracked on a Study Team Log or other comparable log

Supplemental Documents

Does this study include supplemental documents?
No

Background & Purpose of the Research

Describe the purpose, specific aims or objectives and specify the hypotheses or research questions to be studied:

The purpose of this research is to address gaps in understanding of the mechanisms of AAI and how these mechanisms may differ across special populations hinder progress in the application of AAI, and limit the acceptability and availability of this integrative health care practice. Our bio-social mechanistic hypothesis contends that dogs elicit physiological responses related to arousal of EF systems, thereby enhancing response to treatments. Furthermore, candidate individual differences potentially mediate outcomes. This work will explore these hypotheses; 1) we suspect AAI will result in enhanced social-behavioral outcomes and improved diurnal patterns of HPA and ANS activity for these children and 2) we suspect acute physiological responses to AAI (markers of HPA & ANS) and social interaction quality (child/child and child/dog) will mediate main outcomes. Specific Aims Specific Aim 1: To replicate previous findings that social-behavioral outcomes are improved for children with ADHD when they participate in an 8- 10 week manualized AAI with therapy dogs. Specific Aim 2: To explore if diurnal patterns of physiological markers of Hypothalamic Pituitary Adrenal axis (HPA) activity (salivary cortisol; Cort and uric acid; sUA) and Autonomic Nervous System (ANS) activity (heart-rate variability; HRV, and salivary alpha-amylase; sAA) are improved over time for children with ADHD in response to an 8- 10 week manualized AAI with therapy dogs. Specific Aim 3: To explore if potential individual differences in children with ADHD are manifested during intervention sessions and if these differences mediate primary and exploratory main outcomes from an 8- 10 week manualized AAI with therapy dogs. Specific individual differences explored include; acute physiological responses during intervention sessions as measured by markers of HPA & ANS activation (Cort, sUA, sAA, & HRV) and the quality of social interaction (child/child and child/animal) during sessions.

Provide the scientific or scholarly rationale for the research and describe the relevant background information and the specific gaps in current knowledge that this study intends to address:

This project explores physiological mechanisms thought to underlie the positive effects of AAI for children with ADHD and posits that interaction with dogs during treatment improves social behavioral and physiological outcomes and that individual differences in bio-markers and interaction style mediate outcomes for this group. Rationale & Background Despite decades of research aimed to optimize outcomes for children with ADHD, the condition remains a significant public health problem adversely impacting individuals, families and schools. The annual cost of ADHD is estimated at $266 billion (Doshi et al., 2012). Pharmacotherapy (e.g., methylphenidate) is the mainstay of traditional medical intervention for ADHD, but treatment failures are common (Caye, Swanson, Coghill, & Rohde, 2018; Schneider & Enenbach, 2014; Swanson et al, 2018), and affected children often require medications during what are now recognized as critical periods of growth and development. It is not surprising that parents find alternative therapies, including Animal Assisted Intervention (AAI), to be more acceptable than medication (Rabbit, Kazdin, & Hong, 2014). Our research found AAI to be effective in reducing ADHD symptoms and improving social skills and self-perception (Schuck et al., 2015; Schuck et al., 2018a, Schuck et al., 2018b). Gaps in Current Knowledge While we demonstrated the effectiveness of AAI for this group, the underlying mechanisms of these effects is unknown; a critical gap in our developing body of evidence for AAI needed to increase the acceptability and accessibility of this integrative health care strategy. The research proposed in this application will break ground in this nascent area and contribute to the rapidly developing discipline of HAI research by (1) contributing to our understanding of bio-social mechanisms which may underlie outcomes, (2) identifying individual responses thought to mediate outcomes and (3) informing the development of future large scale, multi-site trials aimed to informing best practices for delivering AAI in special pediatric populations and improving accessibility to this practice.

Provide relevant preliminary data (animal and/or human):

N/A

Describe the primary outcome variable(s), secondary outcome variables, and predictors and/or comparison groups as appropriate for the stated study objectives/specific aims:

N/A

List up to ten relevant references/articles to support the rationale for the research:

Berry, D., Blair, C., Willoughby, M., & Granger, D. A. (2012). Salivary alpha-amylase and cortisol in infancy and toddlerhood: Direct and indirect relations with executive functioning and academic ability in childhood Psychoneuroendocrinology, 37(10), 1700-1711. doi:http://dx.doi.org/10.1016/j.psyneuen.2012.03.0 Chen, F. R., Raine, A., Glenn, A. L., & Granger, D. A. (2015). Hypothalamic pituitary adrenal activity and autonomic nervous system arousal predict developmental trajectories of children's comorbid behavior problems. Developmental Psychobiology, doi:http://dx.doi.org/10.1002/dev.21379 Esposito, L., Gee, N. R., Freund, L. S., McCune, S., & McCardle, P. (2016). Future research: Needs and promise. In L. S. Freund, S. McCune, L. Esposito, N. R. Gee & P. McCardle (Eds.), The social neuroscience of human animal interaction; the social neuroscience of human-animal interaction (pp. 249-253, Chapter x, 271 Pages) American Psychological Association, Washington, DC. doi:http://dx.doi.org/10.1037/14856-016 Griffiths, K. R., Quintana, D. S., Hermens, D. F., Spooner, C., Tsang, T. W., Clarke, S., & Kohn, M. R. (2017). Sustained attention and heart rate variability in children and adolescents with ADHD. Biological psychology, 124, 11-20. Keller, P. S., El-Sheikh, M., Granger, D. A., & Buckhalt, J. A. (2012). Interactions between salivary cortisol and alpha-amylase as predictors of children's cognitive functioning and academic performance. Physiology & Behavior, 105(4), 987-995. doi:http://dx.doi.org/10.1016/j.physbeh.2011.11.005 Lee, S. H., Shin, D., & Stein, M. (2010). Increased cortisol after stress is associated with variability in response time in ADHD children. Yonsei Med J, 51, 206-211 Loo, S. K., Hale, T. S., Macion, J., Hanada, G., McGough, J. J., McCracken, J. T., & Smalley, S. L. (2009). Cortical activity patterns in ADHD during arousal, activation and sustained attention. Neuropsychologia, 47(10), 2114-2119. doi:http://dx.doi.org/10.1016 Schuck, S.E.B., Emmerson, N., Abdullah, M.M., Fine, A.H., Stehli, A. & Lakes, K. D. (2018a). A randomized controlled trial of traditional psychosocial and canine-assisted interventions for ADHD. Human Animal Interaction Bulletin (6) 1, 64-80 (2 citations) Schuck, S. E. B., Emmerson, N., Fine, A. H., & Lakes, K. D. (2015). Canine-assisted therapy for children with ADHD: Preliminary findings from The Positive Assertive Cooperative Kids Study. Journal of Attention Disorders, 19 (2): 125-137. doi: 10.1177/1087054713502080 Schuck, S.E.B., Johnson, H.L., Abdullah, M. M., Stehli, A., Fine, A. H. & Lakes, K. D. (2018b). The Role of Canine Assisted

Intervention on Improving Self-Esteem in Children with Attention Deficit/Hyperactivity Disorder. Frontiers in Veterinary Science, 08, November 2018 Shin, D. W., & Stein, M. A. (2010). Increased cortisol after stress is associated with variability in response time in ADHD children. Yonsei medical journal, 51(2), 206-211. Thayer, J. F., Åhs, F., Fredrikson, M., Sollers III, J. J., & Wager, T. D. (2012). A meta-analysis of heart rate variability and neuroimaging studies: implications for heart rate variability as a marker of stress and health. Neuroscience & Biobehavioral Reviews, 36(2), 747-756. Van West, D., Claes, S., & Deboutte, D. (2009). Differences in hypothalamic–pituitary–adrenal axis functioning among children with ADHD predominantly inattentive and combined types. European child & adolescent psychiatry, 18(9), 543-553.

Subject Population(s) (Individuals/Records/Biospecimens)

Check all subject populations/data sources that apply to the research:

Adults Competent to Provide Informed Consent

Children

Use of identifiable or coded data, specimens, records, charts

Maximum and Expected Number of Persons/Records/Biospecimens to be Enrolled

1. Click "Add Line" button above Enrollment Table to add a Category/Group
    a. To change visibility of columns, click "Columns" button above Enrollment Table and select which Column rows to view.
2. Specify the maximum and expected numbers of individual-level information and/or biospecimens to be accessed/analyzed within each Category/Group

Category/Group

Parents

Age Range

18 or older

Maximum Number of Subjects, Subjects to be Consented or Reviewed/Collected

160

Number Expected to Complete the Study or Needed to Address the Research Question

48

Category/Group

Children

Age Range

7 years to 9 years, 11 months

Maximum Number of Subjects, Subjects to be Consented or Reviewed/Collected

80

Number Expected to Complete the Study or Needed to Address the Research Question

48

Will this study only take place at UCI and does not involve other sites?

Yes

Eligibility Factors (Inclusion/Exclusion Criteria)

1. Click "Add Line" button above Eligibility Factors Table to add a inclusion/exclusion criteria
    a. To change visibility of columns, click "Columns" button above Eligibility Factors Chart and select which Column rows to view.
2. Identify the factors for limited eligibility and provide a scientific rationale. Include additional rows for factors, as needed.

Category/Group Eligibility

Children

Inclusion Criteria

Participating children ages 7 to 9 years with ADHD and up to two parents per participating child among 4 cohorts across 2 years will be included. Children who are at least 7 years of age on the day of their consent and who are no older than 9 years, 11 months, and 30 days of age (not 10 years of age) on the day of their consent may be included in the samples. Eligibility will be determined utilizing a multi-gate screening procedure, including a semi-structured diagnostic interview schedule for mental disorders of childhood, standardized parent and teacher rating scales, and a brief assessment of intellect. Eligible and consenting participants and their parents will then be randomly assigned to intervention groups. Initial assessment visits, and randomization will take place within a 21-day window prior to the commencement of the treatment phase.

Exclusion Criteria

This study aims to explore specific candidate physiological mechanisms of HPA and ANS activation during intervention that are suspected to be different in young children with ADHD from typically developing children and children with other mental health disorders, as such this study will exclude children with a primary or comorbid diagnosis of Autism Spectrum Disorder (ASD) and/or Major Mood Disorder, in efforts to maximize power with a feasible sample size. Additionally, a careful screening for child and/or family history of mistreatment, neglect, or cruelty to animals will be used to excluded children or families that may put the participating animals at risk. Children with a known allergy or phobia of dogs will also be excluded.

Is eligibility based on age, gender, pregnancy/childbearing potential, social/ethnic group, or language spoken (e.g., English Speakers only)?

Yes

Limited Eligibility Factors (Special Populations)

1. Click "Add Line" button above Limited Eligibility Factors Table to add a special population
    a. To change visibility of columns, click "Columns" button above Limited Eligibility Factors Table and select which Column rows to view.
2. Identify the special populations and provide a scientific rationale. Add additional rows, as needed.

Eligibility Limited to the Following Factors

Gender

Specify the rationale for this group:

ADHD reportedly occurs in a 3:1 boy to girl ratio in epidemiological samples. We therefore expect our sample to be disproportionately male. The proportion of girls in this study will likely reflect the typical population distribution of girls with ADHD. Recruitment strategies aim to be non-bias in the selection of females and minorities.

Eligibility Limited to the Following Factors

Age

Specify the rationale for this group:

The sample of this study is composed of individuals under the age of 18. As Attention Deficit/Hyperactivity Disorder (ADHD) is by definition a neurodevelopmental disorder of childhood onset exclusive of intellectual deficiency, the sample for the proposed project is restricted to children with at least low-average estimated intellectual capabilities (estimated IQ>79). School-aged children between the ages of 7 and 9 will be studied as the first aim of this study is to replicate previous research conducted with this age group.

Subpart D - Children

Select the category that best describes your proposed research (45 CFR 46 - Subpart D):

Category 1 (§46.404) This proposed research poses no greater than minimal risk to children. (Note: for research that qualifies for Expedited level of review)

Indicate why the proposed research poses no greater than minimal risk to children:

The risk to children involved in the study poses no greater risk than that of the risks children experience in their everyday lives at school, in social situations or sports teams, or in the presence of family pets

If there is more than one group of children being enrolled in the research (e.g., patients, healthy controls) and the groups fall into different risk/benefits categories, describe the groups below listing the applicable category for each group:

N/A

Parental Permission

Select one statement that best describes how you will obtain parental permission:

I will obtain the permission of one parent or guardian

Assent

Select which best describes how you will be obtaining assent and answer the corresponding questions:

I will obtain assent from all children

Enrollment of People Under 18 Who Can Consent for Themselves

Will people under the age of 18 who are permitted under California law to consent for themselves be enrolled in this study?

No

Children who are Wards of the State (45 CFR 46.409; 21 CFR 50.56)

Do you intend to enroll wards of the state or any other agency, institution, or entity?

No

Does the study fall under §46.406 or §46.407 (FDA §50.53 or §50.54)?

No

Pre-Screening and Determining Eligibility without Informed Consent

Will Identifiable information be obtained for the purpose of screening, recruiting, or determining eligibility of prospective subjects?

Yes

The 2018 Common Rule allows for Pre-Screening activities (i.e., determining if potential subjects may be eligible to participate in research) performed without the written informed consent of the prospective subject or legally authorized representative (LAR). This means that the IRB does not need to grant a waiver of informed consent.

Provide a complete list of the data points, variables, and/or information that will be collected during Pre-Screening (i.e. data abstraction form):

Or specify variables or information required for Pre-Screening:

The following variables will be collected at the Screening Visit to help determine eligibility: 1. K-SADS-PL DSM-5 Eligibility Screening Visit Parent The Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children, Present & Life-Time Version (K-SADS-PL DSM-5; Kaufman, et al., 2016) is a semi-structured interview designed capture dimensional and categorical assessment to the contribute to the diagnosis of current and present levels of psychopathology in children according to the DSM-5. Parents will complete the K-SADS interview at the Screening Visit to help determine eligibility. 2. ASRS-Short Form Eligibility Screening Visit Parent The Autism Spectrum Rating Scales-Short Form (ASRS; Goldstein & Naglieri, 2013) is a brief assessment designed to provide an estimate of symptoms of Autism Spectrum Disorder and takes 5-10 min to complete. Parents will complete the ASRS-Short Form at the Screening Visit to determine help eligibility. 3. ADHD-RS Eligibility Screening Visit Parent The Attention Deficit/Hyperactivity Disorder Rating Scale, (ADHD-RS; DePaul, 2012) takes about 10-15 minutes to complete. Parents will complete the ADHD-RS at the Screening Visit to help determine eligibility. 4. WASI-II Eligibility Screening Visit Participant The Wechsler Abbreviated Scale of Intelligence-Second Edition (WASI-II, Wechsler, 2011) is a brief assessment designed to provide an estimate of intellectual skills. The assessment takes about 10-15 minutes to complete each of 4 sub-tests, or a total of 40-60 minutes. Participants will complete the WASI-II at the Screening Visit to help determine eligibility for the trial. 5. TOWRE-2 Eligibility Screening Visit Participant The Test of Word Reading Efficiency-Second Edition (TOWRE-2, Torgesen, Wagner & Rashotte, 2012) measures reading skills and takes about 5-10 minutes to complete. Participants will complete the TOWRE at the Screening Visit to help determine eligibility for the trial. 6. PERM-P Eligibility Screening Visit Participant The Permanent Product test (PERM-P, Wigal & Wigal, 2006) is a validated written mathematics test designed to determine math fluency skills in children ages 7-9 and takes about 5-10 minutes to complete. Participants will complete the PERM-P at the Screening Visit to determine basic math achievement levels at eligibility and inform level appropriate assessment prior the trial baseline data collection day.

Check all the Pre-Screening activities that apply:

Study team will obtain information through oral or written communication with the prospective subject or LAR (i.e. self-report of medical information; medical records will not be screened)

Will the study team screen stored identifiable biospecimens?

No

Will the study team contact subjects for eligibility or recruitment purposes?

No

Recruitment Methods

Will this study involve NO direct contact with participants (i.e., passive observation of public behavior)?

No

Indicate all methods that will be used to recruit subjects for this study:

Recruitment Method

Flyers/Brochures

Specify Where Posted

UCI Zot Mail

Type of Space

Public (i.e., site/media that allows open access to content)

Recruitment Method

Center for Clinical Research (CCR) Find a Trial web page

Confirm that the study from the Center for Clinical Research (CCR) Find a Trial web page is registered on ClinicalTrials.gov

Recruitment Method

Clinicaltrials.gov

Confirm that the ClinicalTrials.gov statement is in all applicable consent documents

Recruitment Method

Colleagues provide subjects with information about the research and how to contact investigators

Confirm that colleagues may provide a copy of the consent and other UCI IRB approved materials but do not obtain subjects' consent for the research or act as representatives of the investigators

Recruitment Method

Colleagues, who are treating physicians, will send UCI IRB approved recruitment letter to their patients

Confirm that:

1. The recruitment letter to be signed by the treating physician will be submitted in the Attachments Section
2. Colleagues do not obtain subjects' consent for the research or act as representatives of the investigators

Recruitment Method

Online/Social Media

Specify Where Posted

Research Unity website

Type of Space

Public (i.e., site/media that allows open access to content)

Informed Consent Process

Does this study involve the creation, use, or disclosure of Protected Health Information (PHI)?

No

Methods of Informed Consent

Identify the consent or assent process as applicable for each participant population (check all that apply):

Paper-based signed informed consent/assent

Paper-based Signed Informed Consent

Indicate the paper-based signed informed consent/assent (check all that apply):

Signed Informed Consent

Signed Child Assent

Does this recruitment method include all subjects?

Yes

REQUIRED! Submit the Adult Consent Form, Child Assent Form and/or Parental Permission Form in the Attachments Section.

Circumstances of Consent

Indicate the location where the consent process will take place (**check all that apply**):

Private room

Specify how the research team will assure that subjects, their parents, or their legally authorized representative (LAR) have sufficient time to consider whether to participate in the research:

Subjects or their LAR will be allowed 'X amount of time' to consider whether to consent

Specify hours, days or weeks for subjects, parents or their LAR will be allowed to consider whether to consent:

1 hour

Describe the parental permission process:

Informed parent consent will be obtained prior to children beginning the screening assessment. If parents do not wish to have children in the room during informed consent process, child care will be provided by the research team in the waiting room (see signed written consent forms attached).

Describe the child assent process:

Once parents provide informed consent, the research team will review the child assent form prior to beginning the screening assessment to determine eligibility (see assent forms attached).

This study does NOT include Non-English Speaking Participants. Scientific justification/rationale is required in the Eligibility Criteria Section for Subject Populations.

Research Procedures

Check all boxes that apply to the research:

Audio, Video, Digital or Image Recording and/or Photography for Collection of Research Data
Clinical Investigation involving an Investigational Device
Collection of Other Samples/Specimens (e.g.,tissue, saliva, urine)
Other Non-invasive Physical Measurements (e.g., ECG, EEG, moderate exercise, muscular strength testing, body composition assessment)
Surveys/Questionnaires/Interviews/Oral Histories

Will deception or incomplete disclosure be involved in the research?

No

Study Design

Include an explanation of the study design (e.g., randomized placebo-controlled, cross-over, cross-sectional, longitudinal, etc.) and, if appropriate, describe stratification/ randomization/blinding scheme:

The proposed research will run a Parallel-Group Randomized Controlled Trial, employing an exploratory parallel-group randomized controlled trial study design and utilizing a multi-method and multi-source assessment protocol. a. The study is currently planned to take place at The Children's School at 3400 Michelson #200, Irvine, CA 92612 b. We will use a repeated-measure within-subject design, gathering measurement of main outcomes at three time points to assess the efficacy of AAI for children with ADHD who are participating in a short-term intervention with or without the assistance of therapy dogs. A linear, repeated measures design will be utilized for our primary, and exploratory main outcome. c. Over the course of about 4 months, children will participate in treatment and assessment for a total up to approximately 16-20 hours) and parents will participate in approximately 6-9 hours of assessment. d. Children and their parents will first attend a screening visit that will last 2-3 hours to determine eligibility. e. If eligible, participation will require participants to attend group sessions for integrative, non-medical treatments for ADHD, once weekly (one weekday after school to be determined as space permits for about 2 hours per session (for a total of about 16-20 hours). These play group sessions may or may not include the participation of up to 3-4 certified therapy dog/handler dyads. These group sessions will be video recorded to capture child-child, child-dog, and dog behavior. f. Participation will also require child participants to attend three (3) Saturday "Laboratory School" assessment visits, immediately prior to and after the intervention period and then five weeks later. Each of these assessments will last approximately five to six (5-6) hours (about 18 total hours over three visits) for child participants and up to 2 hours each of three visits for parents (about 6 hours total). "Laboratory School" recess sessions will be video taped to capture observed child-child interactions. g. Participants will also be requested to wear a device used to collect heart rate (FirstBeat monitor) during the assessment days (3) and intervention sessions (3) and on the night prior to participation in the three (3) Saturday "Laboratory School" assessment visits. The FirstBeat monitors which have been found to be acceptable, feasible, safe and reliable for collection in several youth samples. For heartrate collection, parents will be instructed on how to affix a

small heartrate monitor device, the FirstBeat Bodyguard 2 on their child's chest the night before (and then again on the morning of each of the Laboratory School visits. The devices are small, unobtrusive and do not require an uncomfortable halter band as they easily affix with two small hypo-allergenic adhesive electrodes designed to remain comfortable and has been found to remain in place during moderate to heavy physical activity, safe and acceptable in children ages 7-9. Additionally, this device has been found safe and feasibly deployed in studies in both typically developing children and specials population as young as 4 years of age. FirstBeat devices will be distributed to parents at the same time as the saliva kits and parents will receive verbal and written instructions on how and when to affix and remove the device. At the conclusion of each Laboratory School visit, parents will remove the device from their child prior to departure. De-identified heartrate data collected on the device will be immediately downloaded to Dr. Schuck's protected drive in Health Sciences for analysis.

Provide precise definitions of the study endpoints and criteria for evaluation; if the primary outcomes are derived from several measurements (i.e., composite variables) or if endpoints are based composite variables, then describe precisely how the composite variables are derived:

See above

Statistical Considerations

Is a statistical analysis plan appropriate for this qualitative study design?

Yes

Describe the statistical methods for the stated specific aims and hypotheses. Your analysis plans should match the stated study specific aims and hypotheses:

Statistical Method per Outcome Specific Aim 1: Replicate Previous Favorable Behavioral Response to AAI Primary Main Outcome: Behavior responses. This parallel-group randomized design and will utilize a multi-method and multi-source assessment protocol. The assessment protocol will use a repeated-measure within-subject design, gathering main outcomes at three time points to assess the efficacy of AAI on outcomes for children with ADHD who are participating in a short-term intervention with or without the assistance of certified therapy dogs (see Figure 1). Our previous research indicated that after just 2 weeks of intervention, participants in the AAI condition showed significantly greater improvement in symptoms compared to control participants and that these gains were maximized by 10 weeks and then maintained at 6 weeks post intervention (Schuck et al., 2018a), suggesting that 10 weeks is an ideal duration of treatment to detect significant benefits from AAI with dogs. Outcomes from AAI utilizing a manualized treatment with therapy dogs (AAI) will be compared to standard of care evidence-based psychosocial treatment at usual (control). Specific Aim 2: Determine Physiological Response over time to AAI for children with ADHD. Exploratory Main Outcome: Diurnal HPA and ANS responses. To determine if children with ADHD present with measurable changes in physiological responses to a short-term AAI (10 weeks) on measures of HPA and ANS we will gather candidate salivary analytes (salivary cortisol, uric acid, and alpha-amylase; Cort, sUA, sAA, respectively) and measures of cardiac rhythm, (heart rate variability; HRV) prior to and post intervention for children participating in both treatment conditions before, immediately after, and upon treatment follow up. Specifically, for each domain we will ascertain changes in diurnal patterns of candidate physiological measures utilizing a linear, repeated measures design gathered across three (3) points in time; establishing individual baseline patterns, end of treatment patterns, and then patterns at 6 weeks post-treatment. Specific Aim 3; Explore Individual Differences as potential mediators of response to AAI in children with ADHD. Secondary Outcome Exploratory Mediator Analysis; In the proposed study, we will explore how children’s individual (a) acute physiological responses during intervention sessions and their individual (b) social interaction quality during intervention sessions may play a role in each of the Main Outcomes. Specifically, we will a) ascertain acute HPA activity (as measured by Cort, and sUA) and acute ANS activity (as measured by HRV and sAA) during intervention sessions across

both treatment conditions and we will b) ascertain the quality of in-session social relationships (child-child) across both treatment conditions as well as the quality of in-session child animal interaction (child-dog) during the AAI sessions (observed child/child & child/dog interaction) at three (3) time points across the 10-week study intervention period (weeks 1, 5, & 10). The acute response and interaction quality measures from each of the three sessions will then be correlated with the degree of change in the primary main outcomes. (e.g., pre-post change in ADHD symptoms, social skills, regulation) and the exploratory main outcomes (e.g., pre-post change in diurnal HPA activity and ANS activity) to examine the potential mediation of individual differences on response to AAI with therapy dogs for children with ADHD. Here we provide an example of one mediation analysis for treatment group (AAI vs Control) as the primary predictor, salivary cortisol response slope at session 5 the potential mediator, and behavioral change (pre-post change) the outcome: First, cortisol response slope2 means will be compared between the groups (the mediator must be related to the predictor). If significant, then the relationship between cortisol response slope2, and behavioral change will be evaluated for a significant correlation/slope (the mediator must be related to the outcome). Finally a model will be run with both treatment group and cortisol response slope2 predicting behavioral change. If the relationship between treatment group and behavioral change is reduced compared to the primary analysis (i.e., with treatment group alone), saliva cortisol response2 is interpreted as providing a mediated effect. To obtain estimates of the size and significance of the indirect effects, bootstrapping procedures as described by Shrout and Bolger (2002) will be implemented. Due to the fact that bootstrapping procedures are still limited in the case of multilevel models, an approximation of the Sobel test will also be performed, along with Monte Carlo estimation of confidence intervals but because this aim is exploratory and this is not a fully powered study, results presented will include descriptive and confidence intervals.

Describe the statistical method(s) that will be used to analyze the primary outcome(s) or endpoints:

see previous section

If appropriate describe secondary or post hoc analyses of primary outcome(s) or other exploratory analysis and if necessary, provide a breakdown of the methods used per outcome or endpoint:

Statistical Method to Inform Randomization Bias: Intent to treat bias. To establish equivalence of randomly assigned groups pre-intervention, t-tests will be performed on outcome measures comparing the groups. Means and standard deviations will be obtained and effect sizes calculated. Demographic profiles will be obtained and bivariate significant tests performed to assess the balance expected with randomization. Cohort effects on outcome as well as participation rates will be evaluated to assess any bias related to location, calendar time, or other session characteristics. Participation rates across the intervention will be tracked and compared between the randomized groups. In the spirit of the intent to treat principle (White, Carpenter, and Horton 2012) every effort will be made to conduct follow-up assessments on all randomized participants. Withdrawals will be documented with reason provided. In addition, multi-level modeling allows all cases to remain in a repeated measures model and will be done as a sensitivity analyses to primary analyses done on individuals with at least one follow-up point.

Sample Size Determination: Explain how the overall target sample size was determined (e.g., power analysis; precision estimation), providing justification of the effect size for the primary outcome based on preliminary data, current knowledge/literature and/or cost consideration; if appropriate, provide sample size justification for secondary outcomes. Power analysis should (at least) match the primary outcome/endpoint:

Sample Size. This exploratory study will employ a parallel-group randomized clinical trial design in which 48 participants will be randomly allocated to one of two (2) treatment/intervention groups (AAI and Control) delivered across four (4) cohorts in two (2) waves over the span of two (2) years (n = 12 per parallel ten-week cohort) in efforts to inform the specific aims of the study. Power & Expected Effect Size. Sample size analysis was conducted for randomized controlled design, using SAS PROC power. For the primary analysis of the main outcome domain (Aim 1: ADHD Behavior) with type I error rate of .05 was implemented for a repeated measures analysis evaluating group main effect, treatment main effect, as well as the group*treatment interaction. Effect size estimates from the authors' previous parallel-group randomized study of HAI demonstrated large AAI vs control effect size for problem behaviors (.86) and moderate effects on inattention (.45) (Schuck et al., 2018a). For Aim 1, with a projected analysis of n=48, this exploratory study will exceed 90% power to detect effect sizes of .19 and above. At a level of 80% power, the minimum detectable effect was determined to be .21. For Aim 2, n= 48 will, for each of the two primary physiological outcome domains (Aim 2: Diurnal Pattern Hypothalamic Pituitary Adrenal axis activity; HPA and Autonomic Nervous System activity; ANS), a multilevel model will be constructed to assess pre-post intervention change, post-follow up change, group differences at each assessment, and group differences in degree of change. Models will account for within-subject correlation and within-cohort correlation. Four (4) cohorts of 13 participants each will be recruited for a total enrolled target sample size of 52 families over Years 1 and 2, accounting for an anticipated attrition rate of about 8% which is based on our recently completed study of AAI with ADHD (Schuck, et al., 2018a) in efforts to yield a total sample of 48.

Research Procedures

Provide a detailed chronological description of the clinical or treatment plan:

See Study Design

List all procedures involving the use and/or collection of photographs, or audio/video recording:

Facial image will be in video or photo Participants' first names may be collected or recorded in either video or audio recording

Specify the total duration of a subject's participation in the study and clearly outline the duration of participation for each study visit and sub-study, as applicable:

See Study Design

List data collection tools (e.g., measures, questionnaires, observational tool) below by clicking the 'Add Line' button. Include additional rows for study instruments, as needed:

The 'Columns' button allows you to display or hide columns in the Study Instrument List.

Name of Tool:

The Child's Sleep Habits Questionnaire (Owens, Spirito, & McGuinn 2000)

Is the data collection tool standardized or validated?

Yes

Please provide data collection tool citation:

Owens, J. A., Spirito, A., & McGuinn, M. (2000). The Children's Sleep Habits Questionnaire (CSHQ): psychometric properties of a survey instrument for school-aged children. Sleep-New York-, 23(8), 1043-1052.

Will this study require clinical items/ services from UC Irvine Health?

No

Does the research involve the use of identifiable private information?

No

Sharing Results with Subjects

Will Individual results be shared with subjects?

No

Will overall study results will be shared with subjects?

The overall study results will be listed on Clinicaltrials.gov

Medical Devices

Risk Assessment

Risks and Discomforts

1. Describe and assess any reasonably foreseeable risks and discomforts associated with each procedure for each subject population — physical, psychological, social, legal or other:

2. If this study will involve the collection of identifiable private information, even temporarily, for which the disclosure of the data outside of the research could reasonably place the subjects at risk, include the risk of a potential breach of confidentiality:

The greatest potential risk for children interacting with dogs include the danger of an animal bite or that a dog might carry diseases with potential transmission to humans.

Also, should there be a breach in confidentiality of data, there is a slight risk that private health information could be shared with individuals who are not members of the study team.

This study involves the collection of participant identifiable data (even if temporary such as for recruitment or compensation purposes), and as such, a breach of confidentiality is a risk associated with the research.

Discuss what steps have been taken and/or will be taken to prevent and minimize any risks/potential discomforts to subjects:

Though these are potential dangers, risks of interacting with participating therapy dogs are minimized by a strict safety screening protocol including a review of animal health, history, certification by reputable therapy animal certification organizations, and dog/handler interview. This safety protocol was developed in a prior study by the Lead Investigator which included eight-one children and over a dozen therapy animals over the course of 4 years and resulted in zero incidents of injury or disease transmission (Schuck, Emmerson, Abdullah, Stehli, Fine, & Lakes, 2018) and has since been used in clinical treatment in a wide variety of settings across the nation for over 10 years now. The FirstBeat Bodyguard 2 device is small, unobtrusive and does not require an uncomfortable halter band as they easily affix with two small hypo-allergenic adhesive electrodes designed to remain comfortable and has been found to remain in place during moderate to heavy physical activity, and is safe and acceptable in children ages 7-9 [Martinez, et al, 2016]. Additionally, this device has been found safe and feasibly deployed in studies in both typically developing children and specials population as young as 4 years of age [Jerger et al., 2018, Riquelme, et al, 2018]. There is a minimal risk of discomfort from removing the adhesive discs, similar to removing an adhesive bandage. Wiping the skin with a clean cloth or alcohol prep pad will minimize the risk of irritation. All paper and digital records and saliva samples are de-identified using a coding system in which there is only one linking document for record keeping, recruitment and compensation purposed. Only the LR and the study coordinator have access to this document. All identifying information and digital images and recordings are destroyed immediately after analysis unless participants have given explicit consent to use those images or names for explicit media purposes as designated in the Release Form. Only de-identified data will be shared with non-UCI collaborating researchers.

Certificate of Confidentiality

Is the research partially or wholly funded by NIH (including NIH Institutes and Centers), or does the research involve identifiable sensitive information that require CoC protections?

Yes

Indicate whether the research is protected by a NIH Certificate of Confidentiality (CoC):

This research is partially or wholly funded by NIH, including NIH Institutes and Centers. A CoC is automatically issued

Indicate in what situations identifiable private information protected by a CoC will be disclosed (**check all that apply**):

As required by Federal, State, or local laws, excluding instances of disclosure in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others

Potential Benefits

Is there the prospect of a direct benefit anticipated for subjects?

Yes

Describe the potential benefits subjects may expect to receive from participation in this study:

Participants and their parents may experience improved social skills including improved self-esteem and pro-social behavior and reduced symptoms of inattention and oppositional behavior.

Specify the expected potential societal/scientific benefit(s) of this study:

The possible benefits to science and society include providing information about how potential biological responses to animals may enhance treatments for children with ADHD. This information is important as there are few evidence-based non-pharmacological interventions for this group of individuals who remain at risk for poor life outcomes despite the effectiveness of medicines for the symptoms of ADHD.

Alternatives to Participation

Describe the alternatives to participation in the study available to prospective subjects. Include routine (standard of care) options as well as other experimental options, as applicable (**check all that apply**):

Routine standard of care available

Specify the routine standard of care:

The known alternative procedures for decreasing the symptoms of ADHD include treatment with medicines that have been found to decrease symptoms (e.g., Dexedrine®, CONCERTA®, Focalin®, Adderall®, Adderall® XR, Ritalin®, Ritalin LA®, etc.). The known alternative procedures for improving social skills for children with ADHD include behavioral parent training. These alternatives will not be administered during the course of this study.

Participant Compensation

Will subjects be compensated?

Yes

Specify whether compensation is applicable and, if so, the method, amount and schedule of compensation (**Check all that apply**):

Cash

Cash Compensation

Specify cash amount:

$60.00

Cash schedule:

Other

Specify 'Other' cash schedule:

After each Laboratory School Day (3)

Will the cash compensation method include all subjects?

Yes

Will subjects be reimbursed for out-of-pocket expenses?

No

Confidentiality of Research Data

Information and/or Biospecimens Storage

Indicate how information and/or biospecimens (including signed consent forms) will be stored (check all that apply):

Biospecimens will be stored in a locked lab/refrigerator/freezer that is not accessible to non-study team members
Information will be maintained electronically. Information will be password protected and maintained in an encrypted format
Information will be maintained in hard copy. Information will be stored in a locked area that is not accessible to non-study team members

Biospecimens Storage

Specify where the biospecimens will be stored in a locked lab/refrigerator/freezer:

Biospecimens will be stored in a locked lab freezer at the contracted lab, Salimetrics, Inc.

Encrypted Format

Specify where the information will be maintained electronically:

All electronic information is maintained in Redcap

Hard Copy

Specify where the information will be maintained in hard copy:

Hard copy data will be stored in a locked cabinet in the private office of the LR and not accessible to non-study team members.

Will subject/patient identifiers be collected or retained?

Yes

Subject/Patient Identifiers

Will any subject/patient identifiers be collected or retained for data analysis, recruitment, consenting and/or compensation (check all that apply)?

All elements of dates (except year) for dates that are directly related to an individual: birth date, admission date, discharge date, death date, and all ages over 89

All geographic subdivisions smaller than a state: street address, city, county, precinct, ZIP code, and geocodes

Any other unique identifying number, characteristic, or code

Email addresses

Full-face photographs and any comparable images

Names

Telephone numbers

Specify any other unique identifying number, characteristic or code:

audio-video recordings

Will a code be used to link subject/patient identifiers with the information and/or biospecimens?

A code will be used. Subject/Patient identifiers will be kept separately from the information and/or biospecimens. The code key will be destroyed at the earliest opportunity, consistent with the conduct of this research

Will research data/biospecimens be transported or maintained on portable devices (e.g., laptop, smartphone, external hard drive, etc.)?

Yes

Specify the device(s) or method(s) of transportation:

portable devices

Explain why transporting or maintaining subject/patient identifiable data/biospecimens on portable devices is necessary:

Audio and video recordings will be recorded on portable devices, which will be placed in a locked cabinet following evening sessions and then immediately downloaded to a secure server within 24 hours of recording and deleted from the portable device.

Specify who will have access to subject/patient identifiable information/biospecimens as part of this protocol (**check all that apply**):

Authorized UCI personnel (such as the research team) and appropriate institutional officials: such as the Office of Human Research Protections (OHRP) Regulatory entities such as the Food and Drug Administration (FDA), the National Institutes of Health (NIH)

Specify whether subject/patient identifiers be disclosed in presentations and/or publications:

Subject/Patient identifiers will not be disclosed

Specify how long all subject/patient identifiers will be retained. This includes identifiers stored in paper format, stored electronically as well as video recordings, audio recordings, photographs, etc.:

Destroyed after publication/presentation or end of protocol

Will any identifiable photos or audio/video recordings be collected or used?

Yes

Collection of Photographs, or Audio/Video Retention & Recording

Will identifiable audio recordings be collected?

Yes

How will the audio recordings be transcribed?

Identifiable audio recordings transcribed by the study team

Specify timeframe for the audio transcription:

within 2 years of the study completion

Will the identifiable audio recordings be de-identified?

No

Provide rationale on why identifiable audio recordings will not be de-identified:

First names may be called during the audio recording of intervention group sessions. No identifiable information will be used in the labeling of audio recordings

Will identifiable video recordings be collected?

Yes

How will the video recordings be transcribed?
Identifiable video recordings transcribed by the study team

Specify timeframe for the video transcription:
within 2 years of the study completion

Will the identifiable video recordings be de-identified?
No

Provide rationale on why identifiable video recordings will not be de-identified:
Provided parents or LAR provide explicit permissions, photographs and/or audio/video recordings may be used as specifically specified (i.e., training, presentation). See Release Form

Will identifiable photographs be collected?
Yes

Will the identifiable photographs be de-identified?
No

Provide rationale on why identifiable photographs will not be de-identified:
Provided parents or LAR provide explicit permissions, photographs and/or audio/video recordings may be used as specifically specified (i.e., training, presentation). See Release Form

Research Information and/or Biospecimens Retention

Indicate how long research information/biospecimens will be retained:
In accordance with UCOP policy, information/biospecimens will be retained for 10 years after the end of the calendar year in which the research is completed, unless otherwise specified in the award agreement

Will research information and/or biospecimens be shared?
No

Attachments

If required documentation is not provided, the submission is incomplete and your Application will be returned to you. Be sure to upload each document as required. If changes are needed, go back to

the sub-section to revise your selections.

Maximum file size is 30MB

All UCI templates are available on the Human Research Protections Applications & Forms page or Human Stem Cell Research Applications & Forms page.

To access approval documents where UCI will rely on another IRB, including commercial IRBs, visit their respective online portals. Frequently used commercial IRB portals include:

- WIRB Copernicus Group's WCG IRB Connexus
- Advarra's CIRBI
- SMART Online Reliance System (ORS)

Attachment

2020-6069 Phone Scripts 10-21-20_normal_397124.docx

Attachment Type

Recruitment Material

File Comments

File Name

Status (IRB/hSCRO Use Only)

Approved

Attachment

2020-6069 Phone Scripts 10-21-20_approved_397124.pdf

Attachment Type

Recruitment Material

File Comments

File Name

Status (IRB/hSCRO Use Only)

Approved

Attachment

2020-6069 Release Form 10-21-20_normal_397126.doc

Attachment Type

Other

File Comments

File Name

Status (IRB/hSCRO Use Only)

Approved

Attachment

2020-6069 Assent Form 08-27-21_normal_418576.doc

Attachment Type

Assent Form

File Comments

File Name

Status (IRB/hSCRO Use Only)

Approved

Attachment

2020-6069 Assent Form 08-27-21_approved_418576.pdf

Attachment Type

Assent Form

File Comments

File Name

Status (IRB/hSCRO Use Only)

Approved

Attachment

2020-6069 Flyer 08-27-21_normal_418577.doc

Attachment Type

Recruitment Material

File Comments

File Name

Status (IRB/hSCRO Use Only)

Approved

Attachment

2020-6069 Flyer 08-27-21_approved_418577.pdf

Attachment Type

Recruitment Material

File Comments

File Name

Status (IRB/hSCRO Use Only)

Approved

Attachment

20206069 Parent Consent 10-19-2022.doc

Attachment Type

Consent Form

File Comments

Word version

File Name

Status (IRB/hSCRO Use Only)

Approved

Attachment

20206069 Parent Consent 10-19-2022.pdf

Attachment Type

Consent Form

File Comments

stamped pdf version

File Name

Status (IRB/hSCRO Use Only)

Approved

Attachment

Measures.png

Attachment Type

Data Collection Tool/Instrument

File Comments

File Name

Status (IRB/hSCRO Use Only)

Attachment

FirstBeat_Bodyguard2_Manual.pdf

Attachment Type

File Comments

File Name

Status (IRB/hSCRO Use Only)

Attachment

20206069 Renew & Amend Approval Letter 10-19-2022.pdf

Attachment Type

UCI IRB Approval Letter

File Comments

File Name

Status (IRB/hSCRO Use Only)

Approved

Lead Researcher Certification

Investigator's Assurance

As Lead Researcher, I have ultimate responsibility for the performance of this study, the protection of the rights and welfare of the human subjects, and strict adherence by all co-investigators and research personnel to all Institutional Review Board (IRB) requirements, federal regulations, and state statutes for research involving human subjects.

I hereby assure the following:

1. The information provided in this application is accurate to the best of my knowledge.
2. The information provided in this application has been discussed and shared with my Department Chair. Any requests for changes based on this discussion are included in this application upon submission or will be initiated by the research team either during the IRB review process or via an amendment.
3. All named individuals on this project have read and understand the procedures outlined in the protocol and their role on the study.
4. All named individuals on this project have completed the required Educational research tutorials and have been made aware of the "Common Rule" (45 CFR Part 46), applicable Food and Drug Administration (FDA) regulations (21 CFR Parts 50, 56, 312 and 812), have read the Belmont Report, and UCI's Federalwide Assurance (FWA) that are available on the Human Research Protections Program (HRP) website.
5. All experiments and procedures involving human subjects will be performed under my supervision or that of another qualified professional listed on this protocol.
6. I understand that, if the study described in this IRB application is supported by a federal award or used as a basis for a proposal for funding, it is my responsibility to ensure that the description of human subjects activities in the proposal/award is identical in principle to that contained in this application. I will submit modifications and/or changes to the IRB as necessary to assure the proposal/award and application are identical in principle.

I and all co-investigators and research personnel agree to comply with all applicable requirements for the protection of human subjects in research including, but not limited to, the following:

1. Obtaining the legally effective informed consent of all human subjects or their legally authorized representatives (unless waived) and using only the currently approved, stamped consent form (if applicable).
2. Per federal regulations, once a human research study has received IRB approval, any subsequent changes to the study must be reviewed and approved by the IRB prior to implementation except when necessary to avoid an immediate, apparent hazard to a subject. See Reporting of Unanticipated Problems.
3. Reporting any unanticipated problems involving risk to subjects or others, including protocol violations per UCI IRB policy. In addition, HIPAA privacy violations must be PROMPTLY disclosed to the UCI Privacy Officer. There are time requirements for reporting these breaches of confidentiality, which, if not met, may result in monetary damages to the researcher and the institution.
4. Responding appropriately to subjects' complaints or requests for information about the study; and reporting to the IRB any subject complaints that are not resolvable by the study

team.

5. Promptly providing the IRB with any information requested relative to the project.
6. Assuring the appropriate administration and control of investigational test articles (i.e., investigational drugs, biologics or devices) by a qualified investigator or other appropriate individual or entity (e.g., UCI Health pharmacy), and assuring use and maintenance of an Investigational Drug/Biologic Accountability Log or Device Accountability Log.
7. Registering applicable clinical trials with clinicaltrials.gov. For more information about this topic, visit the ClinicalTrials.gov web page or the HRP webpage. The consequences of not meeting the registration and reporting requirements include monetary damages to the researcher and the institution.
8. Obtaining continuing review prior to study expiration (I understand if I fail to apply for continuing review, approval for the study will automatically expire, and all human research activities must cease until IRB approval is obtained).
9. Promptly and completely complying with an IRB decision to suspend or terminate its approval for some or all research activities.
10. Submitting to a routine review of human subject research records. The Compliance & Privacy Office at UCI Health performs ongoing routine reviews of open biomedical research protocols, in an effort to ensure in part that human subject research activities are conducted in accordance with regulations, laws and institutional policies regarding the protection of human subjects. In addition, the HRP unit of the Office of Research has developed the Education Quality and Improvement Program (EQUIP). Through EQUIP, HRP staff conduct periodic quality improvement monitoring and educational outreach.
11. For clinical trials initially approved by the IRB on or after January 21, 2019, posting one (1) IRB-approved clinical trial consent form at a publicly available federal website. The consent form must be posted after recruitment closes, and no later than 60 days after the last study visit. For additional guidance, refer to the OHRP FAQs on Informed Consent.
12. Filing a final report with UCI HRP at the conclusion of this project.

As the Lead Researcher, I assure all of the above

Financial Disclosure

Investigators' Disclosure of Financial Interest

In order to inform research subjects of circumstances that may affect their decision to participate in this study, all researchers are required to disclose their financial interests with outside institutions.

The Lead Researcher of the protocol must ask the following question of all study team members:

"Do you, your spouse/registered domestic partner, and dependent children together have any disclosable financial interests (i) that would reasonably appear to be affected by the research; or (ii) in entities whose financial interests would reasonably appear to be affected by the research?"

A member of the study team who answers in the affirmative will be contacted by the Conflict of Interest Oversight Committee (COIOC) to obtain additional information regarding their specific financial interest(s).

IMPORTANT! If there has been a change in the financial disclosures of the LR or the study team, please also request a 'Change in Financial Interests'.

As Lead Researcher, I certify that the disclosures for all study team members are accurate

End of form. Please review responses for accuracy and completeness.

Please ignore the Admin Details Section below. This section is for IRB/hSCRO use only.

Administrative Details Form

Project Status

Committee:
IRB C

Project Status:
Approved

Date of Project Determination:
October 19, 2022

Amendment Status:
Approved

Date of Amendment Determination:
October 19, 2022

Date of ERA Transcription:
November 10, 2021

Pre-2018 Common Rule:
No

Date of Transition to 2018 Common Rule:
No date entered