Date: February 1st, 2022

Study Protocol and Statistical Analysis Plan

Study Title	A Novel, Non-pharmacological, Intervention for the Management of ADHD in Adolescents
Protocol ID	VIZO_004
ClinicalTrials.gov ID	NCT05835336

Device Name	VIZO Glasses
Objectives	To Assess the Efficacy and Safety of a Novel Device (VIZO Glasses) in the Management of ADHD in Adolescents.
Study Group Investigational Group	VIZO Glasses: Eyeglasses with personalized peripheral retinal stimuli
Key Eligibility Criteria	
Inclusion Criteria	• Documented history of primary ADHD diagnosis by certified clinicians • Age 12-17 y • Minimum total of 24 on the parent ADHD-IV Rating Scale (ADHD-RS) • Written informed consent • Able and willing to complete all required ratings and assessments
Exclusion Criteria	• Any current psychiatric/neurological comorbidity (e.g., epilepsy, Autism, depression, TBI, etc.), other than ADHD • ADHD Medications (stimulants, non-stimulants, other) • Undergoing Neurofeedback, cognitive training • Any other reason that, in the opinion of the investigator, prevents the participant from participating in the study
Endpoints	
Primary	Primary Outcome Measure: Change in the ADHD Rating Scale (ADHD-RS) Parent-report Questionnaire - Total Score [Time Frame: Baseline, 2-month] The ADHD-RS is a parent report questionnaire that is used to aid in the diagnosis of ADHD in children ranging from ages 5-17. The questionnaire contains 18 symptom items corresponding to the DSM-V criteria for ADHD. The parent rates each symptom item on a 4-point Likert scale ranging from 0 ('Never or Rarely') to 3 ('Very Often'). The total score goes from 0 up to 54. Higher scores mean more symptoms and higher ADHD impairments. Change in the ADHD Rating Scale (ADHD-RS) Parent-report Questionnaire - Inattention Subscale [Time Frame: Baseline, 2-month] The Inattention subscale of the ADHD-RS contains 9 symptom

	items, that are designed to measure the child's attention level on tasks or play activities.The items are rated by the parent on a 4-point Likert scale ranging from 0 ('Never or Rarely') to 3 ('Very Often'). The total score goes from 0 up to 27. Higher scores mean more symptoms and higher ADHD impairments. Change in the ADHD Rating Scale (ADHD-RS) Parent-report Questionnaire - Hyperactivity-Impulsivity Subscale [Time Frame: Baseline, 2-month] The Hyperactivity-Impulsivity subscale of the ADHD-RS contains 9 symptom items, that are designed to measure the child's hyperactivity level and impulsivity level. The items are rated by the parent on a 4-point Likert scale ranging from 0 ('Never or Rarely') to 3 ('Very Often'). The total score goes from 0 up to 27. Higher scores mean more symptoms and higher ADHD impairments. Change in Behavior Rating Inventory of Executive Function (BRIEF) - Metacognitive Index [Time Frame: Baseline, 2-month] The Metacognition Index (MI) of the BRIEF reflects a child's ability to self-manage and monitor tasks cognitively. The subscale is composed of the Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor scales of the BRIEF. It uses a Likert-type response format ranging from 1 to 3, where 1 is never, 2 is sometimes, and 3 is often. High scores indicate executive deficit.
<u>Secondary</u>	Secondary Outcome Measures: Clinical Global Impression-Improvement (CGI-I) [Time Frame: 2-month] Based on an interview with the participant, the clinician rates the total improvement on a 7 point scale as follows: 1=very much improved since the initiation of treatment; 2=much improved; 3=minimally improved; 4=no change from baseline (the initiation of treatment); 5=minimally worse; 6= much worse; 7=very much worse since the initiation of treatment. Change in Behavior Rating Inventory of Executive Function (BRIEF) - Global Executive Composite [Time Frame: Baseline, 2-month] The BRIEF is a standardized measure that captures views of

	executive functions or self-regulation in the everyday environment. The BRIEF is composed of 86 items, where each item is rated by the parent, using a 3-point Likert scale ranging from 1 ('Never') to 3 ('Often'). The Global Executive Composite (GEC) is an overarching summary score that incorporates all of the BRIEF clinical scales. High scores indicate executive deficit.
Other Outcomes	Adverse events will be monitored and documented.
Follow-up Visits Schedule	This was a two-month, open-label study in which eligible ADHD-diagnosed adolescents were provided with a pair of VIZO-Glasses featuring a personalized visual stimuli pattern for each participant. A baseline assessment of the participants' ADHD clinical profile pre-intervention included the ADHD-RS and the Behavior Rating Inventory of Executive Function (BRIEF) questionnaires. In addition, participants completed the Conners' Continuous Performance Test-3 (CPT-3). Optical centration parameters and demographic information were collected for each participant. Participants were then invited to complete a personalization process in which they were fitted with personalized VIZO-glasses. Participants were instructed to wear their Vizo-glasses for at least two hours daily for two months. A follow-up assessment at the end of the intervention re-assessed ADHD performance on the ADHD-RS and BRIEF questionaries. In addition, participants completed the CPT-3 test while wearing their VIZO-glasses. The Clinical Global Impression-Improvement (CGI-I) rating scale was administered by a clinician.
Sample Size	Given the exploratory nature of the study, the sample size was chosen to be sufficiently large to detect significant within subject effects of at least 0.5 (Cohen's D) for a 2-Tailed test, at anlpha-0.05 with a power of 80%.
Analysis Plan	Paired samples t-tests will be used to test the effect of the VIZO-glasses intervention, comparing the baseline and end-of-intervention performances. No corrections for multiple testing will be applied due to the exploratory nature of the study. The safety analysis will include all available data on the intent-to-treat (ITT) population.