Date: February 1st, 2022

Study Protocol and Statistical Analysis Plan

Study Title	A Pilot Study to Assess the Efficacy and Safety of a Novel Device (VIZO Glasses) in the Management of ADHD in Adults
Protocol ID	VIZO_003
ClinicalTrials.gov ID	NCT05777785

Device Name	VIZO Glasses
Objectives	To Assess the Efficacy and Safety of a Novel Device (VIZO Glasses) in the Management of ADHD in Adults.
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 18-40 y • 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) • Neurofeedback, cognitive training
Endpoints	
Primary	Adult ADHD Self-Report Scale (ASRS) - Total Score at Baseline and 2 Months Follow up The Adult ADHD Self-Report Scale (ASRS) is a self-report instrument that comprises eighteen items that correspond with the DSM-V-TR criteria for ADHD. Subjects are asked to rate 18 symptom items using a 5-point Likert scale ranging from 0 ('Never') to 4 ('Very Often'). Total scores range from 0 to 72, based on the sum of all 18 questions. Higher scores mean more symptoms and higher ADHD's impairments. Lower values represent better outcomes. The ASRS has two subscales that can be used to identify ADHD subtypes - Inattentiveness and Hyperactivity/Impulsivity. Each subscale contains 9 questions. Adult ADHD Self-Report Scale (ASRS) - Inattentiveness Subscale Score at Baseline and 2 Months Follow up The inattentiveness sub-scale of the ASRS measures difficulties with focusing on details, organisation, remembering appointments, making careless mistakes, and concentration. It includes 9 symptom items using a 5-point Likert scale ranging from 0 ('Never') to 4 ('Very Often'). Total scores range from 0 to 36, based on the sum of all questions. Higher scores mean more symptoms and higher inattentiveness' impairments.

Secondary	Clinical Global Impression-Improvement (CGI-I) - Rate at 2 Months Follow up 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. Conners' Continuous Performance Test-3 (CPT-3) - Detectability (d') at Baseline and 2 Months Follow up Conners' Continuous Performance Test-3 (CPT-3) is an objective test of attention and impulsivity that has been validated in individuals aged 8 years and older. d-prime (d') is a measure of how well the respondent discriminates nontargets (i.e., the letter X) from targets (i.e., all other letters). This variable is also a signal detection statistic that measures the difference between the signal (targets) and noise (non-targets) distributions. In general, the greater the difference between the signal and noise distributions, the better the ability to distinguish non-targets and targets. CPT scores are age and gender standardized T-scores, in which the mean is equal to 50 and the standard deviation is equal to 10. d' is reverse-scored so that higher raw score and T-score values indicate worse performance (i.e., poorer discrimination). Atypical scores are higher than 60 indicating "elevated" to "very elevated" performance. Behavior Rating Inventory of Executive Function Adult Version (BRIEF-A) - Metacognitive Index - at Baseline and 2 Months Follow up The Behavior Rating Inventory of Executive Function Adult Version (BRIEF-A) is a standardized measure that captures views of adults' executive functions or self-regulation in their everyday environment. The BRIEF-A comprises 75 items, each rated by the individual, using a 3-point Likert scale ranging from 1 ('Never') to 3 ('Often'). BRIEF-A includes a Behavioral Regulation index, a Metacognition index, and a summary score-Global Executive Composite. The Metacognition Index (MI) reflects the individual's ability to initiate activity and generate problem-solving ideas, to sustain working memory, to plan and organize problem-solving approaches, to monitor success and failure in problem solving, and to organize one's materials and environment. The MI

	subscale includes 40-items with score ranges between 40 to 120. Higher values represent worse outcome and greater difficulties with executive functions.
Other Outcomes	Adverse events will be monitored and documented.
Trial Design and Follow-up Visits Schedule	This study was designed as a pilot single-center, open-label study of 2 months treatment. Following the enrollment, the participants will go through an adjustment process where they will be fitted with a personalized pair of VIZO Glasses. The participants will be instructed to wear the glasses throughout the day for two months. A follow-up visit at the end of the 2-month treatment will be conducted to assess the efficacy of VIZO Glasses on managing ADHD symptoms, using the Conners Continuous Performance Test-3, the Adult ADHD Self-Report Scale (ASRS), Behavior Rating Inventory of Executive Function Adults (BRIEF-A), and Clinical Global Impression-Improvement (CGI-I).
Sample Size	Power analyzes determined that a sample size of 90 participants will have 80% power to detect an effect size of 0.30 (Cohen's D) using a paired t-test with a 0.05 two-sided significance level. Assuming a 20% attrition rate over the course of the study, 108 participants were targeted for inclusion.
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. Paired samples t-tests will be used to test the effect of the VIZO-glasses intervention, comparing the baseline and end-of-intervention performances. Normality distribution of data will be assessed using the Shapiro–Wilk test. Due to the exploratory nature of the study, no corrections for multiple testing will be applied. The safety analysis will include all available data on the intent-to-treat (ITT) population. Additionally, Mixed model ANOVA will was used to explore any potential effect of covariates such as gender, age, eyeglasses, learning disabilities, treatment naïve, and ASRS total score.