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Validating an EEG-based test for ADHD: a case-control study on brain connectivity during executive task

Submission date
04/02/2025

Recruitment status
No longer recruiting

Registration date
20/02/2025

Overall study status
Completed

Last Edited
19/02/2025

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental condition that affects about 5-7% of children and 2-5% of adults worldwide. It is characterized by symptoms like inattention, hyperactivity, and impulsivity. Diagnosing ADHD can be challenging because there is no specific medical test for it, and current methods rely heavily on clinical interviews and behavioral assessments, which are subjective and can lead to misdiagnosis. This study aims to improve the accuracy of ADHD diagnosis by using brain activity data collected through electroencephalograms (EEGs). Researchers will analyze brain connectivity patterns during tasks that require executive control, using advanced computer algorithms to identify specific biomarkers (biological indicators) associated with ADHD. The goal is to develop an EEG-based diagnostic tool that can accurately identify ADHD in children.

Who can participate?
The study will involve at least 162 children aged between 7 and 12 years. Participants will be divided into three groups:
- Children diagnosed with ADHD, predominantly inattentive type.
- Children diagnosed with ADHD, predominantly combined or hyperactive type.
- Healthy children without ADHD, who are serving as the control group.
Children must have the consent of their parents or guardians to participate. Some medical conditions or the use of certain medications may exclude children from the study to ensure accurate results.

What does the study involve?
Participants will undergo several assessments:
- Clinical Interview: To gather detailed medical and behavioral history.
- Neuropsychological Tests: To evaluate cognitive functions like attention, memory, and problem-solving.
- EEG Recording: To measure brain activity while the child is at rest and during a simple attention task called the "go/no-go" task.
The EEG cap with 64 sensors will record the brain's electrical activity. The task will involve

responding to certain visual stimuli on a computer screen, designed to engage attention and impulse control.

What are the possible benefits and risks of participating?
Benefits:
- Participants will receive a thorough assessment of their cognitive and brain function, which may help in understanding their attention-related difficulties.
- The study may contribute to the development of a new, more accurate diagnostic tool for ADHD, potentially benefiting many children in the future.
Risks:
- The procedures are safe and non-invasive. EEG is commonly used in clinical settings and poses no known risks.
- Some children might feel uncomfortable wearing the EEG cap or sitting still during the test. Breaks will be provided to minimize discomfort.

Where is the study run from?
The study is conducted at the Puerta de Hierro Hospital in Majadahonda, Madrid, Spain.

When is the study starting and how long is it expected to run for?
The study started in June 2023 and is expected to run until November 2024. The analysis of the collected data will continue until early 2025, with results anticipated in the first half of 2025.

Who is funding the study?
The study is funded by the sponsor, Bitsphi Diagnosis. Specific details about the sponsor are managed by the study's administrative team.

Who is the main contact?
Sandra Ortiz Hernández (Clinical Trial Manager), bitsphiclinico@bitsphi.com

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Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
HUPH-BP-BMCCEEG-CC22

Study information

Scientific Title
Retrospective/prospective case-control study to determine the concurrent criterion validity of a diagnostic test for attention-deficit/hyperactivity disorder based on the classification of brain connectivity patterns evoked during an executive control challenge

Acronym
SINCRONIA

Study objectives
The characterization, refinement, and concurrent validation of an ADHD diagnostic test based on biomarkers of attentional control and executive function will identify the minimal set of brain connectivity patterns that optimize diagnostic performance. Furthermore, the index test will demonstrate non-inferiority or superiority compared to the best available reference standard.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 16/02/2023, Drug Research Ethics Committee of the Puerta de Hierro University Hospital (Joaquín Rodrigo, 2, Majadahonda, Madrid, 28222, Spain; +3491 191 76 62; secreceic.hpth@salud.madrid.org), ref: 207/22

Study design
Non-interventional case-control cross-sectional non-randomized blinded study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied

Attention deficit/hyperactivity disorder (ADHD)

Interventions
This is an observational study investigating electroencephalogram (EEG)-based biomarkers for ADHD diagnosis in children aged 7 to 12.

Participants undergo a comprehensive assessment that includes clinical interviews, standardized neuropsychological tests (such as the WISC-V for intelligence; CPT-3 and ENFEN for attention, processing speed, and executive functions; SDQ, CABI, and ADHD Rating Scale-IV for behavioral and emotional regulation; PROLEXIA for dyslexia screening; and CCI-2 for slow cognitive tempo), alongside EEG recordings during both resting state and a go/no-go interference task with varying stimulus ratios to evaluate brain connectivity, response inhibition, and cognitive control.

Intervention Type
Other

Primary outcome(s)
The diagnostic accuracy of the EEG-based index test for ADHD, defined by its sensitivity (true positive fraction) and specificity (false positive fraction). These metrics are derived from EEG functional connectivity patterns recorded during a standardized go/no-go interference task.

Key secondary outcome(s))
1. Comparison with CPT-3 Performance measured by comparing classification probabilities (e.g., sensitivity and specificity) of the EEG-based index test with those obtained from the Continuous Performance Test (CPT-3).
2. Influence of Demographic and Clinical Factors assessed via regression analyses correlating participant characteristics (such as age, sex, ADHD subtype, and comorbidities) with the diagnostic performance metrics.
3. Construct Validity of Slow Cognitive Tempo (SCT) measured using scores from the Child Concentration Inventory-Version 2 (CCI-2) and correlating these with EEG biomarkers.
4. EEG Biomarker Identification determined through dimensional reduction techniques and fuzzy deep neural network analyses to identify the most informative EEG connectivity metrics.

Completion date
12/11/2024

Eligibility

Key inclusion criteria
1. Aged between 7 and 12 years (inclusive).
2. Right-handed dominance.
3. Written informed consent from a legal representative and assent from the participant.
4. (Cases) Diagnosed with ADHD within the past 3 years or at the time of the study, with hyperactive/impulsive, combined, or inattentive presentation, including cases with dyslexia or slow cognitive tempo (SCT).
5. (Controls) Patients from the Pediatrics Department at HUPHM, whose medical care will not be compromised by participation (e.g., those monitored for short stature, hypercholesterolemia, early pubarche, or heart murmurs/chest pain).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
7 years

Upper age limit
12 years

Sex
All

Total final enrolment
189

Key exclusion criteria
1. Color blindness or any other condition affecting sensorineural perception, which may interfere with study procedures.
2. Cognitive or behavioral difficulties (pathological or not) or insufficient capacity, as determined by the investigator, to maintain a minimum level of relaxation and rest or to understand and follow study procedures.
3. Regular use of medications (excluding ADHD treatment) that may affect attentional or executive function, such as opioid analgesics, benzodiazepines, hypnotics, or sedative antihistamines, or any other drug deemed relevant by the investigator.
4. (Cases) Subjects for whom stopping ADHD medication for 24 hours (methylphenidate /atomoxetine) or 48 hours (other ADHD medications) poses a medical, behavioral, or other risk.
5. (Cases) Subjects for whom a medication change (different drug) was required after initial stabilization for clinical stabilization reasons, except for adjustments made during holidays or weekends.
6. Diagnosis of ADHD subtypes not considered in the inclusion criteria or presence of other neurological or psychiatric disorders significant enough to interfere with study evaluations, such as autism spectrum disorders, Tourette's syndrome, or epilepsy (or epileptic foci).
7. (Control) Participants who meet the diagnostic criteria for ADHD or other significant mental health conditions, as determined by the research team using DSM-5 criteria and the SDQ questionnaire.

Date of first enrolment
18/07/2023

Date of final enrolment
12/11/2024

Locations

Countries of recruitment
Spain

Study participating centre
Puerta de Hierro University Hospital
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Sponsor information

Organisation
Bitsphi Diagnosis

Funder(s)

Funder type
Industry

Funder Name
Bisphi Diagnosis

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to their use in training proprietary algorithms that will be part of a commercial diagnostic product and to protect participant confidentiality and intellectual property rights.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	12/12/2022	19/02/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes