A Longitudinal Follow-up Study of Neuroimage and Neuropsychological Endophenotype Study on ADHD

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ClinicalTrials.gov Identifier: NCT03679403

Recruitment Status: Recruiting
First Posted: September 20, 2018
Last Update Posted: September 20, 2018
See Contacts and Locations

Sponsor:
National Taiwan University Hospital

Information provided by (Responsible Party):
National Taiwan University Hospital

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Study Description
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Brief Summary:
Attention deficit/hyperactivity disorder (ADHD) is a common (3-10%), early-onset, clinically and genetically heterogeneous neuropsychiatric disorder with lifelong neuropsychological deficits. Despite many imaging studies on ADHD across countries, only few longitudinal studies investigated the developmental changes of structural and functional brain connectivity and some imaging studies using unaffected sibling design in western countries. There is no published data regarding developmental changes in brain functions assessed by neuropsychology/physiology/image in Asia and Taiwan as well. The ultimate goals of this 3-year project are to identify which neuropsychological, functional and structural connectivity, and neurophysiological variables can be effective endophenotypes (biomarkers) for ADHD based on this follow-up unaffected sibling study design. Due to the limitation of diffusion tensor image (DTI), original analysis of diffusion spectrum image (DSI), and single-echo resting-state functional MRI (SE rsfMRI), the investigators will adopt Mean Apparent Propagator (MAP)-MRI, tract-based autonomic analysis (TBAA) and multi-echo (ME) rsfMRI in this project. With the accomplishment of the following study goals, this study will be the first longitudinal follow-up neuroimaging/physiological endophenotypes study on ADHD using advanced imaging techniques and comprehensive clinical and neurocognitive data.

Condition or disease

Attention Deficit Hyperactivity Disorder

Detailed Description:

Primary Aim:

1. To examine the developmental changes and stability of neuropsychological functions (NFs, assessed by CPT and CANTAB) and structural (morphometric, cortical thickness, gyrification, fiber tract integrity) and functional connectivity (assessed by SE rsfMRI, counting-Stroop fMRI) from childhood to late adolescence and young adulthood;
Secondary Aims:

2. To validate a wide range of neuropsychological functions (assessed by CPT, CANTAB, CNB), structural and functional connectivity in the frontostriatal (FS), frontoparietal (FP) and other circuitries, and neurophysiological functions (assessed by event-related potential [ERP]: MMN, Gamma ARRS) as effective imaging endophenotypes by demonstrating the intermediate position of unaffected siblings between ADHD probands, and age-, sex-, and handedness-matched neurotypicals at Time 1 and Follow-up;

3. To identify the Time 1 predictors (behavioral symptoms, NFs, and imaging data) for Follow-up neuroimaging data (Morphometric, DSI, rfMRI, task-fMRI, MMN, Gamma ARRS); and

4. To correlate all kinds of neurocognitive data and clinical symptoms profiles stratifying by the presence of ADHD, proband-unaffected sibling dyads, and two time points.

Hypothesis The investigators anticipated despite increasing thinning of cortical thickness, microstructural integrity of several targets fiber tracts, and brain activity of target brain regions and improving neuropsychiatric performance from childhood to late adolescence/young adulthood in neurotypicals and probably in ADHD with lower developmental changes slope in ADHD. These changes of unaffected siblings are in the intermediate position between the ADHD probands and neurotypicals. For the endophenotype part, the investigators anticipate that ADHD probands may have a higher level of altered microstructural integrity and decreased brain activity of the FS, FP, other hypothesized fiber tracts/brain networks, deficits in MMN and Gamma, and impaired a wide-ranging NFs than neurotypicals. These differences in the unaffected siblings would be in the intermediate position between ADHD probands and neurotypicals.

Study Design

Study Type: Observational

Estimated Enrollment: 334 participants

Observational Model: Case-Control

Time Perspective: Cross-Sectional

Official Title: A Longitudinal Follow-up Study of Neuroimage and Neuropsychological Endophenotype Study on ADHD

Actual Study Start Date: August 1, 2017

Estimated Primary Completion Date: July 2020

Estimated Study Completion Date: July 2020

Resource links provided by the National Library of Medicine

MedlinePlus related topics: Attention Deficit Hyperactivity Disorder

U.S. FDA Resources

Groups and Cohorts

<table>
<thead>
<tr>
<th>Group/Cohort</th>
<th>Intervention/treatment</th>
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<tr>
<td>ADHD Probandsf Subjects with DSM-IV ADHD who received the same MRI and CANTAB+CPT assessments during 2010.8-2015.7(NCT00916851, NCT01682915) at their age of 8-17 will be reassessed at the estimated age of 15-25.</td>
<td>Other: Psychiatric diagnosis Kiddie Schedule for Affective Disorders &amp; Schizophrenia (K-SADS) for DSM-5</td>
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<tr>
<td>Unaffected siblings of ADHD</td>
<td>Other: Psychiatric diagnosis</td>
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</table>
The unaffected siblings received the MRI and CANTAB+CPT assessments during 2013.8-2015.7 (NCT01682915) will be recruited and assessed.

Neurotypicals Follow-up
Subjects without any lifetime diagnosis of DSM-IV ADHD or other psychiatric disorders as the control group of the ADHDFU group around 4-8 years ago when they received the same MRI and neuropsychological assessments during 2010.8-2015.7(NCT00916851, NCT01682915) at their age of 8-17 will be reassessed at their estimated age of 15-25.

Outcome Measures

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Primary Outcome Measures :

1. Neuropsychological functions: Continuous Performance Test (CPT) [ Time Frame: 1 day ]
   The 4 dimensions of CCPT: focused attention, hyperactivity/impulsivity, sustained attention, and vigilance.

2. Neuropsychological functions: Cambridge Neuropsychological Test Automated Batteries (CANTAB) [ Time Frame: 1 day ]
   The 4 main cognitive components of CANTAB: Visual Memory, Attention, Working and Planning Memory (Executive Functions), and Decision Making.

3. Structural neuroimaging: Diffusing spectrum imaging (DSI) [ Time Frame: 1 day ]
   Using a pulsed-gradient spin-echo diffusion EPI (echo planar imaging) sequence with a twice-refocused balanced echo to acquire diffusion-weighted images.

4. Functional connectivity: Single-echo (SE) [ Time Frame: 1 day ]
   SE will be used to evaluate functional connectivity.

5. Multi-echo (ME) Resting-state fMRI (rsfMRI) [ Time Frame: 1 day ]
   rsfMRI will be used to evaluate functional connectivity.

Eligibility Criteria

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Ages Eligible for Study: 15 Years to 25 Years (Child, Adult)
Sexes Eligible for Study: All
Accepts Healthy Volunteers: No
Sampling Method: Non-Probability Sample

**Study Population**
This 3-year follow-up study will repeat the same neuropsychological (CANTAB, CPT) and MRI (T1, T2, DSI, SE-rsfMRI, counting stroop fMRI) assessments at Time 1 and additionally assess electrophysiology (MMN, Gamma ASSR), fMRI (ME rsfMRI, tasks fMRI) and Computerized Neuropsychological Battery (CNB) among 138 probands with ADHD, 61 unaffected siblings, and 135 neurotypicals who had the same neuropsychological and imaging assessments in 2010.8-2015.7 (NCT00916851, NCT01682915).

**Criteria**

Inclusion Criteria:
- Subjects who received the same MRI and neuropsychological assessments during 2010.8-2015.7 (NCT00916851, NCT01682915).

Exclusion Criteria:
- Subjects will be excluded from the study if they have (1) neurodegenerative disorder, epilepsy, involuntary movement disorder, congenital metabolic disorder, brain tumor, history of severe head trauma, or history of craniotomy; and (2) visual or hearing impairments, or motor disability which may influence MRI assessment.

**Contacts and Locations**

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**Information from the National Library of Medicine**

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): NCT03679403

**Locations**

Taiwan

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**Sponsors and Collaborators**
National Taiwan University Hospital

**More Information**

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ClinicalTrials.gov Identifier: NCT03679403 History of Changes
Other Study ID Numbers: 201701033RIND
First Posted: September 20, 2018 Key Record Dates
Last Update Posted: September 20, 2018
Last Verified: September 2018
Studies a U.S. FDA-regulated Drug Product:  No
Studies a U.S. FDA-regulated Device Product:  No

Additional relevant MeSH terms:
Attention Deficit Disorder with Hyperactivity
Attention Deficit and Disruptive Behavior Disorders
Neurodevelopmental Disorders
Mental Disorders