Purpose

Introduction: Attention deficit/hyperactivity disorder (ADHD) is one of the most prevalent mental disorders in children and is associated with important negative functional outcomes throughout development. The first signs and symptoms become apparent in preschool age. Therefore, early interventions in this population have the potential of limiting the disorder's negative impact and preventing future impairments in affected individuals. The first-choice medication for treating ADHD is methylphenidate, which has evidence of efficacy and safety in preschool children. However, non-evidence based worries and pressure from the media placed parent training as the first-line treatment for ADHD in clinical guidelines. Parent training is a behavioral intervention implemented with the parents, with weekly sessions for 8 to 12 weeks, adequate for treating ADHD dysfunctional symptoms and behaviors. However, the level of evidence for this intervention is reduced. Furthermore, the need of trained therapists in the public health system, added to the difficulties on adherence and comprehension from parents, limit its generalization and raise questions regarding its indications. Until now, no study has compared pharmacological treatment with methylphenidate to parent training in preschool children with ADHD regarding their clinical efficacy and cost-effectiveness. Moreover, no study has evaluated the impact of pharmacological intervention and psychotherapy on neurobiological mechanisms of ADHD, which is crucial for determining their impact on neurodevelopment.

Objectives: This is a double-blind randomized clinical trial that aims to evaluate the efficacy, tolerability and acceptability of treatment with methylphenidate compared to parental training and placebo in preschool children with ADHD. Furthermore, the investigators propose the use of advanced neuroimaging techniques for the assessment of changes in brain connectivity from the institution of treatment.
Methods: This study will be a randomized, double-blind, parallel-group, evaluating two active interventions and placebo control group. One hundred and fifty children aged 3 years and 11 months and 5 years and 11 months, diagnosed with ADHD, will be randomized to receive treatment with methylphenidate and information (50 children), parental training and treatment with placebo medication (50 children) or belong to active control group with educational information for parents and placebo treatment with no treatment (active control, 50 children). The treatment will last eight weeks, the neurobiological outcomes will be assessed before and after treatment and clinical outcomes will be assessed at weeks 0, 4 and 8 will also be evaluated 50 children with typical development in relation to neurobiological measures.

Implications: This study proposes an innovative and relevant analysis, which will enable the field to advance the knowledge of biological mechanisms related to ADHD and to treatment response. Also, the study will expand the evidence to guide early prevention strategies and early intervention.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
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</table>
| Attention Deficit Disorder With Hyperactivity Preschool Child | Drug: Methylphenidate  
Behavioral: Parental training  
Other: Psychoeducational groups for parents  
Drug: Placebo pill | Phase 4 |

Study Type: Interventional

Study Design: Allocation: Randomized
Endpoint Classification: Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: Early Interventions in Children With Attention Deficit/Hyperactivity Disorder: Randomized Controlled Trial Comparing Methylphenidate Parental Training in Treating Preschool Children With Attention Deficit / Hyperactivity Disorder

Resource links provided by NLM:

MedlinePlus related topics: Attention Deficit Hyperactivity Disorder Toddler Health

Drug Information available for: Methylphenidate Methylphenidate hydrochloride

U.S. FDA Resources

Further study details as provided by University of Sao Paulo:

Primary Outcome Measures:

- Change in attention deficit and hyperactivity symptoms [ Time Frame: Baseline and after 8 weeks (post intervention). ] [ Designated as safety issue: Yes ]

The child will be assessed with the Swanson, Nolan and Pelham (SNAP) scale.
• Change in symptom severity [Time Frame: Baseline and after 8 weeks (post intervention).] [Designated as safety issue: Yes] The child will be assessed by a blinded rater with the Clinical Global Impressions Scale (CGI).

Estimated Enrollment: 150

Study Start Date: June 2016

Estimated Study Completion Date: December 2017

Estimated Primary Completion Date: December 2017 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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</thead>
<tbody>
<tr>
<td>Experimental: Methylphenidate and psychoeducational groups</td>
<td>Drug: Methylphenidate</td>
</tr>
<tr>
<td>Methylphenidate treatment with a initial dosage of 0,3 mg/kg per</td>
<td>Methylphenidate treatment with a initial dosage of 0,3 mg/kg per day (weekly dosage</td>
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<td>day (weekly dosage adjustments) and weekly psychoeducational</td>
<td>adjustments).</td>
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<tr>
<td>groups during 8 weeks.</td>
<td>Other: Psychoeducational groups for parents</td>
</tr>
<tr>
<td></td>
<td>Weekly psychoeducational groups conducted by educators.</td>
</tr>
<tr>
<td>Experimental: Parental training and placebo medication</td>
<td>Behavioral: Parental training</td>
</tr>
<tr>
<td>Weekly parental training conducted by behavioral psychologists and</td>
<td>Weekly parental training conducted by behavioral psychologists.</td>
</tr>
<tr>
<td>placebo pill during 8 weeks.</td>
<td>Drug: Placebo pill</td>
</tr>
<tr>
<td></td>
<td>Placebo pill during 8 weeks.</td>
</tr>
<tr>
<td>Placebo Comparator: Psychoeducational groups and placebo mediation</td>
<td>Other: Psychoeducational groups for parents</td>
</tr>
<tr>
<td>Weekly psychoeducational groups and placebo pill during 8 weeks.</td>
<td>Weekly psychoeducational groups conducted by educators.</td>
</tr>
<tr>
<td></td>
<td>Drug: Placebo pill</td>
</tr>
<tr>
<td></td>
<td>Placebo pill during 8 weeks.</td>
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</tbody>
</table>

Eligibility

Ages Eligible for Study: 3 Years to 5 Years

Genders Eligible for Study: Both

Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:
• Attention deficit hyperactivity disorder DSM-5 diagnosis
Score above 32 on the Swanson, Nolan, and Pelham-IV scale

Child is registered in a school or day care center

Children without the use of stimulants in the last 30 days

Exclusion Criteria:

Intelligence quotient <70

Presence of clinical condition or history of neurological disorder or head trauma with conscience loss

Presence of affective and psychotic disorders, as well as autism spectrum disorders

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02807870

Contacts

Contact: Guilherme V Polanczyk 55112661-7560  gvp@usp.br

Contact: Guilherme V Polanczyk 55112661-7560

Locations

Brazil

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Sponsors and Collaborators

University of Sao Paulo

Conselho Nacional de Desenvolvimento Científico e Tecnológico

Investigators

Principal Investigator: Guilherme V Polanczyk  University of Sao Paulo Medical School

More Information

Responsible Party: Guilherme Vanoni Polanczyk, Professor, University of Sao Paulo

ClinicalTrials.gov Identifier: NCT02807870  History of Changes

Other Study ID Numbers: 466859/2014-7

Study First Received: June 9, 2016

Last Updated: June 20, 2016

Health Authority: Brazil: Ethics Committee

Keywords provided by University of Sao Paulo:
Parental training

Additional relevant MeSH terms:

<table>
<thead>
<tr>
<th>Term</th>
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<tbody>
<tr>
<td>Attention Deficit Disorder with Hyperactivity</td>
<td>Methylphenidate</td>
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<td>Hyperkinesis</td>
<td>Central Nervous System Stimulants</td>
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<td>Attention Deficit and Disruptive Behavior Disorders</td>
<td>Dopamine Agents</td>
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<tr>
<td>Dyskinesias</td>
<td>Dopamine Uptake Inhibitors</td>
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<td>Mental Disorders</td>
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<td>Nervous System Diseases</td>
<td>Molecular Mechanisms of Pharmacological Action</td>
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<td>Neurodevelopmental Disorders</td>
<td>Neurotransmitter Agents</td>
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<tr>
<td>Neurologic Manifestations</td>
<td>Neurotransmitter Uptake Inhibitors</td>
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<tr>
<td>Signs and Symptoms</td>
<td>Physiological Effects of Drugs</td>
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ClinicalTrials.gov processed this record on June 20, 2016