ADDITIONAL MATERIAL: Protocol

PROTOCOL

Introduction

Despite the high prevalence of Attention-Deficit/Hyperactivity Disorder (ADHD), estimated as 5.9 to 7.1% in school aged-children (Willcutt, 2012), there is still a lack of consensus on how best to ascertain the disorder (Polanczyk et al., 2007). This is reflected in continuing public concern regarding presumed over-diagnosis, despite evidence of both under- and over-diagnosis (Sciutto and Eisenberg, 2007b). The diagnosis continues to be completely based on clinical history despite the salience of observable characteristics such as increased locomotor activity. Advances in approaches quantifying locomotor activity motivated this review of such methods for differentiating individuals with ADHD from healthy comparisons, as an initial step in defining the potential role of such methods in clinical practice.

Objectives

Our aim is to perform a systematic review and meta-analysis of studies including measures of locomotor activity in individuals with ADHD to assess the accuracy of such measures in the diagnosis of ADHD.

Methods

Methods for this systematic review/meta-analysis follow the recommendations from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, PRISMA (Liberati et al., 2009a)

Selection criteria

Study type: All types of published peer-reviewed controlled studies will be included; abstracts and book chapters will not. As we want to assess the accuracy of locomotor measures for the diagnosis of ADHD, the inclusion of a control group is a requirement. We will include all types of movement measures for ADHD diagnosis, but no other indices such as sleep parameters. As suggested by the Cochrane group (2011), the inclusion of unpublished data may introduce bias, due to the fact that contacted authors may provide requested data in a selective way; therefore, we will not include data from unpublished studies and we will not contact experts in the field to gather unpublished data.

Population: ADHD: To be included, ADHD groups needed a categorical diagnosis of ADHD per DSM (III,III-R, IV, IV-TR or 5) or Hyperkinetic Disorder according to ICD-10 or previous ICD versions. We did not include studies assessing only symptoms of ADHD, without a formal diagnosis of the disorder. We will also exclude studies based on the diagnosis of minimal brain dysfunction, which would not be comparable with DSM definitions of ADHD, or with DAMP syndrome (deficit in attention, motor control and perception), since this category has not been broadly embraced. In addition, deficits in motor control may impact on physical activity levels in individuals with this syndrome, consequently introducing possible bias in this systematic review. No restrictions of age, sex or socioeconomic status (SES) will be applied. The presence of comorbid neuropsychiatric disorders will not be an exclusion criterion. No restriction of medication status will be applied. We will perform subgroup analyses according to the medication status of the subjects (psychostimulant-naïve or treated with medications for ADHD) if sufficient numbers of studies are detected.

Comparisons: Preferably healthy controls, i.e., individuals without ADHD as well as without any other neuropsychiatric disorder. In case of two control groups, we will choose the healthy one.

Setting: Studies including participants recruited in any setting will be retained.

Outcomes:

Primary outcome:

The primary outcome will be the effect sizes of objective measures of locomotion when used to contrast individuals with ADHD and controls.

Search methods for identification of studies

Electronic searches

Electronic searches will be performed in the following databases, accessed from the New York University Medical Library: PubMed, Ovid databases, and Web of Knowledge databases, with the following search terms and syntax:

Pubmed:

(ADHD OR adhd OR attention deficit disorder with hyperactivity OR minimal brain disorders OR syndrome hyperkinetic OR hyperkinetic syndrome OR hyperactivity disorder OR hyperactive child

syndrome OR childhood hyperkinetic syndrome OR attention deficit hyperactivity disorders OR attention deficit hyperactivity disorder OR adhd attention deficit hyperactivity disorder OR adhd OR overactive child syndrome OR attention deficit hyperkinetic disorder OR hyperkinetic disorder OR attention deficit disorder hyperactivity OR attention deficit disorders hyperactivity OR child attention deficit disorder OR hyperkinetic syndromes OR syndromes hyperkinetic OR hyperkinetic syndrome childhood) AND (actigraph OR McLean Motion and Attention Test OR MMAT OR QbTest plus OR actigraphy OR Quantified Behavior test plus OR OPTAX)

Ovid databases *(Ovid MEDLINE®, Biological Abstracts®, EMBASE Classic+EMBASE, PsycINFO)*
(ADHD OR adhd OR attention deficit disorder with hyperactivity OR minimal brain disorders OR syndrome hyperkinetic OR hyperkinetic syndrome OR hyperactivity disorder OR hyperactive child syndrome OR childhood hyperkinetic syndrome OR attention deficit hyperactivity disorders OR attention deficit hyperactivity disorder OR adhd attention deficit hyperactivity disorder OR addh OR overactive child syndrome OR attention deficit hyperkinetic disorder OR hyperkinetic disorder OR attention deficit disorder hyperactivity OR attention deficit disorders hyperactivity OR child attention deficit disorder OR hyperkinetic syndromes OR syndromes hyperkinetic OR hyperkinetic syndrome childhood OR Attention deficit disorder / OR ((atteni$) adj3 (deficit$ OR disorder$ or hyperactiv$ OR hyper?activ$ OR adhd OR addh OR ad??hd)) OR ((hyperkin$ OR hyper?kin$) adj3 (deficit$ OR disorder$ OR hkd))) AND (actigraph OR McLean Motion and Attention Test OR MMAT OR QbTest plus OR actigraphy OR Quantified Behavior test plus OR Qb Test OR OPTAX)

Web of Knowledge databases *(BIOSIS Previews®, Inspec®, Science Citation Index Expanded (SCI-Expanded), Social Sciences Citation Index (SSCI), Arts & Humanities Citation Index (A&HCI), Conference Proceedings Citation Index - Science (CPCI-S), Conference Proceedings Citation Index - Social Sciences & Humanities (CPCI-SSH), CABI: CAB Abstracts® and Global Health®, Food Science and Technology Abstracts (FSTA)®)*

(ADHD OR adhd OR attention deficit disorder with hyperactivity OR minimal brain disorders OR syndrome hyperkinetic OR hyperkinetic syndrome OR hyperactivity disorder OR hyperactive child syndrome OR childhood hyperkinetic syndrome OR attention deficit hyperactivity disorders OR attention deficit hyperactivity disorder OR adhd attention deficit hyperactivity disorder OR addh OR overactive child syndrome OR attention deficit hyperkinetic disorder OR hyperkinetic disorder OR attention deficit disorder hyperactivity OR attention deficit disorders hyperactivity OR child attention deficit disorder OR hyperkinetic syndromes OR syndromes hyperkinetic OR hyperkinetic syndrome childhood) #1

(actigraph OR McLean Motion and Attention Test OR MMAT OR QbTest plus OR actigraphy OR Quantified Behavior test plus OR Qb Test OR OPTAX) #2

Searching other resources

Manual searches will include scanning of reference lists of relevant papers retrieved.

No a priori limitations on language or period of publication will be applied.

Identification and selection of studies:

Studies identified with electronic and manual searches will be listed with citation, titles and abstracts in Endnote (Microsoft, Redmond, Washington, USA); duplicates will be excluded using the Endnote function 'remove duplicates.' The eligibility process will be conducted in two separate stages:

1. Two authors (LG-M and SC) will independently screen title and abstracts of all non-duplicated papers and will exclude those not pertinent. A final list will be agreed with discrepancies resolved by consensus between the two authors. When consensus is not reached, a third author (FXC) will act as arbitrator. If any doubt about inclusion exists, the article will proceed to the next stage.

2. The full-text version of the articles passing stage 1 screening will be downloaded and assessed for eligibility by two authors (LG-M and SC), independently. Discrepancies will be resolved by consensus between the two authors and, if needed, a third author (FXC) will act as arbitrator.

Data from multiple reports of the same study will be linked together. Where required, we will contact the corresponding author to inquire regarding study eligibility.

Data extraction

Two authors (LG-M and SC) will independently perform data extraction; any discrepancies will be resolved by consensus between the two authors. If this is not possible, another author (FXC) will make a judgment on the data entered and act as an arbitrator. The following data will be extracted:

1. Publication detail: year and language of publication, country where the study was conducted.

2. Design: Study temporality (prospective, retrospective); patient enrollment (consecutive, non-consecutive); method use to define ADHD/non ADHD (type of instrument).

3. Study participant details: number, mean age (SD), sex distribution, SES and ethnicity of participants with and without ADHD; psychiatric and other comorbidities (type and prevalence); method to establish the diagnosis of ADHD [structured or semi-structured interview according to DSM (III, III-R, IV and IV-TR) or ICD (ICD-10 or previous versions) criteria]; medication status of individuals with and without ADHD (type of medication and percentage of treated participants, during and prior to the study).

Statistical analysis

All analyses will be performed using Rev Manager 5.3.

We will assess the feasibility of combining effect sizes from each studies using the inverse-variance method, in which the reciprocal of their variance is used to weight the standardized mean difference from each trial before being combined to give an overall estimate (2011). Given the heterogeneity of ADHD assessments and sample characteristics, we will choose *a priori* to use random-effects models, as recommended by Field and Gillett (Field and Gillett, 2010). The I^2 statistic will be calculated, *a posteriori*, as an estimate of between study heterogeneity in effect size.

Subgroup meta-analyses will be conducted according to participants' age (children vs. adults) and motion measure (actigraphy vs. infrared camera measures) if sufficient numbers of studies are identified. We will explore the feasibility of conducting meta-regression analyses to assess the moderating effect of age, sex, socioeconomic status, methods to assess ADHD, psychiatric comorbidities, and medication status.

Cochrane Handbook for Systematic Reviews of Interventions. In Green JPHaS, editor. The Cochrane Collaboration, 2011.

Field AP, Gillett R. (2010). How to do a meta-analysis. *British Journal of Mathematical and Statistical Psychology, 63*(3), 665-94. doi: 10.1348/000711010X502733

Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, Clarke M, Devereaux PJ, Kleijnen J, Moher D. (2009). The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. *PLoS Med, 6*(7), e1000100. doi: 10.1371/journal.pmed.1000100

Polanczyk G, de Lima McS, Horta BL, Biederman J, Rohde LA. (2007). The worldwide prevalence of ADHD: a systematic review and metaregression analysis. *The American journal of psychiatry, 164*(6), 942--8. doi: 10.1176/appi.ajp.164.6.942

Sciutto MJ, Eisenberg M. (2007). Evaluating the Evidence For and Against the Overdiagnosis of ADHD. *Journal of Attention Disorders, 11*(2), 106-13. doi: 10.1177/1087054707300094

Willcutt EG. (2012). The prevalence of DSM-IV attention-deficit/hyperactivity disorder: a meta-analytic review. *Neurotherapeutics : the journal of the American Society for Experimental NeuroTherapeutics, 9*(3), 490-9. doi: http://dx.doi.org/10.1007/s13311-012-0135-8