

# INPLASY PROTOCOL

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## The neural correlates of attention deficit hyperactivity disorder: an ALE meta-analysis

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**Review Stage at time of this submission:** Piloting of the study selection process.

**Conflicts of interest:**  
None declared.

**Review question / Objective:** The authors conducted a comprehensive meta-analysis of task-based functional magnetic resonance studies in children with attention deficit hyperactivity disorder (ADHD).

**Condition being studied:** Attention deficit hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder in children, with a global prevalence of approximately 5.2–7.2%. Although considered to be a childhood disease, it is reported that in most cases (approximately 65%), symptoms persist in adulthood. ADHD can result in poor educational performance, job unemployment, marital failure, crimes, and various mental illness, including personality disorder, self-harm, affective disorder, and drug abuse.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 May 2023 and was last updated on 11 May 2023 (registration number INPLASY202350046).

### INTRODUCTION

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**Condition being studied:** Attention deficit hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder in children, with a global prevalence of approximately 5.2–7.2%. Although considered to be a childhood disease, it is reported that in most cases (approximately 65%), symptoms persist in adulthood. ADHD can result in poor educational performance, job unemployment, marital failure, crimes, and various mental illness,

including personality disorder, self-harm, affective disorder, and drug abuse.

## METHODS

**Participant or population:** Attention deficit hyperactivity disorder children.

**Intervention:** None.

**Comparator:** Typical developing child.

**Study designs to be included:** Using task state functional magnetic resonance imaging (fMRI) methods.

**Eligibility criteria:** Studies were excluded if they 1) used a neuroimaging method other than fMRI; 2) included participants with ADHD symptoms but without a formal diagnosis of ADHD; 3) assessed the effect of medication without reporting fMRI data at baseline or after washout; 4) reported only within-group contrasts; 5) conducted a priori region-of-interest analyses (as these violate the assumption, under the null hypothesis, that the likelihood of locating activated foci is equal at every voxel); 6) reported only deactivations (this occurred in only one study [12], which was thus not comparable to the others); or 7) Under 18 years of age.

**Information sources:** Databases were search (PubMed, The Cochrane Library, Web of Science, EBSCO (MEDLINE, APA PsycInfo Em, base ERIC), , Scopus, and ProQuest, ) up until 20th March 2023. Reference lists of included studies will be scanned for further relevant literature. No restrictions will be placed on study design, sample size or language.

**Main outcome(s):** Based on the perspective that ADHD is a disorder reflecting dysfunction of large-scale neuronal systems , we interpreted abnormally activated brain regions from our meta-analysis as dysfunctional nodes of large-scale networks described in the current neuroscience literature.

**Quality assessment / Risk of bias analysis:** No appropriate tool exists for assessing

risk of bias in neuroimaging studies. However, due to results from ALE analyses being susceptible to dominance from individual large cohort studies, it may be necessary to conduct sensitivity analyses using the ‘Jackknife’ method or the ‘leave one out’ method.

**Strategy of data synthesis:** Aggregate data will be used for quantitative coordinate-based ALE meta-analyses. Analyses will be performed in Brainmap GingerALE version 3.02 We will adhere to the ALE method (<http://www.brainmap.org/ale/>) of Eickhoff et al. [1, 2] . A p value will be calculated for each voxel based on probabilities of attaining an ALE value which differed from that of the corresponding voxel on a null-distribution map, In all analyses, the threshold was set at  $p < 0.001$  uncorrected with an extent-threshold of 120 mm<sup>3</sup>.

[1] Eickhoff, S.B., et al. Human Brain Mapping, 2009. 30(9): p. 2907-2926

[2] Eickhoff, S.B., et al. Neuroimage, 2012. 59(3): p. 2349-2361.

**Subgroup analysis:** If evidence allows, consideration may be given to the following subgroups: Stimulant naïve participants, all tasks; Participants without comorbidities, all tasks; All participants, inhibition tasks; All participants, working memory tasks.

**Sensitivity analysis:** We will also do a sensitivity analysis removing studies with fewer than 10 participants. In the present paper.

**Country(ies) involved:** China; Republic of Korea.

**Keywords:** Attention deficit hyperactivity disorder; child; Executive Functions.

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