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Shared symptomatology between atopic dermatitis, ADHD and autism spectrum disorder: a protocol for a systematic scoping review

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ABSTRACT

Introduction Children with atopic dermatitis (AD) are more at risk for the neurodevelopmental disorders attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) with parallel increases in global prevalences. Children afflicted with these conditions appear to share similar problems in sensory modulation but investigational studies on the underlying aetiology are scarce. This scoping review aims to find knowledge gaps, collate hypotheses and to summarise available evidence on the shared pathophysiology of AD, ADHD and ASD in children.

Methods and analysis Our study will follow the methodological manual published by the Joanna Briggs Methodology for Scoping Reviews and will be reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses Extension for Scoping Reviews. The following electronic databases will be searched for studies focused on children with AD and symptoms of ADHD and/or ASD: Medline ALL via Ovid, Embase, Web of Science Core Collection and the Cochrane Central Register of Controlled Trials via Wiley.

Ethics and dissemination This review does not require ethics approval as it will not be conducted with human participants. We will only use published data. Our dissemination strategy includes peer review publication and conference reports.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This scoping review marks the pioneering attempt to explore the relation between atopic dermatitis, and symptoms of attention-deficit/hyperactivity disorder and autism spectrum disorder in children.
⇒ To ensure methodological rigour, we will collaborate with health sciences librarians to construct an established methodology and execute a systematic search, encompassing a wide spectrum of publication types.
⇒ The identification and synthesis of data will be limited to published articles found on the MEDLINE, Embase, Web of Science and Cochrane databases and snowball references.
⇒ Relevant articles in the grey literature or written in another language than English may be missed.

INTRODUCTION

Background

Atopic dermatitis (AD) is a common chronic inflammatory skin disorder characterised by pruritus and recurrent eczematous skin lesions affecting up to 20% of children in high-income countries.[1] Besides other atopic diseases such as allergic rhinitis, food allergies and asthma, children with AD are also more at risk for non-allergic comorbidities including infectious and systemic diseases, as well as neurodevelopmental disorders such as attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD).[2–4] Current studies on paediatric AD focus on the clinical treatment of the disease but there are still gaps in knowledge regarding aforementioned neurodevelopmental comorbidities. Complex pathomechanisms, involving both genetic and environmental factors, combined with global increases in prevalence of AD, ADHD and ASD in the past decades has led to many hypotheses on the underlying etiological associations between these conditions.[5–9]

ADHD is one of the most common neurodevelopmental disorders in children, characterised by symptoms of inattention, hyperactivity and impulsivity.[10] Children with ADHD often have sensory processing problems, which is the inability to effectively regulate and organise a graded and adaptive response to sensory stimuli.[11–13] Similar to ADHD, children with AD also exhibit symptoms of altered sensory processing, expressing sensory hyporeactivity or hyper-reactivity compared with controls.[14 15] Epidemiologically, individuals with AD are more at risk for ADHD with an estimated OR=1.32 (95% CI, 1.20 to 1.45) for all ages to OR=1.56 (95% CI, 1.38 to 1.77) in children and adolescents.[16 17]

ASD is a heterogeneous neurodevelopmental disorder, encompassing former diagnoses such as autistic disorder, Asperger syndrome and pervasive developmental disorder not otherwise specified.[18] Traits displayed by diagnosed individuals include persistent difficulties with social communication and interaction, and the presence of restricted and repetitive patterns of behaviour from an early developmental period.[18 19] Comparable to both AD and ADHD, children with ASD have also been found to have more sensory hyporeactivity or hyper-reactivity symptoms.[20] The risk for developing ASD in individuals with AD has been estimated to be OR=1.49 (95% CI 1.20 to 1.83) in all ages to OR=2.57 (95% CI 1.47 to 4.51) in children and adolescents.[17 21] Moreover, children with ASD with AD may have more pronounced ASD symptoms overall and on the social domain outcomes, relative to children with ASD without AD.[22]

Due to the parallel rises in the global prevalences of AD, ADHD and ASD, an increasing interest among many research groups emerges for the potential influence of atopic diseases on the skin–brain axis within the field of neurodevelopment.[17 22] A positive association between paediatric AD and the neurodevelopmental disorders ADHD and ASD has consistently been found in epidemiologic studies,[17] but studies on the underlying pathophysiological mechanisms are scarce, leaving an ambiguous underlying interplay between dermatological, neurodevelopmental, and behavioural elements.

Objectives

The main goal for this proposed scoping review is to provide an extensive overview on the shared symptomatology between paediatric AD, and ADHD and ASD, and to highlight knowledge gaps regarding this matter. Extracted data will be mapped according to the following research questions:

1. What are mutual traits in AD, ADHD and ASD?
2. What are current hypotheses for the shared symptomatology of AD, ADHD and ASD?
3. What are gaps in the current evidence for a potential underlying shared aetiology of AD, ADHD and ASD?

METHODS AND ANALYSIS

Scoping review

Scoping reviews allow for the exploration of broad research questions with the goal of discovering key concepts, theories and knowledge gaps in an upcoming field. The aim of this study is to provide a comprehensive overview of etiological theories on overlapping traits between paediatric AD and neurodevelopmental comorbidities ADHD and ASD, and to map, report and discuss the concepts in current literature. Due to the broad research question and the exploratory nature of this study on an emerging field of interest with great heterogeneity in literature, we expect a scoping review to be more suitable than a systematic review.[23]

This scoping review will follow the methodological manual published by the Joanna Briggs Methodology for Scoping Reviews and will be reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR).[24 25]

Inclusion criteria

Participants

Children and adolescents <18 years old must have been diagnosed with AD by a healthcare provider. Additionally, subjects either must have a diagnosis or documented signs or symptoms of ADHD and/or ASD, as identified through validated psychological measuring instruments by a healthcare provider, parent, teacher or as self-reported. Studies solely focusing on sleeping problems, cognitive functioning or school performance were excluded. Peer-reviewed primary and secondary studies in children and adolescents under the age of 18 that were published in English between 1 January 1946 and 1 June 2024, will be eligible for inclusion. Translational research and theoretical studies on AD and ADHD and/or ASD are eligible. Studies with a mix of both children and adults will be excluded, unless separate data for children are provided. Exclusion criteria are non-peer-reviewed publications such as textbooks, commentaries, dissertations, and conference abstracts.

Search strategy

The search strategy will be developed by an information specialist (CN). The following databases will be searched from inception until August 2023: Medline ALL in Ovid, Embase, Web of Science Core Collection and the Cochrane Central Register of Controlled Trials via Wiley.

An exemplary search string for Medline:

(exp *'Eczema'/ OR exp *'Dermatitis, Atopic'/ OR *'Pruritus'/ OR (eczema* OR ((atopic*) ADJ3 (dermatit* OR neurodermat*)) OR eczematous* OR prurit* OR itch*).ti.) *AND* ('Attention Deficit Disorder with Hyperactivity'/ OR (((attention*) ADJ3 (deficit*) ADJ3 (disorder*)) OR ((attenti* OR concentrat*) ADJ3 (defici*)) OR ADHD).ti.) *AND* (exp 'Child'/ OR exp 'Infant'/ OR 'Adolescent'/ OR exp 'Paediatrics'/ OR (adolescent* OR teenager* OR child* OR toddler* OR boy OR boys OR girl OR girls OR infant OR infants OR baby OR babies OR newborn* OR paediatric* OR paediatric*).ab,ti,kf.)

For the full search strategy, see online supplemental file S1. The search will be supplemented by forward and backward citation searches of all included papers.

Study selection

After removal of duplicates from the initial search, two reviewers (NTN and AR) will independently screen all articles on title and abstract for potential eligibility using Rayyan Software.[26] Potentially eligible articles that answer any of the research questions will be read in full. References from included articles will be manually screened for additional eligible articles. Any differences and discussions will be resolved by a third author (RS) and justified in a group meeting with all the authors. The study

selection process will adhere to recommendations in the PRISMA-ScR checklist.[24]

Data extraction

Data from the final articles that will be included in this scoping review will be independently added into an electronic standardised template by two researchers (NTN and AR), see also online supplemental file S2. This form will include at least the following: author, year of publication, title, design, study aim, country and characteristics of study population such as age, sex, ethnicity, socioeconomic status and use of ADHD medication. Measures of AD, ADHD, ASD diagnosis or symptoms (either clinically diagnosed, self-reported, retrospective or structured assessments and questionnaires) will be extracted. Any discrepancies or uncertainties during the data extraction process will be discussed and resolved by the entire study team.

Presentation of results

The search results and study selection process will be presented in a flow chart following the PRISMA statement.[27] Extracted data from included studies will be mapped to each of the relevant research questions in a tabular format and graphically if needed. A narrative summary will accompany the tabulated or charted results and will describe how the results relate to the review objectives and questions. This study will be conducted from June 2024 and is expected to finalise in October 2024.

Patient and public involvement

No patients were involved in developing this protocol. No involvement from patients, nor from the general public will be pursued for this scoping review.

ETHICAL CONSIDERATIONS

Due to the nature of this study, there are no ethical or safety considerations to be made. Approval by a local ethics committee is therefore not needed. Findings will be disseminated widely through a peer-reviewed publication and conference reports.

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Contributors NTN, AR and RS conceived the study and NTN and AR were in charge of overall direction, planning and writing this protocol. NTN, AR, ABR, TN and RS will contribute to the analysis of the results and to the writing of the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

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