Review paper

Heart rate asymmetry in children: a scoping review

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Abstract

Heart rate asymmetry (HRA) is a nonlinear measure reflecting unequal contributions of heart rate decelerations and accelerations to heart rate variability (HRV). This scoping review, conducted in line with the PRISMA extension for Scoping Reviews (PRISMA-ScR) guidelines, aimed to summarize current evidence on HRA in pediatric populations. A systematic search of PubMed, Scopus, Web of Science, Embase, and Google Scholar (2000–2025) identified four eligible studies involving 192 children aged 3–18 years, including healthy individuals and those with attention deficit/hyperactivity disorder (ADHD), depression, or cardiac conditions. All studies were single-center and used electrocardiography (1000 Hz); one used 24-hour Holter monitoring, whereas the others used 5-minute recordings. One study also used a Pneumonitor (250 Hz). HRA was assessed using Porta's index, Guzik's index, and Ehlers' index. Some studies included orthostatic testing. The findings suggest HRA may help detect neurocardiac dysregulation in both healthy children and those with specific diagnoses and may serve as a prognostic tool. Further research is needed to confirm its clinical relevance.

Introduction

Dysfunctions of the autonomic nervous system (ANS) frequently manifest in pediatric patients with specific diagnoses, including cardiac conditions [1–3]. The ANS regulates many involuntary bodily functions, such as the modulation of heart rate (HR). The fluctuation in the time intervals between successive RR intervals (RRi) originating from sinus rhythm, measured in milliseconds, is known as heart rate variability (HRV) [4]. HRV is extensively used as a non-invasive method for the clinical assessment of autonomic regulation due to the association between ANS activity and HRV [5]. HRV arises from fluctuations in RRi resulting from variations in HR accelerations (AR) and decelerations (DR). These variations in HR contribute differentially to short-term, long-term, and total HRV, resulting in a phenomenon known as heart rate asymmetry (HRA). The HRA concept, as elucidated in studies by Guzik (2006), Piskorski (2007, 2011) and Porta (2008), may provide a novel framework for investigating the cardiovascular system and its interactions with ANS [6–9]. Guzik and Piskorski proposed two principal domains for HRA analysis:

1) assessment of the contributions of AR (a) and DR (d) to short-term (SD1) and long-term (SD2) variability, expressed as the percentage of the cumulative distance of points; and

2) analysis of monotonic runs of AR, DR, and neutral changes.

Within short-term variability, the authors defined the indices C1a and C1d (Guzik's index – GI) as the relative contributions of AR (SD1a) and DR (SD1d) to the total SD1 variance. Analogously, for long-term variability they defined C2a and C2d as the relative contributions of AR (SD2a) and DR (SD2d) to the SD2 variance. The Porta index (PI) is based on the percentage of negative RRi_ii differences (points below the line of identity in the Poincaré plot) relative to all points not lying on that line [6–9].

Short series of HRA could be valuable for evaluating the risk of long-term mortality from any cause, as well as specifically from cardiovascular-related causes. HRA has been documented in adult populations [6, 10–12]. HR DR have a greater impact on short-term HRV and a lesser impact on long-term and total HRV in electrocardiography (ECG) recordings of varying lengths in adults [6, 7, 9, 13–15]. Furthermore, the phenomenon of HRA exists, where the increased contribution of HR DR to short-term HRV balances out the greater influence of HR AR on long-term HRV [13].

In pediatric populations, HRA was observed in a group of healthy children [16], children with untreated major depressive disorder (MDD) [17], children with attention deficit/hyperactivity disorder (ADHD) [18], and children with cardiac conditions [19].

This study aimed to review the existing findings of HRA in pediatric patients.

Table 1. Search strategies for scoping review

Concept	Search terms
Heart rate asymmetry in children	(„heart rate asymmetry"[Title/Abstract]) AND („children"[Title/Abstract])
Heart rate asymmetry and patients	(„heart rate asymmetry"[Title/Abstract]) AND („patients"[Title/Abstract])

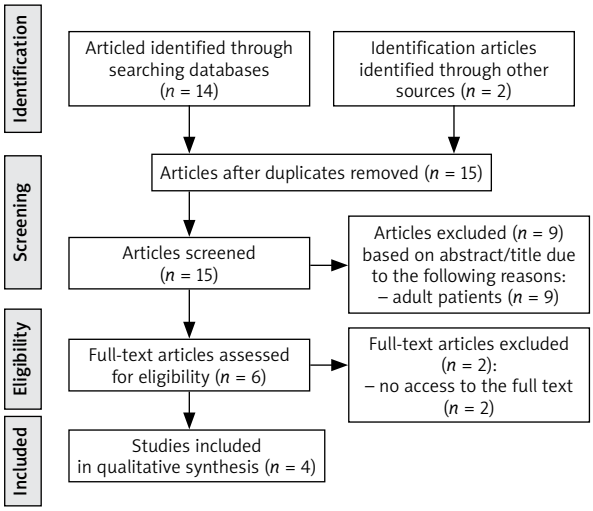

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for the search process

Methods

This scoping review investigated HRA in children. The study adheres to the PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) guidelines, the most widely accepted reporting framework for scoping reviews, thereby ensuring transparency and methodological rigor [20, 21]. The PRISMA-ScR checklist has been provided as supplementary material. A comprehensive literature search was performed in April 2025 using electronic databases, including PubMed, Scopus, Web of Science, Embase and Google Scholar, to identify studies published between 2000 and 2025. The search strategy incorporated Medical Subject Headings (MeSH) terms and Boolean operators (AND, OR) to enhance specificity. In Google Scholar, the first 150 results (equivalent to the first 15 results pages) were screened using a predefined stopping rule: screening was discontinued once consecutive records no longer met the inclusion criteria or were clearly irrelevant to HRA or pediatric populations. The inclusion criteria were restricted to English-language publications. Additional relevant articles were sourced through manual examination of reference lists. Two independent researchers determined the search terms to ensure exhaustive inclusion of pertinent studies (Table 1). The inclusion criteria for this scoping review were delineated using the PICO framework. Eligible studies in English focused on HRA in healthy children or those with specific diagnoses, aged 0–18 years. Comparative studies evaluating differences between HRA in children with specific diagnoses and healthy children were also considered when available. Studies that exclusively focused on adult populations were excluded from this review. Additionally, grey literature, including conference proceedings, dissertations, and unpublished studies, was not considered. Furthermore, studies not available in English or lacking a reliable translation were excluded. Two independent researchers (I.W., J.G.) conducted an initial screening of the titles and abstracts of the retrieved studies. Subsequently, the full texts of the selected articles were meticulously reviewed. Any discrepancies between the researchers were resolved through deliberation with a third reviewer (B.W.).

Results

Study selection

Our database search identified 16 studies. After removing duplicates, we screened the remaining 15 studies, and only 6 were eligible for full-text retrieval. Ultimately, only 4 studies met our inclusion criteria and were included in the review [16–19] (Figure 1).

Study characteristics

The studies included in this review reported data on a total of 192 pediatric subjects: 136 healthy, 20 diagnosed with ADHD, 20 with MDD, 5 with congenital heart disease, 4 with cardiac arrhythmia, and 7 with cardiomyopathy. The age of participants ranged from 3 to 18 years. In 2 of the included studies, the experimental group was compared to an age-matched cohort of children serving as the control group. All studies were conducted at a single center. Summaries and detailed baseline characteristics of the included studies are provided in Table 2.

RRi recordings

Details concerning RRi acquisition are provided in Table 2. ECG recordings are considered the gold standard for acquiring RRi for HRV analysis. In one of the included studies, long-term recordings were performed using 24-hour ECG (Holter monitoring) with a 1000 Hz sampling frequency [16]. Three studies used 5-minute short-term RRi recordings obtained via ECGs with a 1000 Hz sampling frequency [17–19]. Additionally, one study employed both ECG and an alternative device, the Pneumonitor, with a 250 Hz

Table 2. Detailed data from studies included in the literature review on heart rate asymmetry in children

First author, year of publication [Ref.], type of study	Aim of the study	Experimental group	RRi acquisition	Software for RRi acquisition, sampling frequency, and duration of recordings	Conclusions
Tonhajzerova *et al.*, 2012 [17], case-control observational study	Study of HR time irreversibility, a nonlinear characteristic of HRV, indicating cardiac autonomic control complexity	*N* = 40 (40 ♀) Age: 15–18 years Diagnosis: never-treated MDD Groups: Study group – *n* = 20 with MDD Control group – *n* = 20 healthy age-matched girls Exclusion criteria: a history of disorders affecting HRV, including cardiovascular, respiratory, endocrinological, neurological, infectious conditions, as well as obesity, weight issues, alcohol and drug abuse and smoking	Instructions: Avoid caffeine and alcohol for at least 12 hours before the recording. Empty bowel and bladder before the examination. Lie down comfortably and avoid speaking or moving unless necessary Time of the day: between 8:00 and 11:30 a.m. after a normal breakfast consumed 2 h prior Room: quiet room with standard temp. of 23°C and minimalization of stimuli Rest before the recording: 15 min	Software: ECG VorCorPF6 (Dimea, CZ) Sampling: 1000 Hz Duration: 5 min in both positions Position: I supine II postural change from lying to standing (orthostasis) Artifact correction: manually HRA analysis: Indices (Porta's, Guzik's, Ehlers')	HRA is disrupted in never-treated adolescent girls with MDD at rest, suggesting intricate autonomic dysregulation. Exploring the link between depression and cardiac dynamics through nonlinear methods may elucidate essential pathophysiological aspects. Assessing HRA could aid in identifying neurocardiac dysregulation in adolescent MDD, potentially acting as a prognostic indicator for future adverse cardiac events.
Tonhajzerova *et al.*, 2014 [18], case-control observational study	Study of HR time asymmetry as a nonlinear qualitative feature of HRA indicating complexity of cardiac autonomic control	*N* = 40 (40 ♂); Age: 8–12 years Diagnosis: ADHD Groups: Study group – *n* = 20 with ADHD Control group – *n* = 20 healthy age-matched boys Exclusion criteria: As above	Instructions: No data Time of the day: between 8:00 and 12:00 a.m. after a normal breakfast consumed 2 h prior Room: quiet room with standard conditions (temp., minimization of stimuli) Rest before the recording: 10 min	Software: VorCorPF6 (Dimea, CZ) Sampling: 1000 Hz Duration: 5 min in both positions Position: supine position and postural change from lying to standing (orthostasis) Artifact correction: manually HRA analysis: Indices (Porta's, Guzik's, Ehlers')	Altered HRA is observed in children with ADHD, both at rest and during orthostatic challenge (posture change from lying to standing). These findings suggest a potential deficiency in the complex cardiac regulatory system, which may contribute to future adverse cardiac outcomes. Nonlinear analysis of HRV based on HR irreversibility could serve as a novel indicator to elucidate the connection between neurocardiac integrity and ADHD in untreated children without comorbidities.
Zalas *et al.*, 2023 [16], cross-sectional observational study	Analysis of the presence and expression of short-, long-term, and total HRA in 24-h Holter ECGs Study the presence of HRA compensation in children Comparison of the expression and rate of HRA and HRA compensation between girls and boys Exploration of the association between age and HRA	*N* = 96 (50 ♀, 46 ♂) Age: 3–18 years Diagnosis: none, healthy children Exclusion criteria: additional medical conditions, ≥ 100/hour of supraventricular and ventricular extrasystoles, pairs or tachycardias, pathological bradycardia, non-sinus rhythm, atrioventricular conduction disturbances, or < 90% sinus rhythm on 24-hour ECG Holter monitoring	Instructions: No data Time of the day: No data Room: No data Rest before the recording: No data	Software: Holter monitoring – Medilog Darwin 2, 3-channel (Schiller, CH) Sampling: 1000 Hz Duration: min 18 h (included night hours) Position: N/A Artifact correction: manually HRA analysis: HRAExplorer (v. 1.55) developed by Piskorski and Guzik	HRA is present in 88% of healthy children aged 3–18 years, based on 24-hour ECG recordings. Short-term HRA is more pronounced in boys, but overall prevalence shows no gender differences. Long-term and total HRA increase with age. Further research is required to understand HRA mechanisms and clinical significance in children.

Table 2. Cont.

First author, year of publication [Ref.], type of study	Aim of the study	Experimental group	RRi acquisition	Software for RRi acquisition, sampling frequency, and duration of recordings	Conclusions
Gąsior *et al.*, 2024 [19], cross-sectional observational study, validation study	Assessment of the validity of Pneumonitor for acquisition and analysis of short-term RRi in the context of HRA in comparison to ECG Analysis of the association between HRA parameters and RespRate	*N* = 16 (6 ♀, 10 ♂) children Age: 7–18 years Diagnosis: congenital heart disease (*n* = 5), cardiac arrhythmia (*n* = 4), cardiomyopathy (*n* = 7) Exclusion criteria: infection, change in medications in the last 3 months (in cases of constant pharmacological treatment)	Instructions: Abstain from physical activity the day before and the day of the study. Avoid junk food, sugary drinks, and snacks. Use the toilet before examinations if necessary Time of the day: between 8:00 a.m. and 2:00 p.m. at least one hour after breakfast Room: hospital room with stable, controlled temperature and humidity Rest before the recording: No data	Software: PC ECG – Custo cardio 100, 12-channel (DE) Pneumonitor (academically developed) records RRi, RespRate and tidal volume equivalent Sampling: ECG 1000 Hz, Pneumonitor 250 Hz Duration: 5 min Position: stationary Artifact correction: manually HRA analysis: HRAExplorer (v. 1.55) developed by Piskorski and Guzik	HRA should be analyzed before conducting HRV analysis. The Pneumonitor is considered valid for recording RRi, which can then be used to calculate time- and frequency-domain HRV parameters, as well as selected HRA parameters, and consequently cardiorespiratory coupling, in pediatric cardiac patients at rest. However, it is important to note that RRi recorded with devices having a sampling frequency lower than 250 Hz may not be adequate for reliable HRA analysis.

ADHD – attention deficit hyperactivity disorder, HRA – heart rate asymmetry, HR – heart rate, HRV – heart rate variability, MDD – major depressive disorder, RespRate – respiratory rate, RRi – R–R interval.

sampling frequency, for RRi acquisition [19]. Two studies provided detailed information about when the data were collected, the room conditions during the study, and the circumstances before the recordings. In all four studies, short-term recordings were made while participants were lying down. Additionally, in two of these studies, recordings were made during the transition from lying down to standing (orthostasis).

HRA analysis

For HRA analysis, Porta's, Guzik's, and Ehlers' indices were quantified in two studies, while the freely available HRAExplorer software, developed by Piskorski and Guzik, was used in two other studies. This software is accessible at https://hraexplorer.com [7].

Discussion

This study reviewed HRA findings in pediatric patients. Linear methods for HRV analysis are inadequate for capturing the complex dynamics of HR. Consequently, advanced nonlinear methodologies are being increasingly employed to quantify qualitative characteristics such as HR complexity, asymmetry, and recurrent patterns in HR dynamics [22]. HRA may help identify neurocardiac dysregulation in both healthy children and those with specific diagnoses; however, its prognostic relevance for future adverse cardiac events remains unconfirmed and requires larger, preferably multicenter, prospective studies.

HRA is present in 88% of healthy children aged 3–18 years, based on 24-hour ECG recordings. Short-term HRA is more pronounced in boys, but overall prevalence shows no gender differences. Long-term and total HRA increase with age [16].

In adolescent girls with untreated MDD, HRA is disrupted at rest, indicating complex autonomic dysregulation. Nonlinear methods examining the link between depression and cardiac dynamics may reveal important pathophysiological details. Evaluating HRA might help detect neurocardiac dysregulation in adolescents with MDD and might, pending further validation, potentially serve as a prognostic marker for future adverse cardiac events [17]. Adolescence is a critical period when depression can impair neurocardiac control due to developmental changes [23]. This makes adolescence a key period for studying heart function in depression and preventing potential cardiac complications [24].

Similarly, children with ADHD show altered HRA both at rest and during orthostatic challenges (posture change from lying to standing). These findings suggest a deficiency in the cardiac regulatory system, which may lead to future adverse cardiac outcomes. Nonlinear analysis of HRV based on HR irreversibility may clarify the relationship between neurocardiac

integrity and ADHD in untreated children without comorbidities [18].

Importantly, HRV study authors should adhere to methodological guidelines to ensure comparability [25]. Many studies lack detailed information on RRi acquisition timing, room conditions, pre-recording periods, patient positioning, and recording duration.

Limitations

Although the manuscript employed a narrow search strategy, additional screening using related concepts (e.g., heart period asymmetry, Poincaré plot asymmetry, time irreversibility, acceleration/deceleration asymmetry) and broader pediatric age descriptors (e.g., adolescent, youth) did not change the number of eligible studies. Nevertheless, future reviews should employ broader, synonym-inclusive search queries and explicitly incorporate specific index names to increase search sensitivity and completeness.

Conclusions

HRA may help identify neurocardiac dysregulation in both healthy children and those with specific diagnoses and might have prognostic value for future adverse cardiac events. Researchers conducting HRV studies should adhere to methodological guidelines and recommendations, as this would facilitate direct comparisons between their studies. Further research is needed to understand HRA mechanisms and clinical relevance in pediatric populations, ideally in larger, multicenter, prospective cohorts.

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Ethical approval

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Conflict of interest

The authors declare no conflict of interest.

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