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ORIGINAL PAPER

Vestibular Function in Children with Neurodevelopmental Disorders: A Systematic Review

Ruth Van Hecke[1] · Maya Danneels[1] · Ingeborg Dhooge[2,3] · Hilde Van Waelvelde[1] · Jan R. Wiersema[4] · Frederik J. A. Deconinck[5] · Leen Maes[1,2]

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Abstract

This review was performed to investigate the characteristics of vestibular dysfunctions in children with neurodevelopmental disorders (NDDs). The majority of the included studies reported central and/or peripheral vestibular aberrations in a subset of these children. These alterations may result in symptoms of distorted motor coordination or postural instability, and might explain some of the balance problems observed in this population. However, high-quality studies with an extensive vestibular test battery are required to further characterize the vestibular function in NDDs since current findings are ambiguous and mainly based on evaluation of the horizontal semicircular canals alone. Importantly, since vestibular dysfunctions may result in comparable characteristics as found in NDDs, clinicians should be aware of these similarities when establishing the NDD diagnosis.

Keywords Systematic review · Vestibular function · Neurodevelopmental disorders · Children

While the clinical features and consequences of a vestibular dysfunction in adults are frequently discussed, vestibular failure in childhood has less often been described and only gained more attention the last few decades. However, the overall reported prevalence of vertigo and dizziness in children is as high as 0.5–15% (Humphriss and Hall 2011; Jahn et al. 2011; Gioacchini et al. 2014; Jahn 2016; Li et al. 2016; Wiener-Vacher et al. 2018) and is probably even underreported (Weiss and Phillips 2006; Rine 2009; Antoine et al. 2017). Children are often not able to communicate their complaints properly and a vestibular dysfunction often has a different clinical course compared to that in adults. In addition, vestibular examination in this population can be quite difficult, as these tests require cooperation, alertness and test conditions that may be frightening for children (e.g. some vestibular assessments have to be performed in the darkness in order to eliminate visual suppression of vestibular responses). Therefore, making a diagnosis in this population is challenging and often based on a parent's report, which might suggest that the prevalence remains underestimated (Casselbrant and Mandel 2005; Medeiros et al. 2005; Maes et al. 2014).

A severe peripheral vestibular dysfunction may have a significant impact on quality of life (Mendel et al. 1999; Zingler et al. 2009; Guinand et al. 2012; Sun et al. 2014; van de Berg et al. 2015). When a vestibular dysfunction occurs at birth or in early stages of life, one might expect that it may be even more debilitating compared to when it occurs in adulthood (Byl et al. 1989; Medeiros et al. 2005; Rine and Wiener-Vacher 2013; Cushing and Papsin 2018). In recent years, there has been growing attention and evidence that a congenital or early acquired vestibular problem may considerably influence children's development at many levels.

Firstly, the vestibular system is known to be involved in various *motor tasks* and contributes to the *maintenance of postural stability*. This is perhaps not surprising given the primary role of the three semicircular canals and two otolith

✉ Ruth Van Hecke
ruth.vanhecke@UGent.be

1 Department of Rehabilitation Sciences, Ghent University, Corneel Heymanslaan 10, 9000 Ghent, Belgium

2 Department of Otorhinolaryngology, Ghent University Hospital, Corneel Heymanslaan 10, 9000 Ghent, Belgium

3 Department of Head and Skin, Ghent University, Corneel Heymanslaan 10, 9000 Ghent, Belgium

4 Department of Experimental Clinical and Health Psychology, Ghent University, Henri Dunantlaan 2, 9000 Ghent, Belgium

5 Department of Movement and Sports Sciences, Ghent University, Watersportlaan 2, 9000 Ghent, Belgium

organs in providing information about rotational and translational head movements relative to gravity. In case of a severe vestibular dysfunction in children, several studies found an association with poor motor development and delayed psychomotor milestones, especially in gross motor functions like head control, independent walking and sitting (Kaga et al. 1988; Kaga 1996; De Kegel et al. 2012; Wiener-Vacher et al. 2012; Inoue et al. 2013). Later in life, these children are known to have a greater step width during gait, which is reflective of balance problems. This unsteadiness exacerbates when the other sensory input systems are challenged, e.g. walking in the dark or on uneven surfaces (van de Berg et al. 2015; Strupp et al. 2016). In contrast, knowledge of the influence of a partial or unilateral dysfunction on a child's postural development is still lacking.

Secondly, *fine motor skills* may be related to vestibular function too. A well working vestibulo-ocular reflex (VOR), responsible for gaze stabilization, is crucial for an optimal eye-hand coordination and therefore necessary for several fine motor performances (Ottenbacher et al. 1984; Cohen and Keshner 1989; Ayres et al. 2005; Wiener-Vacher et al. 2013). As diagnosing vestibular failure in children is challenging, children presenting these secondary motor dysfunctions are often incorrectly labeled as clumsy or only having poor fine or gross motor coordination (Casselbrant and Mandel 2005; Rine 2009; McCaslin et al. 2011; O'Reilly et al. 2011; Maes et al. 2014).

Thirdly, although past research has mainly focused on adults, it has been suggested that a vestibular dysfunction may influence a child's *cognitive development* as well (Wiener-Vacher et al. 2013; Besnard et al. 2015; Bigelow and Agrawal 2015). In vestibular-impaired adults, cognitive symptoms (e.g. loss of concentration, inability to multitask, short-term memory loss or extreme fatigue) frequently occur in addition to the more typical vestibular symptoms (e.g. vertigo and imbalance) (Jacob et al. 1996; Jacob and Furman 2001; Yardley et al. 2001; Black et al. 2004; Bigelow and Agrawal 2015). The appearance of these cognitive symptoms has been explained by the cognitive-motor interference to ensure adequate gaze stabilization or balance (Kahneman 1973; Nascimbeni et al. 2010; Gurvich et al. 2013; Bigelow and Agrawal 2015) and has been related to the extensive vestibular projections throughout the cerebral cortex and subcortex (Barmack 2003; Lopez and Blanke 2011; zu Eulenburg et al. 2012; Gurvich et al. 2013; Stiles and Smith 2015; Frank and Greenlee 2018; Brandt and Dieterich 2019), especially the connection with the hippocampus, playing a prominent role in visuo-spatial memory and self-perception of position and movement in the environment (Maguire et al. 2000; Burgess et al. 2002; Brandt et al. 2005; Hanes and McCollum 2006; Hitier et al. 2014; Bigelow and Agrawal 2015; Kremmyda et al. 2016; Popp et al. 2017; Smith 2017). In children, evidence on the vestibular involvement in cognition is currently lacking, however, several studies suggested that the cognitive-vestibular interactions found in adults may be extrapolated to the pediatric population and that adequate cognitive development is heavily reliant upon accurate sensory input, including vestibular function (Wiener-Vacher et al., 2013; Besnard et al. 2015; Bigelow and Agrawal 2015; Cushing and Papsin 2018).

Since the abovementioned skills are important for scholastic achievement, *educational development* may be affected too, which have been suggested by the following studies in the pediatric population. When the VOR is lacking in a severe vestibular dysfunction, oscillopsia or an unstable gaze will occur while moving the head. As oscillopsia is associated with an impaired visual acuity (Tilikete and Vighetto 2011), vestibular-impaired children can be expected to have difficulties with drawing, writing and reading, resulting in a sloppy handwriting and impaired reading performances compared to the performances seen in their peers (Braswell and Rine 2006; Rine and Wiener-Vacher 2013; Wiener-Vacher et al. 2013; Janky and Givens 2015). In addition, visuo-spatial skills, which are thought to be strongly related to the vestibular system, are necessary for other scholastic achievements like mathematics and other non-spatial disciplines where spatial relationships are involved (e.g. syntax, biology, geography etc.) (Szucs et al. 2013; Wiener-Vacher et al. 2013; Cornu et al. 2018). Just as with motor deficits, if the vestibular dysfunction stays undiagnosed, these manifestations may erroneously be labeled as attention deficits and poor cognitive and educational capacities.

Lastly, the vestibular system is very closely related to *emotional and social behavior*, and vestibular-impaired children may, as adults, develop affective symptoms (e.g. anxiety and depression) due to the substantial consequences of a vestibular dysfunction (Reale et al. 2011; Gurvich et al. 2013; Lee et al. 2014; Jahn et al. 2015). In addition, the incomprehension of vestibular symptoms and the sustained cognitive demand for gaze and postural stabilization may lead to avoidance behavior, lower self-esteem, anxiety (of movement), angriness or frustration (Bart et al. 2009; Lee et al. 2014; Kreivinienė 2016). Furthermore, emerging evidence suggests that the vestibular system has reciprocal projections with neural networks involved in social cognitive and emotional processing (Gurvich et al. 2013; Deroualle and Lopez 2014). Again, since vestibular disorders in young children are often dismissed by professionals, symptoms may consequently be attributed to behavioral problems (e.g. autism-related symptoms, ways to draw attention, signs of overactive behavior, lack of empathy).

In summary, a vestibular dysfunction is associated with a range of problems, which may affect motor, cognitive, and behavioral development and which tend to overlap with symptoms found in neurodevelopmental disorders (NDD)

(O'Reilly et al. 2011). Neurodevelopmental disorders are, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM 5th edition), a heterogeneous group of psychiatric conditions arising early in life and characterized by abnormalities in the development of the central nervous system, which can lead to emotional and behavioral problems and impairments in psychological, social, academic and occupational functioning (American Psychiatric Association 2013; World Health Organization 2018). Since a standard neuro-clinical examination often does not include a vestibular screening, it remains unclear to what extent symptoms like poor coordination, attention difficulties, reading disability or lack of empathy may be linked to a vestibular dysfunction. On the other hand, in literature it is already suggested that children with NDDs have more difficulties in static and dynamic balance than typically developing children (Brookes et al. 2010; Fournier et al. 2010b; Enkelaar et al. 2012; Blomqvist et al. 2013; Liu et al. 2015; Bucci et al. 2016; Mitsiou et al. 2016). Most of these studies have based their suggestions on postural and sensory organization tests. However, literature concerning whether these balance problems are accompanied with a (peripheral) vestibular dysfunction which may contribute to the phenotype or behavioral features of these NDDs is rather scarce.

To examine the potential link between vestibular function and neurodevelopmental disorders and to investigate the presence and characteristics of vestibular dysfunctions in this population, a systematic review was performed.

Methods

This systematic review is reported following the international Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Liberati et al. 2009).

Search Strategy

A systematic literature search was performed using the following electronic databases: MEDLINE (PubMed), EMBASE and Cochrane Register of Controlled Trials (CENTRAL). According to the guidelines, the search strategy and eligibility criteria were derived from the Population, Intervention/Exposure, Comparison and Outcomes (PICO/PECO) structure. Articles were required to assess vestibular function (E/O) in children younger than 18 years old, diagnosed with a neurodevelopmental disorder (P) (American Psychiatric Association 2013). Vestibular function tests were defined as specific tests used in clinical settings, which measured (at least) the function of the peripheral vestibular system. Therefore, studies using oculomotor tests alone were not sufficient to be rated as eligible studies. Because of the limited amount of data in this research topic, all types of group designs (C and S) were accepted. The Medical Subject Heading (MeSH) terms, represented in Table 1, completed with all their subheadings, their free text word variants and synonyms, were used in the MEDLINE search, and were adapted appropriately for each database.

Study Selection

Eligibility of the search results was assessed by applying the abovementioned selection criteria. Additionally, only human studies in English were accepted and duplications of data published in other included papers were excluded. Firstly, title and abstract of all retrieved articles were screened, followed by a full-text screening of the selected articles. If the study did not correspond to the selection criteria, the article was excluded. In addition, the reference lists of the eligible studies were hand searched in order to prevent missing useful citations. The literature search and screening procedure was conducted by two independent researchers (RVH and MD), with calculation of Cohen's Kappa score (Landis and Koch 1977) to determine the level of interrater agreement. Disagreements between the two reviewers were resolved by consensus. If consensus could not be reached, a decisive opinion was provided by a third researcher (LM). The cut-off date for articles to be included was September 2018.

Data Extraction

For each article included in this review, the following data were extracted: characteristics of the study (author, publication year, study design), of the study population (number of participants, mean age (or range if the average was not determined), gender, diagnosis, used diagnostic criteria, and additional comorbidities), the control group, the study methodology (used vestibular function tests), and vestibular outcome data.

Risk of Bias Assessment

All included papers were critically evaluated for methodological quality using the Newcastle–Ottawa Scaling (NOS) for nonrandomized studies (Herzog et al. 2013; Wells et al. 2014) or the modified form for cross-sectional studies (Modesti et al. 2016). In this scale, papers are judged on eight items, categorized into three groups of methodological study parameters: selected population (four items), comparability of groups (one item), and assessment of either the exposure or outcome of interest (three items). According to the scales, each study was assigned an overall score from 0 to 9 (case control or cohort studies) or 10 (cross-sectional studies), with a higher score indicating higher quality. To make a comparison of the included studies, studies with a cumulative score of 7 or more were arbitrary considered as

Table 1 The used MeSH terms in the search strategy

Population		Exposure/outcome
("child"[MeSH] OR "adolescent"[MeSH]) **AND** ("Neurodevelopmental Disorders"[MeSH] OR "Communication Disorders"[MeSH] OR "Neuropsychological Tests"[MeSH] OR "Attention"[MeSH] OR "Executive Function"[MeSH] OR "Memory"[MeSH] OR "Cognitive Reserve"[MeSH] OR "Space Perception"[MeSH] OR "Spatial Navigation"[MeSH] OR "Depth Perception"[MeSH] OR "Imagination"[MeSH] OR "Cognition"[MeSH] OR "Neurocognitive Disorders"[MeSH] OR "Orientation"[MeSH] OR "Memory Disorders"[MeSH] OR "Motion Perception"[MeSH] OR "Thinking"[MeSH] OR "Learning Disorders"[MeSH] OR "Postural Balance"[MeSH] OR "Psychomotor Disorders"[MeSH] OR "Psychomotor Performance"[MeSH] OR "Motor Activity"[MeSH] OR "Locomotion"[MeSH])	**AND**	("Labyrinth Diseases"[MeSH] OR "Bilateral Vestibulopathy"[MeSH] OR "Vestibular Evoked Myogenic Potentials"[MeSH] OR "Vestibular Function Tests"[MeSH] OR "Head Impulse Test"[MeSH] OR "Electronystagmography"[MeSH] OR "Reflex, Vestibulo-Ocular"[MeSH] OR "Pursuit, Smooth"[MeSH] OR "Nystagmus, Optokinetic"[MeSH])

relatively high quality studies, 4–6 to be of moderate quality, and less than 4 to be of low quality (Chen et al. 2018; Grgic et al. 2018). Due to the limited existing literature on this topic, the overall methodological quality score was not used as criterion for eligibility. However, bias assessment was conducted to enhance the consistency of the results and to reveal further information about flaws in the literature.

Results

Study Selection and Characteristics of the Included Studies

A total of 2509 records were retrieved from the electronic databases (MEDLINE: 1317; EMBASE: 1104; CENTRAL: 88). A summary of the collection procedure and reasons for exclusion are presented in the PRISMA flowchart (Fig. 1) (Liberati et al. 2009).

The additional hand search did not reveal any other relevant citation. The percentage of interrater agreement between the two investigators was almost perfect (99%), yielding a very good interrater agreement kappa score of 0.91 (SE = 0.021) (Landis and Koch 1977).

All included studies were observational studies, using a cross sectional study design (n = 19; 95%), except for the study of Dannenbaum et al. (2016), where a cohort study design was used. The year of publication ranged from 1969 (Ritvo et al. 1969) to 2017 (Carson et al. 2017; Isaac et al. 2017; Lotfi et al. 2017b) and the overall sample size of the study participants diagnosed with a neurodevelopmental disorder was 604 (range 13–79) for the twenty included papers. The mean age of the studied population varied from 4 (Ornitz et al. 1985) to 17.5 years (Zur et al. 2013). In the study of Westerman et al. (1982), the age of the study population was not specified. In addition, in all studies that specified the gender of the participants, a male predominance was observed with an overall ratio of 3.9:1. A detailed overview of the study population, control group, and characteristics of the included studies is listed in Table 2.

Risk of Bias Assessment

Based on the appraisal for risk of bias, none of the studies reached the maximum score. The mean NOS score was 4.6/10, and ranged from 1/10 (Westerman et al. 1982) to 8/10 (Lotfi et al. 2017b). Ten of the included studies (50%) were rated as moderate (Ritvo et al. 1969; Stockwell et al. 1976; Ornitz et al. 1985; Polatajko 1985; Horak et al. 1988; Levinson 1990; Franco and Panhoca 2008; Dannenbaum et al. 2016; Carson et al. 2017; Isaac et al. 2017). Four studies (20%) were judged as relatively high quality studies (Brown et al. 1983; Goldberg et al. 2000; Furman et al. 2015; Lotfi

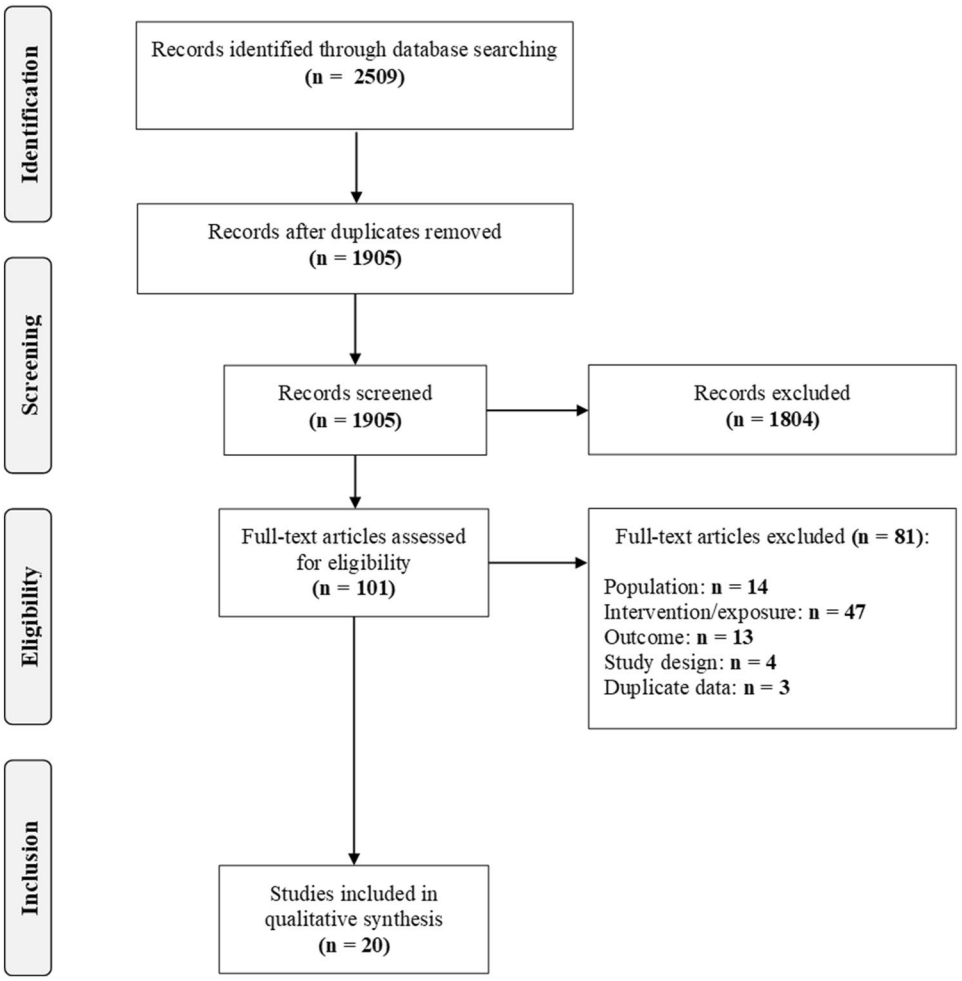

Fig. 1 PRISMA flowchart of the selection procedure

et al. 2017b) and the remaining six studies (30%) were found to have a high risk of bias, thus having a poor study quality (Frank and Levinson 1973; Ornitz et al. 1974; Westerman et al. 1982; Sumerson 1985; Jerabek and Krejcova 1991; Zur et al. 2013). The quality analysis of the included articles and, consequently, the potential risk of bias, is shown in Table 3.

Synthesis of the Included Studies

Neurodevelopmental Disorders (NDDs)

Based on the current version of the Diagnostic and Statistical Manual of Mental Disorders (5th edition; DSM-5) (American Psychiatric Association 2013), study populations in which vestibular assessment had been performed, could be arbitrary subdivided in four of the seven current categories of NDDs; intellectual developmental disability (IDD), autism spectrum disorder (ASD), attention deficit/hyperactivity disorder (ADHD), and specific learning disorder (SLD). As depicted in Table 2, six studies (30%) reported vestibular outcomes in children with ASD, two (10%) in children diagnosed with ADHD, and in ten of the studies (50%) vestibular findings of children with SLD were discussed. In the two remaining studies (10%) vestibular function was assessed in children diagnosed with IDD. One of these two studies reported vestibular outcomes in children with global developmental delay (GDD) (Dannenbaum et al. 2016). Although the authors used a different definition than the one described by the American Psychiatric Association (2013), this study will be discussed within the paragraphs of IDD for practical reasons and because this diagnosis is currently categorized as a subgroup of IDD in the 5th edition of the DSM. None of the included studies assessed the association between vestibular function and the remaining NDDs (communication and motor disorders).

As the present version of the DSM was only published in 2013, several other terms and categories were used in the studies. Moreover, only two studies used the diagnostic criteria, as described in the DSM-5 or previous editions, for the selection of the study participants (Ornitz et al. 1985; Isaac et al. 2017). In the other included studies a wide range of clinical and/or behavioral tests was used to establish the neurodevelopmental diagnosis (Kanner 1943; Gray and Test 1963; Ornitz 1973; Lord et al. 1994, 2000; Rutter et al. 2003;

Table 2 Evidence table of the included studies

Article	Patient information	Control group	Vestibular (related) assessments	Main findings
Attention/deficit hyperactivity disorder				
Isaac et al. (2017)	n = 13 Mean age (years) = 7.8 Gender (M/F) = 9/4	n = 13 Mean age (years) = 7.3 Gender (M/F) = 3/10	cVEMP, SVV, computerized posturography, and DGI	For the overall DGI performance and LOS test, lower scores in children with ADHD compared to controls were found. Additionally, cVEMP responses were found to be bilaterally absent in 23% (3/13) children with ADHD, while in the others the amplitudes were significantly reduced in comparison with the control group. However, no significant differences could be seen between these groups during the SVV test.
Lotfi et al. (2017b)	n = 33 Mean age (years) = 9 Gender (M/F) = 19/14	n = 30 Mean age (years) = 9.5 Gender (M/F) = 15/15	cVEMP and rotatory testing at 0.01, 0.02, 0.08, 0.16 and 0.32 Hz	Based on cVEMP testing, no significant differences could be found. However, significantly higher VOR gains were observed in children with ADHD at all frequencies (except for 0.02 Hz). Additionally, visual fixation performances were significantly lower in children with ADHD in comparison to their unaffected peers at 0.16 and 0.32 Hz.
Intellectual disability disorder				
Dannenbaum et al. (2016)	n = 20 Mean age (years) = 7.9 Gender (M/F) = 13/7	n = 11 Mean age (years) = 7.2 Gender (M/F) = 4/7	DVA, m-ECVCT at 0.5 Hz and CTSIB	33% of the children (6/18) had abnormal DVA scores and the CTSIB scores were significantly lower in the GDD group. The modified rotatory testing did not reveal significant differences, although GDD children demonstrated larger variance in the duration of postrotatory nystagmus.
Zur et al. (2013)	n = 21 Mean age (years) = 17.5 Gender (M/F) = 18/3	N/A	HIT, DVA, CTSIB, SLS and Romberg testing	62% (13/21) of the children with IDD had positive HIT results, suggestive for a horizontal VOR deficit. Additionally, six of the thirteen patients had a positive DVA test. In these patients with a decrease in vestibular function, a trend towards a poorer static balance control was established as well.
Specific learning disorder				
Brown et al. (1983)	n = 34 Mean age (years) = 11.1 Gender (M/F) = 34/0	n = 33 Mean age (years) = 11.4 Gender (M/F) = 33/0	Rotatory testing at 0.01, 0.04 and 0.16 Hz	There were no detectable and significant differences in phase, gain or asymmetry between the two groups.
Franco and Panhoca (2008)	n = 43 Age range (years) = 7-12 Gender (M/F) = 29/14	n = 45 Age range (years) = 7-12 Gender (M/F) = 23/22	Nystagmus and oculomotor tests, rotatory testing (unspecified), positional and air caloric test	Mean saccade accuracy to the right and cold caloric stimulation thresholds differed significantly. Taken together all test results, in 67.4% of the children with learning impairment, a uni- or bilateral peripheral vestibular dysfunction could be seen, which was significantly different in comparison to the children without learning impairments.

Table 2 (continued)

Article	Patient information	Control group	Vestibular (related) assessments	Main findings
Frank and Levinson (1973)	n = 30 Age range (years) = 6.5-14 Gender (M/F) = ?	N/A	Nystagmus and oculomotor tests, positional and caloric test	87% (26/30) of the SLD group showed ENG abnormalities and revealed spontaneous and positional nystagmus, asymmetric smooth pursuit, and asymmetric functioning of the vestibular system (not further specified). Based on cold caloric stimulation, two additional cases showed unilateral canal paresis.
Horak et al. (1988)	n = 15 Mean age (years) = 9.4 Gender (M/F) = 10/5	n = 54 (TD) Mean age (years) = 9.2 Gender (M/F) = 28/26 n = 30 (HI) Mean age (years) = 9.2 Gender (M/F) = 12/18	Computerized posturography and rotatory testing at 0.2 and 0.05 Hz	In 20% (3/15) of the SLD children an abnormal VOR was seen. One child had abnormal phase and asymmetry and a normal gain, while another had abnormal asymmetry, but normal gain and phase score. The last child had abnormal phase but normal gain and asymmetry. In addition, all but one SLD child fell in the two sensory conditions wherein vestibular input was the most crucial.
Jerabek and Krejcova (1991)	n = 52 Mean age (years) = 10.5 Gender (M/F) = 46/6	n = 41 Mean age (years) = 10 Gender (M/F) = ?	Nystagmus and oculomotor tests, rotatory testing (unspecified) and caloric test	In 11-29% of the SLD group, oculomotor abnormalities, gaze-evoked or spontaneous nystagmus were found. Based on rotatory test results, 27% of the patients had a hyperfunction, while in 8% a hypofunction was found. For caloric testing, only 44% had normal test results. Additionally, in one half of the cases poor visual suppression of vestibular nystagmus could be seen during caloric and rotatory testing.
Levinson (1990)	n = 35 Mean age (years) = 16.9 Gender (M/F) = 19/16	n = 35 Mean age (years) = 16.9 Gender (M/F) = 19/16	Oculomotor tests, finger-to-finger sequencing, diadochokinesis, positional test, tandem stance, Romberg and caloric test	No significant vestibular differences between the adolescents with SLD and the control group could be disclosed. However, the results of monopedal Romberg stance, finger-to-finger sequencing and tandem dysmetria differed significantly between the two groups.
Polatajko (1985)	n = 40 Age range (years) = 8-12 Gender (M/F) = 36/4	n = 40 Age range (years) = 8-12 Gender (M/F) = 36/4	Nystagmus and oculomotor test and low-acceleration ($6°/s^2$) velocity step test at 120°/s	No significant differences could be found between the SLD children and the control group and none of the correlations between vestibular function and academic performance were significant.
Stockwell et al. (1976)	n = 21 Age range (years) = 7-17 Gender (M/F) = ?	n = 5 Age range (years) = 9-16 Gender (M/F) = ?	Nystagmus and oculomotor test, positional and caloric test	None of the children showed clinically significant evidence for vestibular dysfunctions.
Sumerson (1985)	n = 27 Mean age (years) = 10 Gender (M/F) = 21/6	N/A	Nystagmus and oculomotor test, positional testing, Romberg test, caloric test and evaluation of the gait	One child had positional nystagmus and in two an asymmetrical optokinetic nystagmus could be found. Additionally, only the caloric results of one child indicated vestibular deficits. In 12-31% of the SLD children, a poor coordination could be suspected.

Table 2 (continued)

Article	Patient information	Control group	Vestibular (related) assessments	Main findings
Westerman et al. (1982)	n = 41 Mean age (years) = ? Gender (M/F) = ?	N/A	Nystagmus and oculomotor test, past-pointing test, rotatory testing (unspecified), positional testing and caloric test	Taken together all test results, 31 children (76%) showed deficits during ENG testing (unspecified). Seventeen of these children had a hypofunction during cold caloric testing and in this group 14 patients had poor past-pointing results. Half of the group (20/41) had oculomotor abnormalities.
Autism spectrum disorder				
Carson et al. (2017)	n = 16 Mean age (years) = 8.8 Gender (M/F) = 16/0	n = 24 Mean age (years) = 9.2 Gender (M/F) = 22/2	Oculomotor screening, high-acceleration (125°/s^2) velocity step test at 100°/s (in light, dark and with visual fixation)	Children with ASD showed increased VOR gain in all conditions. Although not significant, a trend towards a longer time constant decay during and after rotation could be seen for the ASD group in both dark and suppression conditions, respectively. While no group differences in the number of postrotatory nystagmus beats could be found, the ASD group also exhibited less regular or periodic horizontal eye movements.
Furman et al. (2015)	n = 79 Mean age (years) = 17 Gender (M/F) = 71/8	n = 62 Mean age (years) = 16.5 Gender (M/F) = 56/6	Oculomotor tests, rotatory testing at 0.05, 0.1, 0.5 and 1.0 Hz and a low-acceleration (10°/s^2) velocity step test at 90°/s (in dark, with visual fixation and tilt-suppression)	No significant differences in the VOR, visual-vestibular and semicircular canal-otolith interaction could be detected. Also saccade accuracy and velocity were similar in both groups, while saccade latency was significantly increased.
Goldberg et al. (2000)	n = 13 Mean age (years) = 13.6 Gender (M/F) = 7/6	n = 10 Mean age (years) = 10.9 Gender (M/F) = 8/2	Velocity step test (acceleration unspecified) at 60°/s (In dark and with tilt-suppression)	For both positions, no differences in postrotatory nystagmus could be seen between the two groups.
Ornitz et al. (1974)	n = 21 Mean age (years) = 4.1 Gender (M/F) = 20/1	n = 25 Mean age (years) = 4.7 Gender (M/F) = 16/9	High-acceleration (unspecified) velocity step test at 180°/s (in light, dark and with visual fixation)	The nystagmus durations were significantly shorter in the ASD group compared to the control group in the light and fixation conditions, while no or only marginal significant differences could be found in complete darkness. Only in these conditions, a significant difference in number of nystagmus beats could be seen as well, with less nystagmus beats in the ASD group. However, frequency of nystagmus revealed less significant contrasts between the two groups.
Ornitz et al. (1985)	n = 22 Mean age (years) = 4 Gender (M/F) = 18/4	n = 25 Mean age (years) = 4.1 Gender (M/F) = 16/9	Low-acceleration (10°/s^2) velocity step test at 180°/s	The time constant of the primary nystagmus in autistic children was significantly longer, while the gain was found to be equal between the two groups. Additionally, the amount of nystagmus beats was significantly reduced during the secondary reversed nystagmus in the ASD children relative to the normal children.

Table 2 (continued)

Article	Patient information	Control group	Vestibular (related) assessments	Main findings
Ritvo et al. (1969)	n = 28 Mean age (years) = 5.3 Gender (M/F) = 21/7	n = 22 Mean age (years) = 6.8 Gender (M/F) = 7/15	Manual postrotatory nystagmus test (in light and dark)	When tested in the dark, no significant difference could be found in the duration of postrotatory nystagmus between the two groups, while a significantly shorter duration could be found in the ASD group compared to the control group in the light condition.

cVEMP cervical Vestibular Evoked Myogenic Potentials, *SVV* Subjective Visual Vertical, *DGI* Dynamic Gait Index, *LOS* Limits Of Stability, *ADHD* Attention Deficit/Hyperactivity Disorder, *VOR* Vestibulo-Ocular Reflex, *DVA* Dynamic Visual Acuity test, *m-ECVCT* modified Emory Clinical Vestibular Chair Test, *CTSIB* Clinical Test of Sensory Interaction and Balance, *GDD* Global Developmental Disorder, *N/A* not applicable, *SLS* Single Leg Stance, *IDD* Intellectual Disability Disorder, *HIT* Head Impulse Test, *SLD* Specific Learning Disorder, *ENG* ElectroNystagmoGraphy, *TD* Typically Developing, *HI* Hearing Impaired, *ASD* Autism Spectrum Disorder

Shevell et al. 2003; Wechsler and Hsiao-pin 2011) or the diagnostic criteria remained unspecified (Frank and Levinson 1973; Westerman et al. 1982; Polatajko 1985; Sumerson 1985; Horak et al. 1988; Levinson 1990; Jerabek and Krejcova 1991; Franco and Panhoca 2008; Lotfi et al. 2017b). Due to the latter, differences in prevalence rates between the included papers should be interpreted carefully.

Performed Vestibular Assessments

Concerning the types of vestibular examinations, in the vast majority (70%; 14/20) of the eligible studies *rotatory testing* was used, *examining the mid-frequency range of the horizontal semicircular canals (SCCs) and superior vestibular nerve*. A summary of all vestibular assessments applied in the included studies is given in Table 4. This test was even the preferred and only test used for peripheral vestibular assessment in nine (45%; 9/20) studies. Since multiple types of rotatory tests are available, a large variety of stimulus and response parameters were applied. Four authors performed the Sinusoidal Harmonic Acceleration Test (SHAT) within a frequency range of 0.01–0.2 Hz and a peak velocity of 50°/s, while for one study (Horak et al. 1988) the peak velocity and for another study (Franco and Panhoca 2008) both the peak velocity and frequencies had not been described. Six other studies used low- or high-acceleration Velocity Step Tests (VST), which also provide some information about the velocity storage mechanism and central processing of the rotational VOR (Bertolini and Ramat 2011). Similar to the SHAT approach, a wide variety of different protocols were utilized to perform VST testing which is described more in detail in Table 2. Only in the study of Furman et al. (2015), both SHAT and VST were implemented. Most studies using rotatory testing, performed the tests in a dark environment, although the test conditions were not described in three (Westerman et al. 1982; Jerabek and Krejcova 1991; Franco and Panhoca 2008). To test the visual-vestibular interaction and involvement of the cerebellar system, testing in a light environment and with visual fixation were performed as well (Ritvo et al. 1969; Ornitz et al. 1974; Furman et al. 2015; Carson et al. 2017). Additionally, to examine the semicircular canal-otolith interaction, tilt-suppression or dumping was applied to the rotatory test protocol in the studies of Furman et al. (2015) and Goldberg et al. (2000). In two studies using the SHAT approach, 'gain', 'phase' and 'symmetry' were the elected response parameters for analysis (Horak et al. 1988; Lotfi et al. 2017b). In the study of Brown et al. (1983) the parameters 'gain' and 'symmetry', and in the study of Furman et al. (2015) 'gain', 'phase' and 'fixation suppression' were chosen. Besides the standard parameters 'gain' and 'symmetry' evaluated in the studies of Polatajko (1985), Ornitz et al. (1985) and Carson et al. (2017), studies using the VST approach, evaluated 'time constant' (TC) (Ornitz

Table 3 Risk of bias assessment

Author (year)	Study design	Selection (max 4/5 stars)	Comparability (max 2 stars)	Exposure/outcome (max 3 stars)	Total scores (max 9/10)
Brown et al. (1983)	Cross-sectional	★★★	★★	★★	7
Carson et al. (2017)	Cross-sectional	★★	★	★★★	6
Dannenbaum et al. (2016)	Cohort	★★★	★	★	5
Franco and Panhoca (2008)	Cross-sectional		★	★★★	4
Frank and Levinson (1973)	Cross-sectional	★	N/A	★	2
Furman et al. (2015)	Cross-sectional	★★★	★	★★★	7
Goldberg et al. (2000)	Cross-sectional	★★★	★	★★★	7
Horak et al. (1988)	Cross-sectional		★	★★★	4
Isaac et al. (2017)	Cross-sectional	★★	★	★★★	6
Jerabek and Krejcova (1991)	Cross-sectional	★		★	2
Levinson (1990)	Cross-sectional	★★	★	★★★	6
Lotfi et al. (2017b)	Cross-sectional	★★★	★★	★★★	8
Ornitz et al. (1985)	Cross-sectional	★★	★	★★	5
Ornitz et al. (1974)	Cross-sectional	★		★★	3
Polatajko (1985)	Cross-sectional	★★	★	★★	5
Ritvo et al. (1969)	Cross-sectional	★	★	★★	4
Stockwell et al. (1976)	Cross-sectional	★★	★	★★	5
Sumerson (1985)	Cross-sectional		N/A	★★	2
Westerman et al. (1982)	Cross-sectional		N/A	★	1
Zur et al. (2013)	Cross-sectional	★	N/A	★★	3

max maximum, *N/A* not applicable

et al. 1985; Goldberg et al. 2000; Furman et al. 2015; Carson et al. 2017), 'Postrotatory nystagmus (PRN) duration'(Ornitz et al. 1974, 1985) and the amount of nystagmus beats (Ornitz et al. 1974, 1985; Carson et al. 2017) as well. Carson et al. (2017) performed the most detailed analysis by far, since the authors additionally analyzed frequency and regularity of the response by spectral analysis, and sample entropy. Besides objective rotation stimuli, manual rotations by the investigators and consequently more subjective test approaches, were performed as well (Ritvo et al. 1969; Dannenbaum et al. 2016). In the study of Dannenbaum et al. (2016), the response parameter (duration of PRN) was visually evaluated by the investigators (i.e. Frenzel goggles), while the same parameter was measured by electronystagmography (ENG). Additionally, in a few studies (Westerman et al. 1982; Jerabek and Krejcova 1991) the way rotatory testing was performed remained undetermined.

Also, the *evaluation of the low-frequency function of the SCCs and superior vestibular nerve by caloric testing* was performed in seven studies (Table 4). Six studies used water caloric irrigations, with three studies using bithermal caloric stimulation (30–44 °C), two performing cold caloric stimulation and in the study of Stockwell et al. (1976) monothermal caloric testing (44 °C) was performed, based on the criteria by Barber et al. (1971). Besides bithermal caloric stimulation, Levinson (1990) also applied simultaneous binaural bithermal caloric testing, introduced by Brookler in 1971. Additionally, one study used air caloric stimulation at 18 °C and 42 °C (Franco and Panhoca 2008). Although the stimulation approach was specified, the parameters and criteria for the responses to be classified as abnormal were lacking in the studies of Jerabek and Krejcova (1991), Westerman et al. (1982) and Sumerson (1985). In the study of Franco and Panhoca (2008) responses were rated as normal if the values corresponded to the normative data described by Ganança et al. (2000) and the results were additionally compared to those found in the control group. In two studies, their judgement was based on left–right differences only; with 20% unilateral weakness in the study of Stockwell et al. (1976) and 30% unilateral weakness and/or directional preponderance in the study of Levinson (1990). Since Frank and Levinson (1973) based their assessment on the method described by Kobrak (1920) for ice cold water caloric stimulation, vestibular hypofunction was assumed if there was only a reaction after 10 or 20 cc stimulation and no response after 40 cc of cold water irrigation was an indication of areflexia.

In more recent studies, relatively new vestibular tests, as the *Vestibular Evoked Myogenic Potentials (VEMP) for the evaluation of the otolith organs and the Head Impulse Test (HIT)* (Halmagyi and Curthoys 1988), from which the computerized variant (video HIT) has become nowadays the gold standard *to assess the high-frequency function of*

Table 4 Overview of the applied vestibular function tests in the included studies

Vestibular function testing	Article (Neurodevelopmental Disorder)	
Horizontal semicircular canal		
Caloric testing (low-frequency function)	Franco and Panhoca (2008) (SLD)	
	Frank and Levinson (1973) (SLD)	
	Jerabek and Krejcova (1991) (SLD)	
	Levinson (1990) (SLD)	
	Stockwell et al. (1976) (SLD)	
	Sumerson (1985) (SLD)	
	Westerman et al. (1982) (SLD)	
Rotatory chair testing (mid-frequency function)	Brown et al. (1983) (ASD)	Jerabek and Krejcova (1991) (SLD)
	Carson et al. (2017) (ASD)	Lotfi et al. (2017b) (ADHD)
	Dannenbaum et al. (2016) (IDD)	Ornitz et al. (1974) (ASD)
	Franco and Panhoca (2008) (SLD)	Ornitz et al. (1985) (ASD)
	Furman et al. (2015) (ASD)	Polatajko (1985) (SLD)
	Goldberg et al. (2000) (ASD)	Ritvo et al. (1969) (ASD)
	Horak et al. (1988) (SLD)	Westerman et al. (1982) (SLD)
(video) Head Impulse Test (vHIT) (high-frequency function)	Zur et al. (2013) (IDD)	
Otolith organs		
cervical Vestibular Evoked Myogenic Potentials (cVEMP)	Isaac et al. (2017) (ADHD)	
	Lotfi et al. (2017b) (ADHD)	
Vestibular output/postural performances		
Subjective Visual Vertical (SVV)	Isaac et al. (2017) (ADHD)	
Dynamic Visual Acuity (DVA)	Dannenbaum et al. (2016) (IDD)	
	Zur et al. (2013) (IDD)	
Clinical Test of Sensory Interaction and Balance (CTSIB)	Zur et al. (2013) (IDD)	
	Dannenbaum et al. (2016) (IDD)	
Computerized Posturography (CP)	Isaac et al. (2017) (ADHD)	
	Horak et al. (1988) (SLD)	
Gait Analysis/Dynamic Gait Index (DGI)	Isaac et al. (2017) (ADHD)	
	Sumerson (1985) (SLD)	
Single Leg Stance (SLS)	Zur et al. (2013) (IDD)	
	Levinson (1990) (SLD)	
Romberg Stance	Zur et al. (2013) (IDD)	
	Sumerson (1985) (SLD)	
	Levinson (1990) (SLD)	

SLD Specific Learning Disorder, *ASD* Autism Spectrum Disorder, *IDD* Intellectual Disability Disorder, *ADHD* Attention Deficit/Hyperactivity Disorder

the semicircular canals (Halmagyi et al. 2017), were performed as well. Saccular function and inferior vestibular nerve function were assessed in two studies concerning ADHD (Isaac et al. 2017; Lotfi et al. 2017b) based on cervical Vestibular Evoked Myogenic Potentials (cVEMP). Both studies compared the outcome measures with the control group and evaluated the presence of the responses, and the parameters 'latency' and 'amplitude'. In the study of Lotfi et al. (2017b) 'threshold' and 'amplitude ratio' were discussed too. In addition to the cVEMP Isaac et al. (2017) indirectly assessed otolith function with a Subjective Visual Vertical (SVV) test, using the bucket method. None of the eligible studies performed ocular Vestibular Evoked Myogenic Potentials (oVEMP) to evaluate the function of the utricle and superior vestibular nerve. The clinical HIT was used in the study of Zur et al. (2013) to assess the horizontal VOR function in children and young adults diagnosed with IDD. Three to five trials were performed on each side and if correction saccades were present in three trails, this was found to be indicative of a vestibular dysfunction on that side. None of the included studies performed the objective variant; the video HIT.

As shown in Table 4, only one study gave information about both the horizontal SCCs and the saccule by using a

complementary test battery of multiple objective tests (Lotfi et al. 2017b). Isaac et al. (2017) evaluated the otolith function alone and in the other eighteen studies only the function of the horizontal SCCs was assessed.

Furthermore, the *static and dynamic visual acuity (DVA) test* was used in the two studies concerning IDD (Zur et al. 2013; Dannenbaum et al. 2016) *to assess VOR performances during head movements*. In both studies, the participant's head was oscillated from side to side (15°) at a frequency of 2 Hz (provided by a metronome) and the DVA score was considered to be abnormal when the difference between the static and dynamic acuity was three or more.

Vestibular Abnormalities in Children with NDDs

Based on the vestibular assessments in the included studies, the overall reported amount of vestibular abnormalities in NDDs ranged from 0% (Stockwell et al. 1976; Brown et al. 1983; Polatajko 1985; Levinson 1990; Furman et al. 2015; Lotfi et al. 2017b) to 87% in the study of Frank and Levinson (1973). Since NDDs are a heterogeneous group with diverse characteristics, the vestibular outcomes will be discussed for each NDD separately.

Firstly, in the *studies on children with ADHD* (n = 2), both peripheral and central vestibular abnormalities could be found. Isaac et al. (2017) observed that cVEMP amplitudes were significantly reduced in children with ADHD and in three of these children (23%) cVEMP responses were completely absent. Moreover, a significant negative correlation between the individual average amplitude of bilateral cVEMPs and total sensory processing measure (SPM) score could be detected, showing that lower cVEMP amplitudes are associated with more sensory processing problems. With regard to the other response parameter 'latency' and SVV perception, there were no significant differences between the two groups. Contrary to the previous study, Lotfi et al. (2017b) did not find any differences in cVEMP parameters between the two groups. However, significantly higher VOR gains at all frequencies except for 0.02 Hz, and reduced ability to fixate at the highest frequencies (0.16 and 0.32 Hz) were observed in children diagnosed with ADHD.

Secondly, the results of both *studies concerning IDD* were suggestive of peripheral vestibular abnormalities. In the study of Zur et al. (2013), 13 of 21 (62%) participants who were able to complete the test, had correction saccades during horizontal HIT testing and six of them had positive DVA results too, indicating a VOR deficit. Also, in the study of Dannenbaum et al. (2016) 6 of 18 (33%) children diagnosed with GDD had abnormal DVA scores. The evaluation of postrotatory nystagmus (PRN) did not reveal any differences between children with global developmental delays and the control group, while a greater variance in the duration of PRN was found in children with GDD.

Although findings were inconsistent, some *studies on children with SLD* (n = 6) were suggestive of higher incidences of vestibular dysfunction in children with SLD as well. The oldest study (Frank and Levinson 1973) described that 87% of their participants exhibited ENG abnormalities, which mainly included deviations in oculomotor function (dysmetric smooth pursuit) and spontaneous and positional nystagmus. The authors also reported two other participants with unilateral canal paresis after cold caloric stimulation, however, vestibular findings were not discussed in detail and remained rather vague. This was also the case in the studies of Westerman et al. (1982) and Jerabek and Krejcova (1991). In the study of Westerman et al. (1982) 76% of the participants showed ENG abnormalities, with about half of these children having hypofunction during cold caloric testing and one half of the study participants exhibited oculomotor dysfunctions (during optokinetic and smooth pursuit testing); however specification of the response parameters and the nature of vestibular abnormalities lacked. The other study (Jerabek and Krejcova 1991) also reported that 10–39% of the subjects had dysmetric saccades and/or spontaneous or gaze evoked nystagmus. In addition, 27% and 8% of the participants had abnormally high or low VOR gain during rotatory chair testing, respectively. With respect to the caloric responses, 56% of the children had abnormal responses, while the response parameters remained unclear. In addition, it is interesting to mention that the latter study emphasized that about one half of all cases had an abnormal visual suppression of vestibular nystagmus during rotational and/or caloric testing. In the final study concerning vestibular dysfunction in children who significantly underperformed at school, only 32.6% of the children had normal vestibular responses (Franco and Panhoca 2008). However, whereas only for cold air caloric stimulation a significant difference between the SLD group and children without difficulties at school could be demonstrated, no differences in oculomotor (except for saccade accuracy to the right) and rotatory chair testing could be detected. In the study of Horak et al. (1988), SHAT testing revealed abnormal VOR responses in three children (more specific in Table 2) and one child had abnormal caloric test results in the study of Sumerson (1985); however compared to the control groups no significant incidence of abnormal ENG results could be detected in both studies. Based on the applied tests, no significant peripheral vestibular abnormalities were found in the studies of Stockwell et al. (1976), Brown et al. (1983), Polatajko (1985) and Levinson (1990) either (Table 2).

Finally, four *ASD studies* revealed suggestions for (mainly central) vestibular lesions, while in the other two studies no difference in vestibular response between the ASD and control group could be observed (Goldberg et al. 2000; Furman et al. 2015). In the oldest study (Ritvo et al. 1969) included in this systematic review, the mean duration of postrotatory

nystagmus was significantly shorter in children diagnosed with ASD when tested in the light condition, while this difference disappeared when the tests were repeated blindfolded in a dark environment. The same findings in several light, fixation and dark conditions were observed by Ornitz et al. (1974). Furthermore, the total number of nystagmus beats appeared to be lower in the light and fixation conditions in the ASD group, compared to the control group. On the other hand, the measurement of nystagmus frequency in different conditions disclosed fewer and less significant contrasts between the two groups, while the frequency was substantially more variable in the ASD group. In a later study, Ornitz et al. (1985) did not detect a difference in gain, but longer perrotatory time constants in children with autism were observed when tested in the dark. In contrast to the previous study, a significant decrease in the number of nystagmus beats was found in the ASD group in the dark. Additionally, in the ASD group irregularities in the slow component velocity were described and a greater incidence of slow phases that failed to be followed by a quick phase in comparison to the control group. The most recent study in children with ASD, confirmed the latter findings with a trend towards longer per- and postrotatory time constants in the ASD group in the dark and visual fixation condition, respectively. Additionally, based on sample entropy the authors confirmed the suggestion that ASD participants have much more irregularity in eye positions during postrotatory nystagmus. However, in contrast to the study of Ornitz et al. (1985), Carson et al. (2017) found that the ASD group had significantly higher per- and postrotatory VOR gain in both the dark and visual conditions. Also the finding that there were no group differences in the number of postrotatory nystagmus beats in any of the test conditions conflicts with the study of Ornitz et al. (1985).

Vestibular Function and Postural Stability

Six studies (30%) evaluated postural stability and vestibulospinal reflexes too (Table 4). In the IDD study of Zur et al. (2013) postural stability was evaluated by the *Clinical Test of Sensory Interaction and Balance (CTSIB)* and both *single leg stance (SLS)* and *Romberg stance under eyes open and eyes closed conditions*, and was linked to VOR function. The authors established that children with a VOR dysfunction (based on HIT and DVA, Table 4) had significantly more difficulties to maintain balance in condition 5 of the CTSIB test (standing on a foam with closed eyes). For SLS and Romberg testing, no significant differences were found between the two groups, although a marginally significant difference was observed in the eyes closed condition during SLS. These findings were confirmed by Dannenbaum et al. (2016), where children with GDD, with one-third having abnormal DVA scores, scored significantly worse in condition 5 and 6 of the CTSIB (standing on foam and wearing a visual dome) compared to the healthy control group.

In one ADHD study postural stability and gait were evaluated by the *dynamic gait index (DGI) and computerized posturography (CP)* (Isaac et al. 2017). Here it was shown that children with ADHD had significantly reduced total DGI scores and scored significantly worse for several balance tasks during CP investigation.

Three studies about SLD included some tests to evaluate postural control. In the study of Sumerson (1985) 3 of the 26 participants had abnormal *gait patterns* when walking with their eyes closed, while no child demonstrated a positive/abnormal *Romberg test*. Whether one of these three children was the same child with abnormal caloric responses or not, remained unclear. Levinson (1990) found significantly more positive monopedal Romberg responses in children with dyslexia in comparison to the control group, however no difference was observed in terms of bipedal Romberg responses. Also in the third study on SLD, it was suggested that children with SLD had much more difficulties in maintaining stability during *sensory organization test (SOT)* (Horak et al. 1988). However, no correlation between the SOT results and VOR function could be demonstrated. In none of the studies concerning ASD postural stability was measured.

Discussion

Since several symptoms in children with NDDs may resemble those of children with known vestibulopathy or since reports indicate that (at least a proportion of) children with NDDs have difficulties with postural stability, the current systematic review was conducted to provide an overview of the knowledge and evidence about the presence or characteristics of vestibular dysfunctions in children diagnosed with NDDs.

Attention Deficit/Hyperactivity Disorder (ADHD)

Attention deficit/hyperactivity disorder is one of the most commonly occurring NDDs which affects 3–7% of school-age children (Polanczyk et al. 2007; Thomas et al. 2015; Sayal et al. 2018) and is characterized by pervasive and impairing symptoms of hyperactivity, inattention, and impulsive behavior (American Psychiatric Association 2013). Currently, only two recent studies evaluated vestibular function in children with ADHD (Isaac et al. 2017; Lotfi et al. 2017b). In these studies, it was hypothesized that vestibular dysfunction could be associated with the diagnosis of ADHD, since gait and balance performances, in which a well working vestibular system is crucial, were found to be

abnormal in a subset of children with ADHD (Buderath et al. 2009; Papadopoulos et al. 2014). Additionally, cerebellar abnormalities in patients with ADHD are well established, resulting in poor postural performances (Buderath et al. 2009; Goetz et al. 2017; Kim et al. 2017). Since the cerebellum is inseparably linked to the vestibular system (Barmack 2003; Gurvich et al. 2013), it was hypothesized that altered vestibular function may exist and contribute to these balance and gait disturbances.

Since cVEMP amplitudes were significantly reduced, Isaac et al. (2017) concluded that saccular function was altered in a significant number of ADHD children. Conversely, Lotfi et al. (2017b) tested 33 children in which no significant differences in cVEMP parameters could be found. The majority of the methodological parameters, such as stimulus, stimulus frequency, stimulation rate, head positioning, test equipment, electrodes placement etc., were identical, yet the contradictory results may originate from other methodological differences. Firstly, in contrast to Lotfi et al. (2017b), Isaac et al. (2017) did not use the electromyographic (EMG) activity to compute rectified amplitude, although this is highly recommended as this value permits more reliable amplitude comparisons between patients (Welgampola and Colebatch 2005). Therefore, the cVEMP amplitudes found by Isaac et al. (2017) should be interpreted with some caution. Nevertheless, Isaac et al. (2017) also identified bilaterally absent cVEMP responses in 23% of the study participants, which implies that complete saccular dysfunction was present in a significant portion of the ADHD group. Another major difference between both studies was related to the study population; hearing loss was a reason for exclusion in the study of Lotfi et al. (2017b) and all children received pharmacological therapy (methylphenidate), while neither of these criteria was used by Isaac and colleagues. Hearing loss may have been a confounding factor in the study of Isaac et al. (2017) resulting in an overestimation of vestibular dysfunction in ADHD, since hearing loss is frequently linked to poor cVEMP responses (Singh et al. 2012; Maes et al. 2014; Verbecque et al. 2017). Nevertheless, if vestibular alterations frequently co-occur in this population, vestibular assessment and rehabilitation should be taken into account in the diagnosis and treatment of patients with a comorbid diagnosis of ADHD and vestibular dysfunction. Additionally, the second difference may play a role as well, since recent studies found that postural control abilities in ADHD children improved after a month of methylphenidate treatment, especially in conditions where they mainly had to rely on vestibular function (when somatosensory and visual information were missing/disturbed) (Bucci et al. 2016). Moreover, structural cerebellar differences were not seen in children receiving therapy, in comparison to the children who did not receive the treatment (Bledsoe et al. 2009; Makris et al. 2015). As proposed by Isaac et al. (2017) as well, further research should focus on whether vestibular responses can be altered or normalized with methylphenidate treatment too.

Lotfi et al. (2017b) also performed rotatory chair testing, which revealed significantly higher VOR gains and reduced ability to fixate in the ADHD group, indicating central vestibular alterations in the connections between the vestibulocerebellum and the vestibular nuclei (VN). Since these central vestibular dysfunctions may also result in motor coordination problems, it is recommended that further studies confirm and expand the known findings about both the peripheral and central vestibular dysfunctions. Moreover, the individual average cVEMP amplitudes appeared to correlate with the severity of ADHD symptoms (SPM score). Interestingly, the correlation between vestibular dysfunction and hyperactive behavior has been described in a recent animal study as well (Antoine et al. 2017). Therefore, research on whether the presence of several ADHD symptoms indicates an underlying vestibular dysfunction could be interesting as well (Antoine et al. 2017; Isaac et al. 2017).

Besides vestibular function, the overall dynamic gait index (DGI) and the limit of stability (LOS) were tested and found to be significantly reduced in this population (Isaac et al. 2017), which is in accordance with several posturography studies in patients with ADHD (Zang et al. 2002; Wang et al. 2003; Hassan and Azzam 2012; Papadopoulos et al. 2014; Hove et al. 2015; Manicolo et al. 2017). Unfortunately, an association with the established saccular function lacked. To verify the possible involvement of the vestibular system into these balance alterations, a correlation with vestibular assessment should be taken into account in future posturography studies.

In this respect, it is also interesting to note that Lotfi et al. (2017a) found that vestibular rehabilitation in children with ADHD had positive effects on saccadic accuracy, smooth pursuit gain, VOR gain during rotatory chair testing, balance and choice reaction time performances. It is obvious that further examination is required, yet these findings do suggest that vestibular rehabilitation therapy may be beneficial for (a subset of) patients with ADHD.

In summary, although research is limited, current literature suggests that the (peripheral and/or central) vestibular system may be involved in the phenotype of ADHD. Since the high prevalence of ADHD, this research area should be elucidated further with respect to the abovementioned shortcomings in the available literature. Moreover, as was emphasized by both studies, the recently growing evidence about cognitive-vestibular interactions, as earlier described, should be considered in research concerning cognitive and developmental disabilities such as ADHD.

Additionally, it would be interesting to compare vestibular outcomes in children with different presentations of ADHD (inattentive, hyperactive-impulsive and combined

type), since up to now research focused on the combined type only.

Intellectual Disability Disorder (IDD)

Intellectual disability is a neurodevelopmental disorder that begins in childhood and is characterized by limitations in both intellectual functioning and adaptive skills in at least one of three adaptive domains (conceptual, social, and practical) (American Psychiatric Association 2013). The estimated overall prevalence of IDD in the global population is 1%, but a wider range has been reported (0.05–1.55) due to the variability across countries, age groups, and heterogeneity in study design, methodology and definitions (Karam et al. 2016; McKenzie et al. 2016). Also in children with IDD, a higher risk for vestibular dysfunction could be assumed. Patients with IDD are known to be at higher risk for sensory impairments, such as hearing loss, which is more frequently occurring in people with IDD compared to the general population (Driscoll et al. 2003; Meuwese-Jongejeugd et al. 2006; Herer 2012; Hey et al. 2014). Because of the close anatomical relationship between the auditory and vestibular end organs, it seems evident that whatever reason causes damage to the auditory structures, may also negatively affect the vestibular organ. In addition, multiple studies have reported abnormalities in gait, fine and gross motor performances and postural stability in both children and adults with IDD compared to the control group (Frey et al. 2006; Simons et al. 2008; Dellavia et al. 2009; Hartman et al. 2010; Vuijk et al. 2010; Enkelaar et al. 2012; Blomqvist et al. 2013, 2014; Pitetti et al. 2017). As mentioned earlier, in addition to the known cognitive deficits in this population, a concomitant vestibular (and auditory) dysfunction may result in poor academic, psychosocial and motor performances (e.g. gross motor skills, postural control). Moreover, IDD is a major concern throughout the world but besides genetic and environmental causes, a specific cause of intellectual disability often remains unknown in 30–50% of these patients (Daily et al. 2000; Rauch et al. 2006; Bhowmik et al. 2011; El-Bassyouni and Zaki 2015). Therefore, it is interesting to verify if a vestibular dysfunction is a component in the underlying pathophysiology and contributes to the poor postural stability seen in a subset of these patients. Yet, literature on the vestibular function in patients with IDD is limited, especially in children. Zur et al. (2013) were the first authors who tested 21 children and adolescents with IDD and concluded that a VOR dysfunction was highly prevalent (62%) in these patients. It is noteworthy that the vestibular outcomes were linked to postural performances and that children with a vestibular deficit had poor static postural control when the other sensory input systems were challenged (standing on foam with the eyes closed) compared to those without a VOR deficit. Although these findings are in accordance with studies in children with Down Syndrome (the most common genetic origin of IDD) (Costa 2011; Inagaki et al. 2011), the small sample size may have led to overestimation. Furthermore, caution is warranted given the lack of a control group and the use of rather subjective tests (HIT and CTSIB). On the other hand, Zur et al. (2013) excluded children with known hearing deficits, which could rather result in an underestimation of vestibular dysfunction as auditory impairment is frequently co-occurring in patients with a vestibular deficit. In 2016, Dannenbaum et al. suggested that vestibulopathy in children with GDD is highly prevalent as well. Although m-ECVCT scores revealed no statistically significant difference between both groups, significantly lower CTSIB scores during the subtask which is the most demanding for vestibular processing and abnormal DVA scores were observed and might suggest a deficit in vestibular processing. However, more research is needed to confirm these assumptions, since CTSIB assesses 'balance' and DVA measures 'gaze stability during head movements' rather than attempting to assess peripheral or central vestibular function more directly. Generally, to confirm these suggestions about high occurrence of vestibular dysfunction in children with IDD, further research is needed and may contribute to the growing evidence on the cognitive-vestibular interaction.

Specific Learning Disorder (SLD)

Specific learning disorders are a heterogeneous group of disorders characterized by significantly lower educational skills (reading, spelling, writing and/or mathematics) as would be expected according to age and which considerably affects academic/occupational performances and daily activities. In order to confirm the diagnosis of SLD, these symptoms must have continued for at least 6 months despite providing interventions that target those difficulties. The prevalence of SLD has been reported as 5–15% in school-age children (American Psychiatric Association 2013).

Literature on vestibular dysfunction in SLD is mainly focused on children with reading disabilities. Interest for vestibular function in this neurodevelopmental disorder arose in the 1970s (Frank and Levinson 1973), since similar symptoms were seen in children with SLD and vestibular impairments; poor postural stability and motor coordination (Bucci et al. 2014; Razuk et al. 2018), spatial orientation (Lipowska et al. 2011; Giovagnoli et al. 2016) and oculomotor function (Lukasova et al. 2016). This has led to the theory described by Levinson (1988), which suggested that cerebellar-vestibular deficits exist in dyslexia. This hypothesis was supported by several occupational and physical therapy studies performed in the 1970s and 1980s (Ayres 1978; Ottenbacher 1978; Ottenbacher et al. 1984; Byl et al. 1989) and similar data were found

in the included studies reporting vestibulo-cerebellar dysfunction in children with learning disabilities compared to normal controls (Westerman et al. 1982; Levinson 1990; Jerabek and Krejcova 1991; Franco and Panhoca 2008). However, these deficits in vestibular function were not consistent across all studies (Stockwell et al. 1976; Brown et al. 1983; Polatajko 1985; Sumerson 1985; Horak et al. 1988). Importantly, a huge amount of variability in the measurement and definition of vestibular impairment exists across this literature. Additionally, as was depicted in Table 3, most of these studies showed to be at high risk for bias and in several studies the applied methods and vestibular outcomes were rather vague or even not described. Moreover, all these studies performed rather old techniques and evaluated the horizontal SCC function by rotatory and caloric testing only. It is generally known that the cerebellar/vestibular hypothesis was heavily debated and considered wrong due to methodological shortcomings and has therefore lost its interest as theory of dyslexia (Silver 1987; Stoodley and Stein 2013; Ferrè and Harris 2017). However, several authors suggested the cerebellar hypothesis of dyslexia should not be completely rejected, since evidence is required for the motor and postural deficits which are frequently occurring in dyslexia (Beaton 2002; Pope and Whiteley 2003). As a result of improved screening procedures for dyslexia and other learning disorders, and improved research techniques such as neuroimaging and enhanced vestibular assessments, a reevaluation of this hypothesis may be performed (Pope and Whiteley 2003). However, it seems apparently premature to relate dyslexic difficulties exclusively or even predominantly to vestibular/cerebellar disturbances or to state that antimotion sickness medications may be therapeutically useful to treat children with learning disabilities, as was previously reported (Levinson 1991). Nevertheless, it needs to be emphasized that children with a severe vestibular dysfunction may have poor reading acuity (Braswell and Rine 2006), and that children with reading difficulties may present with similar complaints as children with a vestibular dysfunction of which clinicians should be aware and should take into account when establishing the diagnosis of dyslexia.

The same applies for children with other specific learning disorders, such as dysgraphia and dyscalculia. As previously discussed, children with a vestibular dysfunction may have poor handwriting skills and may show difficulties in some educational performances (e.g. mathematics), which was also concluded in the included study of Franco and Panhoca (2008). Research whether the difficulties and complaints in children with dysgraphia and dyscalculia are accompanied with a vestibular dysfunction is lacking. However, several studies in adults emphasized a possible connection between vestibular function and math performance or dyscalculia (Risey and Briner 1990; Smith 2012; Moser et al. 2017). Moreover, emerging literature concerning vestibular involvement in cognitive function (Gurvich et al. 2013; Hitier et al. 2014; Bigelow and Agrawal 2015; Smith 2017), especially the link with visuo-spatial skills crucial for mathematics, and suggestions that a functional vestibular system is important for normal cognitive development and learning (Wiener-Vacher et al. 2013; Bigelow and Agrawal 2015), supports the need for research on a possible (peripheral and/or central) vestibular contribution in these learning disorders.

Autism Spectrum Disorder (ASD)

Autism spectrum disorder, with a prevalence of 1.5% (Lyall et al. 2017; Morales-Hidalgo et al. 2018; Xu et al. 2018), is characterized by a neurodevelopmental onset of persistent deficits in social communication and interaction and restricted/repetitive behavior, interests and/or activities (American Psychiatric Association 2013).

In the recent study of Carson et al. (2017), children with high functioning autism had increased VOR gains on rotatory chair testing, indicative of a possible lack of cerebellar inhibition to the vestibular nuclei in the brainstem. This was in accordance with previous studies, in which poor regulation of sensory input and brainstem-cerebellar dysfunctions following vestibular stimulation were suggested (Ritvo et al. 1969; Ornitz et al. 1974, 1985). Also, the significant increase in the postrotatory VOR time constant in children with ASD compared to the control group could confirm these findings (Ornitz et al. 1985; Carson et al. 2017). The VOR time constant improves the efficiency of the vestibulo-ocular reflex to transduce low-frequency components of head rotation and may be increased by lesions of the nodulus/uvula in the cerebellum (Waespe et al. 1985; Leigh and Zee 2015; Rambold 2017). Conversely, Furman et al. (2015) performed a larger study (n = 79) with both the SHAT and VST and suggested that the vestibulo-cerebellar structures (lobules IX and X) are spared in children with high functioning autism, which was also the main result of Goldberg et al. (2000). These contradictory results are most likely due to differences in methodology, rotatory test approach and study population. Inconsistent findings are also seen in neuroimaging studies, with some studies supporting vestibulo-cerebellar aberrations and others who do not (Stanfield et al. 2008; Webb et al. 2009; Becker and Stoodley 2013; Carson et al. 2017; Traut et al. 2018).

However, currently three main cerebellar abnormalities have been observed in patients with ASD: diminished Purkinje cells (PC) and two related consequences; reduced cerebellar volume, and interrupted cerebro-cerebellar feedback pathways (Phillips et al. 2015). As PCs are inhibitory in nature and make synapses with neurons within the vestibular nuclei, loss of cerebellar inhibition of the VOR (Carson et al.

2017) may be related to these findings of PC reduction in the vestibulocerebellum (Fatemi et al. 2012; Skefos et al. 2014; Donovan and Basson 2017). Nevertheless, due to the conflicting results, further assessment of these cerebellar alterations in the vestibulocerebellum, as well as correlation with vestibular examination is warranted.

It needs to be emphasized that well-documented structural and functional differences, such as in the basal ganglia, are found throughout the brain of patients with ASD as well (Subramanian et al. 2017). Therefore, motor coordination problems and postural instability found in these patients should apparently not be attributed to cerebellar and vestibular alterations only. However, investigations on whether an accompanying central vestibular dysfunction is present too is limited and should be elucidated further, which was also suggested in a recent narrative review of Christy (2018). Since poor postural performances are usually one of the earliest identifiable and highly prevalent (up to 80% of the patients) clinical abnormalities in ASD and have been argued to be included as main ASD features (Phagava et al. 2008; Fournier et al. 2010a; Mosconi and Sweeney 2015; Stins and Emck 2018), research including a complementary vestibular test battery to assess peripheral vestibular function may be interesting as well and is currently lacking. All included studies used exclusively (variants of) rotatory chair testing with the principal aim to elucidate the neural circuitry in ASD. With this test a mild or compensated unilateral vestibular dysfunction would be missed and assesses horizontal SCC function only.

In addition, vestibular function testing in children with ASD would be interesting since there is evidence that, compared to the control group, postural performances are the most aberrant in conditions were patients could rely on vestibular input only, suggestive for a vestibular deficit (Molloy et al. 2003; Minshew et al. 2004; Doumas et al. 2016; Goulème et al. 2017). Also, several symptoms (e.g. avoidance behavior, fine or gross motor dysfunctions, delayed motor milestones, poor coordination and postural instability) are highly prevalent in both children with ASD (Ornitz 1983; Fournier et al. 2010a; MacDonald et al. 2013; Harris 2017; Lim et al. 2017; Stins and Emck 2018) or a severe vestibular disorder, as was previously discussed. Lastly, it would be interesting to know whether the vestibular function is involved in the known preoccupation with spinning objects or repetitive movements (e.g. spinning or shaking their head) in patients with ASD (Goldberg et al. 2000; Goldman et al. 2009).

Noteworthy, to our knowledge, no study directly measured central or peripheral vestibular function in children with language disorders and motor disorders, like tic disorders and developmental coordination disorder (DCD). For this latter NDD particularly vestibular assessments may be interesting and have been recommended by several authors (Inder and Sullivan 2005; Grove and Lazarus 2007; Fong et al. 2012; Christy 2018; Niklasson et al. 2018), because it has been shown repeatedly that children with DCD have more difficulty to maintain balance than typically developing children when vestibular feedback is the sole accurate source of sensory information (Inder and Sullivan 2005; Grove and Lazarus 2007; Deconinck et al. 2008; Fong et al. 2012).

Based on all included studies, in which vestibular function tests were performed, vestibular research has shown to be useful in all types of NDDs. In nearly all types evidence for peripheral and/or central vestibular dysfunction was found in a subset of patients, however conflicting results have been reported and prevalence ranges of vestibular dysfunction in these children were very wide. As discussed in the previous paragraphs, some of the results should be interpreted with some caution and further research is appropriate, taking into account the existing gaps and flaws in the current literature (i.e. wide range of different diagnostic criteria, low methodical quality, the lack of control groups or guard against potential confounding factors, the use of subjective measurements and outdated data). As was also mentioned before, several different methodological approaches were used for the assessment of the vestibular function and most studies focused on the function of the horizontal SCCs only. This supports the recommendation to replicate several findings and to expand literature with an enhanced test battery (i.e. oculomotor testing, caloric and rotatory chair testing (including fixation suppression), vHIT, cVEMP and oVEMP) for the evaluation of both the semicircular canals and otolith function, and also the central vestibular processing to improve evidence on the involvement of the different vestibular components in NDDs. Noteworthy, testing in this population may be even more challenging than in the general pediatric population. Therefore, an adequately adapted and child-friendly complementary test battery should be performed (Dhondt et al., 2018). Lastly, none of the included studies further explored the potential causes of the established vestibular dysfunctions. However, this information would be useful to gain more thorough understanding of the potential link between vestibular dysfunction and NDDs.

Importantly, although comparable symptoms may occur in both patient groups, an evaluation of the vestibular function, in contrast to the function of other sensory input systems as the auditory and visual system, is (very often) not included in the standard neuro-clinical examination to establish the NDD diagnosis. Therefore, it remains unclear to what extent symptoms like poor coordination, reading disability, lack of empathy etc. may be linked to a (concomitant) vestibular dysfunction or not. If vestibular dysfunctions indeed turn out to be highly prevalent, vestibular screening should be included in the standard evaluation in this population, since a vestibular dysfunction may result

in a diminished quality of life (Guinand et al. 2012; Cohen 2013), especially in these patients for whom it may be more difficult to identify or communicate about their complaints.

The current review has several limitations. First of all, the NDDs were subdivided following the DSM-5 for practical and structural considerations. Although grouping of these NDDs was useful, it is important to recognize important distinctions between the different groups, the heterogeneity and wide range of different applied diagnostic criteria within the groups, and the possible overlap or comorbidity between different types of NDDs (Thapar et al. 2017). Secondly, it was not appropriate to perform a meta-analysis because of the poor methodical quality of several studies and the wide heterogeneity in study methodologies and analyses. Although several studies had a low methodological quality, studies at high risk for bias were included as well, since these studies could provide additional and important information in the context of this systematic review. Finally, since non-English articles were excluded from the review, language bias may have occurred.

In conclusion, a normal functioning vestibular system is thought to be critical in a child's development on many levels. In case of a vestibular dysfunction motor, cognitive, psychosocial and educational symptoms may occur which tend to overlap with those found in patients with NDDs. Moreover, in nearly all NDDs it is known that postural instability, balance, gross and fine motor disturbances are frequently occurring in a subset of patients, which may assume a possible association between vestibular function and NDDs. Although one cannot assume that a vestibular dysfunction is solely responsible for the wide range of symptoms observed in these children, the hypothesis of the possible connection has been supported by the majority of the included studies. To get a representative overview and to better understand the potential association and characteristics (i.e. the cause, origin, symptoms, whether there is a partial/complete, bi-/unilateral, or central/peripheral problem) of a (concomitant) vestibular dysfunction in children with various neurodevelopmental disorders, more research with more scientific rigor and an extensive vestibular test battery is required. Nevertheless, since comparable symptoms may occur in both children with NDDs and vestibular-impaired patients, the authors of this systematic review would like to encourage clinicians to be aware of these similarities when determining the vestibular or NDD diagnosis.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Research Involving Human Participants and/or Animals This article does not contain any studies with human participants or animals performed by any of the authors.

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