Ankle Audiometry: A Clinical Test for the Enhanced Hearing Sensitivity for Body Sounds in Superior Canal Dehiscence Syndrome

Audiology and Neurotology

Research Article

Audiol Neurotol
DOI: 10.1159/000528407

Received: May 21, 2022
Accepted: November 7, 2022
Published online: January 12, 2023

Ankle Audiometry: A Clinical Test for the Enhanced Hearing Sensitivity for Body Sounds in Superior Canal Dehiscence Syndrome

Luca Verrecchia[a, b] Karl-Johan Fredén Jansson[c] Magnus Westin[a]
Aleksandr Velikoselskii[a] Sabine Reinfeldt[c] Bo Håkansson[c]

[a]Audiology and Neurotology Department, ENT, Karolinska University Hospital, Stockholm, Sweden; [b]Department of Clinical Science, Intervention and Technology, ENT Unit, Karolinska Institutet, Stockholm, Sweden; [c]Department of Electrical Engineering, Chalmers University of Technology, Gothenburg, Sweden

Keywords
Superior canal dehiscence · Superior canal dehiscence syndrome · Autophony · Hyperacusis · B250

Abstract
Introduction: The aim of this study was to develop a clinical test for body sounds' hypersensitivity in superior canal dehiscence syndrome (SCDS). ***Method:*** Case-control study, 20 patients affected by SCDS and body sounds' hypersensitivity and 20 control matched subjects tested with a new test called ankle audiometry (AA). The AA consisted of a psychoacoustic hearing test in which the stimulus was substituted by a controlled bone vibration at 125, 250, 500, and 750 Hz, delivered at the medial malleolus by a steel spring-attached bone transducer prototype B250. For each subject, it was defined an index side (the other being non-index), the one with major symptoms in cases or best threshold for each tested frequency in controls. In 3 patients, the AA was measured before and after SCDS surgery. ***Results:*** The AA thresholds for index side were significantly lower in SCDS patients (115.6 ± 10.5 dB force level [FL]) than in control subjects (126.4 ± 8.56 dB FL). In particular, the largest difference was observed at 250 Hz (−16.5 dB). AA thresholds in patients were significantly lower at index side in comparison with non-index side (124.2 ± 11.4 dB FL). The response obtained with 250 Hz stimuli outperformed the other frequencies, in terms of diagnostic accuracy for SCDS. At specific thresholds' levels (120 dB FL), AA showed relevant sensitivity (90%) and specificity (80%) for SCDS. AA did not significantly correlate to other clinical markers of SCDS such as the bone and air conducted hearing thresholds and the vestibular evoked myogenic potentials. The AA thresholds were significantly modified by surgical intervention, passing from 119.2 ± 9.7 to 130.4 ± 9.4 dB FL in 3 patients, following their relief in body sounds' hypersensitivity. ***Conclusion:*** AA showed interesting diagnostic features in SCDS with significantly lower hearing thresholds in SCDS patients when compared to healthy matched subjects. Moreover, AA could identify the affected or more affected side in SCDS patients, with a significant threshold elevation after SCDS surgery, corresponding in body sounds' hypersensitivity relief. Clinically, AA may represent a first objective measure of body sounds' hypersensitivity in SCDS and, accordingly, be an accessible screening test for SCDS in not tertiary audiological centers.

Introduction

The superior canal dehiscence syndrome (SCDS) is an audio-vestibular disorder in which the presence of a bone dehiscence at the dome of the superior semicircular

Karger@karger.com
www.karger.com/aud

Correspondence to:
Luca Verrecchia, luca.verrecchia@ki.se

Table 1. Clinical features in case group

#	Index side			Non-index side		
	AC PTA (dB HL)	BC PTA (dB HL)	VEMP	AC PTA (dB HL)	BC PTA (dB HL)	VEMP
P1	8.8	−5.0	2.6	1.3	−6.7	0.3
P2	28.8	25.0	2.5	7.5	3.3	0
P3	15.0	0.0	1.8	12.5	−3.3	0
P4	22.5	−6.7	1.5	6.3	−1.7	0
P5	16.3	−10.0	1.0	5.0	1.7	0
P6*	7.5	−10.0	2.0	2.5	3.3	0.8
P7*	26.3	−8.3	1.0	12.5	−6.7	0.67
P8	2.5	−3.3	1.1	0.0	−5.0	0
P9	10.0	−10.0	1.0	7.5	−10.0	0
P10	27.5	3.3	1.1	17.5	13.3	0.4
P11	8.8	−8.3	1.7	2.5	−8.3	0
P12	13.8	5.0	1.9	11.3	3.3	0
P13	16.3	−1.7	2.0	11.3	3.3	0.5
P14*	33.8	5.0	0.8	33.8	6.7	1.2
P15	12.5	5.0	1.6	6.3	1.7	0
P16*	21.3	−1.7	0.9	17.5	−3.3	1.1
P17*	22.5	0.0	2.1	23.8	3.3	2.1
P18	18.8	−5.0	1.0	8.8	1.7	0.3
P19	21.3	−6.7	2.3	16.3	0.0	0.7
P20	15.0	−1.7	2.2	7.5	−8.3	0.5

* Indicates patients with bilateral SCDS. AC PTA: hearing thresholds' average calculated on frequencies 500-1,000-2,000-4,000 Hz for air conduction stimulus; BC PTA: hearing thresholds' average calculated on frequencies 500-1,000-2,000-4,000 Hz for bone conduction stimuli. VEMP: cervical vestibular evoked myogenic potential amplitude in response to 90-dB clicks normalized on the background electromyographic activity. A corrected amplitude ≥1 characterized a SCDS-specific vestibular hypersensitivity [Brantberg and Verrecchia, 2012].

canal modifies the inner ear micro fluid dynamics. The vestibular organ becomes sensitive for intense sounds/vibrations and pressure gradients; the cochlea shows a hypersensitivity to internal body sounds/vibrations and a less response for environmental sounds [Ward et al., 2017]. Defined as an "otological mimicker" [Zhou et al., 2007], SCDS has an inconstant and challenging clinical presentation, most often debuting in middle age (30–50 years) with a slow clinical progression, in some cases promoted by a skull trauma. A major SCDS feature is the hearing hypersensitivity for internal body sounds (HIBS) which is variably described as an enhanced hearing of one's own pulse, borborygmi, joints movements, eye movements, voice, crunching, and stepping.

HIBS characterizes the SCDS clinical presentation, together with ear fullness and dizziness [Naert et al., 2021], and responds successfully to surgical treatment [Alkhafaji et al., 2017]. Despite its prominence, HIBS remains hardly quantifiable. At the moment, few validated surveys [Crane et al., 2010; Voth et al., 2018] and a weber test with forks applied on the ankle [Watson et al., 2000] are the proposed assessments for HIBS. However, a measure of HIBS is worth consideration for monitoring of surgical outcomes but more in general for the quantification of a major symptom in SCDS.

In Brantberg et al. [2016], an experimental method for the measure of HIBS was presented, consisting of a psychoacoustic hearing test in which the sound was substituted by controlled sinusoidal bone vibrations delivered at different distant body sites. The stimulus was generated by a bone transducer, the Bruel & Kjaer 4810 Minishaker, and consisted of vibrations at different frequencies between 125 and 1,000 Hz delivered at three different sites: the skull vertex, the spinous process of 7th cervical vertebra, and the medial malleolus of ankles. The study showed how the low frequency distant vibrations could be heard at significantly lower intensities by SCDS patients. In our opinion, the Brantberg's psychoacoustic hearing test represents the best approach for the study of HIBS, and the

Fig. 1. Test setting for AA. The B250 was placed in contact with the medial malleolus with a velcro band, with an adjusted tension corresponding to a pressure at contact point of 10 N. The subjects during testing wore hearing protection against air conducted hearing contamination and disposable foam ear tips in connection with audiometer to deliver masking noise to the not stimulated side ear.

purpose of this work is to reproduce the results obtained by Brantberg et al. but adapting the procedure to clinical use. We have thus set up a similar experimental protocol, substituting the Minishaker with the novel bone transducer prototype, the Ortofon B250 [Fredén Jansson et al., 2021]. B250 represents a precommercial prototype with the specific property to deliver low frequency vibrations at sufficiently loud intensities to match the Minishaker but overcoming its drawbacks in terms of lower weight and smaller size. Moreover, the new procedure was limited to the only ankle stimulation, since the pressure at contact point could be more easily controlled at ankle in comparison to vertex or neck. Moreover, the ankle stimulation would resemble the well-established ankle weber, commonly used in SCDS clinical assessment. For simplicity, the test described in detail below has been termed ankle audiometry (AA).

Materials and Methods

Sample

Study reporting follows the STROBE statement [von Elm et al., 2007]. This is a case-control study in which the psychoacoustic hearing thresholds obtained by AA in a sample of 20 subjects with confirmed SCDS diagnosis was compared with the thresholds obtained in 20 age-/sex-matched healthy control subjects. The study was approved by the national Ethical Committee (ref. No. 2019-05214), and all subjects gave their written consensus before inclusion.

All patients complained about autophony and met the diagnostic criteria for definitive SCDS, according to the International Classification Vestibular Diseases Committee's recent release [Ward et al., 2021]. Since a SCDS may be clinically and radiologically evident on both sides, an "index side" was defined, when (in order of importance): 1. only one ear met the SCDS diagnostic criteria; 2. both sides met the diagnostic criteria (bilateral SCDS), while (a) one ear gave predominant symptoms or (b) one ear had a larger amplitude at VEMP (according to the procedure described in Brantberg and Verrecchia [2009]),

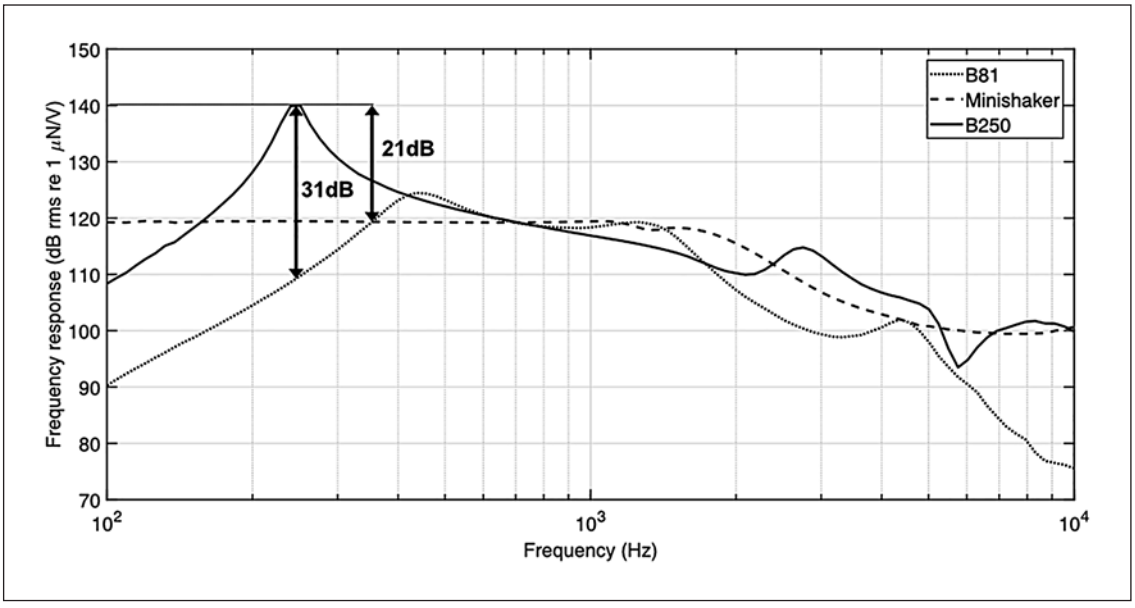

Fig. 2. The frequency response in units of decibel root mean square relative 1 μ Newton per volt (dB RMS re 1 μN/V) for B250 (solid line), Minishaker (simple dashed line), and Radioear B81 (double dashed line) between 100 and 10,000 Hz normalized to 1 V RMS input voltage. The 31 dB difference at 250 Hz between B250 and Radioear B81 is highlighted [Fredén Jansson et al., 2021].

or (c) one side showed a larger dehiscence at the temporal bone CT scans. The "non-index side" was consequently assigned as the other side. In this perspective, the present study differed from the reference experiment by Brantberg et al. [2016], in which it was only analyzed patients affected by unilateral SCDS. In the authors' opinion, when translating Brantberg's experiment into a clinical procedure, both sides should be taken in account, since the bilateral forms may represent up the 50% of the SCDS [Ward et al., 2021].

The control subjects were included only if presenting normal hearing thresholds for age, without any history of relevant audiovestibular, otologic, or medical disorders. They were age- and sex-matched with the case group. The index side in controls represented the side which alternatively returned the best AA threshold for each specific stimulus frequency. Consequently, the non-index side in controls was the side that gave the worse hearing threshold for each tested frequency. In this sense, the index side (the opposite for the non-index side) may have shifted ipsilaterally or contralaterally with respect to the stimulated ankle for stimuli at different frequencies. By this approach, the study permitted to compare the AA thresholds at the symptomatic/more symptomatic ear in SCDS patient with the best between the two AA thresholds obtained for each tested frequency in control subjects. Finally, when the ankle stimulations gave the same threshold on both sides, the index/non-index side was assigned randomly.

Despite the already good study power in Brantberg et al. [2016], obtained with only 10 subjects for group, we have extended the sample size to 20 subjects/group, to have a better control over the variability of the study outcomes. Three patients got surgery as treatment of the SCDS with a capping technique and with a transmastoidal approach, all by the same surgeon. They could be tested with AA before and after surgery.

In Table 1, there are listed the air conduction (AC) and bone conducted (BC) pure tone averages (PTA) and VEMP amplitudes for SCDS patients, referred to the index and non-index sides. Control subjects' PTA are not shown as those were normal for age according to inclusion criteria, in particular the $PTA_{125–750}$ was within 25 dB hearing level for all included subjects.

The two groups did not differ in age (SCDS: 51.8 ± 11 years; control: 49.4 ± 8.6 years, t test = 0.785, p = 0.44) or sex (females/males in SCDS: 11/20 and in control: 12/20, Fisher exact test, p = 0.50), according to subjects' matching.

AA: Test Procedure and Technical Specifications

All subjects were tested in a soundproof booth (T-Room; CA Tegnér AB, Stockholm, Sweden) with B250 transducer held in contact with the medial ankle malleolus by an elastic velcro band (EPISystem MP1022; Orthoservice AG, Chiasso, Switzerland) giving a constant pressure of approximately 10 N at the contact point (Fig. 1).

The B250 is a specially designed bone transducer that has a resonance peak at around 250 Hz. The frequency response was measured with the B250 attached to an artificial mastoid (B&K 4930) and calibrated for a static load of 10 N. For comparative purposes, also the frequency responses of the Minishaker B&K 4810 and audiometric transducer B81 are shown in Figure 2.

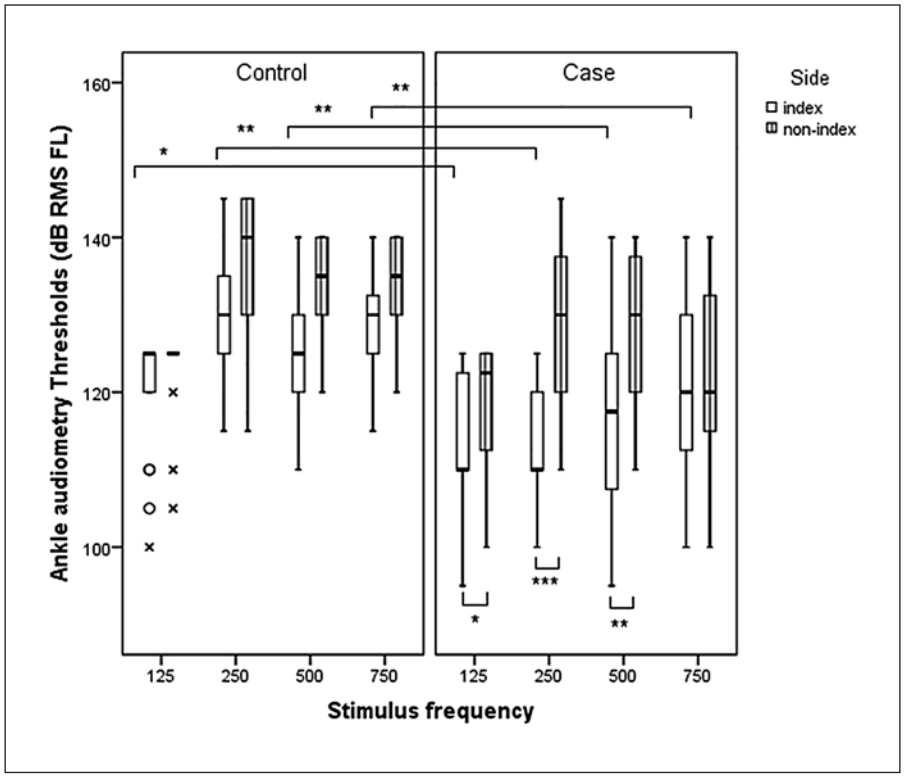

Fig. 3. Box plots indicating the AA distribution in the two groups (case/control). On Y axis, the value of AA given in dB FL; on X axis the four tested frequencies. The data were further sub-grouped relating to the index and non-index sides. o = outliers; x = extremes. Only significant between and within groups' differences related to the index side is shown with the relative level of significance (* <0.05; ** <0.01; *** <0.001); the within groups' differences in control group are expected significant but not shown, as a result of the assignment of index/non-index sides.

The B250 was connected with an audiometer (Madsen Itera; GN Otometrics A/S, Taastrup, Denmark) and generated sinusoidal warble stimuli at 4 frequencies 125, 250, 500, and 750 Hz. The stimulus intensity was calibrated in root mean square force level (FL; expressed in decibels relative to 1 μN) and was varied from 80 dB FL to the maximum force level related to the frequency tested (125 Hz – 120 dB FL; 250 Hz – 140 dB FL; 500 Hz – 135 dB FL; 750 Hz – 135 dB FL). This limitation is given by the audiometer output in relation to the frequency characteristics of the B250 bone transducer. In order to promote the lateralization of vibrational hearing to the ear ipsilateral to the stimulated ankle, a narrow-band masking noise (ISO 389-4) was applied in two steps (at 40 and 60 dB hearing level) to the contralateral ear for the tested side in all patients and controls. For the masking E-A-RLINK 3A (13.7 mm), disposable foam ear tips were used and connected to insert earphones E-A-RTONE 3A (3M Auditory Systems, Indianapolis, IN, USA). The tips were deeply inserted in both ear canals to minimize the risk of creating an occlusion effects [Stenfelt and Reinfeldt, 2007]. Moreover, to avoid the BC hearing contamination by AC each subject wore bilateral passive hearing protectors, Peltor Optime III H540A (3M, St. Paul, MN, USA).

The mode of threshold examination was the same as in routine audiometry (modified Hughson-Westlake method), i.e., after a positive response, the stimulus intensity was decreased by 10 dB, and after a negative response, it was increased by 5 dB. Subjects were instructed to respond when hearing a sound and to disregard any vibrotactile sensations. Further, if there was no response at the highest stimulus intensity, a substitute value exceeding 5 dB was used. We have noticed that some subject did refer a better hearing threshold to the contralateral ear, especially in SCDS patients tested at non-index side. This is irrespective to the applied contralateral masking. This aspect was judged relevant in a clinical perspective; consequently, the response lateralization was added as a variable in the analysis: the subject was asked to express which was the predominant side for vibrational hearing, ipsilateral to the stimulated ankle, contralateral to stimulation, or not defined (centralized).

Outcomes and Statistical Analysis

The AA thresholds obtained in each subject and different frequencies are listed in tables and showed in graphics (box plots or dot plots), referred to the index/non-index side. Response lateralization, ipsilaterally/contralaterally/indifferently to the stimulated ankle (1 = ipsi; −1 = contra; 0 = indifferent), was also taken in account. The AA results before and after surgery for the three operated subjects were listed separately in tables.

A first study hypothesis was that the AA data showed a significantly different distribution between the two groups. The difference in data distribution was studied with mixed model ANOVA, with one between subjects' condition (group belonging) and two within subjects' factors (stimulus frequency and side). A specific analysis was done for response lateralization.

A second aim of this study was to define the diagnostic properties of AA for SCDS. The diagnostic accuracy of AA for SCDS was studied with receiver operating characteristic analysis

Table 2. AA thresholds in dB FL and response lateralization (1 = ipsilateral; 0 = central; –1 = contralateral) for index and non-index sides in patients (P) and controls (C)

AA	Index side thresholds and lateralization								Non-index side thresholds and lateralization							
	125 Hz	Lat	250 Hz	Lat	500 Hz	Lat	750 Hz	Lat	125 Hz	Lat	250 Hz	Lat	500 Hz	Lat	750 Hz	Lat
P1	110	1	100	1	125	1	130	1	115	–1	125	–1	140	1	130	1
P2	110	1	110	1	140	0	140	0	120	–1	125	–1	135	–1	140	0
P3	110	1	110	1	125	1	115	1	125	0	135	1	135	1	115	1
P4	110	1	115	1	105	1	105	1	120	–1	130	1	120	–1	105	1
P5	110	1	110	1	105	1	120	1	100	–1	110	1	110	–1	120	1
P6	125	0	120	1	115	1	115	1	125	0	145	1	140	0	115	1
P7	110	1	115	1	115	1	100	1	115	1	115	1	130	1	100	1
P8	95	1	110	1	115	1	120	1	110	1	130	1	120	1	120	1
P9	125	0	110	1	120	1	120	1	125	0	145	1	140	0	120	1
P10	125	0	120	0	130	1	125	1	125	0	130	0	140	0	125	1
P11	110	1	110	1	110	1	120	1	125	0	130	1	135	1	120	1
P12	125	0	125	1	125	1	140	1	125	0	145	1	140	0	140	1
P13	95	1	120	1	95	1	115	1	125	0	140	1	130	1	115	1
P14	110	1	120	1	125	1	135	1	110	1	125	1	115	1	135	1
P15	120	1	125	1	125	1	130	1	125	0	135	1	130	1	135	1
P16	120	1	110	1	120	1	100	1	110	1	115	1	115	1	105	1
P17	105	1	120	1	120	1	120	1	105	1	125	1	125	1	120	1
P18	115	1	110	1	100	1	130	1	125	0	145	0	135	1	135	1
P19	125	0	100	1	95	1	110	1	125	0	115	–1	120	–1	120	–1
P20	110	1	105	1	115	1	100	1	120	1	115	1	110	1	100	1
C1	125	0	130	1	130	1	135	1	125	0	130	1	130	1	135	1
C2	120	1	130	1	130	1	130	1	125	0	140	1	130	1	130	1
C3	120	1	135	1	125	1	130	1	120	1	140	1	135	1	140	0
C4	125	0	140	–1	125	1	130	–1	125	0	140	1	130	–1	140	0
C5	125	0	145	1	115	1	120	0	125	0	145	1	135	1	135	1
C6	125	0	130	1	140	0	130	1	125	0	145	0	140	0	140	0
C7	105	1	115	1	120	1	120	1	110	1	115	1	120	1	125	1
C8	100	1	120	1	120	1	125	1	105	1	120	1	120	1	125	1
C9	125	0	125	1	120	1	130	1	125	0	140	1	135	1	130	1
C10	125	0	130	1	135	1	135	0	125	0	130	1	140	0	135	0
C11	125	0	120	1	125	1	130	1	125	0	145	0	140	0	140	0
C12	120	1	130	1	130	1	140	0	125	0	135	1	135	1	140	0
C13	125	0	130	1	125	1	125	1	125	0	140	1	135	1	130	1
C14	125	0	145	1	140	0	140	0	125	0	145	1	140	0	140	0
C15	125	1	125	1	130	1	125	1	125	1	130	1	140	0	130	1
C16	110	1	115	1	110	1	115	1	125	0	130	1	125	1	120	1
C17	110	1	135	1	120	1	120	1	125	0	140	1	125	1	125	1
C18	125	0	145	0	130	1	130	1	125	0	145	0	130	1	140	0
C19	125	0	125	1	130	1	140	0	125	0	145	0	140	0	140	0
C20	125	0	125	1	125	1	130	1	125	0	130	1	135	1	130	1
Patients	113.25±9.2		113.25±7		116.25±12		119.5±12		118.75±7.5		129±11		128.25±11		120.75±12	
	115.56±10.52								124.19±11.40							
Controls	120.5±7.8		129.75±9		126.25±7.6		129±7		123±5.5		136.5±9		133±7		133.5±6.5	
	126.37±8.56								131.50±8.50							

The last rows indicating "average ± SD" for each frequency and for all subgroups of frequencies.

(ROC). The area under the curve (AUC) was compared among the two groups (reference standard: SCDS diagnosis) for the four tested AA frequencies calculating the sensitivity/specificity values for different threshold levels only in case of AUC ≥0.8.

A third aim was to define in SCDS patients the correlation between AA and other objective measures in SCDS patients, as the VEMP responses, PTAs, and age, but also the effect of surgical correction on AA in the three operated patients (paired *t* test). All statistics were calculated assuming a significance level of $\alpha = 0.05$.

Results

AA Thresholds

The AA thresholds measured at the index side and non-index side at the four different stimulus frequencies in the two groups are represented in Figure 3. The AA thresholds are listed in detail in Table 2.

The difference in data distribution in the two groups was evaluated with a two-way ANOVA. The analysis included some assumptions' violations: $AA_{125\ Hz}$ in control group distributed not normally and presented outliers; $AA_{750\ Hz}$ showed no homogeneity of variance according to Levene's test ($p = 0.035$). However, given the clinical focus on the $AA_{250\ Hz}$, we did not alter the dataset with any transformation or exclusion.

The index side AA thresholds distributed differently between the groups ($F(1,38) = 4,676.4$, $p < 0.001$, partial $\eta^2 = 0.423$) and within the groups differently in the different tested frequencies ($F(3,114) = 371.08$, $p < 0.001$, partial $\eta^2 = 0.145$) with a frequency/group interaction ($F(3,114) = 158.07$, $p = 0.047$, partial $\eta^2 = 0.067$). The thresholds given by cases were on the average 7–10 dB lower than the ones given by controls. Moreover, the non-index thresholds in cases distributed not differently than the index thresholds in controls, except for the responses at 750 Hz. Among the cases, the thresholds of the index side differed significantly between the tested frequencies ($F(3,57) = 352.1$, $p < 0.001$, partial $\eta^2 = 0.361$). This was not true for the control group ($F(3,57) = 177.8$, $p = 0.104$, partial $\eta^2 = 0.102$). A two-way repeated ANOVA was applied in the only case group to study the differences among the tested frequencies between the two sides. Only one outlier was detected with a studentized residual value of 3,37 and was kept in the data analysis. To be noted that the data showed also a not normal distribution for the 125 Hz AA and for the non-index side also only for 500 Hz AA. There was a statistically significant two-way interaction between frequency and side, $F(3,52) = 13.11$, $p < 0.001$. The thresholds in the case group were significantly lower at index side compared to non-index side at frequencies 125 Hz (diff: 5.5 ± 2.1 dB), 250 Hz (diff: 15.7 ± 2.3 dB), and 500 Hz (diff: 12 ± 2.9 dB) but not for 750 Hz (diff: 1.2 ± 0.6 dB). Frequencies thresholds did not significantly differ at the index side ($F(3,57) = 2.152$, $p = 0.104$) but were significantly different among the tested frequencies at the non-index side ($F(3,57) = 8.9$, $p < 0.001$), specifically for 125 Hz when compared with 250 Hz (−10.25 ± 1.97 dB) and 500 Hz (−9.50 ± 1.84 dB).

Table 3. SCDS diagnostic accuracy for different thresholds levels of AA_{250}

AA_{250} thresholds (dB FL)	Sensitivity (%)	Specificity (%)
≤110	55	100
≤115	65	90
≤120	90	80
≤125	100	60

Diagnostic Accuracy of AA for SCDS

The diagnostic value of AA for SCDS was further determined by a ROC analysis. SCDS diagnosis was the reference standard for the analysis of the pooled AA thresholds obtained in the SCDS group (target condition) and healthy group (control condition). The analysis was repeated for each of the four tested frequencies.

Accordingly, the AA_{250} was the only test frequency with a clinically relevant diagnostic accuracy: $AUC_{250} = 0.928$; $AUC_{125} = 0.723$; $AUC_{500} = 0.765$; $AUC_{750} = 0.736$. The sensitivity/specificity was calculated at different AA_{250} threshold levels are listed in Table 3.

The highest diagnostic accuracy for AA_{250} was obtained with 120 dB FL as a test criterion. AA thresholds better than 120 dB FL detected SCDS patients with 90% sensitivity and 80% specificity. Moving to 125 dB FL, test sensitivity increased to maximum (100%) but the specificity lowered to 60%.

Hearing Lateralization during Ankle Vibration

SCDS patients referred mostly ipsilaterally when stimulated on the index side, with a remaining 5–25% of stimulations that could not be lateralized. When stimulated on the non-index side, they referred to the same side or centered, however, up to 20% reported the best hearing threshold contralaterally, i.e., heard on the affected or more affected ear. In contrast, only 5% in the control group referred their AA responses contralaterally to the stimulated ankle. Focusing on the AA_{250}, the thresholds' lateralization acquired a specific pattern, shown in Figure 4.

In patients, all the ipsilateral responses referred to index side stimulation were perceived within 125 dB FL. Interestingly, also the contralateral responses secondary to the non-index side stimulations were confined within 125 dB FL. Contrarily, in controls, the ipsilateral and central referred responses distributed widely through the limit level of 125 dB FL and the few responses referred contralaterally to ankle stimulation were all placed over 125 dB FL threshold. This configured a clinically relevant

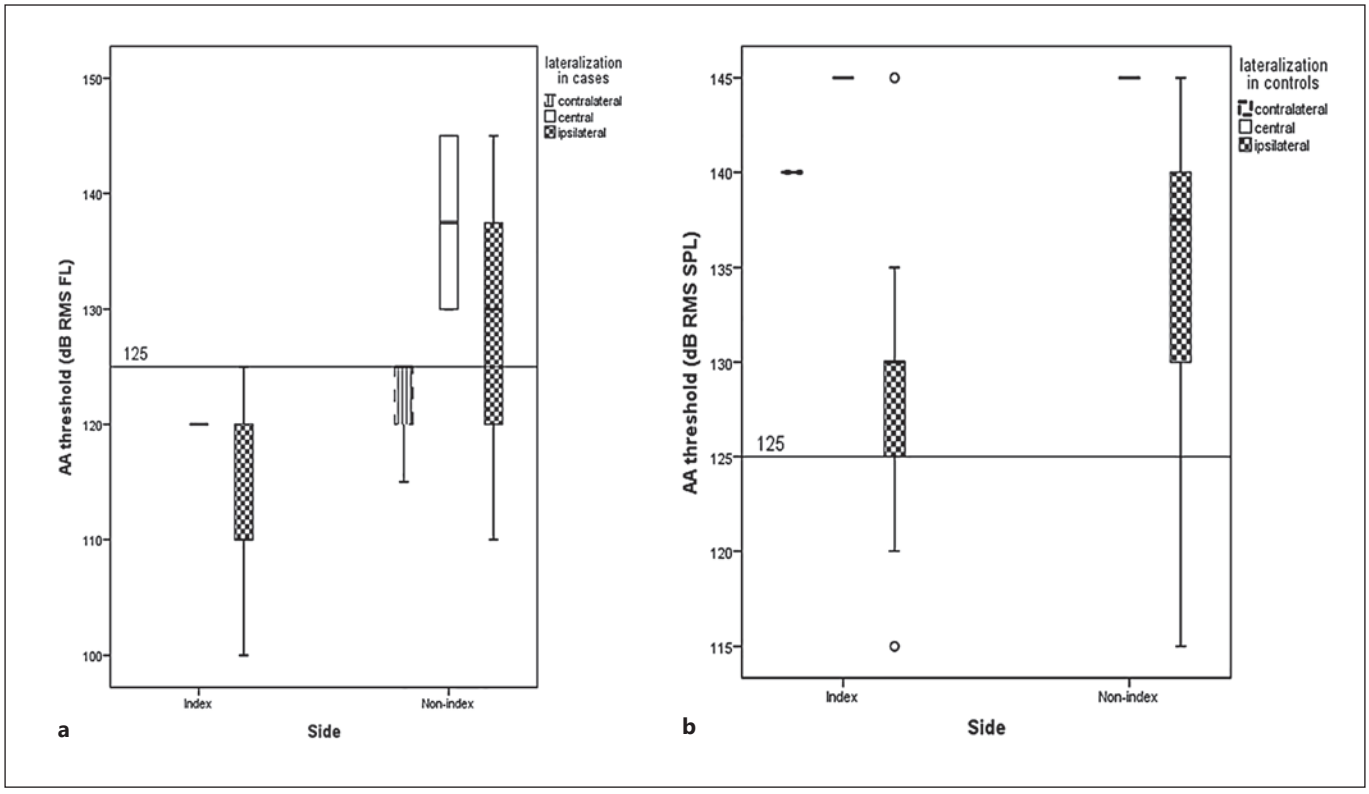

Fig. 4. Box plot: AA hearing lateralization in cases (**a**) and control subjects (**b**) for index and non-index sides. Chequered boxes indicate the ipsilateral responses, the white ones the responses referred centrally, and the striped ones the responses given contralaterally. **b** The centrally and contralaterally given responses show a ceiling effect.

pattern: all AA_{250} thresholds ≤125 dB FL referred contralaterally to the ankle stimulation were associated to the presence of a contralateral SCDS.

Patients with bilateral SCDS (5 cases) referred always ipsilaterally regardless the prominence of the symptoms, with all responses confined within 125 dB limit level. The same pattern (ipsilateral response ≤125 dB FL) was present in only 10% of controls and 27% of unilateral cases.

AA and Other SCDS Markers

No significant correlation was found between the AA_{250} and other SCDS markers (index side) in SCDS patients: BC 250 Hz hearing threshold (Person's $r(18) = 0.353$, $p = 0.127$), AC $PTA_{250–1,000\ Hz}$ ($r(18) = 0.182$, $p = 0.447$), and cVEMP corrected amplitude ($r(18) = -0.242$, $p = 0.305$). Moreover, no significant association was noted between AA and age ($r(18) = 0.105$, $p = 0.661$).

Effect of SCDS Surgery on AA

The effect of a SCDS surgical repair on AA could be studied in only three operated patients, comparing the pre- and postoperative AA. Patients were a male, 44 years, unilateral SCDS, another male, 33, with bilateral SCDS, and a female, 55, with bilateral SCDS. Once operated, the patients had a significant relief in HIBS at the operated side. Their responses are listed in Table 4.

Taking together the responses at different frequencies, all AA thresholds except one shifted upward postoperatively: $AApreoperative_{all\ frequencies}$: 119.2 ± 9.7 dB FL versus $AApostoperative_{all\ frequencies}$: 130.4 ± 9.4 dB FL (paired t test = 5.745 $p = 0.000$). The highest threshold elevation (20 dB) was observed in 25% of the measures, and the smallest (5 dB) in another 25%.

The highest threshold elevation was seen for 250 and 500 Hz stimuli, 15 dB and 16.7 dB respectively. For completion, these 3 patients improved also in their BC hearing at 250 Hz (8 dB) and 500 Hz (18 dB) and their cVEMP response normalized (corrected amplitude: 2.6, 2.0, and 1.0 before and 0, 0.4, and 0.3 after, respectively. A value <1 is within the normative range [Brantberg and Verrecchia, 2009]).

Table 4. AA thresholds for the operated ear before and after surgery

#	AA thresholds pre-operatively (dB FL)				AA thresholds postoperatively (dB FL)				Difference (dB)			
	125 Hz	250 Hz	500 Hz	750 Hz	125 Hz	250 Hz	500 Hz	750 Hz	125 Hz	250 Hz	500 Hz	750 Hz
1	110	100	125	130	125	120	140	140	15	20	15	10
6	125	120	115	115	125	130	135	120	0	10	20	5
14	110	120	125	135	115	140	135	140	5	20	10	5

The difference in thresholds for each patient and frequency tested is shown separately. All data referred to the index side (the operated one).

Discussion

This new hearing test, the AA, has shown relevant clinical and diagnostic features for SCDS. AA thresholds were significantly lower in SCDS patients when compared to matched healthy subjects. This was true for each frequency tested in the low/middle frequency spectrum (125–750 Hz), which was the frequency band affected in the reference experiment [Brantberg et al., 2016]. This frequency spectrum overlaps also with the one (250–1,000 Hz) mostly affected in conventional audiometry in SCDS patients [Ward et al., 2021]. Thresholds between the two groups differed majorly with the 250 Hz stimuli, with on the average 16 dB lower thresholds in cases. AA thresholds were also significantly lower at index side when compared to the non-index side within the case group. When patients were stimulated on the non-index side, the AA thresholds did not differ from the best ones reported by the control subjects, at least for frequencies 125, 250, and 500 Hz. Regarding the first study aim and according to these results, the AA not only identified the affected ear, or the more affected ear in SCDS subjects, but it also differed significantly when compared to healthy subjects.

The diagnostic value of AA for SCDS was studied with ROC analysis. It resulted that the AA by 250 Hz was the most accurate marker of SCDS diagnosis. Thresholds lower or equal to 120 dB FL could detect SCDS patients with 90% sensitivity and 80% specificity. By moving this level to 125 dB FL, the AA reached its maximum sensitivity but with a consistent reduction in specificity (60%). The 125 dB limit could also detect all the SCDS patients among those that referred a hearing sensation contralaterally to the stimulation. A SCDS clinical work-up based on a multistep diagnostic strategy could be initiated with AA_{250} as an accessible SCDS screening test. In a future scenario, a subject complaining symptoms compatible with HIBS may be easily screened with AA at non-tertiary audiological centers and when positive (at least one tested side having a $AA_{250} \leq 125$ dB FL) be addressed to tertiary centers for further diagnostics with VEMP and computer tomography.

In fact, AA has all the necessary requirements in terms of accessibility, cost containment, commercial devices' compatibility/feasibility to permit a wide diffusion of the procedure in clinical audiological testing. In this regard, a major role is played by the transducer B250 which maintains an optimal electro-mechanical output at low frequencies but with substantial weight advantage and easy handling in contrast to the Minishaker B&K 4810, as used in the reference experiment of Brantberg et al. With B250 it was possible to standardize the transducer pressure at contact point with a common adjustable velcro based attachment device. In contrast, the use of Minishaker B&K 4810 in the reference experiment was more operator specific given its vertical suspension at contact point. So, looking at the second aim of this study, the AA with a diagnostic accuracy up to 90% sensitivity and 80% seemed to provide diagnostic accuracy valuable for clinical purposes.

The AA may represent a clinical marker of HIBS in SCDS: the AA stimulation at ankle is today one of the most standardized methods to reproduce a controlled bodily transmitted vibration to the ear, reproducing the body sounds which are loudly perceived by SCDS patients. A fork test at ankle was proposed as a clinical test for bodily transmitted vibration hypersensitivity in SCDS [Benamira et al., 2015]; however, its diagnostic accuracy had never been systematically studied. Brantberg's experiment could show a good separation between SCDS and healthy controls by controlled bone vibrations at extremities. In similar experimental conditions, i.e., when the air conducted hearing contamination is abolished, also healthy subjects can hear body vibrations delivered at distant points from the ears [Ishikawa et al., 2021]. It is still a matter of discussion how these body vibrations are transmitted to the ear and, specifically, in which way these vibrations are perceived more loudly by SCDS patients. According to the speculation given by

Brantberg et al., a major role for HIBS would have been played by the soft tissue conduction (STC) [Sohmer, 2017]. A vibration at distant point may be transmitted by a column of soft tissues/liquids through the whole body up into the inner ear fluids compartments through the bony opening at the superior canal. In SCDS models [Songer and Rosowski, 2007], it was demonstrated that a bone vibration is facilitated in the vestibular partitions of the inner ear. This has been given as the basis for the enhanced BC hearing (BC hyperacusis) characteristic of SCDS [Pisano et al., 2012]. A finite-element model for prediction of BC hearing was recently presented [Chang et al., 2016] and used for predictions of SCDS related hearing changes [Stenfelt, 2020]. The model could predict a SCDS-specific BC hearing increase at 250/300 Hz with an enhancement of 15/23 dB in case of superior canal dehiscence. Moreover, the model seemed to downsize the role of STC for the HIBS, as the STC would have involved majorly the BC hearing at higher frequencies than the one resulted in the model. Looking at the data in this study, the largest difference in AA thresholds was observed at 250 Hz (−15.7 dB in SCDS patients), very similar to the BC hearing prediction made by the finite-element model of Stenfelt. By these considerations, it may be argued that HIBS is a direct consequence of BC hyperacusis (i.e., by an intrinsic SCDS ears' feature to enhance BC cochlea stimulation, regardless the mode of vibratory transmission to the ear through the body). This interpretation seems also to be predominant in the newly released international SCDS criteria [Ward et al., 2021] in which the HIBS has been defined "BC hyperacusis." A recent clinical study in bone-anchored hearing aids' recipients seems to reinforce the BC hyperacusis as the principal HIBS source, by demonstrating that the STC hearing is mostly determined by BC mastoid vibrations secondary to soft tissue conduction [Chordekar et al., 2018].

Looking at the final aim of this study, AA, in the specific the AA_{250}, showed no significant correlation with the BC hearing at 250 Hz, neither with AC PTA or cVEMP values in non-operated SCDS subjects. However, AA showed significant thresholds elevation after surgery, following the relief in HIBS reported by patients. In fact, the surgical correction shifted the AA_{250} from 119.2 dB FL, i.e., lower than the proposed limit level of 120–125 dB FL for SCDS diagnosis, to 130.4 dB FL, a value measured in healthy subjects not affected by HIBS. Moreover, this AA_{250} elevation, corresponding to HIBS relief, was accompanied by an elevation of BC PTA observed in these three operated patients, particularly enhanced at 250 Hz and 500 Hz. This is to remark, one more time, the strong association between AA, HIBS and BC hyperacusis above mentioned. If these results will be confirmed by larger series, AA would not only assume a role of accessible SCDS screening test but also of HIBS marker and a surgical outcome.

Conclusion

The AA is a new accessible test based on the BC stimulation at distance (ankle) with a novel prototype of bone transducer, the B250, which has shown promising diagnostic features for SCDS. It most probably represents a specific measure of the hypersensitivity for body sounds, commonly suffered in SCDS. AA hearing thresholds have not only been shown to be enhanced in SCDS when compared to matched healthy subjects, but they may also identify the affected or more affected side in SCDS patients. Moreover, AA thresholds elevation secondary to SCDS surgical correction seems to hint the relief of body sounds hypersensitivity referred by the operated patients. The introduction of new B250 bone transducer may promote the diffusion of AA as a hearing screening test for SCDS using conventional audiometric equipment. Larger studies are needed to confirm these results. In particular, AA must be studied in SCDS compared to alternative clinical conditions characterized by excessive hearing of body sounds, for example, patulous eustachian tube (breath, voice) and Meniérè's disease (pulsatile tinnitus).

Acknowledgments

Ortofon A/S is acknowledged for supplying prototypes of the B250 and Promobilia Foundation is acknowledged for financing a Postdoc for Luca Verrecchia. Luca Verrecchia thanks for supporting the SCAPA (scientific center for advanced pediatric audiology) research group and Foundation for support of innovation and research at Karolinska Institutet, Stockholm, Sweden. The authors thank also Anders Sjöstrand at Karolinska University Hospital, ENT Audiology and Neurotology Department, Stockholm, Sweden for helping in test conduction.

Statement of Ethics

The study was reviewed and approved by the Swedish National Ethical Committee, approval number: 2019-05214. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

Bo Håkansson has been supported by Ortofon A/S for this and other related projects. No other conflicts of interest, financial, or otherwise to be reported.

Funding Sources

This study was funded by Promobilia Foundation (F20605) and Tysta Skolan Foundation (FB20-0020).

Author Contributions

Luca Verrecchia designed and performed experiments, analyzed data, and wrote the paper; Luca Verrecchia, Karl-Johan Fredén Jansson, Magnus Westin, Aleksandr Velikoselskii, and Bo Håkansson performed testing; Luca Verrecchia and Aleksandr Velikoselskii collected data; Luca Verrecchia analyzed data and provided statistical analysis; Karl-Johan Fredén Jansson, Magnus Westin, Aleksandr Velikoselskii, Sabine Reinfeldt, and Bo Håkansson provided critical revision.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

Alkhafaji MS, Varma S, Pross SE, Sharon JD, Nellis JC, Santina CCD, et al. Long-term patient-reported outcomes after surgery for superior canal dehiscence syndrome. Otol Neurotol. 2017;38(9):1319–26.

Benamira LZ, Maniakas A, Alzahrani M, Saliba I. Common features in patients with superior canal dehiscence declining surgical treatment. J Clin Med Res. 2015;7(5):308–14.

Brantberg K, Verrecchia L. Testing vestibular-evoked myogenic potentials with 90-dB clicks is effective in the diagnosis of superior canal dehiscence syndrome. Audiol Neurootol. 2009;14(1):54–8.

Brantberg K, Verrecchia L. Effectiveness of different click stimuli in diagnosing superior canal dehiscence using cervical vestibular evoked myogenic potentials. Acta Otolaryngol. 2012;132(10):1077–83.

Brantberg K, Verrecchia L, Westin M. Enhanced auditory sensitivity to body vibrations in superior canal dehiscence syndrome. Audiol Neurootol. 2016;21(6):365–71.

Chang Y, Kim N, Stenfelt S. The development of a whole-head human finite-element model for simulation of the transmission of bone-conducted sound. J Acoust Soc Am. 2016;140(3):1635.

Chordekar S, Perez R, Adelman C, Sohmer H, Kishon-Rabin L. Does hearing in response to soft-tissue stimulation involve skull vibrations? A within-subject comparison between skull vibration magnitudes and hearing thresholds. Hear Res. 2018;364:59–67.

Crane BT, Lin FR, Minor LB, Carey JP. Improvement in autophony symptoms after superior canal dehiscence repair. Otol Neurotol. 2010;31(1):140–6.

Fredén Jansson KJ, Håkansson B, Reinfeldt S, Persson AC, Eeg-Olofsson M. Bone conduction stimulated VEMP using the B250 transducer. Med Devices. 2021;14:225–37.

Ishikawa H, Otsuka S, Nakagawa S. Basic properties of distantly-presented bone-conduction perception. Annu Int Conf IEEE Eng Med Biol Soc. 2021;2021:6376–9.

Naert L, Ocak I, Griet M, Van de Berg R, Stultiens JJA, Van de Heyning P, et al. Prospective analysis of an evidence-based symptom set in superior canal dehiscence syndrome. Otol Neurotol. 2021;42(2):e186–e192.

Pisano DV, Niesten MEF, Merchant SN, Nakajima HH. The effect of superior semicircular canal dehiscence on intracochlear sound pressures. Audiol Neurootol. 2012;17(5):338–48.

Sohmer H. Soft tissue conduction: review, mechanisms, and implications. Trends Hear. 2017;21:2331216517734087.

Songer JE, Rosowski JJ. A mechano-acoustic model of the effect of superior canal dehiscence on hearing in chinchilla. J Acoust Soc Am. 2007;122(2):943–51.

Stenfelt S. Investigation of mechanisms in bone conduction hyperacusis with third window pathologies based on model predictions. Front Neurol. 2020;11:966.

Stenfelt S, Reinfeldt S. A model of the occlusion effect with bone-conducted stimulation. Int J Audiol. 2007;46(10):595–608.

von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, STROBE Initiative, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. PLoS Med. 2007;4(10):e296.

Voth BL, Sheppard JP, Barnette NE, Ong V, Nguyen T, Jacky Chen CH, et al. The Gopen-Yang Superior Semicircular Canal Dehiscence Questionnaire: development and validation of a clinical questionnaire to assess subjective symptoms in patients undergoing surgical repair of superior semicircular canal dehiscence. J Laryngol Otol. 2018;132(12):1110–8.

Ward BK, Carey JP, Minor LB. Superior canal dehiscence syndrome: lessons from the first 20 years. Front Neurol. 2017;8:177.

Ward BK, van de Berg R, van Rompaey V, Bisdorff A, Hullar TE, Welgampola MS, et al. Superior semicircular canal dehiscence syndrome: diagnostic criteria consensus document of the committee for the classification of vestibular disorders of the Bárány Society. J Vestib Res. 2021;31(3):131–41.

Watson SR, Halmagyi GM, Colebatch JG. Vestibular hypersensitivity to sound (Tullio phenomenon): structural and functional assessment. Neurology. 2000;54(3):722–8.

Zhou G, Gopen Q, Poe DS. Clinical and diagnostic characterization of canal dehiscence syndrome: a great otologic mimicker. Otol Neurotol. 2007;28(7):920–6.