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Influence of tonotopic cochlear stimulation on subjective visual vertical – a pilot study

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Abstract. – OBJECTIVE: This pilot study aimed at evaluating the effect of tonotopic (basal) stimulation on the Subjective Visual Vertical (SVV) in patients unilaterally treated with a Cochlear Implant (CI).

MATERIALS AND METHODS: Ten adult subjects with severe to profound sensorineural hearing loss, who were implanted with a CI from Advanced Bionics (AB, Stäfa, Switzerland), model HiRes 90K™ or newer, were included in this prospective pilot study between September and December 2020. A specific CI processor (Naída CI Q90) was used to generate five different stimulation modes: simulation of either basal, medial, or apical electrodes, all electrodes on and all electrodes off. The examination of the verticality was carried out by means of SVV goggles both in the upright body position (head position 0 degrees) and with the head tilted sideways (–30°, –15°, +15°, +30°).

RESULTS: In each stimulation mode, there was a significant difference ($p < 0.05$) in SVV between the straight head orientation and the tilted head position. There were, however, no significant differences between the five CI settings in any given head position ($p > 0.05$). No significant differences could be found regarding the direction of SVV deviation relative to the operated ear ($p > 0.05$).

CONCLUSIONS: SVV could not be influenced by tonotopic CI stimulation. Different stimulation settings, patterns and intensity other than the auditory strategy may have to be developed to provide an adequate stimulus to the otolith organs.

Key Words:

Cochlear implant, Vestibular function, Subjective visual vertical, Vertigo.

Introduction

Vestibular dysfunction results in an impairment of gait, a higher risk of falls, decreased work ability and decreased social engagement[1]. The changing age-pyramid raises a special interest in enhancing mobility und reducing morbidity in the elderly. The treatment of vestibular degeneration is therefore of political, socio-economical, and medical interest[2].

Over the last decades, many attempts have been made to improve impaired vestibular function by electrical stimulation of vestibular afferents in the crista ampullaris either directly through the semi-circular canal (vestibular implant) or indirectly through cochlear implants (CI). However, the use of direct vestibular implants has only been used in experimental settings and has not yet received regulatory approval due to the lack of proof of effectiveness on one hand and, on the other hand, the severe possible side effects, such as hearing loss, that add to an unfavourable risk-benefit ratio[3].

The effects of CI implantation on the vestibular organ have first been suggested through vestibular side effects, such as imbalance and dizziness after cochlear implantation[4,5]. These effects can easily be explained by its close anatomical relationship to the hearing apparatus and thereby vestibular end-organ damage due to manipulation during electrode insertion, but also by postoperative inflammation or due to labyrinth fluid shifts. Thanks to central compensation, vestibular dysfunction after CI implantation is usually temporary[6,7]. Nevertheless, there also have been reported long-term vestibular effects after CI-Implantation even with maintained vestibular function, suggesting a vestibular co-stimulation upon CI-stimulation[8-11]. Some CI-patients even report a sound-induced vertigo, as well as objectified changes in subjective visual vertical (SVV)[12]. These changes can be explained by a saculoutricular co-stimulation of the cochlear implant[12]. The exact pathophysiology remains unknown, but presumably this vestibular co-stimulation is being achieved through a mechanism called ‘spread of excitation’[13].

Therefore, the significant effects on the SVV raise the question of whether there can be a frequency-spe-

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cific effect on the SVV upon selective CI-electrode stimulation and, in particular, upon basal stimulation because of its close proximity to the utriculus. We performed a prospective pilot study to evaluate the effect of tonotopic (basal) stimulation on the SVV in unilateral CI-implanted patients.

Materials and Methods

Study Design

We conducted this prospective pilot study at a tertiary hospital and academic center. The study was approved by the Local Institutional Ethics Committee (Approval protocol number EK 337/19, clinical trial center number 19-062) and in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP (good clinical practice) and the applicable regulatory requirement. We obtained written, informed consent from all study participants.

Eligibility Criteria

Ten (10) adult subjects with severe to profound sensorineural hearing loss, who were implanted with a cochlear implant from Advanced Bionics (Stäfa, Switzerland), model HiRes 90K™ or newer were included in this prospective pilot study between September and December 2020. Patients excluded were those who were not competent and mentally able to follow the instructions of the staff, as well as those with unsuccessful implantation (device or electrode defects, incomplete electrode array insertion, lack of neural stimulus responses) and pregnant women. There was no selection regarding pre- or postoperative neuro-otological examination. Patients were implanted at least 6 months prior to study begin.

Technical Details

A CE-certified CI processor (Naída CI Q90) provided by Advanced Bionics (Stäfa, Switzerland) for the purpose of this pilot study was used to generate five different stimulation modes, using the same strategy (Hi Res Optima S):

1. All electrodes (electrodes 1-16) turned off;
2. Basal (electrodes 12-16) and medial (electrodes 6-11) electrodes turned off;
3. Basal (electrode 12-16) and apical (electrodes 1-5) electrodes turned off;
4. Medial (electrodes 6-11) and apical (electrodes 1-5) electrodes turned off;
5. All electrodes (electrodes 1-16) switched on.

The stimulation parameters were set according to the individual settings of the patient's own processor to ensure that stimulation intensity was equal to or below its individual settings, as mandated by the local ethic commission, according to the original purpose of the medical device (Naída CI Q90). There was no misuse of the device and no change in the performance attributes.

The possible setting ranges were: sensitivity 0-10 dB, input dynamic range 20-80 dB, Pulse width 18-229 us, Charge 0-500 CU (clinical unit).

Clinical examination was performed by one of the authors and a neurotology technical assistant. The study visits included logging demographic data, an otolaryngologic examination, recording of vital signs, as well as height and weight, requesting medication, handing the processor, measuring SVV with the different CI settings (1-5), and recording side effects. The examination of the verticality was carried out by means of the C-SVV goggles (company Interacoustics, Chronos vision, Dortmund, Germany).

The C-SVV goggles allow digital determination of SVV by remote control while the vision is completely darkened. The software enables assessment in different head positions or static tilt positions. Measurements for this study were taken both in the upright body position (head position 0 degrees) and with the head tilted sideways (−30°, −15°, +15°, +30°). For the examination of the SVV, subjects were asked to set a luminous orange line (which is at the beginning randomly tilted by the computer system) in the vertical position using the arrow keys of a remote control. The C-SVV goggles are additionally able to include the head tilt of the subject α[°] in the measurement and the resulting differences or deviations were calculated accordingly (Δ[°]). Each measurement was repeated at least 3 times in every head position.

When measuring the SVV, the deviation of the set line angle from the actual tilt angle of the head is measured (Δ[°]. This results in minus sign ("too far to the left"), plus sign ("too far to the right") or in other words, overestimated or underestimated depending on the head tilting. A maximal deviation of ± 2.5 degrees in upright body position with no head tilt (head position at 0°) is considered normal, whereby the scatter of the measured values in immediately repeated examinations with head tilting without body tilting increases with the degree of head tilting. For example, with head tilts of 30 degrees a precision of ±10 degrees are still within the normal range[14]. All examinations were performed in a clinic room with a background noise of around 40 dB (SPL).

Table I. Patient characteristics.

Case No.	Sex	Age	Location (side)	Implant	Implantation Date	Study inclusion	Implant
1	M	67	links	HiRes 90k	10/2018	09/2020	Unilateral
2	W	41	rechts	HiRes Ultra 3D	01/2020	09/2020	Unilateral
3	W	82	rechts	HiRes 90k	08/2020	09/2020	Unilateral
4	W	54	links	HiRes Ultra 3D	08/2020	10/2020	Unilateral
5	M	72	rechts	HiRes Ultra 3D	06/2019	10/2020	Unilateral
6	M	64	links	HiRes 90k	09/2018	12/2020	Unilateral
7	W	76	links	HiRes Ultra 3D	05/2019	12/2020	Unilateral
8	M	47	links	HiRes 90k	02/2020	12/2020	Unilateral
9	W	78	links	HiRes Ultra 3D	01/2020	12/2020	Unilateral
10	M	64	rechts	HiRes Ultra 3D	10/2020	12/2020	Unilateral

Statistical Analysis

We performed a statistical analysis using SPSS version 22.0 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA). Normal distribution was excluded with the Kolmogorov-Smirnov Test. SVV Scores in different CI-Processor settings (1-5) were compared using the Friedman test and Chi-square. The effect size was determined using Kendall's W test. A p-value ≤ 0.05 was considered statistically significant. No pre-study caseload planning was conducted, and the results are exploratory in nature.

Results

Patient Characteristics

Between September and December 2020, we enrolled ten patients (5 female and 5 male; mean age 65.0 years (SD = 14.0, Range: 41-82 years). Patient characteristics and implantation side are shown in Table I.

SVV Value Testing with Different CI Settings

Absolute SVV deviation was considered, the average values in each head position are shown in Table II.

There were no significant differences between the five CI settings in any head position. For the small effect size (Kendall W=0.024) of head position at zero degrees, a sample size of over 1000 would be required for an adequately powered study using these assessing tools[15]. SVV in different CI settings with head straight and tilted head were compared. In all groups, there was a highly significant difference in SVV between the straight head orientation and the tilted head position. It was found that SVV determination was more accurate with straight head orientation than with head tilt (Table II).

SVV Value Dispersion

As a measurement of the consistency and precision of the SVV in estimation with different CI settings, we determined the average standard deviation values for each setting. No significant differences were found. SVV value dispersion with head straight and in the tilted head position with different CI settings was compared. In all groups, there was a highly significant difference in SVV between the straight head and the tilted head position. It was found that the dispersion of SVV values was lower with straight head orientation than with head tilt (Table III).

Table II. SVV testing with different CI settings.

Head tilt	Setting 1 CI off	Setting 2 Basal and medial off	Setting 3 Basal and apical off	Setting 4 Medial and apical off	Setting 5 CI on	*p*-value (Frieman)	Effect size (Kendall W)
−30°	**6.44**	6.59	7.87	8.36	8.93	0.318	0.131
−15°	**5.23**	7.39	5.32	5.95	7.52	0.511	0.091
0°	**3.10**	3.44	3.48	3.23	3.51	0.931	0.024
15°	7.05	**4.86**	6.87	8.25	6.59	0.070	0.240
30°	**7.13**	8.75	11.03	10.97	8.71	0.777	0.049

Table III. SVV value dispersion.

Head tilt	Setting 1 CI off	Setting 2 Basal and medial off	Setting 3 Basal and apical off	Setting 4 Medial and apical off	Setting 5 CI on	*p*-value (Frieman)	Effect size (Kendall W)
−30°	3.16	**2.60**	3.81	2.95	3.45	0.299	0.136
−15°	2.18	2.17	**1.82**	2.64	2.27	0.57	0.254
0°	1.36	**0.91**	1.63	1.48	1.33	0.308	0.133
15°	2.40	**1.51**	2.26	3.32	3.12	0.171	0.178
30°	3.21	**2.35**	3.78	4.05	3.03	0.431	0.106

Direction of SVV Relative to the Operated Ear

We assessed the direction of deviation relative to the operated ear, using Chi-square ($p > 0.05$). No significant differences could be found. Results are shown in Table IV.

Discussion

Ten adult patients with unilateral CI for rehabilitation of sensorineural hearing loss were successfully enrolled in a prospective study assessing clinical signs of vestibular dysfunctional in dependence of various stimulation CI settings.

The otolith-ocular reflex begins at the utricle for the perception of the SVV[16]. SVV testing operates on the principle that unilateral utricular hypofunction causes ocular torsion away from the side of the lesion and, consequently, deviation towards the side of the lesion[17]. Jin et al[18] have been able to demonstrate changes in otolith function associated with CI activity, which probably occur due to the close anatomic proximity between the otolith organs and cochlea. For the distances from the stapedial footplate to the vestibular end organs and cochlear duct, they range from 1.9 to 2.4 mm to the utricle, while the distance between cochlear duct and inferior border of the footplate is around 0.2 mm[19]. Furthermore, CI has been seen to spread outside the cochlea and stimulate other nearby neural structures[18,20]. Moreover, a vestibular involvement upon CI stimulation has been supported by histopathological evidence and laboratory testing[21].

As such, we hypothesized that SVV testing may be used to assess possible utricular dysfunction that following CI setting modification and its resulting tonotopic stimulation.

SVV was measured in absolute values to adequately characterize the degree of deviation. Patients were shown to overestimate, as well as underestimate SVV in consecutive examinations. The measurement of SVV not taking this in account, could lead to a median SVV deviation of 0, even though there is marked deviation with consecutive over- and underestimation SVV. To eliminate this issue, we considered the absolute values of SVV.

None of the above-mentioned stimulation modes we used in our study resulted in a significant difference in SVV results. As described by other authors, the SVV determination was more accurate with straight head orientation than with head tilt for the different CI settings[22]. Even an intact vestibular system in lateral head position has a less precise fine adjustment of the subjectively perceived earth vertical, which is why torso deflection rather than head deflection is favored in everyday situations[23]. In our study, we could

Table IV. Direction of SVV relative to operated ear.

	Deviation (relative to the operated ear)	
	Away (underestimating)	**Towards (overestimating)**
Setting 1 - CI off	4	6
Setting 2 - Basal and medial off	5	5
Setting 3 - Basal and apical off	3	7
Setting 4 - Medial and apical off	3	7
Setting 5 - CI on	2	8

also confirm this effect with different CI settings, which again supports the finding that utricular function may not tangibly be altered by tonotopic (auditory) cochlear stimulation.

It is possible that SVV may be insensitive in detecting influence of CI electrical activity on otolithic organs. Moreover, our testing was conducted in a room containing background noise of approximately 40 dB. It may be possible that, if testing was conducted with louder background noise or with a standardized acoustic stimulus, resulting in greater implant electrical activity, greater CI current spread would occur. This could potentially increase the likelihood of CI electrical activity influence on the vestibular system. The present study, however, suggests that CI electrical activity does not influence otolith function. Gnanasegaram et al[23] suggested that stimulation by cochlear implant electrodes may assist with recovery from perceptual tilt because electric input from the CI helped to correct tilt perception, especially when provided from the side ipsilateral to the tilt. However, electrical stimulation was provided at a maximally tolerable intensity level[23], which was not granted in our present study.

A methodic similar study by le Nobel et al[5] which, among other parameters, tested the influence of CI on the SVV also did not show any significant differences on SVV with CI on or off. Interestingly, the direction of the deviation (away from the implant ear) was significant, but this could be due to a statistical anomaly. Indeed, we also tested the direction of the deviation and did not find a consistent deviation of SVV to either side. The effect size of the group around Nobel suggested that a sample of around 500 patients would be needed for a powered study. We calculated a sample size to an adequately powered study in the similar order of magnitude (>1000 patients), which may attest for the insufficiency of the C-SVV method to test such subtle electrical changes in the utriculus. In healthy subjects, the vestibular afferent branches of the utriculus fire spontaneously at a rate of 90 action potentials per second in the absence of movement[24]. This study used an auditory simulation strategy, as imposed by our ethic commission, to not misuse the purpose of the CI. It is known that there is a basal stimulation rate of the otolith organs, which is fundamentally different from that of the auditory stimulation. Ramos Macias et al[25] performed a chronic electrical stimulation of the otolith organ with a constant stimulation rate in two patients. The authors showed with this vestibular implant an improvement of SVV from -9.6° to -1.3° on one patient and from 1.1° to 0.6° in the other patient, however – because of the aforementioned sample size – nothing can be said about its statistical significance[25]. This may suggest that stimulation settings other than the auditory strategy applied in our present study may be required to achieve tangible changes in vestibular function and SVV, in particular. Further studies are needed to address this stimulation issue, since although it has been shown that electrical CI activity may spread to the surround neural structures the auditory stimulus is probably not sufficient or adequate to consistently improve vestibular function. Finally, comprehensive tests of static and dynamic balance testing could possibly elucidate more subtle vestibular changes in Patients with CI.

Conclusions

Although some studies suggest that CI Implantation can improve vestibular function, this could not be confirmed in subjective visual vertical testing in a quiet environment. Tonotopic cochlear stimulation using parameters adapted to the hearing function did not have any deleterious effects on the subjective visual vertical as assessed in this study. The over- or underestimation of SVV, as well as the dispersion of SVV did not correlate with implant side or CI stetting. Different stimulation settings, patterns, and intensity other than the auditory strategy may have to be developed to provide an adequate stimulus to the otolith organs.

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Conflicts of interest

The authors declare no conflicts of interest.

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