



Stimulation Crosstalk Between Cochlear And Vestibular Spaces During Cochlear Electrical Stimulation

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Objectives: Possible beneficial “crosstalk” during cochlear implant stimulation on otolith end organs has been hypothesized. The aim of this case-control study is to analyze the effect of electrical cochlear stimulation on the vestibule (otolith end-organ), when using a cochleo-vestibular implant, comparing vestibular stimulation (VI) and cochlear stimulation (CI).

Methods: Four patients with bilateral vestibulopathy were included. A double electrode array research implant was implanted in all cases. Dynamic Gait Index (DGI), VOR gain measured by using vestibular head impulse test (vHIT), acoustic cervical myogenic responses (cVEMP) recordings, and electrical cVEMP were used in all cases. Trans-impedance Matrix (TIM) analysis was used to evaluate the current flow from the cochlea to the vestibule.

Results: While patients did not have any clinical vestibular improvement with the CI stimulation alone, gait metrics of the patients revealed improvement when the vestibular electrode was stimulated. The average improvement in the DGI was 38% when the vestibular implant was activated, returning to the normal range in all cases. Our findings suggest that any current flow from the cochlear space to the otolith organs was insufficient for effective cross-stimulation. The functional results correlated with the data obtained in TIM analysis, confirming that there is no current flow from the cochlea to the vestibule.

Conclusion: The only way to produce effective electrical otolith end-organ stimulation, demonstrated with this research implant, is by direct electrical stimulation of the otolith end organs. No effective cross-stimulation was found from cochlear electrode stimulation.

Key Words: basic science, cochlear implants, vestibular implant.

Level of Evidence: 4

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INTRODUCTION

Cochlear implants (CIs) have become one of the most successful implantable devices for the treatment of severe-to-profound hearing loss. The electrical stimulation produced by the CI system reaches different portions of the spiral ganglion to produce the perception of different tones at different intensities.

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Unwanted interference may happen during electrical stimulation. The most relevant is the stimulation of the VIIth cranial nerve, with a prevalence ranging between 1% and 14.9%, and is related to different inner ear pathologies such as otosclerosis.^{1,2} To manage this unwanted stimulation, the fitting must be modified to reduce the current density near the facial nerve during stimulation. Usually, this can be done by changing the pulse width and reducing the amplitude of the stimulus. However, in the worst cases, the only alternative may be to deactivate some electrodes.¹

In recent times, possibly beneficial “crosstalk” produced during cochlear stimulation on the otolithic maculae has been hypothesized. This idea is based on the same pathophysiology that is observed in cases of unexpected facial nerve stimulation. Although crosstalk seems like an undesirable side effect, improvements in balance may result for some.³

Vestibular diseases and hearing loss are frequently associated. In fact, a large population of CI candidates also have vestibular problems.⁴ In addition, one possible side effect of cochlear implantation is the damage of vestibule in the implanted ear. This damage may produce a vestibular dysfunction after surgery that is usually compensated. This clinical situation suggests possible cross-stimulation in the vestibular area from the CI, giving relief for vestibular symptoms.⁵

Some literature presents positive effects of CI stimulation on balance.³ One of the most promising research projects is the “BalanCI” device.⁶ This device produces different sounds depending on the pitch and roll of the patient’s head.⁶ On the other hand, there are also other authors that had not observed any vestibular effect, or in fact demonstrated a negative effect to the patients’ balance. Other authors consider this effect as a conditioning effect, rather than a direct stimulation effect.⁷

Bilateral vestibulopathy (BVP) is one of the most prevalent etiologies of imbalance that used to be under-diagnosed. Patients with BVP report imbalance and dizziness when maintaining an upright position or when moving. In scenarios of head motion and in darkness, these symptoms are more severe.⁸ In a high number of patients, despite the severe impact on health, vestibular function cannot be restored, and vestibular implantation may be the only solution to improve their clinical situation in the future.

Different research groups are focussed on the development of vestibular implants for the treatment of balance problems.⁹ The otolith end-organ approach has been performed by the European Consortium “Bionic VEST”.⁸ All cases included in this study were implanted with a cochleo-vestibular implant device. The device is a custom-modified CI CI24RE (VEST), from Cochlear Ltd (Lane Cove, NSW, Australia) with a full-banded straight electrode, with three contacts for otolith end-organ stimulation, and a perimodiolar electrode array with 19 half-banded contacts for cochlear stimulation.¹⁰ Having two different arrays brings the possibility to analyze the electrical relation between the cochlear and vestibular space.

Trans-Impedance Matrix (TIM) is an electrical recording system based on electrical field imaging (EFI).^{11,12} In TIM, the CI stimulates one contact and records the decay of the electrical potential along all other contacts. The decay constants, in general, may depend on electrode design and position, cochlear condition, and tissue properties. In this research, patients had an electrode array inserted in the cochlea (19 contacts), and the electrode array inserted in the vestibule (3 electrode contacts). This configuration of the electrodes allowed measurements of the current flow between the two different spaces.

OBJECTIVE

The aim of this study is to study the effect of electrical stimulation in the vestibule when stimulation is made in the cochlea and *vice versa*. For this purpose, a TIM test was recorded in all patients via the cochleo-vestibular implant. The clinical effects of isolated cochlear stimulation and isolated VI were also studied.

MATERIAL AND METHOD

The current study was conducted according to the Ethics Committee of our medical center (CEIC 2020-020-1) and performed in agreement with the 1964 Helsinki Declaration and similar ethical norms. All patients were provided with written informed consent before participating. All the procedures involving human participants were in agreement with the ethical principles of our institutional research committee.

Four cases matched the following criteria and were therefore included in the study: bilateral profound hearing loss, older than 18 years of age, and meeting the criteria of the consensus for vestibular implantation of Bárány Society.¹³

According to Barany’s criteria: *For the diagnosis of BVP, the horizontal angular VOR gain on both sides should be <0.6 (angular velocity 150–300°/s).*

Regarding the etiology: meningitis was found in one case, Cogan Syndrome in another, and in two cases the etiology was unknown. All four cases were male ranging between 39 and 58 years of age. All patients preoperatively presented with all the diagnostic criteria for BVP according to the Consensus of Diagnostic Criteria of the Classification Committee of the Bárány Society.

All cases had participated in previous rehabilitation sessions, in addition to a daily home exercise program. A minimum follow-up of 1 year prior to the implantation was performed in all cases without substantial benefit. Patients also presented with profound sensorineural hearing loss.

The exclusion criteria were: unwilling to participate, not fulfilling cochlear implantation criteria, inner ear anomalies that prevent full insertion of electrode (such as ossification), retro-cochlear or central hearing impairment, general medical contraindications for surgery, chronic depression, dementia, and cognitive diseases, cerebellar ataxias without BVP, downbeat nystagmus syndrome or peripheral neuropathies.

Surgical Procedure

A double electrode array implant, CI24RE-VEST, (Cochlear Ltd., Sydney, NSW, Australia) was used, after European Medical Agency approval for research (September 26, 2020). This implant has two electrode arrays one for cochlear stimulation and one for VI. The vestibular electrode array is full banded, with a 0.2 mm radius. Each contact has a cylindrical band of 0.3 mm in width. The interelectrode space is 0.2 mm on each lead. This electrode design was selected to ensure that the contacts could be facing the closest area of neural tissue related to the saccular area. The cochlear electrode array was based on the Cochlear CI512[®], but with 19 contacts. Vestibular electrode array has three electrode contacts: E1, E2, and E3; whereas the cochlear electrode array has 19 electrode contacts ranging from E4 to E22.

The basic profile of electrical stimulation to obtain the vestibular response consists of an ACE (RE) coding strategy with MP1 + MP2 stimulation, a maximum of 8, with a stimulus speed between 900 and 1200 Hz and a pulse width of 25 μ s, depending on the patient’s response characteristics. Electrodes 1, 2, and 3 were used with the same C value and a dynamic range of 1, based on responses obtained intraoperatively.

The same surgeon performed all procedures (A.R. M.). A temporalis muscle flap was performed, following the same principles as in a standard CI surgery. Regarding the mastoidectomy, the anatomical landmarks were the sigmoid sinus, incus, and lateral semicircular canal, and it was extended to the attic. Posterior tympanotomy is performed at this time with a clear exposure of the long

process of incus, stapes, and round window. After cochlear electrode array insertion and testing, the vestibular electrode array (otolith area) was inserted. Opening of the vestibule was performed by performing a 0.5 mm stapedotomy with CO₂ laser beam just medial and inferior to the anterior crus of the stapes to position the three contacts close to the area of the inferior vestibular nerve afferents (saccular macula). The saccular macula is located on antero-inferiorly, presenting a mean distance from the oval window of 1.4 mm (minimum of 0.8 mm). The utricle is located on the postero-superior region 1.4 mm from the oval window (minimal distance of 0.2 mm).

Trans-Impedance Matrix (TIM)

Vanpoucke et al. described a system of using electric field imaging to produce an electrical distance matrix from differences in the passive voltage measured at adjacent recording electrodes.¹¹ The voltages measured at each recording electrode are normalized, by dividing by stimulating current, to produce impedance values (Ohm's Law) or "transimpedances", and that generate the TIM. TIM procedure, used in this study is as follows: an electrode is stimulated and the observed electric potential along the electrode array is recorded. The neighboring electrode is also named for stimulation and the next set of observations are recorded. This process is automatically repeated until the whole electrode array (cochlear and vestibular) has been stimulated. As the distance from the stimulating electrode increases, the potential values decrease. This test was repeated intraoperative and 1 month postoperative when activation of the vestibular implant was performed.

The applied signal to the electrodes is a biphasic square signal, the amplitude level of which is settled at 200 current levels, corresponding to 1.02 mA. The determinations are performed at the end of the first trailing edge of the biphasic current pulse. The data is recorded in a matrix. The rows define the target electrode, where the measurement is taken, and the columns refer to the active electrode, where the stimulus is produced.

Disyllabic Word Test in Silence in SPANISH

Recorded materials were presented at 65 dB sound pressure level with the patients seated 1 m from the speaker (0° azimuth). A calibrated compact disc was used rather than a live voice. The variable to be recorded for speech in silence was the "correct words" at 65 dB sound pressure level for 2 lists of 25 words.¹⁴

Dynamic Gait Index

The Dynamic Gait Index (DGI) assesses an individual's capability to modify balance while walking in the presence of external demands. It was developed as a clinical tool to assess gait, balance, and fall risk. It evaluates not only the usual steady-state walking, but also walking while performing other challenging tasks. The DGI was developed to assess the likelihood of falling in aged adults by testing eight angles of gait. It was administered

following the published instructions and always with the same observer to increase the reliability of the results. The score ranged from 0 (i.e., lowest position of function, high risk of falling) to 24 (i.e., highest position of function, without risk of falling).^{15,16}

To correlate the TIM results we also analyze the following neurophysiological findings:

- a. We measured angular VOR gain and saccades by video head impulse test (vHIT) (ICS Impulse type 1085 from GN Otometrics A/S, Denmark) with and without vestibular implant stimulation.
- b. All patients underwent acoustic cVEMP recordings, before and after surgery. To obtain electrical cVEMP (EcVEMPs) recordings after surgery, a second test using Cochlear's Custom Sound Evoked Potential Software tool (version 5.2) was used. A monopolar 1 (MP1), Current level: 180, Stimulus Pulse Width: 25 μ s, Stimulus Inter Phase Gap: 7 μ s, Stimulus Nr of Pulse per Burst: 1, Stimulus Duration: 57 μ s, Stimulus Repetition Rate: 35 Hz, Number of Sweeps: 1200, was used as stimulus. In this study, cervical vestibular-evoked myogenic potentials were obtained by using Eclipse EP 15/EP25/VEMPs (Interacoustics AS, Assens, Denmark system).

RESULTS

After surgery, no side effects were found. Pulse train was used in each vestibular electrode array contact (120–180 pulses per second [pps]). The stimulation current range was from 80 to 180 CL and each phase duration was 25 μ s/phase. The vestibular stimulus was not acoustically sensitive.

In all cases, the TIM results show that there was a discontinuity between the cochlear and vestibular spaces. This is shown in Figure 1, where there is a clear change in the transimpedance values in the area where the stimulation is produced, and in another place where it's recorded. For illustration, when we stimulate electrode 1 (vestibular) and record at electrode 5 (cochlear) the transimpedance value is veritably low.

Additionally, patients were asked if, during VI, they perceived any sound; None reported the perception of sound during vestibular-only stimulation.

Intraoperatively, electrically evoked vestibular compound action potentials (VRT) were obtained in all patients. The VRT response morphology consisted of a biphasic waveform with an initial negative peak (N1) followed by a positive peak (P1), and latencies were typically between 180–210 μ s for N1 and 290–360 μ s for P1. We could observe a shorter latency for N1 and P1, and also a small amplitude in N1P1, if compared with regular neural response telemetry (NRT) from the cochlear nerve. (Fig. 2).

All cases improved their hearing perception after implantation. The average improvement was 70% in word recognition score in quiet when cochlear stimulation was active. There was no benefit with vestibular electrode stimulation only. Table I.

Regarding vestibular improvement, patients did not experience any improvement with CI stimulation alone. Preoperatively, 3 out of 4 had a pathological DGI score.

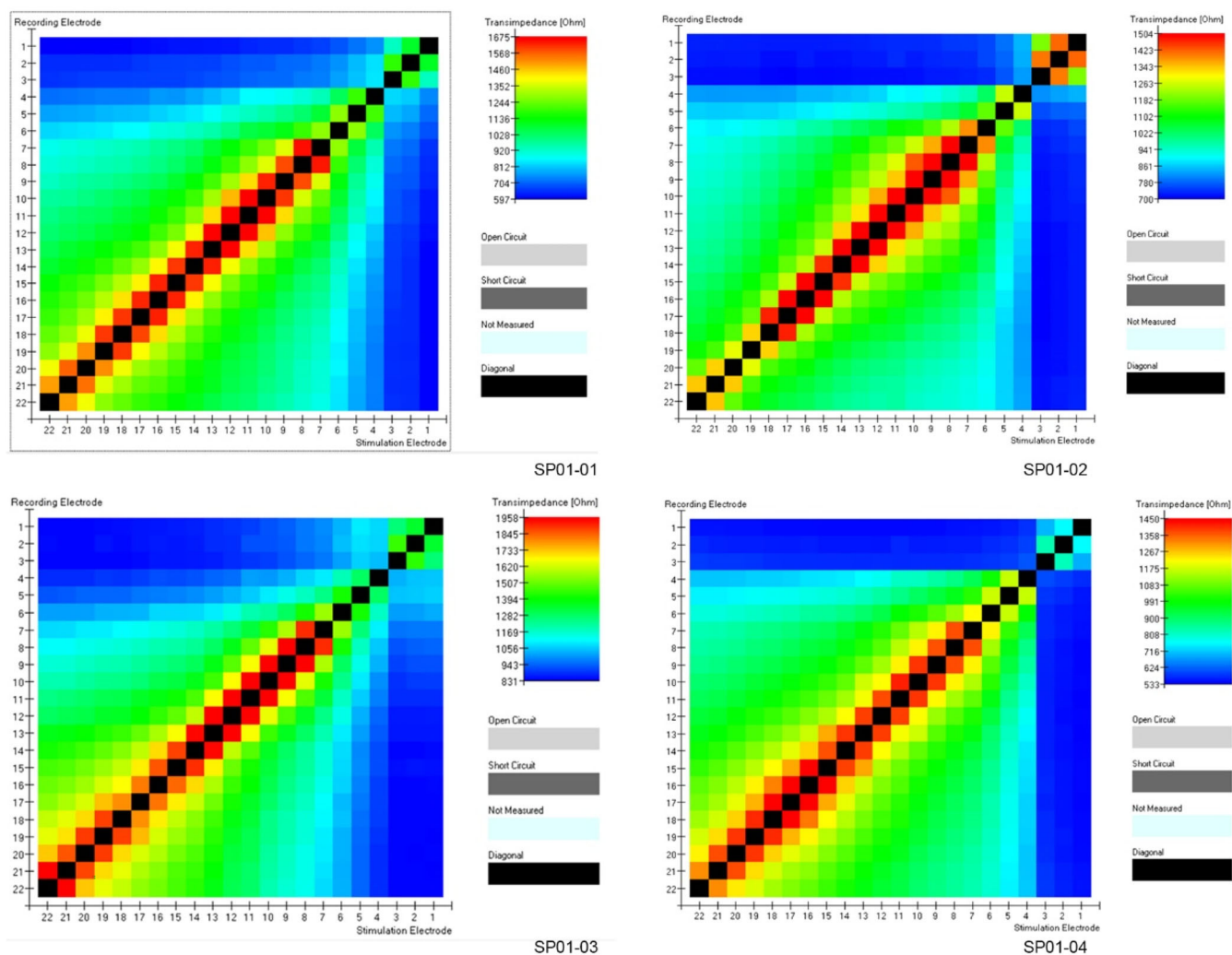


Fig. 1. Trans-impedance recordings with the CI24RE (VEST). All figures show two different spaces: one for the vestibular electrode contacts (E1, E2, and E3) and one for the cochlear electrode contacts (E4 to E22). No current flow could be observed between the cochlea and the vestibular space. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

There was no improvement with only the CI being stimulated. With the vestibular implant active, all four subjects experienced an improvement in DGI scores (between 3 and 9 points), all of them achieving the maximum score. (DGI: Total Score = 24, values $<19/24$ = predictive of falls in the elderly, $>22/24$ = normal situation) (Table II.)

Also, the minimum clinically important difference of the DGI is 4 points, which was achieved in 3 out of 4 cases.¹⁷

We measured angular VOR gain and saccades by video head impulse test (vHIT) with and without vestibular implant stimulation in the same visits to reduce the effect of learning over repeated trials. All patients presented with a bilaterally pathological horizontal angular VOR and at least one pathological vertical angular VOR gain ≤ 0.6 , measured by the vHIT.

In all four patients, acoustic cVEMPs were absent before and after surgery, and electrical cVEMPs were obtained in the implanted side after VI surgery. P1 and N1 latencies range were 11.33–13.6 for P1 and 18.33–21 ms

for N1, respectively. These results were stable, assuming the activation of the vestibulocollic reflex and, consequently, of the otolith organ activation. We consider it interesting to note that in patients with vestibular implants, fast saturation occurs after generating a greater intensity above the threshold used in their daily use.

DISCUSSION

Vestibular dysfunction is prevalent in CI candidates. Abnormal VOR results are associated with an increased possibility of dizziness lasting longer than 1 month postoperatively.¹⁸ The possibility to use the same CI for the treatment of the undesired possible effects of the CI in vestibular function is attractive. Our findings suggest that the current flow from the cochlear space to the otolith organs was very weak and incapable of effective cross-stimulation from the cochlea to the vestibule. Gait and neurophysiological findings of the cases revealed improved outcomes when the vestibular electrode was stimulating, compared

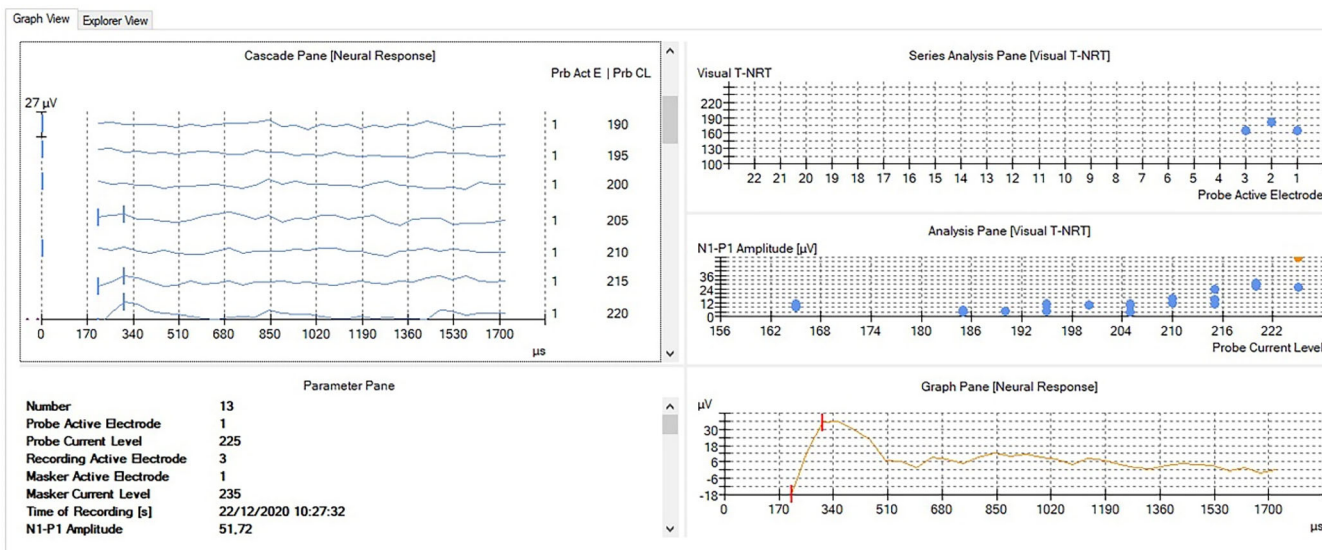
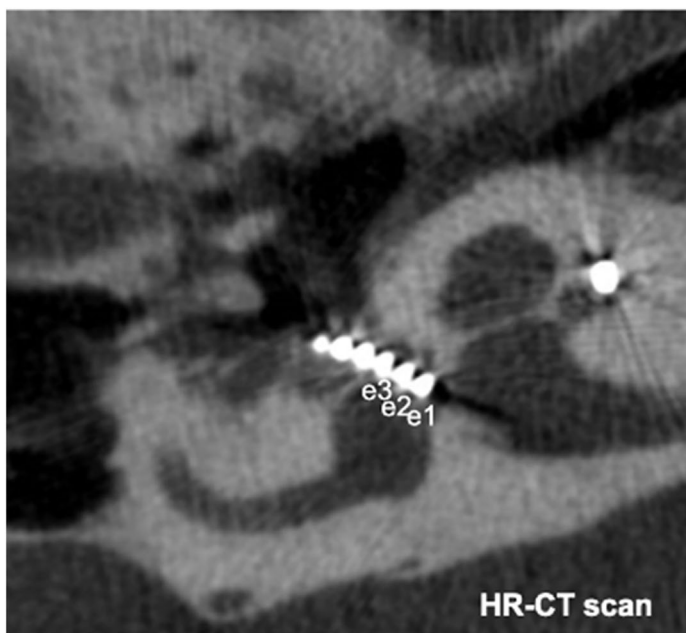


Fig. 2. Electrically evoked compound action potentials were obtained in all patients. The VRT response morphology consisted of a biphasic waveform with an initial negative peak (N1) followed by a positive peak (P1) [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

TABLE I.

Disyllabic Test Evaluation in Quiet. Pre-Operative, Only Cochlear Implant, Cochleovestibular Implant Mode, and Only Vestibular.

Subject	Pre-Op	CI	CI/VI	VI
SP01-01	0%	60%	60%	0%
SP01-02	0%	76%	76%	0%
SP01-03	32%	92%	92%	20%
SP01-04	0%	84%	84%	0%

TABLE II.

Dynamic Gait Index Scores in Three Conditions: Pre-Operative, Only Cochlear and only Vestibular.

Subject	Pre-Op	CI	VI	Improvement VI
SP01-01	19	19	24	+4
SP01-02	21	21	24	+3
SP01-03	16	16	24	+8
SP01-04	15	15	24	+9

to the pre-operative results. In the case of CI-only stimulation, there was no difference in the vestibular function compared to the preoperative condition (Fig. 1). The

functional results correlated with the data from the TIM results and confirm that there is no current flow from the cochlea to the vestibule or *vice versa*.

Although there is a positive impact of the CI on balance described in other publications, these results may be related to the effect of spatial information from the sound information as well as localization of the sound source.¹⁹

Other findings showed a positive impact while using a CI (attached to an inertial motion), by using different sounds for coding the tilt and roll of the head.⁶ Other authors observed improved balance 1 year after cochlear implantation and attributed this to central compensation.²⁰ Based on our results, these positive benefits are substantially based on sensory substitution rather than an effective electrical cross-stimulation of the vestibular peripheral organ. Sensory substitution provides balance information by producing auditory signals that may help to improve balance.

Other sensory substitution systems have demonstrated a positive impact on the management of vestibular pathologies. Haptic feedback devices²¹ or tongue stimulation²² deliver balance information to patients, which helps during the rehabilitation process.^{21,23} CI stimulation can function as a sensory substitution, by providing audible information, which contributes to maintaining their balance as a rehabilitation system.

In this research, we try to clarify whether stimulation of the cochlear electrodes spreads to the vestibule, and vice versa, and also, we report some functional outcomes and neurophysiological findings in patients implanted with a vestibular implant, providing data that both clinical and neurophysiological findings seem to be related to VI and not to cochlear stimulation.

Regarding the mechanism of action, electrical stimulation of utricle- and saccule-targeting electrodes may improve the spatially and temporally distinct responses. Electrical stimulation of the otolith organs was considered more complex to accomplish due to the reversed polarity of the hair cells on both sides of the striola. Several otolith studies have been performed in animals, while only recently the first in-human trial was initiated. As Curthoys et al. suggested, the constant electric stimulation substitutes for the absent saccular neural input to the vestibular nuclei and the cerebellum in these patients and indirectly via these structures to other structures, which have been of great interest in motor control recently. There are projections from midline cerebellum to basal ganglia, including the striatum, which are structures involved in the initiation of gait.²⁴

Limitations

Despite the small number of patients included in the study, it is the first to present the spread of CI electrical stimulation and its relation with the otolith organ function.

We use exclusively a research cochlea/vestibular research implant, approved by the European Medical Agency (CI24RE-VEST, from Cochlear Ltd (Cochlear Ltd., Sydney, NSW, Australia), and the production of this device is very limited, and only for research purposes.

CONCLUSIONS

Within the protocol used in this study, there was no cross-stimulation from vestibular to cochlear electrodes

as demonstrated by TIM. Cochlear stimulation alone did not seem to result in improved DGI scores.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no financial interests or personal relationships that could have appeared to influence the work reported in this article.

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