Vestibular implants: hope for improving the quality of life of patients with bilateral vestibular loss

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Abstract— **The vestibular system plays an essential role in crucial tasks such as postural control, gaze stabilization, and spatial orientation. Currently, there is no effective treatment for a bilateral loss of the vestibular function (BVL). The quality of life of affected patients is significantly impaired. During the last decade, our group has explored the potential of using electrical stimulation to artificially restore the vestibular function. Our vestibular implant prototype consists of a custom modified cochlear implant featuring one to three vestibular electrodes implanted in the proximity of the ampullary branches of the vestibular nerve; in addition to the main cochlear array. Special surgical techniques for safe implantation of these devices have been developed. In addition, we have developed stimulation strategies to generate bidirectional eye movements as well as the necessary interfaces to capture the signal from a motion sensor (e.g., gyroscope) and use it to modulate the stimulation signals delivered to the vestibular nerves. To date, 24 vestibular electrodes have been implanted in 11 BVL patients. Using a virtual motion profile to modulate the "baseline" electrical stimulation, vestibular responses could be evoked with 21 electrodes. Eye movements with mean peak eye velocities of 32°/s and predominantly in the plane of the stimulated canal were successfully generated. These are within the range of normal compensatory eye movements during walking and were large enough to have a significant effect on the patients' visual acuity. These results indicate that electrical stimulation of the vestibular nerve has a significant functional impact; eye movements generated this way could be sufficient to restore gaze stabilization during essential everyday tasks such as walking. The innovative concept of the vestibular implant has the potential to restore the vestibular function and have a central role in improving the quality of life of BVL patients in the near future.**

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I. Introduction

The vestibular system provides essential motion information for the control of balance. It is located in the inner ear and composed of five sub-units (three semicircular canals and two otholitic organs). The vestibular system enables the generation of adequate compensatory eye movements during head or body motion via a three-neuron reflex arc, the vestibulo-ocular reflex, allowing optimal image stabilization on the retina during motion. In addition, the vestibulo-spinal and the vestibulo-collic reflexes allow tuning of the limbs, head, neck, and the axial muscles. They are responsible for postural control. Finally, the vestibular system plays an important role in spatial orientation by providing the cortex with simultaneous information about motion and head position relative to gravity.

The bilateral loss of the vestibular function (BVL) is an often underestimated condition that leads to severe functional consequences. The main complaints of affected patients are chronic imbalance and blurred vision in dynamic conditions (i.e., while walking). Nevertheless there is growing evidence that due to multifocal vestibular projections, emotions, memory, cognitive abilities and personality can also be affected. BVL has a negative impact on the quality of life [1] and imposes an economic burden on patients and society [2]. Currently treatment is limited to physical therapy, which is not effective in the long term in the majority of the cases.

The enormous success of cochlear implants in the rehabilitation of severe to profound deafness has prompted researchers to explore the analogous concept of a vestibular implant to rehabilitate patients with a BVL. Briefly, such a system uses inertial sensors (i.e., a gyroscope and/or accelerometer) to detect motion information. Such information is translated into a pattern of neural excitation by an external signal processor. This pattern is wirelessly transmitted to an implanted stimulator which finally delivers the corresponding patterns of electrical stimulation via electrodes implanted near the ampullary branches of the vestibular nerve afferents. Research both from animal and human studies has demonstrated that electrical stimulation is an effective means to restore the vestibulo-ocular reflex [3-13].

Our research group has a unique pool of 11 BVL patients implanted with three generations of vestibular implant prototypes. In this paper we report on the main characteristics of eye movements that could be evoked in these patients. In addition, to confirm whether electrically evoked eye

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movements are large enough to impact visual function, the impact of artificial eye movements on patients' visual acuity (VA) was assessed.

II. Material and Methods

A. Device, Patients, and Surgery

Eleven BVL patients with bilateral or unilateral severe deafness were recruited between 2007 and 2013 at the ENT Departments of the Geneva University Hospitals in Switzerland and of the Maastricht University Medical Centre in the Netherlands. BVL was defined with 3 criteria: 1) mean peak slow phase velocity of ≤5°/s in bilateral bithermal caloric irrigations, 2) pathological Head-Impulse-Test (HIT) for all 6 canals, and 3) low (<0.2) or no gain at rotatory chair tests(0.05-0.1Hz, ω_{max}=60 deg/s). Video-nystagmography(VNG) and electronystagmography(ENG) were used for vestibular tests. HIT was performed with the Ulmer system(Synapsis©; Marseille, France), the EyeSeeCam(EyeSeeCam VOG©; Munich, Germany) and/or the ICS Impulse (Otometrics, Denmark).

A modified cochlear implant providing one to three-3 extracochlear electrodes was developed in collaboration with MED-EL (Innsbruck, Austria). During surgery, the cochlear array was inserted and each of the extracochlear branches was placed in the proximity of the posterior, lateral, and superior ampullary branches of the vestibular nerve. For simplicity purposes from now on we will refer to PAN, LAN, and SAN for electrical stimulation delivered with each of the extra-cochlear, vestibular electrodes. In five patients (S1-S5), an extralabyrinthine surgical approach was performed [14, 15]. In six patients (S6-S11) an intralabyrinthine approach was used [16]. Details on patient demographics and each of the implanted devices are presented in Table 1.

Device activation took place no earlier than four weeks postoperative, when healing of the surgery site was assumed to be complete.

B. Electrical Stimulation

Cochlear electrodes were always switched off during the experimental procedure. Stimulation was controlled using a custom, computer based setup [17]. Stimulation was delivered to each electrode separately, and consisted of trains of charge-balanced, cathodic-first, biphasic pulses (400µs/phase) presented at 200 pulses-per-second.

A "baseline" stimulation (constant pulse amplitude and pulse rate electrical stimulation) was delivered, with the pulse amplitude arbitrarily chosen in the middle of the previously measured dynamic range (from threshold to the upper comfortable level) for each patient. Once patients were adapted to this "baseline" stimulation [10], the pulse amplitude of the stimulus was modulated using a virtual motion profile consisting in a sinusoidal envelope with a frequency of 3Hz and amplitude corresponding to 75% of each patient's dynamic range. At the end of the experiments, "baseline" stimulation was gradually decreased to zero. Since individual patient results did not follow a normal distribution median values are reported. Group results are presented as mean values ± standard deviation (SD).

C. Visual Acuity (VA) measurements

VA was measured using Sloan optotypes (CDHKNORSVZ) that were displayed one by one on a flat computer screen positioned at eye-height and at a 1 m eye-to-screen distance. Briefly, the VA procedure consisted in presenting a fixed-size sequence of five randomly chosen optotypes. Only one optotype was presented in the computer screen at a time, and patients were requested to read it aloud. The experimenter recorded the patient's response (right or wrong) and the next optotype was then presented. Once all five optotypes in the sequence were presented, the size was decreased by 0.1 logMAR (Logarithm of the Minimum Angle of Resolution) and a new five-letter sequence was prepared. The VA procedure started with an optotype size of 1 logMAR, and was continued until the recognition rate for a

TABLE I. Demographics and implant details for each patient.

Patient	Sex	Etiology	Age at implant	Implant year	Vestibular electrodes	Surgical approach
S1	M	Idiopathic	68	2007	PAN	EL
S2	M	Congenital /idopathic	34	2008	PAN	EL
S3	M	Congenital /idopathic	46	2008	PAN	EL
S4	M	Menière disease	71	2011	PAN	EL
S5	M	Traumatic	63	2012	PAN/LAN	EL
S6	F	Traumatic	67	2013	PAN/LAN/SAN	IL
S7	F	Meningitis	48	2012	PAN/LAN/SAN	IL
S8	M	DFNA9	67	2012	PAN/LAN/SAN	IL
S9	F	DFNA9	68	2013	PAN/LAN/SAN	IL
S10	M	DFNA9	66	2013	PAN/LAN/SAN	IL
S11	M	DFNA9	64	2013	PAN/LAN/SAN	IL

M - male
F - female

EL – extralabyrinthine
IL - intralabyrinthine

given sequence dropped below chance (10%).

Uncorrected VA was determined in two conditions: without stimulation (system OFF) and upon modulation trials (system ON). The VA in each condition was determined as the midpoint of the psychometric fit to optotype recognition rate. VA acuity results were normalized to VA measured in the system OFF condition.

D. Analysis of Eye Movements

Two-dimensional eye-in-head angular position was recorded using a fast monocular 2D video oculography system (EyeSeeCam VOG; Munich, Germany). All eye movement recordings were done in darkness with patients sitting in an upright position.

A segment of 10 cycles was analyzed for each experimental trial. Eye position data were first filtered at 30 Hz with a low-pass moving average filter (zero-phase shift). Eye velocity and acceleration were then obtained via the first and second derivatives of eye position. Blinks and quick eye movements (e.g. saccades and nystagmus quick-phases) were detected as segments where eye acceleration was >1000 deg/s^2. These segments were removed from the data and were not replaced by interpolated values.

Peak horizontal and vertical velocities were estimated using best-fit 3Hz sinusoids. Total peak velocity was then computed as the Euclidean vector norm of these 2D components. The axis of eye movements (angle with respect to the horizontal) was computed using standard triangle trigonometry. Eye movements with an angle >45° were considered as predominantly vertical and those with an angle <45° as predominantly horizontal.

TABLE II. MAIN CHARACTERISTICS OF ELECTRICALLY EVOKED EYE MOVEMENTS.

	PAN		LAN		SAN	
Patient	***Velocity (°/s)***	***Axis (°)***	***Velocity (°/s)***	***Axis (°)***	***Velocity (°/s)***	***Axis (°)***
S1	13.93	84.57				
S2	3.60	73.17				
S3	9.75	56.72				
S4	3.88	58.01				
S5	3.04	78.16	0.73	59.01		
S6	N.M.	N.M.	21.81	31.70	21.27	40.83
S7	26.01	83.16	32.63	16.55	19.11	65.94
S8	6.74	67.20	15.26	80.71	8.22	80.69
S9	1.47	69.02	4.39	49.93	5.76	52.29
S10	9.92	65.34	3.36	65.45	6.61	76.97
S11	N.M.	N.M.	N.M.	N.M.	10.46	75.91
Mean all	***8.70***	***70.59***	***13.03***	***50.56***	***11.90***	***65.44***
SD all	***7.64***	***10.06***	***12.53***	***23.30***	***6.65***	***15.84***

N. M. – Could not be measured even at the highest current level (600μA) tested.

SD – standard deviation.

E. Ethical considerations

Experiments were designed and conducted in accordance with the 1964 Declaration of Helsinki. Local ethical committees of the Geneva University Hospitals (NAC 11-080) and of the Maastricht University Medical Centre (NL36777.068.11/METC 11-2-031) approved this experimental protocol. All participants gave their informed consent prior their inclusion in the study.

III. Results

At the time of writing of this paper, the longest follow-up period was of 7.7 years (patient S1, implantation in July 2007), and the shortest was of 1.7 years (S10 and S11, implantation in July 2013). No complications related to the surgery or to the experimental procedure were reported.

The main characteristics of the eye movements evoked with our electrical stimulation paradigm are presented in Table 2. In spite of different etiologies and different disease durations, in all eleven BVL patients it was possible to elicit controlled eye movements of variable amplitudes and directions, this up to almost eight years after implantation. In two patients (S6 and S7) the elicited eye movements were in the range of the physiological compensatory eye movements present during natural activities such as walking.

Ideally, LAN stimulation should generate mostly horizontal eye movements, while PAN and SAN stimulation should result in eye movements with a relatively larger vertical component along with an unmeasured torsional component. In our experiments, most electrodes generated eye movements predominantly in the expected plane. Stimulation via two LAN electrodes (S6 and S7) resulted in predominantly horizontal eye movements and stimulation via 14 out of the 17 PAN and SAN electrodes resulted in eye movements with a predominantly vertical component. Note however that large misalignment from the expected axis was also observed for stimulation via four LAN electrodes (S5, S8, S9, S10) and one SAN electrode (S6).

Nine patients (S1, S2, S3, S4, S5, S6, S9, S10, S11) were available for the VA experiments. Stimulation of 7 PAN and 4 SAN electrodes induced a significant loss of the visual acuity (Paired t-test; $t(10) = -3.5$, $p<0.01$; see Fig. 1a). In general, we observed lower VA values upon modulation (VA system ON) for larger eye movements. However the correlation between these values and median peak velocities was not significant (Figure 1b).

IV. Discussion

The results show that, by using a virtual motion profile to modulate the baseline electrical stimulation of the ampullary branches of the vestibular nerve, it was possible to artificially generate eye movements in all BVL patients of our group, independently of the disease etiology, duration of implantation, and of the model of the vestibular implant prototype used.

Our results also demonstrate that electrically evoked eye movements resulted in a significant loss of visual acuity.

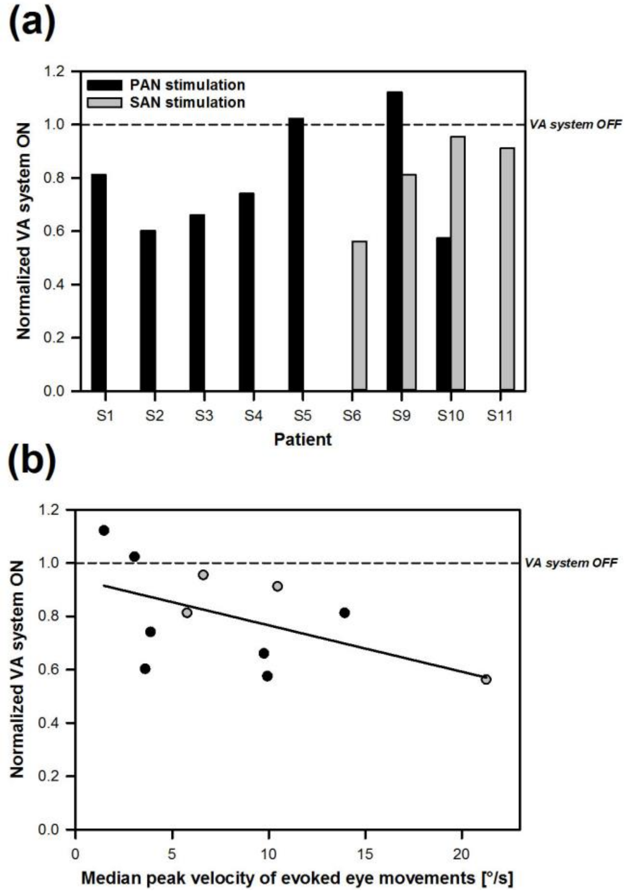

Figure 1. Effects of eye movements evoked upon electrical stimulation of the PAN (black plots) and the SAN (gray plots).

Comparable visual acuity losses have been previously reported in BVL patients while walking on a treadmill [18]. Obviously the goal of the vestibular implant is not to deteriorate visual acuity, but the opposite. However,The fact that the electrically evoked eye moments have similar characteristics to the physiologically induced compensatory eye movements in dynamic conditions such as walking [19], reveals the potential functional impact of the vestibular implant: if it can be fine-tuned to generate appropriate compensatory eye movements in dynamic conditions, retinal slip would be consequently reduced. This should restore gaze stabilization abilities of BVL patients and result in a significant improvement of visual acuity in dynamic conditions.

In conclusion, here we show that it is possible and safe to transfer motion information to the central nervous system using electrical stimulation of the vestibular nerve. Successful tuning of this information could turn this vestibular implant prototype in a successful artificial balance organ that would constitute the first therapeutic alternative to improve the severely impaired quality of life of patients with a BVL.

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