First functional rehabilitation via vestibular implants

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The vestibular system is part of the multisensory balance sense, which is responsible for postural control, gaze stabilization, and spatial orientation. More in particular, the Vestibulo-Ocular Reflex (VOR) is responsible for generating compensatory eye movements relative to head movements while moving. In patients with a bilateral loss of the vestibular function, the VOR is absent or very weak. As a consequence, such patients complain about oscillopsia, the illusory perception of movement of the visual surroundings in dynamic situations. The direct functional consequence of this is an abnormal decrease of visual acuity when in movement1,2, which translates into the difficulty to read signs and recognize faces while walking. This considerably contributes to the significant impairment of the quality of life of affected patients.

Currently, there is no evidence of an effective treatment for these patients. The idea of electrically stimulating the vestibular system emerged about a decade ago and is based on a concept very similar to that of cochlear implants. Briefly, such a system would use inertial sensors (i.e., a gyroscope and/or accelerometer) to detect motion information. Such information is translated into a pattern of neural excitation code 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 vestibular structures to the neural system.

The rapid translation of the cochlear implant concept into a device suitable for stimulating the vestibular system requires two steps: (1) Adaptation of the electrode topology to the neural target to be stimulated, and (2) transformation of the pertinent input signal (in this case motion) into a signal that can be processed by the audio processor of a standard cochlear implant. Today, both steps have been completed. A modified cochlear implant providing 1-3 extracochlear electrodes was developed in collaboration with MED-EL (Innsbruck, Austria). Our research group has developed the necessary interfaces to capture the signal coming from a gyroscope and use it to modulate the stimulation signals delivered by the cochlear implant stimulator (Geneva University Hospitals: Device and method for electrical stimulation of neural or muscular tissue; 2013-01-30; European Patent Application 13153300.2-1652).

A number of studies have contributed to establish the feasibility of the idea of restoring semicircular canal function via electrical stimulation in animal models. At the same time, several important steps have been taken towards the development of a system allowing for the chronic stimulation of the vestibular system in human patients. For example, special extralabyrinthine3 and intralabyrinthine4 surgical techniques have been developed and the feasibility of electrical stimulation of vestibular structures has been demonstrated both in acute5 and chronic configurations6.

To date, 7 volunteer patients with a profound bilateral vestibular loss have received a custom modified cochlear implant in which 1 or 3 electrodes in contact with the vestibular structures (see Table 1). In
addition, since hearing loss due to the implantation of electrodes near the vestibular system remains an important concern, patients were also profoundly deaf in the implanted ear. Two patients (BVL1 and BVL2) were implanted using the intralabyrinthine approach in Maastricht (Ethics committee protocol NL36777.068.11/METC 11-2-031). Five patients (BVL3 – BVL7) were implanted using the extralabyrinthine approach in Geneva (Ethics committee protocol NAC 11-080).

In the present study we attempted to achieve the fundamental milestone of demonstrating whether it is possible to artificially restore the VOR via motion-controlled, amplitude modulated electrical stimulation of the vestibular system. These tests are based on standard clinical procedures, and are similar to preliminary animal experiments.

Patients BVL1, BVL2, and BVL3 participated in these experiments. First, the patient received steady-state electrical stimulation in order to restore an artificial “spontaneous” firing rate in his deafferented vestibular nerve until nystagmic responses vanished. Once the patient was in this “adapted state”, we used a 3-axis gyroscope to code rotational movements in the horizontal plane. This gyroscope signal was used to up- and down-modulate the amplitude of the train of pulses delivered to the vestibular electrode. The

Table 1 | Characteristics of the 7 implanted patients. Patients BVL1 – BVL3 (highlighted in italic bold) participated in the VOR experiments presented here.

<table>
<thead>
<tr>
<th></th>
<th>Sex</th>
<th>Age (implantation)</th>
<th>Etiology</th>
<th>Deafness</th>
<th>Vestibular electrodes</th>
<th>Surgical technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>BVL1</td>
<td>Female</td>
<td>58</td>
<td>Meningitis</td>
<td>unilateral</td>
<td>PAN, LAN, SAN</td>
<td>Intralabyrinthine*</td>
</tr>
<tr>
<td>BVL2</td>
<td>Male</td>
<td>66</td>
<td>DFNA9</td>
<td>bilateral</td>
<td>PAN, LAN, SAN</td>
<td>Intralabyrinthine*</td>
</tr>
<tr>
<td>BVL3</td>
<td>Male</td>
<td>46</td>
<td>Idiopathic</td>
<td>unilateral</td>
<td>PAN</td>
<td>Extralabyrinthine**</td>
</tr>
<tr>
<td>BVL4</td>
<td>Male</td>
<td>68</td>
<td>Idiopathic</td>
<td>bilateral</td>
<td>PAN</td>
<td>Extralabyrinthine**</td>
</tr>
<tr>
<td>BVL5</td>
<td>Male</td>
<td>35</td>
<td>Congenital</td>
<td>bilateral</td>
<td>PAN</td>
<td>Extralabyrinthine**</td>
</tr>
<tr>
<td>BVL6</td>
<td>Male</td>
<td>72</td>
<td>Menière’s disease</td>
<td>unilateral</td>
<td>PAN</td>
<td>Extralabyrinthine**</td>
</tr>
<tr>
<td>BVL7</td>
<td>Male</td>
<td>63</td>
<td>Traumatic</td>
<td>unilateral</td>
<td>PAN, LAN</td>
<td>Extralabyrinthine**</td>
</tr>
</tbody>
</table>

PAN: Posterior Ampullary Nerve
LAN: Lateral Ampullary Nerve
SAN: Superior Ampullary Nerve

Figure 1. Example of the VOR response for patient BVL2 with the system OFF (left panel) and with the system ON (right panel). The inset on the right shows data gathered for healthy volunteer for comparison. Data were analyzed on a cycle-by-cycle basis. Results are presented as the average cycle (±SD) of the total angular velocity vector of the eye (red lines) and head (blue lines) during whole body rotations in the horizontal plane (30°/s peak angular velocity, 1Hz).
patient’s eye movements were recorded while the patient was submitted to whole body rotations in the horizontal plane (sinusoidal 30 °/s peak angular velocity at 1Hz and 2Hz) in complete darkness.

Figure 1 shows an example of the VOR response without stimulation (system OFF) and with motion-modulated stimulation of the vestibular system (system ON) for BVL2 for 1Hz rotations. In the system OFF condition (left panel), the eye movements (red lines) were practically absent. In contrast, in the system ON condition (right panel), a clear VOR response is observed. As expected upon electrical stimulation the time-course of eye movements begins to mirror that of head movements (blue lines), following an inverted compensatory pattern, a typical characteristic of the VOR in healthy subjects. We observed the same pattern of responses for patients BVL1 and BVL3.

At 1Hz the VOR gain (peak eye velocity / peak head velocity) of the 3 tested patients was very low in the system OFF condition (gains < 0.2). In the system ON conditions, the gains in the 3 patients improved significantly (pairwise Tukey test p<0.001) and reached up to 75%-98% of the median VOR gain of healthy volunteers. Furthermore, the gain increased monotonically as we increased the modulation depth (i.e., intensity of stimulation). This dependence of modulation depth was statistically significant (Friedman Repeated Measures Analysis of Variance; BVL1: \( \chi^2(2, N=58)=25.90, p<0.001 \); BVL2: \( \chi^2(2, N=58)=51.14, p<0.001 \); BVL3: \( \chi^2(2, N=59)=53.19, p<0.001 \)).

At 2Hz, results were very similar to those reported for 1Hz rotations. While no clear VOR response could be observed in the system OFF condition, it became clearly visible in the system ON condition. The VOR gain in the system OFF condition was very low while it increased significantly in the system ON condition (Wilcoxon Signed Rank Test; BVL1: \( N=57, z=4.36, p<0.001 \); BVL2: \( N=67, z=5.44, p<0.001 \); BVL3, \( N=57, z=4.45, p<0.001 \)), reaching 51%-69% of that observed in healthy volunteers.

A very interesting additional finding resulted from these VOR experiments. We observed that patient BVL3 could improve significantly his VOR response to whole body rotations in the horizontal plane. But in this patient, electrical stimulation was delivered to the Posterior Ampullary Nerve (PAN), the vestibular nerve branch normally coding movements in the vertical plane. Thus, in this case we obtained a positive functional result while stimulating the “wrong” nerve branch. We designed an additional experimental protocol to further investigate this interesting observation.

The gyroscope was fixed on the frame of the rotating chair, and we recorded the patient’s eye movements, in complete darkness, in three experimental conditions: (1) with the patient sitting on the rotating chair with the system OFF, (2) with the gyroscope and the patient on the rotating chair with the system ON, and (3) with the gyroscope on the rotating chair and the patient sitting aside with the system ON. Note that in all three conditions, the chair rotated exactly in the same way: in the horizontal plane (sinusoidal, 1 Hz, 30 °/s peak angular velocity). Therefore, in conditions (2) and (3) the same motion-modulated electrical stimulus was delivered to the patient’s PAN. The only difference was that in condition (2) the patient rotated with the chair and thus received multisensory (e.g., somesthetetic) information on the rotation while in condition (3) the patient was sitting static, aside the rotating chair.

The results of this additional experiment demonstrated unambiguously that the axis of the VOR response can shift from the vertical (predicted) to the horizontal (unpredicted) axis depending on
whether whole-body rotation information is available to the patient or not. A similar observation was reported in the squirrel monkey\textsuperscript{7} but the adaptation period for the axis shift was much longer (1 week) in the animal.

These results constitute a fundamental milestone towards the development of vestibular implants by demonstrating for the first time in humans that artificial restoration of the VOR is possible via electrical stimulation of the vestibular nerve branches. It allows us to envision clinically useful rehabilitation of bilateral vestibular deficits. Future work will concentrate on extending the present results and to evaluate the benefit of artificially restoring the VOR during every-day tasks. In addition we observed very rapid cross-axis adaptation processes, which appear to be much faster than in animals, as already suggested in our previous studies\textsuperscript{6}. This opens new perspectives on the multisensory processing of motion.

References


