The Vestibular Implant

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Chapter 6

Final discussion and valorisation

Introduction

Inspired from the success of cochlear implants over the last decades in hearing rehabilitation for deaf patients, the concept of the vestibular implant had emerged as a potentially extremely interesting therapeutic option for the rehabilitation of the vestibular function. Persuasive results obtained in animal research led to the transfer to human research, not without having spent considerable amount of time convincing the local ethical committee. Respecting very strict inclusion criteria limiting the research protocol candidacy to patients suffering from a severe bilateral vestibular loss and a concomitant deafness, the first experiments using electrical stimulation of the vestibular nerve were performed at the ENT Department of the University Hospitals of Geneva in 2004 (personal communication).
At the beginning of my thesis, in 2009, I was aware of those extraordinary results. Imagine, it was possible to generate controlled eye movements by using electrical stimulation of the vestibular nerve in patients with a bilateral vestibular loss! Naturally, many questions emerged. They were the driving force behind this thesis in which a selection of essential issues of the vestibular implant project are addressed in a logical, chronological order.

1. Is there actually a need for such a device?

This seems to be the logical question before starting the development of any medical device. When asked, many clinicians were not aware of the existence of a condition such as the bilateral vestibular loss. What could they then say about the patient's complaints? Patients with balance disorders are commonly taken care of by ear nose and throat specialists or neurologists. But even among this subset of physicians the clinical relevance of a bilateral vestibular loss was not uniformly recognized. Several options are presented to us. First, the bilateral vestibular loss is indeed not relevant for Humans and thanks to the redundancy of the multidimensional balance system there is no relevant impact on its function. Second, as reported by some authors, current therapeutic concepts are efficient to tackle the handicap caused by the bilateral vestibular loss. Third, no one is really interested by this group of patients, possibly because there is no efficient treatment available. Fourth, patients with a bilateral vestibular loss have a significant handicap with an impact on their daily life without available efficient treatments. Based on our clinical experience we have always been convinced of the last option. For us the answer to the initial question was a clear yes. Yet we had to demonstrate this. As from the beginning our target group for the vestibular implant project has been the group of patient with a bilateral vestibular loss we decided to assess their quality of life. Chapter 2 deals with this issue. Results demonstrate the significant impact of the bilateral loss of the vestibular function on the quality of life. This has been corroborated in later studies which also revealed the significant social and economical burden on affected patients and on society.[1] Furthermore, in our study a validated handicap index indicated that most of those patients have a moderate to severe handicap. This is worse compared to reported handicap index for other common inner ear pathologies such as superior canal dehiscence or unilateral vestibular loss for example.[2,3] For those both conditions there are available treatments. In conclusion, yes there is a need for therapeutic options for the group of patients presenting a bilateral vestibular loss. Behind the initial question a more global issue appears: the recognition of vestibular disorders and in particular of the bilateral vestibular loss. Fortunately, promising progress is being made. Indeed in 2017, for the first time a consensus document of the Classification Committee of the Bárány Society dealing with the diagnostic criteria of the bilateral vestibulopathy was released (http://www.jvr-web.org/images/Bilateral_vestibulopathy%202017.pdf). This will be a very important reference to standardize research on this topic. In the effort towards a better recognition of vestibular disorders, emphasis should be placed on pre and post graduate education for health specialists, and on dissemination via publications, conferences, media appearances in order to reach as large audience as possible. At a world level and in the same way than for other sensory deficits like deafness and blindness, the bilateral vestibular loss (you notice that there is no specific word to describe this condition…) should be listed WHO health topics (http://www.who.int/topics/deafness/en/ + http://www.who.int/topics/blindness/en/). Together with the vestibular implant project those actions could endeavor to change patient’s life.

2. How to assess the benefit of the vestibular implant?

In order to assess the effect of a treatment it is ideal to have valid objective measurements. This is not trivial with the vestibular system whose evaluation is complex. First the adequate stimuli for the system are accelerations. Unfortunately, it is virtually impossible to deliver such motion stimuli selectively to the vestibular system without activating other sensory systems. Second, there are various outcome parameters which give indications on different aspects of the vestibular function. Recording of eye movements induced by the vestibulo-ocular reflex inform us about gaze stabilization abilities, recording of body sway gives indication about postural control abilities, recording of motion perception threshold involves cortical integration of vestibular information, and other tests such as the measurement of vestibular evoked myogenic potentials gives indication on the integrity of the vestibulo- spinal pathways and presumably on the abilities for head and body stabilization. Third, no significant correlation between symptoms and most of those outcomes is found in patients with vestibular disorders. Therefore we focused our interest on a test assessing gaze stabilization during walking. Although it is not a purely vestibular test we hypothesized that this test would be very sensitive to depict a bilateral vestibular loss. Available data in the literature indicated that it was the case.[4] Visual acuity was measured in standardized walking conditions on a treadmill at different velocities and compared to static values. This study composes the second Chapter of this thesis. Results showed that our dynamic visual acuity test was very sensitive. Significant drop of the visual acuity where found at walking velocity as low as 2 km/h. This indicates that this test should be suited to evaluate the benefit of a vestibular implant whose one of the aims is to restore efficient gaze stabilization. The results also showed that there were no significant differences between patients with a unilateral vestibular loss and healthy subjects, even at quite high walking velocities. This indicates that unilateral restoration of the vestibular function with a vestibular implant could be sufficient to reach a significant improvement of gaze stabilization. This supports our concept of a unilateral vestibular implant. On the other hand no correlation was found between the amount of visual acuity loss and the symptom intensity. Tolerance to retinal slip (image instability in dynamic conditions) may vary from subject to subject. Once more it highlights the difficulty to assess the balance system. With this test we now have an interesting tool to help selecting adequate candidates for a vestibular implantation and to assess the implant performance.

3. What is the potential of each implanted electrode?

Promising results obtained in acute experiments have paved the way for the permanent implantation of the first vestibular implant prototypes, which were modified cochlear implant stimulators with one electrode made available for vestibular stimulation by removing it from the main cochlear electrode array. Using custom modified devices was a crucial strategic choice. This allowed us to avoid the time-consuming, laborious and costly procedures associated with the development of a medical device such as a vestibular implant from scratch. This was possible thanks to a progressive, intelligent, trustworthy collaboration with a private company. This should be noted as it constitutes a fundamental aspect of the project success. In this framework, new versions of the prototype of the vestibular implant were developed. This evolutionary process is still under way, both in the design of the electrodes and the external processor, and should make possible to obtain a commercial version in the near future. Up to know, 13 patients have been implanted with different versions of the vestibular implant prototype. There were no surgical complications and all of them could benefit from the cochlear implant. This last point was a strong argument to obtain the approval of the ethical committee for the permanent implantation of the vestibular implant prototypes. In fact, at the time of writing Chapter 4, 11 patients had been implanted. The purpose of this chapter is to report selective significant objective parameters obtained for each electrode. Interpretation of those parameters should give indications on the potential of each electrode towards rehabilitation of the vestibular function. Three different version of vestibular implant prototypes were implanted in this group of 11 patients, for a total of 24 vestibular electrodes. Although all implantations in our project were made in deaf ears, hearing preservation is a crucial issue for the long term success of the vestibular implant, as the majority of patients with a bilateral vestibular loss has a normal hearing or moderate hearing loss. Depending on the post implantation level of hearing preservation, a purely vestibular implant without cochlear electrode could also be foreseen. If the therapeutic benefit obtained with a vestibular implant is sufficient, patients with bilateral vestibular loss might be ready to take the risk to lose their hearing on the implanted side. Nevertheless, extralabyrinthine surgical approaches, thought to be less traumatic than intralabyrinthine approaches, were initially developed and used for the first experiments.[5,6] In light of animal research findings showing that at least in certain cases it was possible to preserve the hearing after implantation of intralabyrinthine electrodes,[7] specific surgical routes for such an implantation were described and adequate vestibular implant prototype were developed.[8] Among the 11 patients, 4 have vestibular implant prototypes with 1 extralabyrinthine electrode, 1 with 2 extralabyrinthine electrodes and 6 with 3 intralabyrinthine electrodes. Results show that electrical stimulation is a safe and effective means to activate the vestibular system even in a heterogeneous patient population with very different etiologies and disease durations. However, for each electrode, the electrical dynamic ranges, as well as the amplitude of the obtained eye movements were variable. The distance between the electrode and the neural target is of crucial importance to achieve a selective and efficient electrical stimulation. Towards this goal several aspects should be considered: 1. The optimization of the positioning of the electrodes by refining their design and by monitoring intraoperatively the activity of the vestibular nerve during electrode insertion, 2. The increase of anatomic knowledge by creating accurate 3D models based on high tech imaging, 3. The establishment of standard surgical approaches, 4. The exclusion of patients with etiologies inducing neural degeneration. Those issues appear to be essential to turn the vestibular implant prototype into a successful artificial balance organ.

4. Can we make something functionally useful out of it?

Artificial restoration of vestibular reflexes is a remarkable achievement. Nevertheless it does not guarantee a useful functional restitution for the patient. The aim of this final part of the thesis was to demonstrate a useful benefit for implanted patients by using a selected subset of implanted electrodes and the test described in Chapter 3. Can the dynamic visual acuity of implanted patients be improved? For this purpose we chose to use an out the shelf motion sensor which was fixated to the patients head. Motion information captured by this sensor was transmitted to a regular cochlear implant processor, which in turns controlled the electrical stimulation delivered by the implanted stimulator to the ampullary branches of the vestibular nerve. In fact the

strategy for transmitting the motion information to the processor has been patented by members of our research team (M. Pelizzone, A. Perez-Fornos, M. Ranieri and S. Cavuscens, Device for electrical stimulation of neural and/or muscular tissue, has signal processing unit to transform input signal received from signal sensors into modulated electrical output signal to be treated by speech processor., in, vol WO2014118094-A1; EP2762196-A1, 2013.). The main perturbations of the head during walking being vertical translation and head pitch, a subset of electrodes eliciting mainly vertical eye movements was selected for this experimental protocol. The hypothesis made was that those eye movements would compensate for the head movements allowing preservation of the visual acuity while walking. In all 6 implanted patients available for the study the dynamic visual acuity could be significantly improved or even normalized. This represents the first demonstration of a useful functional rehabilitation using a vestibular implant prototype. Results were obtained with a single active electrode by using one-dimensional motion information. It is remarkable that this somehow rudimentary motion information is sufficient in making a significant functional difference in gaze stabilization. We believe that brain plasticity plays a key role, which might mean that perfect restitution of the missing motion information to the central nervous system will not be necessary improve the balance function in a clinically relevant manner. In some respects this is the case for cochlear implants. Indeed a minimum of 6 or 8 independent cochlear electrodes are sufficient for an efficient hearing rehabilitation allowing the development of close to normal speech in a deaf child for instance. In conclusion, the answer is yes, motion modulated electrical stimulation of the ampullary branches of the vestibular nerve can restore a functionally useful vestibular function. With this in mind, it is not anymore utopic to foresee the possibility of having a vestibular implant on the market within the following years.
We hope the horizon of patients with a bilateral vestibular loss will be more stable…

Remarks

On purpose this thesis has been focused on chosen aspects of the vestibular implant project which should provide the reader an interesting, significant glimpse into it. An aspect of interest left somewhat aside is that of more fundamental research. Allowing independent selective activation of the vestibular system, which is unprecedented, the vestibular implant has opened doors in the quest for understanding the physiology of vestibular system.
More information about the project can be found in the numerous publications from our research group.

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