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Vestibular Implants: the First Steps in Humans.

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Abstract—**Currently there is no efficient treatment for patients with severe bilateral vestibular function impairment. Presence of oscillopsia is their main complaint. It has a significant negative impact on their quality of life. Recently it has been shown that angular vestibulo-ocular reflex can be partially restored in animals. In humans it is possible to elicit a nystagmic response by electric stimulation of ampullary parts of the vestibular nerve. Controlled eye movements can be generated by frequency and intensity modulation of the restored baseline firing rate of the vestibular nerve. During adaptation phase to the electric stimulus, patients experience nystagmus with associated inconveniences. By repetition of "on/off periods" the duration of the adaptation phase can be significantly decreased. Results show that permanent electric stimulation is necessary to maintain this "optimal" adaptation state.**

I. INTRODUCTION

The vestibular labyrinth is located in the temporal bone, it is composed of three semicircular canals, almost mutually orthogonal to one another, which are sensitive to angular accelerations in their respective planes and of two otolithic organs, the saccule and the utricle which are sensitive to linear accelerations. As otolithic organs play a key role for postural control, the angular vestibulo-ocular reflex (aVOR) generated by the neurosensory structures located in the ampullae of the three semicircular canals is important for gaze stabilization during head rotation. The aVOR is an extremely fast three neurons reflex, which occurs by up or down modulation of the spontaneous baseline firing rate of the vestibular organ. In less than 10 ms it provides adequate compensatory eye movements in the opposite direction of head rotation, with a gain close to unity, which allow image stabilization on the retina's fovea [1]. In case of a bilateral function loss of the aVOR, gaze stabilization is impaired during high frequency head rotations. Affected patients complain of imbalance, blurred vision and oscillopsia, which can be defined as a sensation that the surrounding is moving when it is not. Impairment of patients' visual acuity during head movements has a negative impact on their physical and social functioning [2]. Significant visual acuity decrease has been reported at walking speed as low as 2 km /h [3].

Currently there is no efficient treatment for patients with bilateral vestibular function loss. It has been shown that their condition does not improve with time in 80% of the cases [4], stressing out the need for new therapeutic options. The idea of an artificial vestibular organ which could register angular accelerations, process the signal and deliver it to the vestibular nerve via electrodes, in a similar way as the cochlear implant for hearing, has raised patients and caregivers hope. Recently, it has been shown that the aVOR can be partially restored on animals [5]. Further, after demonstrating the feasibility of surgical approaches of the posterior and lateral ampullary parts of the vestibular nerve on cadavers [6, 7], the first electric stimulations in human have shown that it is possible to generate a nystagmus in the plane of the stimulated semicircular canal [8]. A crucial step is restoring the baseline spontaneous firing rate in the vestibular system. Recently, for the first time, it was shown that human can adapt to a chronic constant electric stimulation of the vestibular nerve. After less than 30 minutes of continuous stimulation, nystagmic response had ceased and patient could not perceive the signal anymore [9]. It was furthermore possible to elicit controlled eye movements by frequency and intensity modulation of the electric signal. Multiple successive "on/off periods" of electric stimulation were necessary to reach an "optimal" adaption state with acceptable duration of nystagmic response to a stimulation state change (on-off or off-on) [9]. This is promising as it is not conceivable for a patient to experience nystagmus with potential dizziness each time the implant is turned on or off. What happens if the implant is not in use for some time and again turned on? Does "optimal" adaptation state remains? The study objective was to assess "optimal" adaptation state persistence with time.

II. MATERIAL AND METHODS

A. *Patient and surgery*

The subject of this experiment participated to the previous experiment on the adaptation to chronic electrical stimulation of the vestibular system [9]. He is a 70 years old man suffering from an idiopathic bilateral deafness and vestibular loss. He received a custom modified regular Med-El (Innsbruck, Austria) cochlear implant, one electrode being removed from the cochlear array and implanted close to the posterior ampullary nerve, see Figure 1.

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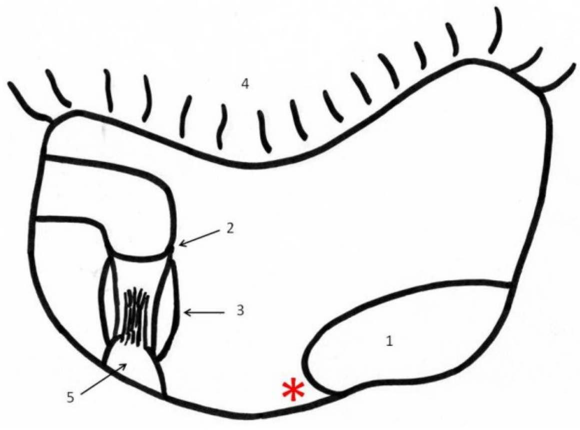

Fig 1. Transmeatal view of the right middle ear medial wall with lifted tympano-meatal flap. 1. Round window, 2. Incudo-stapedial joint, 3. Oval window, 4. Tympanomeatal flap, 5. Pyramidal eminence, * access to the posterior ampullary nerve.

The experimental protocol was approved by the human study committee of our institution and the patient gave his informed consent to participate in the proposed study.

The surgical approach, electrical stimulation, eye movements recording, and eye movements analysis have been described in previous papers [8-10]. Briefly, after the cochlear implantation procedure was completed, an extracochlear electrode was placed near the posterior ampullary nerve.

B. *Electrical stimulation*

The first trials of electrical stimulation of the vestibular system were performed once the adaptation to cochlear implant was fully accomplished, using trains of 400 µs/phase biphasic pulses, delivered at a repetition rate of 200 pulses per second (pps), see Figure 2. During trials of chronic electrical stimulation, the patient was lying in a dark soundproof and electrically shielded room, wearing a black plastic face mask maintaining video cameras in front of his eyes. Eye movements were continuously recorded during the whole experiment, and recorded using 2D binocular video oculography (Difra Instrumentation, Belgium) at 50 samples per second.

Persistence of the “steady state” was challenged by repeating on/off stimulation periods while progressively increasing the delay between the cessation of the “off period” nystagmic response and the following “on period”.

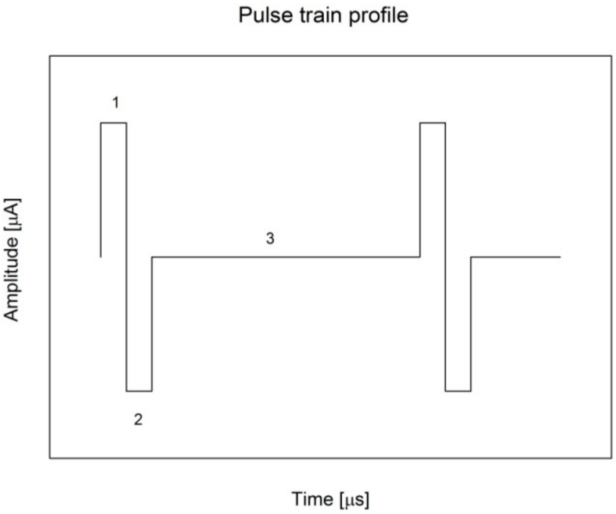

Fig. 2 Train of biphasic pulses with a stimulation rate of 200 pulses per second (pps). 1. cathodic phase and 2. anodic phase have a duration of 200µs at 400µA. 3. Zero current phase.

C. *Analysis of eye movements*

As in previous experiments[8, 10] recordings of eye movements were analyzed off-line to identify artifact free tracings that were not altered by voluntary eye movements. The slow component velocity (SCV) of “nystagmic activity”, was quantified using a custom made Matlab® program so that slope of each beat could be measured manually [8, 10]. The slow component velocity values (expressed in °/s) presented in this paper were computed as the average (and standard deviation) of three consecutive beats. Velocity was considered to be zero when no or only one nystagmic beat could be detected in a period of five seconds.

III. RESULTS

First “on period” in the “not” adapted state elicited a nystagmic response which ceased after 30 minutes. In the following “off period” the duration of the nystagmic response was two point five minutes. Duration of nystagmic response of the seventh “on period” was less than three minutes. During the following “off period”, the registered nystagmic response lasted for 40 seconds. This was considered as the “optimal” adaptation state. After a delay of one hour without stimulation, the first “on period” elicited a nystagmic response which ceased after seven minutes. The first “off period” nystagmic response had duration of one minute. After four “on/off periods” without delay, durations of nystagmic responses were brought back to those of the “optimal” adapted state. Then a delay of two hours without stimulation was observed, the following “on period” nystagmic response lasted for 15 minutes. Duration of the “off period” response was one point five minutes. Again, after four “on/off periods”, nystagmic responses duration of adapted state were reached. The next delay without any stimulation was four hours. The following "on period" nystagmic response had duration of 21 minutes; "off period" nystagmic responses held for two minutes. Repetition of four on/off periods" allowed shortening of the nystagmic responses to duration of those of the "optimal" adapted state. The fourth delay period without stimulation was 18 hours long. Nystagmic response duration of the following "on period" reached 30 minutes, the "off period" nystagmic response lasted two point five minutes. Four cycles of "on/off period" were necessary to obtain nystagmic responses duration similar to those of the "optimal" adaptation state, see Figure 3.

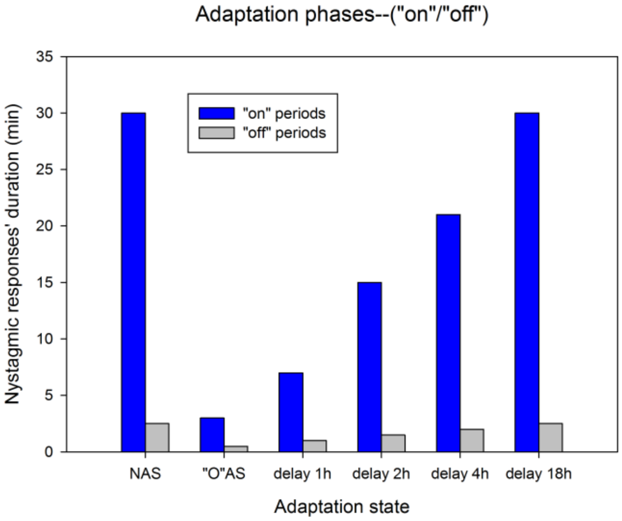

Fig. 3 Duration of the nystagmic responses of the "on and off periods" in function of the adaptation state. NAS: not adapted state, "O"AS: "optimal" adapted state. Delay represents time between "optimal" adapted state "off period" end and beginning of the next "on period".

IV. DISCUSSION

Decreased response to stimuli delivered constantly to a sensory system is defined as adaptation [11]. During the phase of adaptation, the subject perceives the given stimuli, theoretically a rotation perception in case of electric stimulation of the ampullary parts of the vestibular nerve; simultaneously eye movements are registered for aVOR evaluation. By repetition of identical stimuli, duration of the adaptation phase decreases to eventually reach a minimal duration.

This study is an observational case study on one patient with bilateral vestibular loss who received a modified cochlear implant with an electrode implanted near the posterior ampullary part of the vestibular nerve. Even if adaptation phases in the "optimal" adaptation state are shorter than those found under similar conditions in animals [12], our results show that once the "optimal" adaptation state is reached, it can only be maintained with permanent electric stimulation. If the stimulation is turned off for an hour, the adaptation phase will last seven minutes when the stimulation is turned on again. This is about twice as long as in the "optimal" adaptation state. This time is doubled for two hours of delay, three times as long for a four hours delay and will reach the maximum adaptation phase duration of 30 minutes after a delay of more than 18 hours. Even if additional data is needed to confirm those study findings, it is questionable if it is acceptable that adaptation phase and its potentially associated symptoms such as dizziness and nausea last more than a couple of minutes each time the implant is turned on or off. To avoid this problem, permanent stimulation is possible but implies much higher total energy consumption, as the vestibular implant cannot be switched off during periods of time when not useful, such as during sleep. For short interruption of less than an hour such as for battery change or for taking a shower, the possible inconveniences should be acceptable. Permanent stimulation will have an impact on costs on the long term, but that might not be the main obstacle to the release of a functional vestibular implant.

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