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Background

The 7th International Symposium on Objective Measures (IOM 2012), a conference held in Amsterdam on 19–22 September 2012, was organized by two medical institutes: the Department of Otorhinolaryngology of the Radboud University Medical Centre, Nijmegen, and the Leiden University Medical Center. Last year's symposium gathered the largest number of participants in the history of the event, with over 700 scientists from all over the world coming to present current trends in objective evaluations of the physiology and pathology of hearing.

Before the conference started, Cochlear Ltd organized a pre-conference symposium, chaired by Bas Van Dijk (Global Research Coordinator from Cochlear Ltd.), Prof Mark Lutman (Institute of Sound and Vibration Research, University of Southampton, UK), Prof Chris James (Service ORL, Hôpital Purpan, Toulouse, France), and Prof Norbert Dillier (Department of Otorhinolaryngology, Head and Neck Surgery, University Hospital, Zürich, Switzerland). The scientists gave interesting perspectives on the various sound enhancement systems that have been incorporated into the speech processors of cochlear implants (CIs). For day-to-day use by the CI-user, it is clear that optimal types of compression, enhanced noise reduction, and automatic environment detection could improve their quality of life. In addition, for bilateral CI recipients, there is a need to improve speech processing strategies in order to further increase performance and make it closer to normal.

The scientific programme of the conference covered a variety of topics:

a. *Methods of evaluating the auditory system.* These covered cochlear potentials, electrically evoked compound action potentials of the cochlear nerve, intracorporeal cortical telemetry, long latency and cortical potentials, electroencephalography and event-related potentials. There were also sessions on neuroimaging techniques: functional magnetic resonance, near infrared, positron emission tomography, and beam computed tomography.
b. *Evaluation of auditory implants.* The devices included cochlear implants, middle ear implants, auditory brainstem/midbrain/nerve implants, bone conduction devices, and vestibular implants.
c. *Robotics and surgery navigation.*

Opening keynote lecture

Prof. Jay Rubinstein, Director of Virginia Merrill Bloedel Hearing Research Center at the Washington University, opened the conference with a lecture entitled 'Past, present, and future of objective measures'. He presented a brief history of objective measures of the auditory pathway, from auditory brainstem responses, through stapedius muscle reflexes and late responses, to electrically evoked auditory steady-state responses and cortical responses. Prof. Rubinstein showed that each new method of objective measurement raised immense hopes, which were, however, rapidly diminished in everyday practice. He suggested that all techniques are equally important to psychoacoustic measurements and that a patient should never be considered as a 'generator of electric pulses' only.

Professor Rubinstein further elaborated on the relatively short history of using functional imaging methods in the evaluation of auditory function. According to his thorough literature review, the first brain function study in auditory deprivation involved positron emission tomography (F18-FDG PET) and was performed by Truy and colleagues in 1995 [*Auditory cortex activity changes in long-term sensorineural deprivation during crude cochlear electrical stimulation: evaluation by positron emission tomography,* Hear Res. *86(1–2): 34–42]*. The first functional magnetic resonance imaging (fMRI) study of auditory processing was done in 2002 by Lazeyras and colleagues [*Functional MRI of auditory cortex activated by multisite electrical stimulation of the cochlea, NeuroImage 17(2): 1010–17*]. In the same year, the group lead by Sharma pioneered cortical auditory evoked potentials (aERPs) [*Rapid development of cortical auditory evoked potentials after early cochlear implantation.* Neuroreport, *13(10): 1365–68*]. During the last decade the field of neuroimaging has rapidly developed, both in terms of the clinical questions addressed and in applied methodological solutions.

Electrophysiological measures

Electrically evoked compound action potentials were one of the main topics at the conference. The majority of the presenting specialists agreed that registering these potentials is crucial for speech processor fitting. Nevertheless, the extent of measurements differs from clinic to clinic.

Some audiologists (e.g., Dr Joachim Müller-Deile, Kiel, Germany) try to measure all available parameters, such as the threshold of the response, spread of excitation, and refractory time, whereas others focus only on the measurement of auditory thresholds. Moreover, new types of stimuli used to evoke auditory responses were presented (e.g., Andreas Bahmer, Frankfurt), as well as new coding strategies and electrodes penetrating the auditory nerve.

The Institute of Physiology of Pathology of Hearing, Poland, presented two studies. The first was '*ESR, ECAP, and MCL: their relation for charge-based fitting in implants with a 31.5 mm electrode*' (A. Walkowiak, A. Lorens, M. Polak, H. Skarżyński). Here, 14 children and 16 adults participated in the study, all implanted and experienced with the Med-El Pulsar system and the Opus II speech processor (31.5 mm electrode). The mean apical, medial, and basal electrode thresholds were measured for eSR and ART, using the auditory nerve response telemetry (ART) algorithm and most comfortable levels (MCL; only in adults). The thresholds were 19.80 nC, 14.38 nC, and 21.37 nC, respectively. There was no statistical difference found between the means for any of the electrode pairs (electrodes 2, 6, and 11). The results indicate that all parts of the long CI electrode can be effectively stimulated.

The second study was '*Estimation of abnormalities of cochlear implant electrode placement using spread of excitation measurements*' (A. Walkowiak, A. Lorens, B. Kostek, A. Obrycka, A. Wasowski, H. Skarżyński). The study revealed, in an Advanced Bionics HiRes90K implant user, a correlation between postoperative spread of excitation profiles for electrodes 4, 8, and 12, as recorded using RSPOM software and abnormal electrode placement, as shown by CT. Further investigation is necessary in a group of cochlear implant users. Should the results be confirmed, a useful objective tool to assess implant electrode position could supply clinicians with information crucial for speech processor fitting.

Functional imaging

Out of over 100 presentations at the conference around 20 focused on auditory neuroimaging, using event related potentials, functional magnetic resonance, positron emission tomography, and near infrared spectroscopy. A number of experiments were presented below.

Opening the session, Dr Kevin Green, head of the cochlear implant program at the University of Manchester Hospitals, gave a keynote lecture on '*Functional imaging in the age of cochlear implantation*'. Numerous fMRI and PET studies by Dr Green, involving various groups of cochlear implant users, have shown that the auditory brain areas are extremely plastic and re-organize constantly with the duration of CI-use. Dr Green's conclusions were based on segregating users into groups, such as poor vs. good performers, unilateral vs. bilateral, and experienced *vs.* new recipients, as well as individuals with a comorbid visual impairment. In addition, he suggested that other brain regions seem to play an auxiliary role when peripheral auditory function is deprived, including central gyri, prefrontal areas, and the cerebellumIn. Inthe population with hearing loss, visual cortices are found to be more effectively functionally connected to auditory areas, compared to normal, which was shown to translate into enhanced lip-reading abilities [Green et al. (2005), *Auditory cortical activation and speech perception in cochlear implant users: effects of implant experience and duration of deafness, Hearing Research, 205 (1–2), 184–92;* Green et al. (2008a), *Neuronal plasticity in blind cochlear implant users, Cochlear Implants International, 9(4), 177–85;* Green et al. (2008b), *Auditory cortical activation and speech perception in cochlear implant users, Journal of Laryngology and Otology, 122(3), 238–45;* Green et al. (2008c), *Cortical plasticity in the first year after cochlear implantation, Cochlear Implants International, 9(2), 103–17.*]

Electroencephalography (EEG) and event related potentials (ERPs)

1. *Cell biology and cochlear implants: a happy marriage?* Kral et al., Hannover Medical School, Germany. In normal hearing, synaptic density reaches its maximum in the first year of life and drops from the fourth year of age. In hearing-deprived cats, neuronal maturation is delayed, and has an earlier and quicker drop. In animals with unilateral cochlear implants, direct electric stimulation of bilateral auditory cortices revealed Na-Pa-Nb-Pb complexes of potentials, with responses significantly larger in the cortex contralateral to the implant. In unaided unilaterally deaf animals the activity was larger in the cortex ipsilateral to the deaf ear. One can conclude that the available brain areas are recruited by the most trained ear, but the deaf ear is still clearly represented in the cortex.
2. *Simultaneous bilateral cochlear implantation protects auditory pathways in children who are deaf.* Gordon et al., Hospital for Sick Children, Toronto, Canada. In unilateral deafness there is a limited input into the brain from the deaf ear and over-expression of the hearing ear in the cortex. The findings of an auditory ERP experiment were that in a case of unilateral cochlear implantation the over-expression was preserved, with bilateral implantation promoting normal bilateral auditory responses (the more so, the less time elapses between sequential implantations with the critical interval between surgeries being 1.5 years). It was suggested that simultaneous cochlear implantation promotes normal auditory brain development.
3. *Binaural benefit and cortical effort in bilateral CI and bilateral bimodal CI–HA simulations*, Buckley et al., University of Buffalo, USA. Sound localisation is due to differences in sound perceived by the two ears. In unilateral and bilateral cochlear implant users, this experience is altered and requires more cortical effort. In this study the latency of P300 responses under monaural and binaural stimulation was evaluated. It was found that processing the CI-transmitted signal demands more cortical effort than processing natural sounds, although this might not always be reflected in behavioural speech perception scores. No consistent differences in responses were found for the two aided conditions.
4. *Music perception by normal hearing and cochlear implant children: a neuro-electrical imaging study*, Marsella et al., Bambino Gesu Pediatric Hospital, Rome, Italy. Music appraisal is hard to study in young CI users. One objective measure is to record EEG responses while normal and

distorted music is presented. The study showed that, as opposed to normal hearing subjects, desynchronization of alpha bands in the left prefrontal cortex (lPFC) during pleasant stimulation, and the rPFC when the stimulus is unpleasant, does not occur in CI patients. This suggests different musical processing in CI recipients.

5. *Cortical processing of changes in music and speech in children with cochlear implants: role of music*, Torppa et al., University of Helsinki, Finland. In response to piano tones and pseudo-words, varied in frequency, intensity, and duration pitch and timbre perception were studied in single-sided CI users using ERP recordings.. CI patients showed less fluency in detecting change (mismatch negativity, MMN) in timbre, duration, and time interval, and better fluency as regards sound intensity. The latency and amplitude of MMN was similar in the normal hearing group and patients, when piano tones were presented, but with significant differences for speech stimulation. CI users who had some prior musical training (practiced playing an instrument) had results closer to normal.
6. *Neural correlates of tinnitus improved by cochlear implants in patients with single-sided deafness*, Song et al., University Hospital, Antwerp, Belgium.Studies show that in unilateral deafness cochlear implantation can improve tinnitus. On- and off-CI states were analysed with qEEG, the results showing that the improvement might be due to changes in the amount of alpha2 wave in certain brain regions, e.g., decreased in dorsolateral prefrontal cortex and increased in the posterior lateral prefrontal cortex. Longitudinal studies are necessary to assess long-term cortical reorganization after implantation.
7. *Event-related potential evidence for the perception of emotional prosody through cochlear implants*, Buechner et al., Medizinische Hochschule, Hannover, Germany. Cochlear implants impair the transmission of speech melody, and might also affect the processing of prosody, which is indispensable in understanding emotions. This ERP study showed that emotional processing can be reliably measured with ERPs. Moreover, speech coding algorithms used in CI processors seem to determine how prosody is perceived.
8. *Electrophysiological signatures of cortical plasticity in cochlear implant users*, Sandmann et al., University of Oldenburg, Germany. There is large variability among CI users in terms of speech performance. An ERP visual study was done using a parametrically reversing static checkboard. The results showed smaller visual activations in CI users. However, with more CI experience, the amplitude and latency of the P1–N1 complex was found to become closer to normal. In addition, the right auditory cortex was recruited in patients in response to pure visual stimulation, especially in those with poor performance. The amount of cross-modal plasticity was also modulated by the stimulus luminance, which occurs at a very basic sensory level of information processing.

Functional magnetic resonance (fMRI)

1. *Does assessment of brain visual speech circuits in profound acquired deafness support the hypothesis of latent multimodal connectivity?* Truy et al., University of Lyon. Studies indicate that sensory deprivation enhances plasticity across modalities. It has been suggested that during speech-reading tasks, non-aided individuals with acquired profound deafness use visual cortices to a higher extent than auditory cortices, starting 2 years from the onset of deafness. The authors also showed that the amount of visual activations correlates with speech-reading fluency, which is consistently better in hearing-deprived patients than in normal hearing subjects. In cochlear implant users, pathways subserving speech-reading become closer to those in normal hearing subjects, but patients still exhibit more temporal area activity (regions intrinsically processing auditory input). The findings suggest that the cross-modal neural network is already unravelled at the onset of hearing impairment, and is not first established after cochlear implantation.
2. *Bilateral reorganization of posterior temporal cortices in post-lingual deaf subjects,* Lazard et al., Ecole Normale Superiore, Paris. Deafness impairs the processing of phonological aspects of speech. This fMRI study showed that with longer duration of deafness there are: a) decreased brain responses to phonological memory tasks in the left posterior superior temporal gyrus (lSTG) and increased responses in the right posterior superior temporal gyrus; b) decreased responses in the right posterior superior temporal gyrus (rSTG) in tasks involving memorising environmental sounds. It is suggested that the pattern of activations in the rSTG reflects the importance of speech phonology in humans. Further implications are that rehabilitation of phonological processing in hearing impairment should commence earlier in the progress of deafness, and include processing of environmental sounds; these actions could prevent undesired plastic changes.
3. *Visual cross-modal reorganization of phonological pathways in post-lingual deaf subjects,* Lazard et al., Ecole Normale Superieure, Paris. An fMRI reading/rhyming task revealed that: a) deaf subjects perform worse than normal hearing (NH) subjects; b) good hearing-impaired performers have better reaction times that NH individuals; c) the results of the patients correlate with their speech outcomes. Further results suggest that patients using the dorsal phonological route of the speech network to process articulation become good performers after CI implantation, whereas those employing the ventral path, normally subserving semantic operations, perform poorer. In another speech/reading experiment, it was shown that the involvement of the left posterior superior temporal sulcus prior to implantation correlates with good understanding, but at the same time limits the chances of an efficient use of pure auditory cues after implantation. Therefore the authors believe that the neural strategy during phonological reading and lip-reading in CI candidates could serve as a post-CI performance predictor.
4. *Comparison of resting state activity in individuals with unilateral hearing loss and normal hearing,* Firszt et al., Washington University, USA. This fMRI functional connectivity study showed that brain responses at rest differ between hearing individuals and those with unilateral deafness (especially in left-sided deafness). The following areas were shown more strongly 'connected' in patients: frontal eye fields – inferior parietal lobule – motor cortex – auditory cortex. In general, it seems that in hearing-impaired individuals sensory connections are less profound, in favour of attention-related involvement

that is probably required for task-switching. The study provides new data to elucidate reasons of substantially variable speech-performance in the population.

5. *New insights on the tonotopy of the human auditory cortex*, van Dijk et al., UMC Groningen, the Netherlands. Previous studies indicated that the primary auditory cortex (A1) is organized hierarchically, i.e. in sub-areas processing high and low frequency bands. In this study, tonotopic areas of the human primary auditory cortex were mapped using minimally salient stimuli to evoke maximally selective responses in fMRI. The study employed tones of 250–8000 Hz at an intensity of 10–50 dB SL presented in a sparse paradigm (10 s silence, 2 s scanning). The participants performed non-auditory tasks to control the effects of auditory attention. Two tonotopic belts were identified on the Heschl gyri caudally and rostrally, with low-frequency regions in the superior part of the temporal gyrus. A third frequency belt was suggested in the temporal pole. The authors emphasized that numerous variables need to be controlled in tonotopy studies, i.e., i.e.., the effect of attention and stimulation parameters, complex processing occurring on the way from the cochlea to A1, folded surface of the auditory brain areas, as well as inter-subject structural and functional variability, as

Positron emission tomography (PET)

1. An oral presentation was delivered by K. Cieśla from the Institute of Physiology and Pathology of Hearing, Poland. *Cortical activity in bilateral cochlear implant users*, K. Cieśla (IPPH); J. Mathews, K. Green, R. Aggarwal (Central Manchester University, UK). Six adult users of bilateral CIs with postlingual deafness and 6 normal hearing volunteers had up to 12 [15O]H2O-PET scans, listening binaurally to BKB sentences, reversed BKB sentences, and silence. With sentences presented, large activations in bilateral temporal lobes were found in both groups. Responses in CI subjects were significantly more diffuse compared to hearing individuals. For supra-phonological analysis of speech, normal hearing individuals predominantly recruited the left temporal lobe, whereas responses in patients were bilateral. Further investigation is needed to explore the distinct auditory strategies in recipients of bilateral cochlear implants.
2. *PET study of word recognition in binaurally implanted post-lingually deaf patients,* Barone et al., Toulouse, France. An O15-H2O PET study showed that word processing in bilaterally implanted subjects resembles normal cortical processing to a higher extent than is the case in unilateral CI users, especially in response to binaural stimulation.

Near-infrared-spectroscopy (NIRS)

1. *Functional near infrared spectroscopy: a novel imaging technique for cochlear implants,* Kileny et al., University of Michigan, USA. NIRS is a promising neuroimaging method that can be used to study cognitive functions in humans, such as auditory processing in cochlear implant users. Optical imaging is based on the fact that near-infrared wavelengths are differently absorbed by oxygenated and deoxygenated haemoglobin, and therefore task-related molecular concentrations can be assessed. Multiple transmitters and detectors of light are distributed across the skull to collect images. The relative drawbacks of the method include: a) penetration depth limited to 1.5 cm into the brain tissue; and b) relatively low spatial resolution. At the same time, however, the technique is low cost compared to other imaging methods, the equipment is portable, and there is no contamination with cochlear implant or movement artifacts.

Conclusions

The 7{th International Symposium on Objective Measures was of great value for specialists involved in evaluating auditory function. The clear message was that electrophysiology and electroencephalography still provide the most accurate *in vivo* timing data for subcortical and cortical processes, but functional magnetic resonance and positron emission tomography have arrived to compete in localising the areas subserving particular cognitive tasks. For the hearing-impaired population, the additional neuroimaging data afford insights into neuronal re-organization and cross-modal plasticity due to the sensory deprivation itself, and as a consequence of using devices that amplify or restore hearing. Currently, scientific teams are focusing on establishing the optimal interdisciplinary methodology to reliably evaluate the effects of therapeutic interventions, as well as defining patterns in brain activations that could serve as reliable predictors of auditory outcomes following hearing aid fitting or cochlear implantation. Functional imaging, used in a complement to conventional psychoacoustic assessments, is definitely the way of the future.