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Aging, cognitive decline and hearing loss: outcomes of auditory rehabilitation in older adults

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Index

Abstract

Introduction. Restoring a sensory function in older adults might allow a significant improvement in their cognitive status. Although specific clinical conditions could compromise management and drastically reduce the chance of acceptable outcomes, auditory rehabilitation with cochlear implants or hearing aids still remains one of the most effectiveness procedure. Advances in research and technology suggest a functional "adaptation" in central processes that could influence other related or not strictly related activities, such as memory and working memory, frontal and pre-frontal processes, orientation, calculation, logic and executive functions. Since the link between hearing loss and cognitive decline has been clarified, scientific community is currently finding out the lacking evidence of effectiveness of auditory rehabilitation in reducing or counteracting cognitive decline.

Material and Methods. Hearing impaired patients with more than 65 years of age, affected with mild to profound hearing loss were enrolled in the present study; complete audiological assessment and cognitive status evaluation were performed in order to define personal scores for comparison in longitudinal testing after different auditory rehabilitation. A control group was created for statistical purposes and made of cases matched per age and clinical status, without hearing loss and cognitive decline. Different subgroups were created to reduce heterogeneity in terms of entity of hearing loss, duration of auditory deprivation, type of auditory rehabilitation and training. A follow up of 6-12 months has been carried out for selected patients.

Results. To date, 77 subjects have been included in the present study and divided in 5 different groups based on types and degree of hearing loss. Statistical analyses with t-student test and fisher exact test, shows a significant difference in depression and cognitive status scores before and after auditory rehabilitation. In addition there are no differences between the control group (20 subjects) and patients who have a good outcomes after auditory training and rehabilitation.

Discussion. Auditory rehabilitation shows significant effectiveness even among older adults with different degrees of hearing loss, and positive improvements are detectable in terms of social isolation, depression and cognitive performances. In future research, it will be crucially important to unravel how sensory abilities are linked to cognitive functioning in aging. Conventional medical assessment is often not enough to assess older people with multiple comorbidities. In the end, a multidisciplinary approach is still the best option, and geriatrics should include specific sensorineural investigations to manage elderly patients who are generally at risk of cognitive decline and hearing loss.

Key words: elderly, cochlear implantation, hearing aids, cognitive decline, hearing loss, depression.

Invecchiamento, declino cognitivo e ipoacusia: esiti della riabilitazione uditiva negli anziani

Introduzione. Il ripristino di una funzione neurosensoriale negli anziani può consentire un significativo miglioramento del loro stato cognitivo. Anche se condizioni cliniche specifiche possono compromettere la gestione e ridurre drasticamente il raggiungimento di risultati accettabili, la riabilitazione uditiva con impianti cocleari o apparecchi acustici resta ad oggi uno dei mezzi più efficaci. I progressi della ricerca e della tecnologia suggeriscono un "adattamento" funzionale nei processi centrali che potrebbe influenzare le altre attività connesse o meno strettamente correlate con la funzione uditiva, come la memoria di lavoro, processi frontale e pre-frontali, orientamento, calcolo, logica e funzioni esecutive. Dal momento che il legame tra la perdita dell'udito e il declino cognitivo è stato chiarito, la comunità scientifica è ora alla ricerca dell'evidenza scientifica mancante dell'efficacia della riabilitazione uditiva nel ridurre o contrastare il declino cognitivo.

Materiali e Metodi. Soggetti con deficit uditivo con più di 65 anni di età, affetti da sordità lieve-profonda sono stati arruolati in questo studio; la valutazione audiologica completa e la valutazione dello stato cognitivo sono stati effettuati al fine di definire punteggi personali per il confronto longitudinale dopo la riabilitazione uditiva. Un gruppo di controllo di 20 soggetti è stato creato a fini statistici e realizzato con soggetti normo-udenti senza declino cognitive, omogenei per età e condizioni cliniche. Diversi sottogruppi sono stati creati per ridurre l'eterogeneità in termini di entità della perdita di udito, di durata della

deprivazione neurosensoriale, del tipo di riabilitazione e di training uditivo. Un follow up di 6-12 mesi è stata effettuato, ove possibile per pazienti selezionati.

Risultati. Ad oggi, 77 soggetti sono stati inclusi nel presente studio e divisi in 5 gruppi diversi in base ai tipi e gradi di perdita dell'udito. Non tutti i soggetti sono riusciti a completare la batteria di test previsti, tuttavia le analisi statistiche con t-student e fisher test e chi quadro, quando possibile applicarli, hanno mostrato una differenza significativa nei punteggi di depressione e stato cognitivo, prima e dopo la riabilitazione uditiva. Non sono risultate differenze significative tra il gruppo di controllo ed i pazienti con buon esito della riabilitazione.

Discussione. La riabilitazione uditiva presenta una significativa efficacia anche tra gli adulti più anziani con diversi gradi di perdita di udito e miglioramenti positivi sono rilevabili in termini di isolamento sociale, depressione e le prestazioni cognitive. Nella ricerca futura, sarà di fondamentale importanza svelare come le capacità neurosensoriali siano legate al funzionamento cognitivo nell'invecchiamento. Oggi, l'approccio medico convenzionale spesso non è sufficiente per valutare le persone più anziane con comorbidità. In definitiva, un approccio multidisciplinare rimane ancora l'opzione migliore, ed il geriatra dovrebbe includere specifiche indagini neurosensoriali per gestire i pazienti anziani che sono generalmente a rischio di declino cognitivo e perdita di udito.

Parole chiave: anziani, impianto cocleare, apparecchi acustici, declino cognitivo, ipoacusia, depressione.

Introduction

The world's population is continuously rising and it is expected to reach 9 billion by 2045. Available demographic data from the main international research centres indicate that the average lifespan in industrialized countries is increasing (it is currently approximately 80 years): the population's age distribution shows a constant growth in the proportion of people over 65 years old, which has more than doubled in the last 35 years (from 1980 to 2014), rising from 250 million to over 550 million. The median age is also rising continuously, and has gone from 23.5 years in 1950 to 29 in 2014 (Van Bavel 2013). Thus it is expected that also the prevalence of specific conditions could increase with aging, as well as hearing loss or dementia that exceeding 10% beyond the age of 65.

The epidemiological data on hearing-impaired people and patients with cognitive decline are consequently a cause for concern, especially when we consider adults over 65 or 75 years old. There are 360 million people in the world today with disabling hearing loss (5.3% of the world's population) and 91% of them are adults. The prevalence of hearing loss increases with age, so that approximately one in three people over 65 years suffer from disabling hearing loss (http://data.worldbank.org/). Disabling hearing loss refers to a hearing loss greater than 40 dB HL (averaged across 0.5 to 4 kHz) in the better-hearing ear (in adults).

The age-standardized prevalence of dementia varies from 2% to 8.5% among people over 59 years of age, exceeding 10% beyond the age of 65, and rising to 25-30% for people over 85; and more than 90% of dementia patients have hearing problems. The prevalence of dementia was 7.1 million in 2000, and 35.6 million in 2010. What is more, 58% of all people with dementia live in countries with low or mid-range incomes (Wancata et al. 2003; Prince et al. 2013).

In short, as life expectancy has increased, the number of healthy years lost to disability has also risen in most countries (Salomon et al. 2012). But while hearing loss and/or cognitive decline continue to be common among the elderly, that does not necessarily mean that aging and hearing loss or dementia go hand in hand: healthy aging is possible at every stage of life (Kolovou, Kolovou, and Mavrogeni 2014).

Generally, sensorineural systems play a crucial role in the diagnosis, treatment and management of several neurological disorders. The function of the eye and ear represent a unique window for testing various conditions in cognitive decline or dementia. Touch and smell have also been found to be strongly involved in neurodegenerative conditions and their decline has been significantly associated with the progression of the disease; hence, the idea that restoring sensory function in cognitively impaired adults might enable a significant improvement in their cognitive status, reducing the worldwide incidence and prevalence of dementia.

Not all sensorineural "windows" can benefit equally from the same procedures; however; hearing and vision can certainly gain the most from dependable therapeutic and diagnostic options. The ear, including the vestibular system, deserves an honoured place among the sensory organs in this context, due mainly to the sophisticated electrical devices available that have amply demonstrated their effectiveness in treating hearing loss (Prince et al. 2013). The continuously expanding clinical indications for the most advanced auditory-function rehabilitation methods, including digital hearing aids and cochlear implants, have reasonably increased expectations about potential effects on cognitive functions and mood disorders among older adults (Lin et al. 2013; Lin, Thorpe, et al. 2011; Lin, Metter, et al. 2011; Lin et al. 2014; Lin 2011). Several studies have clarified the correlation between hearing loss and cognitive decline. Furthermore, it has become increasingly evident that even very old people can benefit from procedures that were previously recommended for younger patients, such as cochlear implantation. Nevertheless, the direct impact of auditory rehabilitation on cognitive decline remains to be demonstrated. Auditory rehabilitation can reduce the cognitive "load" (the neural activity needed to achieve a task, in particular understanding /recognizing the spoken word), social isolation, anxiety and depression.

Restoring an individual's hearing can reduce the cognitive "load"; i.e. the neural activity needed to understand/recognize the spoken word - an activity that becomes more demanding if the brain is obliged to recruit different neural populations to achieve the same performance, as happens in older adults with sensory impairments.

The sensory interfaces may also facilitate the early diagnosis of conditions characterized by a lengthy pre-clinical phase, as well as enabling non-invasive, follow-up procedures to assess the outcome of rehabilitation measures and distinguish physiological brain aging from neurodegenerative disorders.

Literature review. Systematic research on the connections between hearing loss and cognitive decline began in the 1980s, thanks mainly to publications of several authors [(Uhlmann, Larson, and Koepsell 1986); (Weinstein and Amsel 1987); (Peters, Potter, and Scholer 1988); (Jerger et al. 1989; Jerger 1992). Generally speaking, researchers focused on the significant association between cognitive decline and several factors that might be responsible for neurological diseases or other conditions, including: hearing loss, diabetes, cardiovascular diseases and alcohol consumption. But socio-economic conditions, gender and education also emerged as potentially influencing the risk of dementia (Maggi et al. 1998).

The subsequent scientific publications remained fairly constant until a renewed interest was aroused in the last five years, especially in the light of data from neurophysiological measurements obtained with EEG, MRI/fMRI, genetic investigations and demographic studies. An indirect aspect may have been played by the difficulty of finding effective drug therapies for cognitive decline, and the continuously expanding clinical indications for the most advanced auditory-function rehabilitation methods, including digital hearing aids and cochlear implants. This renewed interest has definitely been sustained by recent works brought to light in the literature (Lin 2011; Lin et al. 2014; Lin, Thorpe, et al. 2011; Lin et al. 2013); (Lazard et al. 2013). The studies are remarkably heterogeneous, but the results all seem to converge on certain, basic shared key issues:

- the neurosensory systems, hearing in particular, are important windows for shedding light on neurodegenerative diseases.

- the cortical activity of patients with hearing loss is characterised by neuron reorganization and adaptive plasticity, but not always with positive results (maladaptive plasticity).
- elderly patients with cognitive impairment, even severe, should not be denied the auditory rehabilitation options currently available.
- changes in anatomy have been documented, such as brain volume shrinkage, synaptic degeneration and subsequent compensatory mechanisms (with greater neural activity) (Kotak et al. 2005; Lin et al. 2014; Lazard et al. 2013).
- working memory has a crucial role in the difficulty of understanding speech in noisy environments.

Modifiable factors. The meaning of a 'risk factor' is strongly linked to a cause-effect correlation on a precise and particular temporal axis: it cannot come after the disease. The early signs of a disease, including hearing loss in patients with dementia, and variability in the risk factors identified may, consequently, be rather confusing. In short, hearing loss and vestibular disorders could be early symptoms of a cognitive decline and, therefore, effects, not causes.

This aspect has been amply cited in relation to the pre-clinical diagnosis of dementias (Wong et al. 2014), as seen for vision and the eye (Kerbage et al. 2013; Chang et al. 2014). So hearing loss can be seen both as a screening method (to test for cognitive decline or dementia) and as a modifiable risk factor for preventing cognitive impairment (Gurgel et al. 2014; Lin, Thorpe, et al. 2011; Parham et al. 2013). Hearing loss can also be considered an independent pathological process that shares some pathophysiological processes and etiologies with cognitive decline (genetics, trauma and vascular diseases, for example) (Kurniawan et al. 2012)].

Auditory rehabilitation. In the auditory rehabilitation of patients with early cognitive impairment, it is important to consider the clinical indications and the feasibility of preventive and diagnostic screening for other diseases. In clinical practice, there is no reason why a cognitively impaired patient should not be able to benefit from valid and documented rehabilitation methods involving hearing aids and/or cochlear implants (Petitot et al. 2007; Allen et al. 2003; Lupsakko, Kautiainen, and Sulkava 2005)]. More timely rehabilitation may yield greater benefits - even in the very elderly (85 years and over). The optimal time window for intervention may be much narrower, however, than the one considered today for children with congenital hearing loss (Arlinger 2003)]. Experimental studies in animal models suggest that some developmental processes may become irreversible even after as little as 30 days (Leake et al. 2008)].

It is well demonstrated that a cochlear implant (CI) dramatically improves auditory function and speech perception for elderly patients, similar to young implanted patients. Recent studies have shown that this procedure improves auditory performance, is well tolerated even in the most elderly, enhances self-confidence, reduces tinnitus and stress – in most cases tinnitus – and increases the health-related quality of life. The risk of anaesthetic and surgical complications remains low provided that a thorough multidisciplinary evaluation is performed before the procedure. The costeffectiveness still remains acceptable, including patients over 70 years of age because, even if healthcare costs are high, the savings in terms of indirect costs and quality of life are important. Among patients with pre-implant severe tinnitus, a partial or total tinnitus reduction was observed in approximately 70% of cases.

Objective measurements. It is widely accepted that auditory rehabilitation with hearing aids or cochlear implants is a valid option even for very old adults, and there are several reports in the literature documenting their benefits. A positive outcome is clearly desirable but stopping, delaying and containing cognitive decline are three different goals of auditory rehabilitation, any and all of which would have positive effects. It is not easy to establish comparable, reliable and valid objective means for measuring the clinical stages of cognitive decline, however. How do we measure the effect of a treatment on a disease that may have begun to develop 20 years earlier, having now reached a time of life characterised by comorbidities and higher incidence of systemic diseases? Objective test methods are needed, generating results that are easy to compare over a lifetime. The data generated through MRI, EEG, and biochemical analyses may help us to elucidate the value of treating hearing loss in cognitively impaired individuals.

Several studies support the use of electroencephalography (including brainstem and cortical potentials) to assess patients with hearing and/or cognitive impairment. Alpha activity has proved essential to the central processes for distinguishing signals from noise (Strauss, Wostmann, and Obleser 2014)]. Particularly in healthy individuals, an increased alpha activity is always needed in the selective attention paid to sound sources in competition. This parameter may help us to differentiate between the peripheral (hearing) and the central contribution (neurodegeneration) to cognitive impairment in patients with hearing loss, especially when combined with data on auditory brainstem responses, and from tonal and speech audiometric tests.

The Mini Mental State Examination (MMSE), the Montreal Cognitive Assessment (MOCA), the Geriatric Depression Scale (GDS), and other such cognitive tests are useful, but can hardly be considered objective.

The potential contribution of new methods such as functional MRI or functional NIRS (near infrared spectroscopy) seems very promising, but these are still mainly only experimental options and are not used routinely at most specialized centres.

Rationales for treatment. From a review of the literature, it is not clear how auditory rehabilitation might actually have direct or indirect effects on cognitive decline, especially at the central nervous system level in a neurodegenerative condition. In general, there are five rationales to consider.

First of all, reducing social isolation and improving depression symptoms could explain some early effects. Social isolation is a risk factor for cognitive decline because speech is the main way to transmit thoughts between individuals (Ertel, Glymour, and Berkman 2008; Boi et al. 2012; Acar et al. 2011)]. Second, there is the preservation of the function and three-dimensional structure of the peripheral and central synapses (Kumar and Foster 2007; Wong et al. 2010)]. Third, partly as a consequence of the second, comes the contraposition and reversibility of negative neuroplastic processes. Fourth, we have the release of biochemical neural factors (Leake et al. 2008)] that may sustain neural cell populations. Fifth, there is the effect of auditory/speech training, which can influence working memory.

Reviewing the literature, we can also establish a hypothetic temporal and audiometric threshold at which auditory rehabilitation should be mandatory, and beyond which treatments would become less effective. This limit could be set at 70 dB HL (PTA 0.5, 1, 2, 4 kHz) in the better-hearing ear, within a month of the hearing loss being diagnosed or suspected (Lazard et al. 2013; Lazard et al. 2011)].

The diagnosis of cognitive decline or dementia requires a multidisciplinary assessment, a battery of tests, and a rather long period of observation. The benefits achievable with these efforts are much greater when the cognitive decline is still mild or in a pre-clinical stage. In fact, some of the most relevant, recent studies have concentrated on the pre-clinical diagnosis of dementia, because this would be the best starting point for efforts to prevent or treat it.

The aim of the present research was to investigate the effects of restoring hearing functions through cochlear implantation or hearing aids on depression and cognitive decline among older adults affected by variable degree of sensorineural hearing loss.

Materials and methods.

The present research is based on a retrospective study of 30 consecutive post-lingual, profoundly hearing impaired elderly adults, previously published in 2015. A selection from approximately 500 patients who were implanted at the Otolaryngology Clinic of Padua Hospital, between May 2010 and December 2014 has been used to collect preliminary data. Selection criteria were age 65 years at surgery, unilateral implantation and absence of neurodegenerative conditions. Pre-implant evaluation consisted of tonal and speech audiometry with and without hearing aids. Post implant evaluation included the same tests that were conducted with and without a cochlear implant one year after surgery. Threshold evaluation was conducted by using the pure tone average (PTA), i.e. the mean of the air-tonal threshold at frequencies 500, 1000, 2000 and 4000 Hz in dBHL. To evaluate speech perception the Speech Detection Threshold (SDT) and Speech Recognition Threshold (SRT) were used. SDT corresponds to the value of sound intensity at which the verbal message is not understood but perceived as generic sound – therefore, with a percentage of intelligibility of 0%. The SRT indicates the level of intensity at which the patient correctly repeats 50% of the words. For the surgical outcome the presence of any medical or surgical major complication related to the implant surgery or to the age of the patients was considered. Significance was determined using the Student's t -test for paired data.

Starting from this data, adults with more than 65 years of age were selected and added in the present study for a longitudinal research; cases were then divided, following clinical indications and entity and types of hearing loss, in 5 groups:

group A, patients with bilateral hearing loss who were candidates for hearing rehabilitation with bilateral hearing aids (first prescription); **group B**, patients who were wearing hearing aids and who were previously trained in the last two years with digital devices (unilateral prescription); **group C**, patients who were eligible for auditory rehabilitation with hearing aids, but without device and prescription (never trained before); **group D**, subjects with profound sensorineural hearing loss, who were scheduled for cochlear implantation, and **group E** (control group), subjects with normal hearing matched for age, sex and clinical conditions that we used as control group. All subjects were adults with more than 65 year of age at the time of the investigation.

The audiological assessment was carried out for each subject by a well-equipped team, with proved experience in the field. Cognitive and depression scores were obtained through Montreal Cognitive Assessment (MoCA) Test, Geriatric Depression Scale and digit span test (figure 1, 2 and table 1).

The MoCA was found to have a 90% sensitivity and a 87 % of specificity that allow the identification of 90% of subject with mild cognitive impairment (MCI) and 100% of patients with mild Alzheimer disease (AD) (Nasreddine et al. 2005). On the other hand, the GDS was found to have a 92% sensitivity and a 89% specificity when evaluated against diagnostic criteria. The validity and reliability of the tool have been supported through both clinical and research practice. In a validation study comparing the Long and Short Forms of the GDS for self-rating of symptoms of depression, both were successful in differentiating depressed from non-depressed adults with a high correlation (r = 0.84, $p < .001$) (Yesavage et al. 1982; Montorio and Izal 1996).

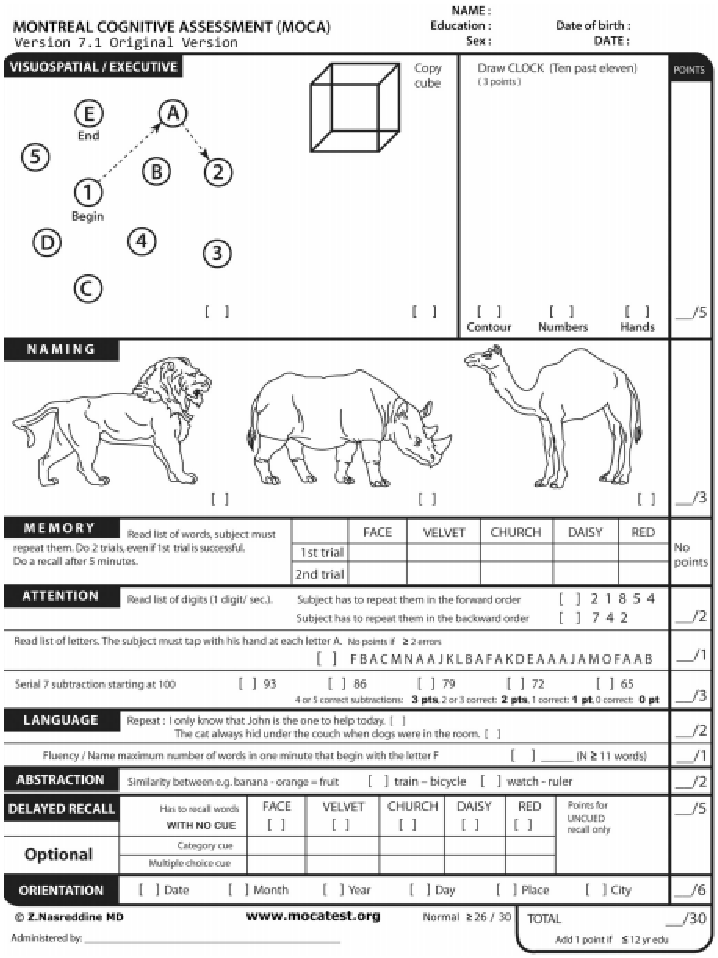

Figure 1 *–The Montreal Cognitive Assessment (MoCA) was designed as a rapid screening instrument for mild cognitive dysfunction. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. Time to administer the MoCA is approximately 10 minutes. The total possible score is 30 points; a score of 26 or above is considered normal.*

Digit span task is a measure of the longest list of numbers that a person can repeat back in correct order immediately after presentation; generally, this task is a common measure of short-term memory (figure 2).

Environments were specifically optimized and chosen for hearing impaired patients; testing was performed with different versions (to avoid learning curve) and given (among profound hearing impaired patients) in written form by 4 different trained professionals. The setting was kept constant throughout the research to reduce systematic errors and allow longitudinal study (GROUP D). Results were corrected with coefficients for different levels of education, as reported in the literature (Nasreddine et al. 2005).

1. Are you basically satisfied with your life ?	16 Do you often feel downhearted and blue ?
2. Have you dropped many of your activities and interests ?	17 Do you feel pretty worthless the way you are now?
3. Do you feel that your life is empty ?	18 Do you worry a lot about the past ?
4. Do you often get bored ?	19 Do you find life very exciting ?
5. Are you hopeful about the future ?	20 Is it hard for you to get started on new projects ?
6. Are you bothered by thoughts you can't get out of your head ?	21 Do you feel full of energy ?
7. Are you in good spirits most of the time ?	22 Do you feel that your situation is hopeless ?
8. Are you afraid that something bad is going to happen to you ?	23 Do you think that most people are better off than you are ?
9. Do you feel happy most of the time ?	24 Do you frequently get upset over little things ?
10. Do you often feel helpless ?	25 Do you frequently feel like crying ?
11. Do you often get restless and fidgety ?	26 Do you have trouble concentrating ?
12. Do you prefer to stay at home, rather than going out and doing new things ?	27 Do you enjoy getting up in the morning ?
13. Do you frequently worry about the future ?	28 Do you prefer to avoid social gatherings ?
14. Do you feel you have more problems with memory than most ?	29 Is it easy for you to make decisions ?
15 Do you think it is wonderful to be alive now ?	30 Is your mind as clear as it used to be ?

Table I *– The Geriatric Depression Scale; This is the original scoring for the scale: One point for each of these answers. Cutoff: normal-0-9; mild depressives-10-19; severe depressives-20-30.*

In addition, selected case underwent electrophysiology measures (EEG), direct functional assessment evaluation (DAFS) and mnemonic tasks in order to score their capacity in memory (FCSRT).

The study was conducted in the complex operative unit of Otolaryngology at the University Hospital of Padua from July 2012 to December 2015. The **group A** was tested after 1 month of auditory training with bilateral behind the ear digital hearing aids; the **group D** was retested 1 year after cochlear implantation surgery.

The results have been analyzed with 2-tailed Student's t-test for paired and unpaired samples, and linear regression analysis for correlations among variables such as age, cognitive function, hearing loss and outcomes after auditory rehabilitation.

Digit span test

	Column 1	Column 2
Forward test	(3) 2−6-5	(3) 2−8-1
	(4) 1−5−2-3	(4) 1−9−5-2
	(5) 2−4−7−6-1	(5) 5−2−1−4-3
	(6) 4-2−1−9−3−7	(6) 8−5−3−1−4-7
	(7) 3−6−4−8−5−2-9	(7) 6−8−1−4−7−2-5
	(8) 7−5−8−2−9−6−1-3	(8) 2−8-5-9−7−3−1-4
	(9) 5−8−6−4−2−7−3−9-1	(9) 4−2−5−8−1−3−9−7-6

Figure 2 ***–*** *The digit span test*

Results

Ultimately, our starting group comprised 30 patients (14 females, 16 males) aged on the day of surgery between 65 and 79 years (median, 70.5 years), which approximately represents 6% of implanted patients during the same period. The group had a high incidence of associated comorbidities such as arterial hypertension, cardiovascular diseases, diabetes, dizziness or other vestibular disorders. Despite these conditions, no surgical events or major complications were observed. The etiology of the hearing loss was unknown in the majority of cases while the most frequent known causes were otosclerosis and sudden hearing loss. Comparison of pre-operative and post-operative examinations revealed a significant improvement in hearing threshold ($p = 0.01$) and speech understanding ($p = 0.001$). In particular, the mean PTA improved in our patients from 111.8dB HL (± 17.8) without hearing aids to 42.6dB HL (± 10) with the cochlear implant. In addition, speech perception scores showed a significant improvement both in the detection threshold (SDT) and the perception threshold (SRT) with the mean value changing from 90dB SPL to 65dB SPL (Table II, Figure 3-4). Dizziness was the most common temporary complication and was observed in six cases (20%). In one case the patient developed a transient facial palsy.

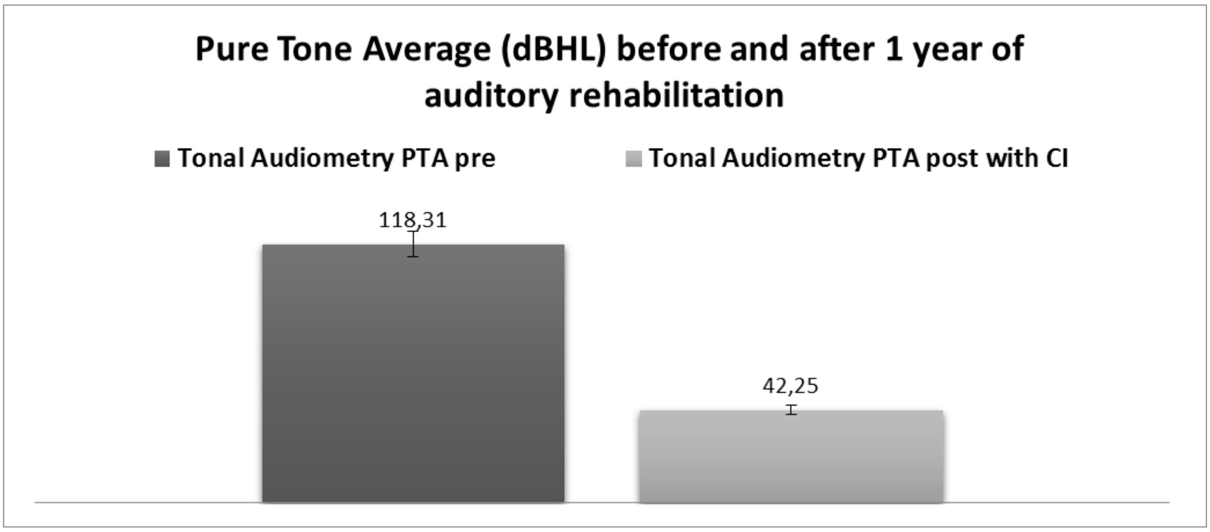

Figure 3 – *The graph shows the difference of PTA (Pure Tone Average 0,5 – 1 – 2- 4 KHz) before and after 1 year from the surgery in a case series of 30 patients who underwent cochlear implantation. The two-tailed t -test of the results revealed a statistically significant difference (p - value < 0.001).*

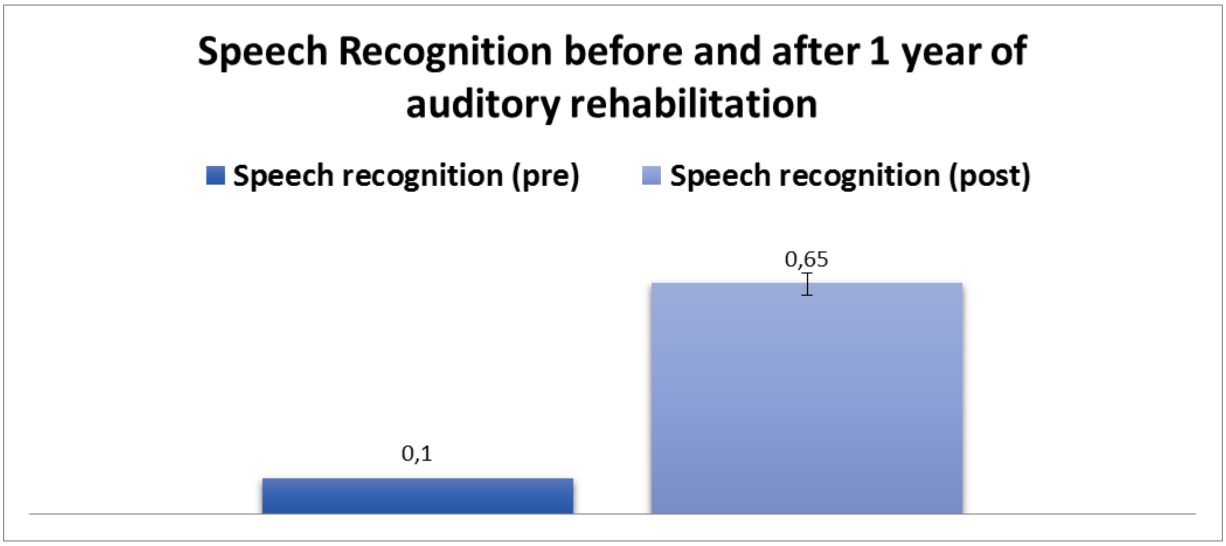

Figure 4 – *The comparison of the Speech Audiometries scores revealed a statistically significant difference (2 tails t test p = 0,003) with cochlear implant.*

Ability/Skill	Number of patients who reached 100%	Number of patients who reached 80–100%	Number of patients who reached < 80%	NE
Identification				
Vowels	17/30	9/30	4/30	–
Disyllabic/trisyllabic words	15/30	6/30	–	9/30
Sentences	11/30	19/30	–	17/30
Perception				
Disyllabic/trisyllabic words	3/30	13/30	12/30	2/30
Sentences	7/30	11/30	6/30	6/30

N.E.: not executable test.

Table II. *Auditory and perceptual abilities before and after cochlear implantation surgery; two patients reached 100% of discrimination after only one month from the activation.*

Starting from this previous report, 77 hearing impaired and 20 normal hearing subjects were added and included in the study between 2012 and 2015; the participants were divided as follows (Table III): GROUP A, 30 cases (15 males and 15 females; range of age 70-80, median 74) with mild to severe hearing impairment and eligible for binaural/bilateral hearing rehabilitation thorough behind the ear hearing aids, who underwent digit span tests before and after auditory rehabilitation; GROUP B, made of 20 subjects (10 males and 10 females, range 65-89, median 74) to whom were previously prescribed hearing aids and compared with group C and E (control group), that respectively were constituted of patients with hearing loss without hearing aids prescriptions (9 males and 3 female, 67-85, median 76), and subjects with normal hearing (9 males and 11 females, 65-80 range, median 70); finally, the GROUP D included 15 profound hearing impaired patients, (8 males and 7 females), with median age of 71 (range 65-75) that underwent cochlear implantation. These patients were retested after 1 year of auditory rehabilitation for longitudinal study. Three subject underwent

EEG with 64 channels during resting state, auditory perception and executive functions. Only one subject (from control group) could successfully complete the exam. Additional functional tests were performed in selected cases and confirmed scores reported during MoCA. A selected group of 17 patients underwent a specific speech tests with adaptative measurements of perception of sentences in noise. These test are thought to be predictive of cognitive decline when results are less than 80% of correct answers.

Generally, as expected, the required auditory rehabilitation was due to entity and type of hearing loss, therefore, the group A was essentially made of patients with mild to moderate symmetrical hearing loss, group B made of patients with asymmetrical conditions and moderate to severe hearing impairment, group C made of patients with mild to moderate hearing loss and group D (cochlear implants) made of patients with profound hearing loss.

Statistical analysis revealed significant improvement in cognitive status or depression in all groups when compared with patients before auditory rehabilitation or patients without hearing aid prescriptions. In addition, no significant differences were found when hearing trained groups were compared with normal hearing subjects in both the MoCA and GDS scores (fig. 5). Furthermore, the GROUP A revealed a significant improvement in digit span tasks after 1 month of auditory training. No gender differences were found.

In order to evaluate the contribution of single tasks or items constituting MoCA, the final scores obtained were divided in different components and compared among groups.

GROUP	N.	AGE	M/F	REHABILITATION	FOLLOW-UPS
A	30	>65 (range 70-80, median 74)	15/15	1 month of bilateral hearing aids (moderate to severe hearing loss)	**1 month** (digit span test), speech test, tonal test
B	20	>65 (65-89; median 74)	10/10	1-2 years of unilateral hearing aid (moderate to severe hearing loss)	MoCA, GDS, speech test, tonal test, 8 sentence tests
C	12	>65 (range 67-85; median 76)	9/3	**None** (mild to moderate hearing loss)	MoCA, GDS, speech test, tonal test
D	15	> 65 (range 65-75; median 71)	8/7	Cochlear Implant (Profound hearing loss)	**1 year**, MoCA, GDS, speech tests, tonal test, 2 EEG, 5 sentence tests
E	20	> 65 (range 65-80; median 70)	9/11	**Normal Hearing (control group)**	MoCA, GDS, speech tests (3 sentence test), tonal test, (1 EEG, 3 DAFS, 3 FRSCT)
TOT.	**77**	**>65 (range 65-89; median 74)**	**42/35**	**Mild to profound sensorineural hearing loss (with or without hearing aids or cochlear implant)**	**MoCA, GDS, DAFS, FRSCT, digit span test, audiological assessment, ABR, P300, EEG**

Table III *– Groups obtained from the subjects enrolled in the present study following clinical indications and degrees of hearing loss. N. = number of subjects; M = males; F = females; REHAB. = type of auditory rehabilitation and entity of hearing loss.*

Surprisingly the improvements might not directly coming exclusively from the restoration of the auditory function: the analysis of the sub-tasks of the MoCA test showed the best increment, after auditory training, respectively in long term memory (average 1.07), visuo-spatial and logical executive skills (average 0.57). As well as, cognitive screening showed positive correlation with auditory and perceptual outcomes.

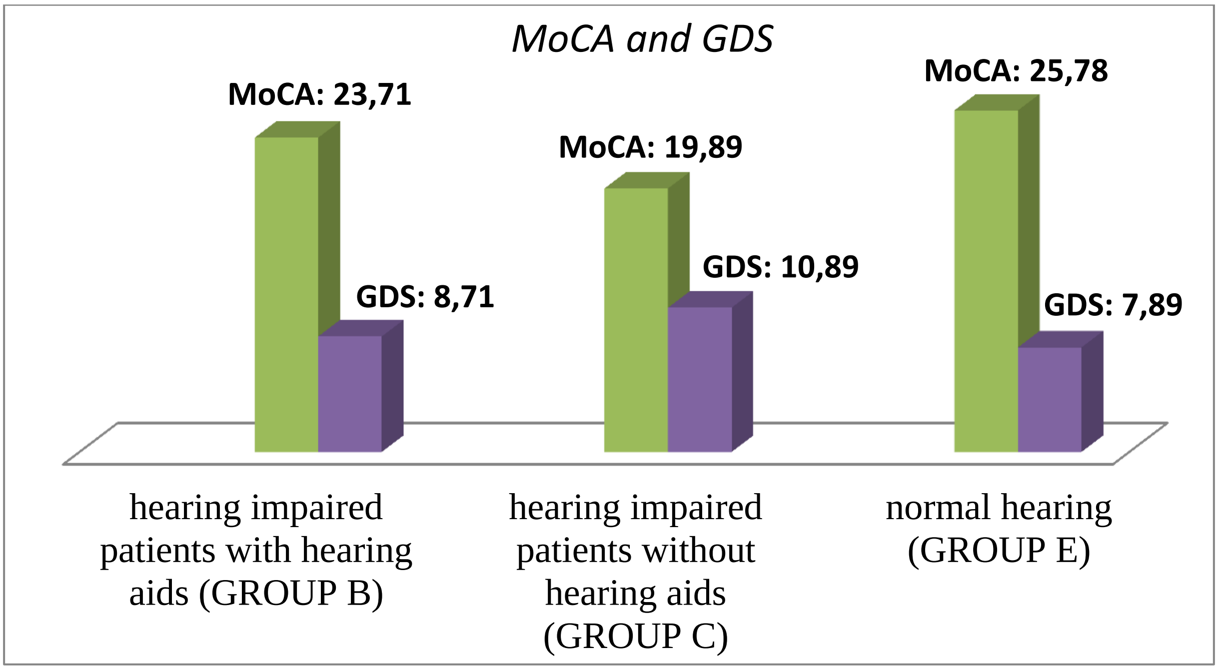

Figure 5 *- The comparison of the MoCA and GDS scores revealed a statistically significant difference between patients with hearing aids and patients without hearing aids (2 tails t test (p < 0,05), as well as between patients without hearing aids and normal hearing (p < 0,05); there is no significant difference between patients with hearing aids and normal hearing.*

Conversely, GDS scores are negatively correlated with outcomes, even if it was quite difficult to assess and to evaluate the real effect of mood disorders among hearing impaired patients. Among patients who underwent cochlear implantation (GROUP D), the auditory training determined a positive effect on cognitive performance and depression (fig. 6). The surgery and the postoperative period were uneventful and the group showed a significant improvement in terms of tonal audiometry and speech perception. The effectiveness of cochlear implantation on tonal and speech audiometry is widely proved by several studies that are available in the literature (Bovo, Ciorba, and Martini 2011; Ciorba et al. 2011; Martini et al. 2013; Chung et al. 2012).

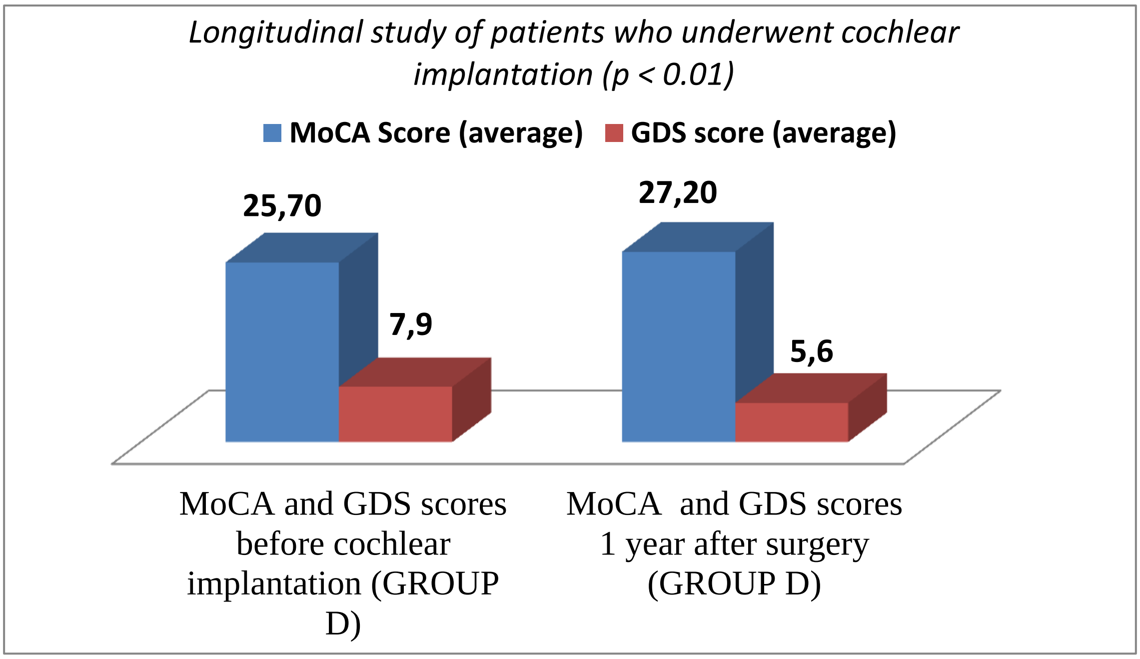

Figure 6 – *The longitudinal comparison of GDS and MoCA scores among patients who underwent cochlear implantation revealed a statistically difference before and 1 year after treatment (2 tails t test p < 0,01; paired data).*

The linear regression confirmed the mild negative correlation between age and cognitive functions, and between cognitive assessment and depression; conversely better outcomes should be expected in patients with higher scores at the MoCA screening (Fig. 7).

When single items of MoCA test were considered separately, the sums of the scores were quite similar to those of patients with cognitive decline, as reported in the literature (Nasreddine et al. 2005) (Tab. 3). The most conspicuous contribute to final score, after auditory rehabilitation, comes from long term memory tasks (Tab. 3). In other terms, long term memory results the most affected skill in hearing impaired patients as well in mild cognitive impaired adults. Interestingly, as mentioned before, the average score obtained was very similar to the average score obtained among patients with mild cognitive impairment (MCI) or, in progressive worsening, with Alzheimer disease (AD) (Tab. 3).

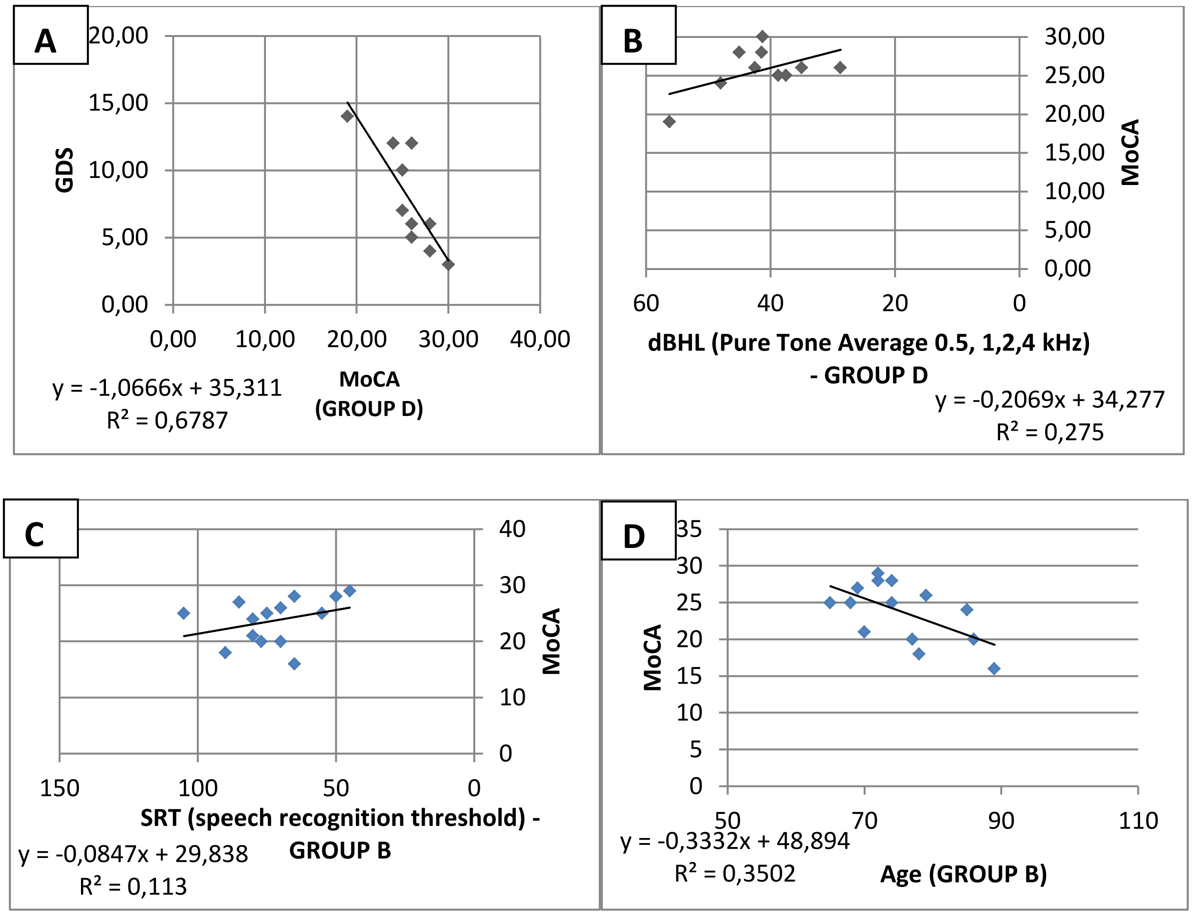

Figure 7 *– A, Negative correlation between MoCA and GDS (GROUP D) and B, conversely, positive correlation between outcomes (in terms of pure tone average after auditory training) and MoCA; C, positive correlation is documented between SRT (speech recognition threshold) and MoCA scores also in GROUP B; all groups show a negative correlation between Age and MoCA scores, especially in group B,*

Discussion and conclusions

Hearing loss is an important public health concern with substantial economic costs and social consequences. Hearing impairment is the most frequent sensory deficit in human populations and affects newborns, children, adults, and elderly people. The population over 65 years old is growing at a faster rate than the population as a whole, and it has been predicted that 20% of the population will be 65 or older by 2030. In 2006, from 35% to 50% of people aged 65 or more reportedly had presbycusis, a sensory impairment that contributes to social isolation and loss of autonomy, and is associated with anxiety, depression, and cognitive decline (Parham et al. 2011).

Conventional medical assessment is often not enough to assess older people with multiple comorbidities, and this acknowledged problem has prompted the development of geriatric assessment procedures that take a broader approach to examining contributors to health in older people, including: hearing impairment, visual impairment, functional decline, balance disorders and falls, urinary incontinence, cognitive impairment, depression, and malnutrition (Rosen and Reuben 2011; Elsawy and Higgins 2011).

Sensory measures are generally good predictors of higher levels of cognitive functioning, especially in older age, although cross-sectional studies have shown that hearing loss is a better predictor than visual acuity of age-related decline in more complex intellectual abilities (Granick, Kleban, and Weiss 1976; Baltes and Lindenberger 1997). Consistent with these earlier works, a recent longitudinal study confirmed that hearing loss is associated with a greater cognitive decline (Lin et al. 2013).

The magnitude of the relationship between sensory and cognitive functioning does not seem to depend exclusively on the level of sensory or cognitive performance, the type of task, or the severity of any brain-related pathology. Other measures of sensorimotor functioning (e.g. balance, gait) correlate with intellectual functioning too, just like visual and auditory acuity. Based on these findings, a common brain-related cause has been suggested to explain the increasingly strong correlation between sensory and intellectual abilities as a function of age (Lindenberger and Baltes 1994), although the evidence to support it is mainly correlational and needs to be confirmed by experiments directly testing this and other hypotheses.

In future research, it will be crucially important to unravel how sensory abilities are linked to cognitive functioning in aging. Understanding these mechanisms will have important implications when it comes to promoting appropriate strategies for better diagnostic or rehabilitation programs.

If a decline in sensory function and intellectual performance share a common cause, as suggested by Lindenberger and Baltes [1994], studies on sensory functioning would generate much the same insight as investigations on more complex cognitive processes, with the added advantage that a greater experimental control could be exerted when studying more straightforward sensory abilities.

If it can be demonstrated that sensory functioning affects cognitive aging, either directly or via some mediating factors (e.g., mood improvement, promotion of social life, and stimulation of cognitive reserves), then rehabilitation protocols designed to boost sensory function are bound to have the effect of improving higher-level cognitive abilities too. Although similar issues have occasionally been investigated with promising results (Mulrow, Tuley, and Aguilar 1992b, 1992a), future experimental research should concentrate more on the cognitive benefits of hearing rehabilitation in aging.

The signs of age-related hearing loss are slow to become apparent in many older adults and hearing loss, consequently, is often perceived as an unfortunate but inconsequential part of the aging process. But then again, research suggests that hearing loss may speed up the age-related cognitive decline and that treating hearing loss more aggressively could help delay cognitive decline and dementia by enabling cognitive rehabilitation through oral communication - the most important tool available for use in patient/operator relations.

It is important to emphasize that healthy aging is possible even in the later stages of life, but this may sometimes rely on behavioural and clinical decisions having been made even decades earlier.

There is still much to be done to improve our understanding of the pathophysiology and treatment of various neurodegenerative disorders, and further studies are needed to investigate the real value of treating sensory deficits in cognitively impaired or very elderly patients. This could influence the way in which elderly patients are assessed by physicians and surgeons who need a better understanding to enable a more effective management of certain conditions. In the end, a multidisciplinary approach is still the best option, and geriatrics should include specific sensorineural investigations to manage elderly patients who are generally at risk of cognitive decline and hearing loss.

Reviewing the literature, revealed 5 possible explanations of these results: (1) reducing social isolation and improving depression symptoms could explain some early effects (Acar et al. 2011; Boi et al. 2012); (2), the electrical stimuli may allow the preservation of the function and three-dimensional structure of the peripheral and central synapses (Ryugo, Kretzmer, and Niparko 2005; Kumar and Foster 2007; Wong et al. 2009; Wong et al. 2014); (3), the auditory rehabilitation can counteract negative neuroplasticity processes (Lazard et al. 2013; Lazard et al. 2011; Lazard et al. 2010); (4) the effect of auditory/speech training, which can positively influence working memory and learning abilities; (5) improvement in self-motivation, self-esteem or self-confidence after rehabilitative procedures, with positive effect on cognitive skills.

Items/Skills	**MCI**	**AD**	**Normal**	**HI-pre***	**HI-post****	**Diff. (post/pre)**
Visuospatial/executive	3.18	2.08	4.23	3.35	3.91	0.57
Naming	2.64	2.19	2.88	2.70	2.80	0.10
Attention	5.41	3.98	5.68	5.27	5.27	0.00
Language	2.2	1.69	2.7	2.43	2.68	0.25
Abstraction	1.43	0.99	1.83	1.40	1.55	0.15
Memory	***1.17***	***0.52***	***3.73***	***1.45***	***2.51***	***1.07***
Orientation	5.52	3.92	5.99	5.75	5.95	0.21

Table IV *– The table shows the average score obtained in different items that are included in MoCA test; it should be noted that the worst scores are obtained in memory skills (long term memory) and that the most increment after auditory training comes from memory and visuospatial items; MCI= mild cognitive impairment; AD=Alzheimer disease; HI-pre =hearing impaired patients before or without auditory rehabilitation; HI-post= hearing impaired patients with or after auditory rehabilitation; Diff. (post/pre) = difference in scores as resulting from different sections among patients before or without auditory rehabilitation and patients after or with auditory training.*

In addition, the hearing system should be considered an important window for investigations in neurodegenerative disorders, and the auditory rehabilitation options currently available should not be denied to elderly patients with cognitive impairment. Working memory has a crucial role in understanding spoken words in noisy environments, consequently long term memory assessment could be a predictive factor for rehabilitative outcomes.

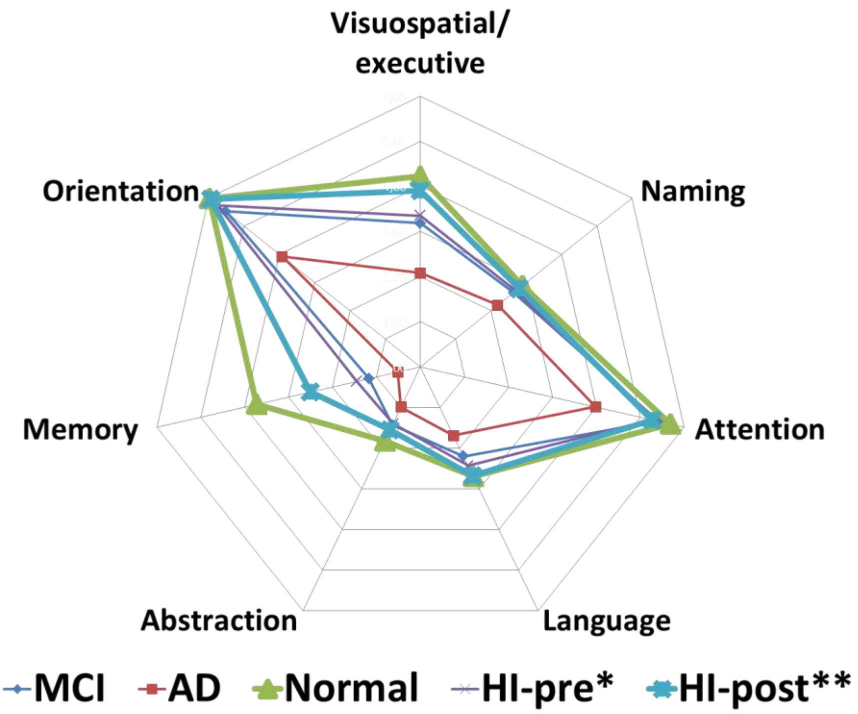

Figure 8 *– Reporting scores from table IV in a graph allows to appreciate the difference between different group in different subtasks: as shown in the graph the most important increment after auditory rehabilitation is essentially due to improvement in memory and executive tasks, that notably are effected in cognitive decline.*

Interestingly, the scores obtained in single sub-tasks of MoCA score are close to those obtained among patients with AD or MCI, as reported in the literature: these results suggest new considerations on cognitive effects of auditory rehabilitation among older adults, confirming the particular correlation between hearing loss and cognitive decline (table IV and figure 8) .

Short term memory also contributes to word identification and correct recall (figure 9): the present study confirmed literature data (Drewnowski and Murdock 1980; Watkins et al. 1992).

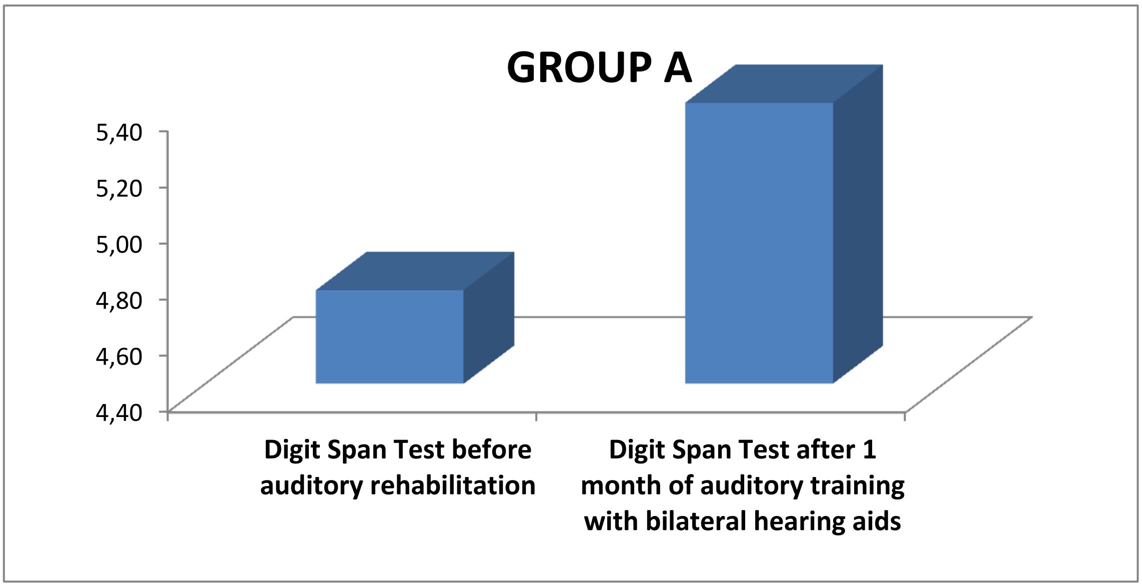

Figure 9 – *Digit span tasks in group A showed a significant improvement after auditory rehabilitation; the test was repeated after 1 month of auditory training with bilateral hearing aids in patients affected with moderate to severe sensorineural hearing loss.*

In conclusion, auditory rehabilitation through cochlear implantation or hearing aids could specifically ameliorate cognitive and psychological conditions with improvements in short and long term memory with positive outcomes in few months as well years after; it should be noted that the effects of auditory restoration is not limited to the improvement in acoustic perceptions, but also due to other cognitive functions that can take advantages from training. In addition, MoCA, GDS and digit span tests have proved to be easy and useful tools for diagnostic and prognostic purposes among older adults with disabling hearing loss.

Hearing loss is an important public health concern with substantial economic costs and social consequences. It is the most frequent sensory deficit in human populations and affects newborns, children, adults, and elderly people. Our results confirmed that CI in older adults is a safe and effective procedure that is similar to those reported in the literature. Furthermore, we observed that elderly patients generally need a longer rehabilitative period compared to younger patients, but regular users can reach similarly good results. The major complication rates are similar to those reported in the literature and do not significantly differ from other younger groups; dizziness or vertigo were not as frequent as might be expected. In our experience, support of the family and professionals, as well as duration of deafness and preimplant scores, greatly influences the results of rehabilitation and its perceived benefit.

Further studies are needed to confirm these data, nevertheless the present study suggest early auditory rehabilitation even among older adults with cochlear implant or hearing aids; in particular cochlear implantation should be considered a safe procedure with good outcomes, low complication rates and extended benefits on cognitive functions and mood disorders (Ciorba et al. 2011; Bovo et al. 2011; Bovo, Ciorba, and Martini 2011; Benatti et al. 2013).

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APPENDIX A

europass Curriculum vitae

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Sesso Maschile | Data di nascita 24/11/1976 | Nazionalità Italiana

TITOLO DI STUDIO Specialista in Audiologia e Foniatria

ESPERIENZA PROFESSIONALE

01/07/2012–30/06/2014 **Assegnista di ricerca**

Università Degli Studi di Padova DNS, Padova (Italia)

Attività didattica e di ricerca orientata all'approfondimento degli aspetti genetici nei quadri malformativi congeniti semplici e complessi, con particolare riferimento alla riabilitazione uditiva con impianto cocleare. Nell'ultimo anno sono state ampiamente esplorate le possibilità riabilitative del paziente anziano con comorbidità, malattie neurodegenerative e/o decadimento cognitivo, per cui sono stati presentati 4 progetti di ricerca nell'ambito dello studio delle funzioni cognitive con e senza riabilitazione uditiva (Ricerca Finalizzata 2013, Strategica 2011, PRIHTA 2013, Giovani Ricercatori 2013).

01/10/2013–30/09/2015 **Docente di Genetica e Fisiologia dell'udito**

Università degli Studi di Padova, Padova (Italia)

Attività di docenza con contratto annuale per lauree triennali e professioni sanitarie, tra cui Corso di Laurea in Teniche Audioprotesiche e Corso di Laurea in Tecniche di Neurofisiopatologia. Gli insegnamenti vertevano sostanzialmente su argomenti di genetica e fisiologia, dall'embriologia ai processi senili involutivi, dall'anatomia comparativa alle misurazioni elettrofisiologiche nella pratica otorinolaringoiatrica.

ISTRUZIONE E FORMAZIONE

16/03/2008–16/03/2012 **Diploma di Specializzazione in Audiologia e Foniatria**

Università di Ferrara, Ferrara (Italia)

COMPETENZE PERSONALI

Lingua madre: Italiano

Altre lingue

	COMPRENSIONE		PARLATO		PRODUZIONE SCRITTA
	Ascolto	Lettura	Interazione	Produzione orale	
Inglese	B2	C1	B1	B1	B2
			FCE IELTS		
Francese	B1	B1	B2	B2	B2

Livelli: A1 e A2: Utente base - B1 e B2: Utente autonomo - C1 e C2: Utente avanzato
Quadro Comune Europeo di Riferimento delle Lingue

Competenze comunicative: Efficiente, cordiale, tenace.

Curriculum vitae   Castiglione Alessandro

Competenze organizzative e gestionali	Buone competenze organizzative maturate durante le esperienze professionali
Competenze professionali	Audiologo e foniatra con provata esperienza in genetica dell'ipoacusia; particolarmente attivo nella ricerca e gestione clinica di condizioni neurodegenerative, malformative congenite e progressive. Abilitato all'esercizio della professione medica e chiurgica presso l'Università degli Studi di Padova il 16/02/2008; iscritto all'Ordine dei Medici dei Chirurghi e degli Odontoiatri della provincia di Pescara dal 28/02/2008.

Competenza digitale

AUTOVALUTAZIONE

Elaborazione delle informazioni	Comunicazione	Creazione di Contenuti	Sicurezza	Risoluzione di problemi
Utente avanzato	Utente avanzato	Utente avanzato	Utente avanzato	Utente avanzato

Informazioni Aggiuntive

ORCID: 0000-0002-5776-0444; ResearcherID: G-7015-2011; Scopus Author ID: 35075634300; https://www.researchgate.net/profile/Alessandro_Castiglione

Esperienze all'Estero

Visiting Physicians Program presso l'HOUSE RESEARCH INSTITUTE, Los Angeles, CA, USA, dal 5 luglio 2011 al 30 settembre 2011.

Elenco titoli di studio

Elenco titoli di studio in possesso del sottoscritto Alessandro Castiglione al 1/01/2016 in ordine cronologico decrescente:

2012 – **Diploma di Specializzazione in Audiologia e Foniatria**, conseguito presso l'azienda ospedaliero-universitaria di Ferrara il 16/3/2012, con votazione **50/50 e lode** discutendo la tesi dal titolo **"Ipoacusia improvvisa: ricerca di nuovi markers molecolari"**; allora relatore Dr.ssa Aimoni C.; correlatore Dr. D. Gemmati; direttore della scuola dal 2008 al 2010 prof. A. Martini, dal 2010 al 2012, prof. S. Pelucchi.

2011 – **Master** di III livello presso l'Università degli Studi Bicocca di Monza in **"Dissezione del temporale e microchirurgia sperimentale per l'impianto cocleare"**

2009 – **Master** di II livello presso l'Università di Brescia in **"Dissezione del temporale e microchirurgia sperimentale per l'impianto cocleare"**

2007 – **Diploma di Laurea** Specialistica in Medicina e Chirurgia ottenuto il 18/10/2007 presso l'Università degli Studi di Chieti-Pescara discutendo la tesi dal titolo **"La chirurgia**

parotidea degli ultrasettantacinquenni”, con votazione **110 su 110 e lode**; relatore Prof. A. Croce.

1995 – **Diploma di Maturità** scientifica ottenuto presso il liceo scientifico statale “G. Galilei” di Pescara con votazione **58/60**.

Partecipazione a Corsi, Convegni, Congressi, In qualità di relatore:

1) 15-17 Dicembre SIAF 2015, Milano, “Ipoacusia e declino cognitivo”

2) 22-23 Ottobre, CRS Amplifon Padova, “Ipoacusia e declino cognitivo”

3) 6 Giugno 2015 - Relatore al convegno "Intervento precoce nei disturbi dell'udito e dell'invecchiamento", Padova, IT

4) 26 Giugno 2014 - Relatore al Corso "Casi difficili" su Genetica della sordità e neuropatie", Padova, IT

5) 12-15 Febbraio 2014 - Relatore al Meeting Annuale Internazionale della Società di Ricerca su Emostasi e Trombosi, nella sezione sul Fattore di coagulazione XIII, Vienna, A

6) 14-15 Novembre 2013 - Relatore al Corso "Top Down & Bottom Up: la plasticità uditiva a tutte le età", del CRS Amplifon, Milano, IT

7) 16-19 Ottobre 2013, Relatore al Congresso Nazionale della Società Italiana di Audiologia e Fonitria "Disabilita Uditiva. Figure Professionali e servizi sanitari" sulla Genetica delle Malformazioni, Venezia, IT

In qualità di frequentatore/partecipante:

1) 27-29 Ottobre 2014 - Workshop in "Neuroanatomia e trattografia", Centro Neuroscienze Cognitive, Padova, IT

2) 18-21 Giugno 2014 - XIII Congresso Internazionale Sugli Impianti Cocleari ed altri dispositivi impiantabili, Monaco, Germania

3) 17-18 Giugno 2014 - II Seminario sull'invecchiamento e soluzioni impiantabili per l'udito, Monaco, Germania

Il sottoscritto Alessandro Castiglione c.f. CSTLSN76S24G141Z nato ad Ortona (CH) il 24/11/1976, e-mail alessandro.castiglione@unipd.it, consapevole delle sanzioni penali richiamate dall’art. 76 del D.P.R. 28 dicembre 2000, n. 445 per le ipotesi di falsità in atti e dichiarazioni mendaci

DICHIARA

di aver regolarmente conseguito i suddetti titoli di studio.

Padova, 1/01/2016

Alessandro Castiglione

APPENDIX B

RESOCONTO ATTIVITA'

XXVIII CICLO – Scuola di dottorato in Neuroscienze UNIPD

Tutor: Prof. Alessandro Martini

Candidato: Dr. Alessandro Castiglione

Progetto di ricerca: "Ipoacusia e declino cognitivo, studio dei rapporti in età avanzata e dei possibili benefici della riabilitazione uditiva con protesi acustiche e/o impianto cocleare".

Background.

In generale, l'approccio specialistico alla perdita uditiva in età avanzata enfatizza, ove possibile, la compensazione periferica di deficit uditivi attraverso apparecchi acustici ed impianto cocleare. Questo approccio però non risponde adeguatamente ai bisogni della popolazione geriatrica generale, di cui un quinto andrà a costituire un gruppo di "molto anziani" dopo alcune decadi.

Un invecchiamento "sano" è sempre possibile, detto questo, generalmente la maggior parte degli over 65 presenterà problemi uditivi di origine periferica e/o centrale, quota che raggiungere l'80% tra quelli con più di 85 anni. Evidenze sempre più consistenti supportano l'associazione tra ipoacusia (age-related hearing loss) e declino cognitivo. Alla luce di queste considerazione, solo in parte nuove, per facilitare una gestione ottimale delle funzioni cognitive del paziente geriatrico è necessario un approccio diverso all'ipoacusia che accompagna l'avanzare degli anni. Una corretta valutazione audiologica e diagnostica dovrebbe ad esempio includere, oltre alla standard batteria di esami, misurazioni delle funzioni uditive centrale utilizzando ad esempio test vocali nel rumore e dicotici. Il trattamento non dovrebbe limitarsi alla sola compensazione periferica, ma prevedere forme di training uditivo riabilitativo (anche per le protesi acustiche) e di consultazione periodica.

Negli USA la popolazione ultrasessantacinquenne era stimata essere di circa 40 milioni di individui nel 2010, il 13,5% della popolazione, con prospettiva di raddoppiare nel 2050 portandosi al 20% della popolazione generale (1/5!!!). Un altro quinto di questo 20% (1/25 della popolazione) è stimata essere la quota di ultraottantacinquenni (4% della popolazione generale). L'80% di questi ultraottantacinquenni (il 3,2% della popolazione generale) sarà affetto da ipoacusia legata all'invecchiamento, condizione mutifattoriale che riconosce cause genetiche, fattori di rischio cardiovascolare, fumo, diabete, esposizione al rumore, farmaci ototossici ed altri disordini otologici. La correzione dell'ARHL (Age Related Hearing Loss), quando e dove possibile, è tipicamente riconducibile all'uso di apparecchi acustici e/o impianto cocleare. Questa strategia orientata a compensare la sola perdita periferica non è sufficiente, per cui persistono, a dispetto dell'amplificazione adeguata, sensazioni di "incapacità a capire le parole, pur sentendole". Così come risulta comune la difficoltà a comprendere il parlato nel rumore, ma non in condizioni di quiete. Il limite concettuale ed epistemologico delle risposte a tali problemi sta nel ritenere, questi problemi, esclusivamente periferici. Le recenti ricerche ci suggeriscono invece che la risposta del paziente geriatrico è influenzata dalle cellule del ganglio spirale (numero, efficienza, sinapsi, connessioni), dalla plasticità centrale (positiva/adattiva vs negativa o "mal-adattiva"), da disordini di processamento uditivo centrale, dalle malattie del sistema nervoso, tra cui condizioni neurodegenerative, e dal declino cognitivo.

Ormai l'utilità della riabilitazione uditiva attraverso gli apparecchi acustici e/o impianto cocleare è universalmente riconosciuta anche nella popolazione più anziana. Tuttavia molti studi rilevano delle differenze all'interno di questo gruppo, condizioni che lasciano emergere considerazioni su quello che può considerarsi un "normale invecchiamento" rispetto " ad "invecchiamento che richiede interventi ulteriori o perlomeno un monitoraggio".

Prima di tutto le performance: ci possono essere notevoli differenze tra individui, anche se ancora soddisfacenti; **secondo**, la durata della deprivazione uditiva soprattutto se confrontata tra "i meno anziani" (< 70 anni) ed "i più anziani" (>70 anni); **terzo,** la curva di apprendimento può essere molto diversa dal "canonico" target raggiunto a 6-12 mesi di comprensione del parlato riportato per i soggetti più giovani. **Quarto**, percezione del parlato nel rumore, che contrariamente ai test in quiete, può non migliorare o rimanere sempre al di sotto delle attese. **Quinto,** la scelta del lato, che risulterebbe più importante rispetto ai più giovani, lasciando supporre un miglior outcome per il lato destro. Questo ultimo punto deve far molto riflettere sulla riabilitazione bilaterale/binaurale nei soggetti anziani e soprattutto dovrà aprire la strada ad una implantologia di genere, perché lo stesso punto potrebbe essere meno evidente per il sesso femminile. Nella popolazione geriatrica alcuni pazienti, soprattutto quelli con disordini di processamento, possono avere esiti migliori con una riabilitazione unilaterale, soprattutto nel rumore, in cui ad esempio fino al 70 % dei soggetti può ritenere più soddisfacente la riabilitazione con un solo dispositivo. Risultano molto importanti in questi casi i test dicotici.

Un modo relativamente semplice ed efficace di valutare una "presbiacusia centrale" è l'uso del DSI (Dichotic Sentence Identification), in cui vengono somministrati bilateralmente segnali in competizione, oppure del SSI (Syntethic Sentece Identification test), in cui il segnale è in competizione unilateralmente sulla base di un rapporto segnale rumore in cui il segnale è rappresentato da frasi corrette grammaticalmente, ma di significato non comune o inatteso (es: *Paolo trascina sette porte nere*, oppure *Rita conosce quattro sedie verdi sul balcone*). I pazienti con declino cognitivo falliscono il target considerato "normale" dell'80% di riconoscimento, e chi sta al di sotto della soglia del 50% di risposte corrette ha un rischio aumentato di 7-12 volte di andare incontro a diagnosi di Malattia di Alzheimer nei successivi 3-10 anni (!). I pazienti affetti da Alzheimer, come noto, hanno particolari difficoltà nello svolgimento di funzioni esecutive, attentive e mnestiche (soprattutto memoria a lungo termine e memoria di lavoro), difficoltà di cui i pazienti possono avere fra l'altro piena consapevolezza, sottostima, oppure sovrastima, magari per rinforzo di altri condizioni quali ansia e depressione.

La relazione per ora più evidente, seppur ancora teorica, tra ipoacusia e declino cognitivo si basa su 1) aumento della carica cognitiva (cognitive load) e 2) l'isolamento sociale. In particolare si è dimostrato che, tra gli anziani, uno spostamento di 25 dB nelle medie ottenute ai test tonali e vocali, corrisponde all'incirca a 7 anni di invecchiamento negli score ottenuti ai test cognitivi. Inoltre i pazienti con ipoacusia, rispetto ai normoudenti, hanno un tasso accelerato di declino cognitivo e minori perfomance anche nei test non-verbali. I soggetti anziani affetti da ipoacusia lieve, moderata, severa hanno rispettivamente un rischio aumentato di 2, 3 e 5 volte di incorrere nella demenza.

Risulta evidente dagli studi riportati che l'ipoacusia nell'età avanzata è un fattore di rischio indipendente per la demenza, per il quale, però, si può quindi speculare sui possibili effetti derivanti da una eventuale riabilitazione uditiva. Ma bisogna tener conto del fatto che una corretta e completa riabilitazione uditiva, soprattutto nell'anziano, non può consistere esclusivamente nel fitting di un apparecchio acustico o di un impianto cocleare.

Il fine ultimo della riabilitazione dovrebbe comunque essere quello di consentire/garantire una sufficiente ed efficiente capacità di comunicazione in tutte le situazioni possibili.

Riassumendo, per ottenere ciò, saranno utili:

1) Test dicotici, in competizione e nel rumore;
2) Adeguata amplificazione/fitting individuale tenendo conto delle differenze di condizione clinica, età e genere, così come dei possibili effetti di una riabilitazione bilaterale vs monolaterale;
3) Adeguato training, counseling e monitoraggio.

In conclusione, è possibile affermare che tali argomenti sono di vitale importanza per la pratica audiologica ed otorinolaringoiatrica e che compito dello specialista e del MMG non è solo quello di conoscere tali aspetti, ma di saperli correttamente gestire e condurre in un'ottica di approccio multidisciplinare. Ulteriori studi sono comunque necessari volti a confermare e verificare alcune affermazioni, così come saranno necessari.

Attività del candidato.

Il candidato ha seguito e realizzato tutti le fasi di ricerca relative al progetto IDECO-PRIHTA 2013, dall'ideazione alla stesura fino alla partecipazione al bando PRIHTA 2013 vinto nel 2014 per un finanziamento complessivo di 450000 euro. Ha inoltre contribuito alla presentazione ed approvazione del progetto da parte del Comitato Etico locale. Ha seguito tutte le fasi di allestimento degli spazi dedicati, implementazione dei software fino alla creazione di una rete logistica ben strutturata sul territorio in grado di realizzare i numerosi test previsti. Ha collaborato in maniera determinante alla realizzazione della fase pilota prevista dallo studio e con un periodo di follow-up di 6-12 mesi. Il candidato ha inoltre sviluppato il data entry informatizzato ed il sito internet del progetto, nonché implementato e realizzato tutte le fasi previste dal comitato etico dalla lettera per i MMG ai consensi informati per esami ed indagini genetiche.

PROTOCOLLO IDECO-PRIHTA 2013

www.progettoideco.it

DATI PRELIMINARI DELLA RICERCA

Sono stati valutati ad oggi oltre 80 pazienti con diversi test dai quali sta emergendo in maniera piuttosto inequivocabile una stretta relazione tra ipoacusia e declino cognitivo. Ben più difficile è risultata la descrizione dei rapporti, nel tempo, con la riabilitazione uditiva. La batteria di test si avvale di semplici questionari, test cognitivi, test semiobiettivi uditivi, misure elettrofisiologiche e indagini genetiche, in particolare *APOE*.

È inoltre presente un gruppo di controllo che viene comparato per patologie ed età. Tutti i gruppi confrontati in maniera trasversale hanno confermato la correlazione tra ipoacusia e declino cognitivo. Anche lo studio longitudinale, pur nei limiti imposti dai test a disposizione, rivela l'utilità della riabilitazione uditiva. Mancando misurazioni obiettive, si è deciso di aggiungere ove possibile uno studio EEG dei soggetti interessati: tale studio prevede una misurazione a riposo, una registrazione durante compito uditivo ed una durante funzione esecutiva. Le misurazioni permettono quindi di valutare l'attività corticale a riposo, l'attività evento correlata prima e dopo riabilitazione uditiva, i tempi di risposta durante specifiche funzioni esecutive che possono essere correlate con test cognitivi.

I test cognitivi sono orientati prevalentemente allo studio di funzioni mnestiche e logico esecutive che sono risultate essere più deficitarie sia nei pazienti con declino cognitivo sia in quelli con ipoacusia. Test specifici sono abbinati a questionari sulla percezione del proprio stato di salute.

I test audiometrici sono invece orientati prevalentemente alla distinzione tra presbiacusia centrale e presbiacusia periferica. La prima sollecita funzioni di processamento centrale soprasoglia, la seconda invece cerca di identificare la minima soglia di udibilità.

Dall'analisi preliminare dei dati risultano correlazioni positive tra punteggi ottenuti ai test cognitivi ed esito della riabilitazione uditiva; risultano differenze significative tra i punteggi ottenuti tra i gruppi divisi per tipo di riabilitazione ed entità rispetto ai soggetti non riabilitati. La differenza si riduce dopo training uditivo e si avvicina al gruppo di controllo di soggetti non ipoacusici.

Sebbene questi risultati non possano considerarsi conclusivi, suggeriscono comunque che la riabilitazione uditiva sia necessaria ed efficace nel soggetto anziano anche se affetto da lieve deficit cognitivo.

Pubblicazioni

Durante il triennio 2013-2016, sono stati pubblicati i seguenti articoli:

1: **Castiglione A**, · Benatti A,· Girasoli L, · Caserta E, Montino ·S, Pagliaro M, Bovo R, Martini ·A. Cochlear implantation outcomes in older adults. Hearing Balance & Communication 02/2015; 13(2). DOI:10.3109/13625187.2015.1030885

2: Busi M, Rosignoli M, **Castiglione A**, Minazzi F, Trevisi P, Aimoni C, Calzolari F, Granieri E, Martini A. Cochlear Implant Outcomes and Genetic Mutations in Children with Ear and Brain Anomalies. Biomed Res Int. 2015;2015:696281. doi: 10.1155/2015/696281. Epub 2015 Jul 5. PubMed PMID: 26236732; PubMed Central PMCID: PMC4506828.

3: **Castiglione A**, Ciorba A, Aimoni C, Orioli E, Zeri G, Vigliano M, Gemmati D. Sudden sensorineural hearing loss and polymorphisms in iron homeostasis genes: new insights from a case-control study. Biomed Res Int. 2015;2015:834736. doi: 10.1155/2015/834736. Epub 2015 Feb 18. PubMed PMID: 25789325; PubMed Central PMCID: PMC4348611.

4: Martini A, **Castiglione A**, Bovo R, Vallesi A, Gabelli C. Aging, cognitive load, dementia and hearing loss. Audiol Neurootol. 2014;19 Suppl 1:2-5. doi: 10.1159/000371593. Epub 2015 Feb 20. Review. PubMed PMID: 25733358.

5: Benatti A, **Castiglione A**, Trevisi P, Bovo R, Rosignoli M, Manara R, Martini A. Endocochlear inflammation in cochlear implant users: case report and literature review. Int J Pediatr Otorhinolaryngol. 2013 Jun;77(6):885-93. doi: 10.1016/j.ijporl.2013.03.016. Epub 2013 Apr 8. Review. PubMed PMID: 23578804.

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APPENDIX C

Publications (H index = 6; TOT I.F. = 22.38)

Aimoni, C., A. Castiglione, A. Ciorba, D. Gemmati, and E. Orioli. "Surdité Brusque (Sb) : Recherche De Nouveaux Marqueurs Moléculaires." *Annales françaises d'Oto-rhino-laryngologie et de Pathologie Cervico-faciale* 129, no. 4 (2012): A18-A19. http://dx.doi.org/10.1016/j.aforl.2012.07.046.

Benatti, A., A. Castiglione, P. Trevisi, R. Bovo, M. Rosignoli, R. Manara, and A. Martini. "Endocochlear Inflammation in Cochlear Implant Users: Case Report and Literature Review." *Int J Pediatr Otorhinolaryngol* 77, no. 6 (Jun 2013): 885-93. http://dx.doi.org/10.1016/j.ijporl.2013.03.016.

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Busi, Micol, Monica Rosignoli, Alessandro Castiglione, Federica Minazzi, Patrizia Trevisi, Claudia Aimoni, Ferdinando Calzolari, Enrico Granieri, and Alessandro Martini. "Cochlear Implant Outcomes and Genetic Mutations in Children with Ear and Brain Anomalies." *Biomed Res Int* (2015).

Castiglione, A., V. Guaran, L. Astolfi, E. Orioli, G. Zeri, D. Gemmati, R. Bovo, A. Montaldi, A. Alghisi, and A. Martini. "Karyotype-Phenotype Correlation in Partial Trisomies of the Short Arm of Chromosome 6: A Family Case Report and Review of the Literature." *Cytogenet Genome Res* 141, no. 4 (2013): 243-59. http://dx.doi.org/10.1159/000353846.

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