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EVALUATION OF AUDITORY CORTICAL PLASTICITY FROM FIRST AMPLIFICATION TO ONE YEAR OF HEARING AID USE: THE RELATIONSHIP BETWEEN AIDED CORTICAL AUDITORY EVOKED POTENTIALS (ACAEPs) AND SPEECH PERCEPTION OUTCOMES AMONG HEARING-IMPAIRED ADULT PATIENTS

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ABR: Auditory brainstem response
ACAEPs: Aided Cortical Auditory Evoked Potentials
APHAB: Abbreviated Profile of Hearing Aid Benefit

CAEPs: Cortical Auditory Evoked Potentials

CVEPS: Cortical Visual Evoked Potentials

EEG: Electroencephalography

FAS: Fatigue Assessment Scale

GFP: Global field power

HINT: Hearing in Noise Test

IQR: Interquartile range

LA: Linear amplification

MMN: Mismatch negativity

MST: Matrix Sentence test

NLFC: Nonlinear frequency compression

PET: Positron emission tomography

PTA: Pure Tone Audiometry

SDT: Speech detection threshold

SIT: Speech intellection threshold

SNHL: Sensorineural hearing loss

SNR: Signal to Noise Ratio

SPL: Sound pressure level

SRT: Speech reception threshold

SSQ: Speech, Spatial and Qualities of Hearing Scale

VOT: Voice onset time

WDRMCC: Wide dynamic range multichannel compression

ABSTRACT

Over the last decade, aided cortical auditory evoked potentials (ACAEPs) have continued to be a focus of interest due to the lack of adequate tools to objectively assess cortical auditory activity in response to amplified stimuli. The majority of authors have investigated the direct relationship between behavioral thresholds and ACAEPs and the evolution of ACAEP waves among children with sensorineural hearing loss (SNHL) undergoing rehabilitation. In contrast, scarce data are available regarding changes in ACAEPs over time in adult hearing aid users, particularly in relation to speech perception outcomes.

The main goal of this project was to investigate the relationship between ACAEPs and speech perception capability over time in post-lingual SNHL adult patients who were first-time hearing aid users. We hypothesized that, in patients with better speech understanding, a modification of the P1-N1-P2 complex could be expected as a result of neuroplastic changes due to hearing aid amplification.

A longitudinal prospective clinical study was conducted on 72 new hearing aid users suffering from symmetrical, sloping SNHL. Patients were assessed at three different time points: baseline (T0), 6 months after the initial assessment (T6), and 12 months after the initial assessment (T12). All the participants went through the same evaluation protocol, which included pure-tone audiometry, speech audiometry tests, ACAEPs recorded with two different stimuli (1000 Hz and 2000 Hz) and questionnaires assessing hearing aid benefit.

Analysis of amplitude values at the three different time points demonstrated an increasing tendency for all waves in both experimental conditions ($p<0.01$). Latencies seemed to become shorter from T0 to T12 for each wave and in the case of 1 kHz and 2 kHz stimuli. ($p<0.05$).

Linear regression analysis found that only P2 amplitude showed a statistically significant increase in its variation while matrix sentence test (MST) and speech intellection threshold (SIT) decreased in both experimental conditions, even when the analysis was adjusted for age and daily hearing aid use ($p<0.05$).

The data collected in this study provide new evidence regarding the relationship between ACAEPs and the speech recognition capability of adults who are new hearing aid users.

In both experimental conditions, we observed larger P2 amplitude in patients with better speech perception outcomes. It should be underlined that, even though P2 may reflect auditory processing beyond sensation, its increase could be an expression of neural activity associated with the acquisition process driven by exposure to sounds and speech. The observation that P2 amplitude tended to improve as SIT and MST scores decreased might be, in the future, a further object of investigation to assess its reliability as a marker of speech perception improvement; it may assist hearing aid dispensers and audiologists as a source of feedback in the evaluation of listening benefits in hard-to-test patients.

1. INTRODUCTION

1.1 Cortical auditory evoked potentials: from the sources to their interpretation

1.1.1. CAEPs: definition and recording technique

Cortical auditory evoked potentials (CAEPs) are the expression of the elaboration made by the higher neuronal centres in response to the perception of a sound stimulus. The ability to detect, process and discriminate between sound cues affects CAEPS and requires the integrity of the auditory pathway as well as good working memory function, attention and pre-attentive auditory processing.

The electrophysiological mechanism behind CAEP recording is based on the stimulus-locked postsynaptic potentials within apical dendrites of pyramidal neurons in the cerebral cortex (Tremblay & Clinard, 2015); in particular, by placing electrodes on the scalp, the clinician can record the voltage differences at the scalp surface which are highly influenced by the number of activated neurons, the extent of neuronal activation and the synchrony of the neural response.

Two parameters are usually associated with the waves that reflect the bioelectrical activity arising from the stimulation of the auditory pathway: latency and amplitude. The former, measured in milliseconds (ms), is defined as the difference between the mean pre-stimulus baseline voltage and the largest positive-going peak of the potential waveform within a time window, and depends on the duration of the electrical stimulus from the excitation of the cochlear hair cells to the generation of the potential by a specific neuronal place along the auditory system. The latter, measured in microvolts (μv), is instead defined as the time from stimulus onset to the point of maximum positive amplitude within a time window, and depends on the strength of the response (Polich, 2007).

CAEPs are represented by a well-defined sequence of waves that can be detected after 50 ms from stimulus onset (Figure 1). They are divided into exogenous potentials, which are mainly determined by the physical properties of the perceived stimulus (e.g., decibel level), and endogenous potentials, whose waveform is influenced by the motivation, concentration and alertness of the subject tested.

The P1-N1-P2 complex belongs to the first group, whereas mismatch negativity (MMN)

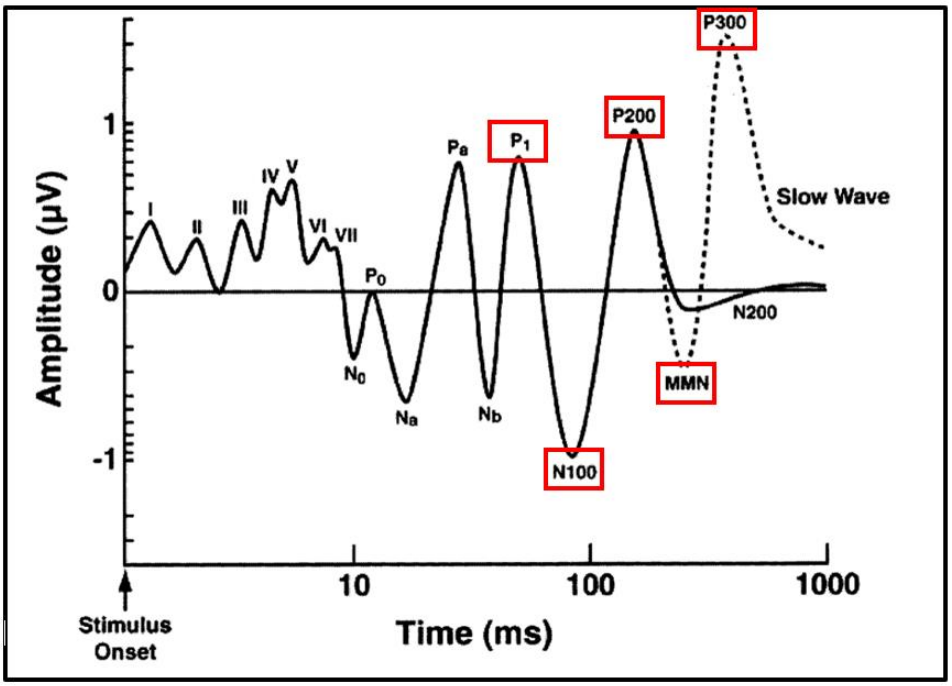

Figure 1: CAEPs: Morphology, latency and amplitude.

and P300 are typical endogenous potentials (Martin et al., 2007; Polich, 2007).

When recording CAEPs, some subjective factors and stimulus characteristics should be taken into account before testing patients (Carter et al., 2013). First of all, even though CAEPs can be evoked just by asking patients to stay alert with their eyes open, improved responses can be obtained by keeping patients busy reading a book or watching a movie, or by simply asking them to count the total number of stimuli. However, when trying to elicit the P300, the patient's active cooperation is essential for making a valid recording. Sleep should be avoided, even though the amplitude of the response may increase depending on the sleep stage.

Stimulus characteristics should be carefully selected before starting with the recording. CAEP waves may arise from the onset or offset of a stimulus, or an abrupt change in it; in particular, considering that the main contribution to the response is the spectral content of the first milliseconds,

the majority of protocols include the use of tone bursts with a 10 to 20 ms rise and fall time.

Tone bursts are universally used when the aim is to estimate a patient's acoustic threshold, though speech signals (e.g., /m/, /g/, /t/) have gained popularity in clinical research because, while they still have spectral emphasis in different frequency regions (though

less compared to tone bursts), they are more comparable to the complexity of acoustic stimuli that surrounds us in everyday life (Kuruvilla-Mathew et al., 2015; Oppitz et al., 2015). However, even though the use of speech signals does not influence the latency of exogenous potentials with respect to tone bursts, it may increase the latency of endogenous potentials due to the higher complexity of the listening task (Oppitz et al., 2015).

Electrode configuration can be changed according to the aim of the recording. In clinical practice, a single recording channel is adequate, with a minimum of three electrodes positioned on the head (Cz, ground, reference). High-density recordings (e.g., 64 channels), instead, can show the variation of CAEPs across different areas of the scalp and are used for pure research purposes due to their scarce applicability in clinical CAEP protocols.

1.1.2 P1

The P1 (or "P50" potential) wave originates from the primary auditory cortex and thalamus, reflecting the summed synaptic transmission along the ascending auditory pathway (Howard et al., 2000); it is represented by a positive deflection (P1) rising around 50 ms after stimulus onset. In children aged 5–6 years, it can be identified at around 85–95 ms, but its latency and amplitude tend to decline over time until they reach the adult values (Shafer et al., 2014).

The presence of even fairly low levels of background noise significantly reduces P1 amplitude. In contrast, binaural presentation of the acoustic stimulus leads to a significantly larger P1 amplitude. From a functional point of view, P1 is thought to reflect a pre-attentive filtering of sensory information in order to enhance cortical responses to novel or relevant stimuli while minimising responses to extraneous or redundant information (Papesh et al., 2014).

1.1.3 N1

The second long latency wave occurs at around 100 ms after stimulus onset. It consists of a negative peak that can be divided into three subcomponents according to the

generation source and recording site. The first subcomponent is a frontocentral negativity whose main source is the auditory cortex. The second, generated in the auditory association cortex of the superior temporal gyrus, is a biphasic T-complex. The third component, instead, has its sources in the frontal motor and premotor cortices and is a negative wave arising at the vertex (Fogarty et al., 2020).

In young children N1 is often absent, though it is sometimes detectable at 100–150 ms in children aged 5–6 years. Peak latency usually declines with age, whereas there is no consensus about the variation of N1 amplitude over time, with some authors demonstrating an increase after 6 years of age and others finding no increase (Gilley et al., 2005; Sussman et al., 2008).

As shown by McCullagh and Shinn (2013), older adults exhibited higher N1 peaks when compared to younger people in quiet conditions, but this difference tended to diminish when a noise was introduced in the test protocol. N1 amplitude may be influenced by low-level background noise, whereas no effect of aural presentation has been demonstrated.

1.1.4 P2

P2 is a positive peak occurring in the latency interval of 150–250 ms; two main sources have been advocated as its generation site: the planum temporale and the auditory association cortex. P2 reaches adult latency value in 3-year-old children, and no significant modification may be observed in the first decades of life, even though a prolongation has been suggested in the elderly (Cardin, 2016). The data concerning its amplitude maturation are conflicting; some studies report higher amplitude over time, while others do not.

Smaller P2 peaks might be seen when recording CAEP in background noise conditions, while, similarly to P1, binaural presentation may enhance P2 amplitude. When tested in quiet conditions, younger subjects show reduced amplitudes with respect to older people. Enhanced P2 waves have been reported in other research fields, such as childhood dyslexia (Ceponiene et al., 2009), sleep (Crowley et al., 2002) and auditory discrimination training (Alain & Snyder, 2008; Ross & Tremblay, 2009), as well as from mere passive

exposure to repeated presentations of stimuli (Ross & Tremblay, 2009); a larger P2 amplitude has been related to aging (Ceponiene et al., 2008).

1.1.5 MMN

MMN originates from the auditory cortical structures located bilaterally in the supratemporal plane which are related to the mechanism of working memory. In the right frontal hemisphere, there is a third MMN generator which is related to the automatic attention-switching process, which may explain the right hemisphere's dominance of MMN scalp distribution.

MMN can be recorded as a negative peak of approximately 0.5–5 μV in amplitude, following N1 in the latency range of 100 to 300 ms (Duncan et al., 2009). Differently from the aforementioned waves, it needs an "oddball" paradigm and a minimum of five electrodes to be recorded; specifically, the oddball paradigm is a protocol in which two tones which differ within a specific parameter (e.g., frequency, intensity, duration, etc.) are administered to the patient who passively waits for them. The second tone typically constitutes 20% of the total stimuli and is sent in an unpredictable way. The two stimuli are usually presented at relatively short interstimulus intervals, such as 500 ms to 1 s. To correctly detect the MMN waveform, it is necessary to subtract the waveform relative to the deviant stimulus from the one relative to the standard stimulus. The remaining "negative" portion of the waveform is the MMN (Cone-Wesson & Wunderlich, 2003).

In terms of the P1-N1-P2 complex, MMN reflects precognitive processes which are involved in the early stages of perceiving stimulus differences; it is generated by mechanisms related to pre-attentive memory and cannot be explained only by the activation of the afferent system nor elicited by a single stimulus per se.

MMN has also been studied as a prognostic predictor in patients suffering from coma, schizophrenia, cognitive decline and dyslexia (Duncan et al., 2009).

1.1.6 P300

Similarly to MMN, P300 (also known as "P3") represents a response to physiological discrimination tasks but requires the patient to pay attention to the stimuli when recording

it. The subject tested is usually asked to count the number of deviant stimuli or push a button every time he/she hears them.

The P300 is produced by multiple, relatively independent generators with major foci in the auditory cortex, centroparietal cortex, hippocampus and frontal cortex (Linden, 2005). It is comprised of two subcomponents named P3a (~230 ms) and P3b (~315 ms). The former results from stimulus-driven frontal attention mechanisms, while the latter stems from temporal-parietal activity associated with attention.

The patient's ability to discriminate may influence the amplitude and latency of P300, with a shorter latency and a larger amplitude in case of easier discrimination tasks. The more complex the stimulus processing required by the task, the longer the latency of P300, which can vary from approximately 250–1000 ms. In addition, P300 amplitude may be affected by the time between stimuli: smaller amplitudes are elicited by shorter interstimulus intervals (Fitzgerald & Picton, 1984); expectations generated by the sequence of stimuli preceding the eliciting stimulus might negatively influence P300 amplitude.

Passive stimulus processing generally produces smaller P300 amplitudes than active tasks because stimulus and non-task events engage attentional resources to reduce amplitude. Individual differences in P300 latency are correlated with mental function speed, such that shorter latencies are related to superior cognitive performance (Polich, 2007).

Aging can prolong P300 latency, and other comorbidities, such as dementia, depression and schizophrenia, may alter its waveform parameters.

1.1.7 Interpretation and clinical application of CAEPs

Until now CAEPs have been used for a variety of purposes, but their main application in clinical practice has been in estimating the hearing thresholds of hard-to-test populations, from patients affected by neuropsychiatric disorders to patients who undergo this test for medical-legal reasons. In this field, the main principle is that the lowest intensity at which a replicable response is obtained can predict the behavioural threshold, with the CAEP threshold generally being 5 to 10 dB higher than the behavioural threshold (Light-foot & Kennedy, 2006); consequently, the audiogram might be rebuilt from the potentials recorded from the main frequencies studied (usually 500, 1000, 2000, 4000 Hz). In

uncooperative patients suffering from hearing loss, a correct threshold estimation may help audiologists in selecting the most appropriate hearing aid and fitting it.

Apart from their use in establishing the hearing threshold of patients, each wave composing the P1-N1-P2 complex has been investigated for clinical applications. Great interest has emerged in using CAEPs clinically to assist with the hearing-aid-fitting process in hard-to-test populations such as infants (Golding et al., 2007; Van Dun et al., 2012) as well as adults (Carter et al., 2013), and to assess the benefits of early intervention treatment with amplification (Gravel et al., 1989; Rapin & Graziani, 1967).

For research purposes, P1 has been investigated as a marker for auditory maturation; in fact, its latency tends to decrease over time from the 300 ms of infants to the 125 ms of 3-year-old children. It is only in adult life that P1 latency reaches 50–60 ms. For this reason, it has been assessed in children with congenital hearing loss, revealing that patients who were provided with hearing aids/cochlear implants before the age of 3.5 years were more likely to have P1 latency within the normal range, whereas subjects who suffered from longer periods of auditory deprivation did not catch-up to their peers. Specifically, the lack of hearing rehabilitation was linked to morphological anomalies of P1-like waveform negativities, polyphasic waveforms and low amplitude waveform morphology.

Obviously, children who were rehabilitated earlier present better speech measurements because receiving appropriate auditory stimulation helps the auditory central pathways develop normally. Such children usually show P1 latency within the normal range, but cases of delayed P1 may be observed among them too; in contrast, normal P1 waves may be found among children with worse speech scores. Clearly the use of P1 to monitor auditory plasticity related to speech discrimination cannot replace behavioural testing, but it can still be considered a precious tool when a reliable behavioural measure cannot be obtained (Nash et al., 2007).

Differently from P1 and N1 waves, P2 has been investigated as a potential biomarker of auditory learning. Based on the evidence that P2 may reflect auditory processing beyond sensation, that gain in P2 is often associated with improved perception and that increased P2 amplitude was observed among patients after different types of auditory training including music, some authors investigated the contribution of auditory learning to such electrophysiological change. In particular, Tremblay et al. (2014) attempted to find

differences in P2 waves among normal-hearing native-English speakers who underwent auditory training; some were trained to learn the voice onset time (VOT) contrast, while others were not. Interestingly, enhanced P2 waves were observed in both groups. These results contribute to the evidence that increases in P2 amplitude may be related to the elements of training (e.g., exposure) more than learning itself. However, the authors hypothesised that enhanced P2 might be the product of neural activity associated with the acquisition process rather than the learned outcome itself (Tremblay et al., 2014).

1.2: Neuroplasticity following auditory deprivation and auditory rehabilitation

1.2.1 Neuroplasticity: general considerations in hearing-impaired patients

From a structural point of view, the auditory cortex consists of a group of areas with different functions that, taken together, form a single functional unit; highly organised connections allow interactions between these areas, which are classified from lower order to higher order areas in a hierarchical perspective (Hackett, 2011).

The transmission of input, either through bottom-up (from lower to higher order) or top-down (reverse) interactions, or through the brain's modulation and processing of the incoming signal, is crucial in the development and functioning of the auditory system (Giraud et al., 2004; Davis & Johnsrude, 2007).

Auditory deprivation as well as auditory training can induce functional changes in the brain and central auditory pathways; this phenomenon, called "neuroplasticity", is based on a dynamic process involving the aforementioned interactions. The anatomical correlate of neuroplasticity in auditory deprivation can be synthesised as follows: the lack of incoming acoustic stimuli may activate a process of pruning and synaptogenesis that modifies the neural circuitry devoted to sound perception, influencing the tonotopic organisation throughout the auditory system; the auditory cortex, when deprived of its normal sensory input, may become responsive to the stimulation of adjacent receptors.

Neurogenesis, which is more active during childhood and early adult development, can help the auditory system reorganise connections after providing hearing restoration; the earlier the intervention occurs, the higher the probability of avoiding sensory deprivation consequences (Kral & Sharma, 2012).

Neuroplasticity is influenced by a number of factors (e.g., acetylcholinergic modulation from the forebrain, behavioural context, etc.); attention can also affect auditory processing, possibly via non-specific modulatory inputs but also via top-down influences (Corbetta & Shulman, 2002). In particular, top-down interactions provide information on cognitive factors that influence the representation of acoustic features, contributing to filling-in phenomena as well. In other words, through cortico-cortical interactions, the cortex may store auditory objects, acting as a filter for acoustic feature perception (Munford, Nelsen). Acoustic stimuli may be compared to information stored in short-

term memory; a complex circuitry involving bottom-up projections from the thalamus to supragranular layers and top-down projections of higher order areas at the level of infragranular layers is thought to play this role (Klinke et al, 1999; Kral et al, 2006). Studies conducted on deaf animals revealed that hearing loss affects cortico-cortical interactions, reducing the effects of top-down modulation, impairing neuroplastic activity and compromising the filling-in phenomena (Kral, 2007).

Considering that synaptic density peaks at about 2–4 years of age in the temporal cortex, it is not surprising that the maximum rehabilitation age limit for achieving good results in deaf children is around 3.5 years; delayed intervention is reflected in an increased latency of CAEPs, particularly P1, which may express a delayed synaptogenesis (Eggermont, 1996).

The existence of sensitive periods was also corroborated by positron emission tomography (PET) measurements of resting cortical metabolic rates and regional cerebral blood flow density. A decrease in spontaneous glucose metabolism in the auditory cortex of children who had received cochlear implants before 4 years of age was demonstrated; children implanted after 6.5–7.5 years of hearing impairment presented a normal metabolism in higher-order auditory cortices, maybe as a consequence of long-term sensory deprivation and functional recruitment of these areas (Lee et al. 2001; Lee et al, 2005). Strelnikov et al. (2013) analysed PET data from adults with post-lingual sensorineural hearing loss (SNHL) who had cochlear implants, finding a positive correlation between metabolic activity in the visual cortex and speech perception recovery 6 months after implantation; the same authors reported a negative correlation between metabolic activity in the superior temporal gyrus and auditory speech perception recovery 6 months after cochlear implantation surgery.

Although cochlear implants provide the best rehabilitation option for deafness as it can reverse the negative effects, the timing of restoring auditory perception may play a crucial role; for example, the time of implantation in children with profound SNHL may influence the morphology of CAEPs. Differently from children implanted at an early age, those implanted later exhibited a lack of the N1 component with a preserved (yet aberrant) P1 component (Sharma et al., 2015); for this reason, P1 latency, which is thought to be a biomarker of cortical maturation, decreases rapidly and reaches the normal age-range in children who receive an implant before 3.5 years of age (Sharma, 2002). Abnormal

CAEPs may persist in children who receive implants later than 7 years of age, even after years of auditory training (Sharma, 2009).
In particular, the absence of N1, which is generated in higher-order auditory areas, may reflect impaired cortico-cortical interaction and a reduction of top-down influences (Ponton & Eggermont, 2001).

1.2.2 Cross-modal plasticity

Following auditory deprivation, a de-coupling of higher order areas from primary auditory cortex may occur that allows non-auditory functions, such as visual and somatosensory functions, to recruit it for different tasks (so-called "cross-modal plasticity") (Fine et al, 2005; Levänen & Hamdorf, 2001). In other words, auditory deprivation makes the auditory cortex more vulnerable to recruitment by the remaining and intact sensory modalities. In addition to cross-modal plasticity, a different neuroplastic process called "intra-modal plasticity" may take place which expresses the functional changes within a particular cortical area as a consequence of increased or decreased stimulation (Glick & Sharma, 2017).
When cross-modal plasticity occurs in deaf people, it may help the visual system by improving visual performance during visual localisation, visual attention and motion detection (Bavelier & Neville, 2002). Both patients with congenital and post-lingual SNHL demonstrated the activation of auditory cortical areas during visual motion processing; the same patients presented decreased performance on speech perception tasks because cross-modal recruitment can limit rehabilitative outcome and understanding of speech (Doucet et al., 2006). Furthermore, implanted children with the poorest outcomes were those whose auditory cortical areas were most recruited for visual tasks, whereas implanted children with good speech recognition results were those who better exploited their dorsolateral prefrontal networks for reasoning, attentional control and working memory (Giraud & Lee, 2007).
It is evident how neuroplastic changes can drive patients' success with amplification. For example, Glick & Sharma (2017) studied the cortical activity of two adult hearing aid users, showing that, in response to visual stimulation, there was an expected activation of visual cortical areas in the subject with good speech perception outcome whereas the one

who performed worse manifested the recruitment of temporal cortices, suggesting cross-modal re-organisation. In particular, in patients who have undergone cochlear implantation, reliance on visual cues may increase over time, even years after surgery (Bergeson et al., 2005).

Cross-modal plasticity seems to show its effects mainly in patients affected by severe to profound hearing loss. However, a study conducted by Campbell et al. underlined how plastic changes may also occur in adults with a lower degree of SNHL. In particular, the authors compared the high-density electroencephalography (EEG) and speech-in-noise perception of a group of adults affected by mild-to-moderate SNHL in the high frequencies with that of a group of normal-hearing adult subjects. As a result of cross-modal plasticity, patients suffering from hearing loss exhibited the recruitment of the temporal cortex for the N1 and P2 Cortical Visual Evoked Potentials (CVEPs) and frontal cortical regions, while the normal-hearing patients showed a dominant activation in cortical areas associated with visual motion processing for all CVEP components (P1, N1, P2). Furthermore, the P1-N1-P2 amplitudes of hearing-impaired subjects were higher, with an early N1 latency negatively correlated to speech recognition in noise tests and an additional P2' component occurring after P2. The increased amplitudes along with the identification of the P2'VEP component, may be considered a sign of faster processing (Tong et al., 2009) or an effort to recruit additional cortical areas to increase speech performance. An increase in CVEP amplitudes across the temporal cortex was also documented in pre-lingual and post-lingual deaf adults with cochlear implants (Buckley & Tobey, 2010; Kim et al., 2016), and it was negatively correlated to behavioural speech perception in noise. However, Buckley and Tobey (2010) found no significant association between length of deafness and N1 CVEP amplitude in both pre-lingually or post-lingually deafened CI adults, hypothesising that cross-modal re-organisation may be influenced by auditory deprivation itself rather than the duration of SNHL.

Campbell's recording of CAEPs with a speech stimulus evidenced decreased temporal activation in patients with early-stage SNHL differently from normal-hearing subjects who showed a normal processing of the auditory stimulus through the inferior temporal, middle temporal and superior temporal gyrus (Glick & Sharma, 2017).

In addition, in SNHL patients, visual stimuli were responsible for a greater activation along the ventral visual stream in temporal areas which are traditionally associated with auditory processing; because of the important role of the ventral stream in processing object and face information (Nasr & Tootell, 2012), it was likely patients with hearing loss had to rely on it more when beginning to pay more attention to lip and facial cues during listening. Similarly, Giraud et al. and Lee et al. also demonstrated a ventral activation in pre-lingually deaf cochlear implanted children and post-lingually deaf cochlear implanted children as well as in adults who had poor speech perception outcomes; in this sense, compensatory activation of the cortical auditory-visual ventral stream may be linked to poorer hearing performance.

Furthermore, cross-modal plasticity in hearing-impaired patients may be the result not only of the purely visual component of the stimulus through a feed-forward neural circuit, but also of the cognitive aspect of the stimulus itself through top-down influences. For example, Que et al. demonstrated how a checkerboard and a visual language stimulus provoked, in the first case, an activation of the right superior temporal cortex and strong functional connectivity with the visual cortex and thalamus; in the second case, there was a bilateral activation of the superior temporal cortex and enhanced functional connections with the anterior temporal cortex and inferior frontal gyrus IFG; the authors concluded that both pathways can activate auditory areas in deaf people, even though they may be functionally segregated with respect to cross-modal plasticity.

As shown in animal studies, auditory deprivation may induce histopathological neural modifications that, in turn, can affect the ability to discriminate because of the loss of the spectral information of the incoming stimulus. In particular, synaptic immaturity, dystrophic changes in neurons and a loss of cochleotopic organisation of the cortex have been proven (Ryugo et al., 2010); a functional loss of neural tissues with an increase in non-responding units and a reduced maximum evoked firing rate was observed (Tillein et al., 2010). More recently, Land et al. (2016), examining the visual responsiveness of the auditory dorsal zone (DZ) of congenitally deaf cats, showed a persistent auditory responsivity of the majority of DZ neurons despite cross-modal plasticity processes, suggesting that the visual takeover of some neuronal populations do not imply a total loss of auditory responsivity.

Cross-modal plasticity has also been reported between auditory and somatosensory modalities. A study conducted on a small group of early and late implanted children revealed that the second group showed a significant activation of the post-central gyrus in the somatosensory cortex in response to a speech stimulus (Gilley et al., 2008), which may be an expression of abnormal functional connectivity for the processing of auditory stimuli, leading to poor outcomes with the cochlear implant. Another study, performed with a 250 Hz vibrotactile stimulus applied to the index fingers of a group of implanted children and an age-matched group of normal-hearing children, noted the activation of both the auditory and somatosensory cortex in the former group, in contrast to the latter group (Cardon et al., 2019).

The question of how much time is needed to observe the first signs of cross-modal plasticity after auditory deprivation remains unanswered. Allman et al. (2009) observed somatosensory cross-modal plasticity after 16 days of the onset of deafness in animal models. Glick & Sharma (2017), examining the CVEPs of a 62-year-old man, observed a recruitment of temporal auditory processing areas and frontal activation in response to a visual-motion stimulus three months after the onset of sudden mild sloping-to-severe bilateral SNHL. A continuous recruitment of visual, temporal and frontal cortices, and a 15% functional improvement in auditory-visual speech perception scores, was recorded after one year in the same patient.

1.3 Aided cortical auditory evoked potentials (ACAEPs)

1.3.1 ACAEPs and hearing aid amplification

Cortical auditory evoked potentials used to study the effect of amplification on the brain in hearing aid users (ACAEPs) were studied for the first time decades ago, along with cortical plasticity induced by auditory rehabilitation. The application of ACAEPs to guide hearing aid fitting and verification and to assist the clinician in the fitting process in hard-to-test populations remains of valuable interest. As reported in the first chapter, CAEPs are routinely recorded to estimate behavioural thresholds (approximately within 10 dB of behavioural thresholds) of both normal-hearing and hearing-impaired populations; however, CAEP thresholds may sometimes exceed behavioural thresholds by more than 20 dB (e.g., Ikeda et al., 2010; Glista et al., 2012; Van Maanen et al., 2005), making the hearing aid fitting more challenging. Since the first ACAEP data was published by Rapin and Graziani, different controversies have emerged regarding the recording of electrophysiology under aided conditions. In particular, the data provided by these authors concerned 8 children of whom only five exhibited improved ACAEPs, while the remaining three did not.

The main body of literature concerning ACAEPs can be divided into three approaches to recording electrophysiology with hearing aids: the first is aimed at determining the physiological response detection, comparing the cortical response recorded in unaided conditions with that in aided conditions; the second addressed the question of whether ACAEPs recorded from two audible stimuli at suprathreshold levels were associated with differences between the waveforms; the third application of ACAEPs focused on monitoring them over time to understand how the continuous use of hearing aids may influence them. It is noteworthy that, even though waveforms were absent or weak in SNHL patients under unaided conditions, compared to robust waveforms in aided conditions, no conclusive data were reported in the case of comparison between ACAEPs recorded at suprathreshold levels (Billings et al., 2007; Billings et al., 2011). In other words, the amplification effect (i.e., differences between unaided and aided conditions) is more likely to occur near threshold than at suprathreshold levels. For this reason, the

effect of amplification by comparing barely audible or inaudible CAEPs with suprathreshold ACAEPs often resulted in significant changes to waveform morphology. From the first ACAEP reports by Rapin and Graziani to the more recent revisions of ACAEP investigations (Rapin & Graziani, 1967; Tremblay, Billings et al., 2006; Tremblay, Kalstein et al., 2006; Billings et al., 2007), various concerns still need to be addressed before their findings can be put into routine clinical practice. The major question remains: "what are the main variables that could affect CAEPs when a hearing aid is worn?" It is evident that hearing aid signal processing causes many acoustic modifications to a stimulus (e.g., rise-fall time, signal level, etc.), but to what extent it can influence ACAEP recording is still a matter of debate.

1.3.2 Recording ACAEPs: characteristics, methods, variables

The first factor that was examined was signal level: when recording CAEPs in quiet conditions, it would be expected that, as the intensity of the stimulus increases there would be a shorter latency and a greater amplitude of the waves (e.g., Adler & Adler, 1989; Picton et al., 1977). Recording CAEPs with a hearing aid means introducing a noise source (through the amplification of background noise or because of circuit noise) into the recording system (Billings et al., 2013); even in quiet conditions, noise is sometimes present in the hearing aid output and can interfere with CAEP intensity/latency patterns (Billings et al., 2007). For this reason, the signal-to-noise ratio (SNR) may need to be taken into consideration when examining the immediate effect of amplification on P1-N1-P2 morphology (Billings et al., 2009; Kaplan-Neeman et al., 2006). Because central auditory system neurons are sensitive to SNR as well as to absolute intensity, the gain provided by a hearing aid might not determine the expected changes in neural processing. Some investigations have reported CAEP differences in unaided and aided conditions, but without equalising SNRs (Korczak et al., 2005; Miller & Zhang, 2014). For example, Korczak et al. (2005) used ACAEPs to test amplification effects in 14 subjects with either moderate or severe-to-profound SNHL who listened to speech syllables (/ba/ and /da/) that were presented in an oddball paradigm. Hearing aid use resulted in the decreased latency and increased amplitude of the ACAEPs. The change in the waveform was greater at the lower speech level than the higher one (either because of a lack of audibility at the

lower intensity when unaided or because of output limitations in the hearing aid with higher intensity sound). Even with hearing aids, SNHL patients had greater latencies than subjects with normal hearing. In addition, the authors found that amplification with hearing aids substantially improved the detectability of all the cortical waves; the amplification of the incoming stimulus may result in better neural encoding of the signal because of the improved audibility that is available immediately after amplification. In contrast, other studies performed in normal-hearing young adults (e.g., Billings et al., 2007; Billings et al., 2011) did not find any changes in ACAEP morphology. Therefore, reported amplification effects might have been influenced by changes in SNRs as well as input modifications from the hearing aid. The interaction between the incoming signal and amplification effect was furtherly studied by Easwar et al. (2012) who did not find evidence of any amplification effect when SNRs were equated at one signal level/noise level combination; Chun et al. (2016) confirmed the findings of Easwar et al. (2012), but, differently from them, they found an amplification effect only for N1 and P2 latencies with a 10 dB SNR condition. They concluded that the effects of amplification may exist only at relatively poor SNRs. Higher absolute signal level was associated with larger amplitudes only when presented in quiet conditions or when background noise was inaudible (Billings et al., 2012), and ACAEPs are mostly influenced by SNR rather than absolute signal level. Specifically, they found that when the amplification effect was absent, the SNR ratios between the unaided and aided conditions were very similar.

To explain the effect of SNR on ACAEPs, Billings et al. (2011) compared CAEP morphology with and without hearing aids, while keeping the incoming signal in the ear canal at the same intensity level. The results showed that ACAEPs tended to present smaller amplitudes and longer latencies when measuring them with hearing aids; SNR decreased as hearing aid gain increased because of the amplification of the background noise, but it may vary depending on the gain setting and the examined frequency. A greater effect of amplification was found for P2 with respect to N1, even though they represent acoustic feature processed in different cortical areas.

Onset characteristics of the stimulus are also a contributing factor in ACAEP morphology, and digital hearings aids can dramatically and differently modify the signal onset and thus ACAEPs in an unpredictable way (Jenstad et al., 2012).

The frequency response as well as the compression filter of the hearing aid may lead to audible background noise in certain spectral ranges but not in others as a result of the programmed fitting, further determining the SNR. In particular, compression modifying the first 30–50 ms of the incoming stimulus (rise slope, rise time, overshoot of the onset) may contribute to determining the morphology of ACAEPs (Onishi & Davis, 1968). Easwar et al. (2012) observed shortened rise times and overshoots at the onset of the stimulus (tone burst) in hearing-aid-processed stimuli with fast compression (attack/release time: 10/60 ms). Because N1-P2 CAEP is an "onset response" generated when many cortical pyramidal cells fire synchronously at the onset of a stimulus, these changes in amplitude or frequency made by hearing aid processing may influence neuronal activity (Onishi & Davis, 1968; Marynewich et al., 2012). Other factors may include channel-specific compression time constants, noise reduction algorithms and adaptive directionality.

Previous studies have explored the effects of digital versus analogue technology on ACAEPs. Marynewich et al. (2012) reported smaller ACAEP amplitudes when recording with digital hearing aids compared to analogue hearing aids, and none of the hearing aids resulted in a reliable increase in response amplitude when compared to unaided across the conditions; digital hearing aids showed significantly delayed ACAEP latencies. Jenstad et al. (2012), studying digital hearing aids with linear amplification, demonstrated that they may alter the rise time of the stimuli so that maximum gain was reached well past 30 ms after stimulus onset, resulting in altered ACAEPs.

ACAEPs are usually elicited by tone-burst stimuli; in contrast, brief and transient stimuli such as clicks and tone pips are not ideal for measuring hearing aid function because they do not effectively and consistently activate hearing aid circuitry.

The use of speech sounds such as vowels and consonants was also tested to record ACAEPs. The acoustic characteristics of complex sounds can be reflected in the form and latency of these potentials; the duration of the spectrum of speech sounds enables the amplified stimulus to have similar performance in relation to its functioning in everyday situations. Depending on the spectral components of the speech sound and on the prescribed fitting algorithm, the effect of amplification on ACAEPs may vary. For example, Durante et al. reported responses that were significantly more present in ACAEPs for the sounds /g/ and /t/ than for the sound /m/; they explained this difference

on the basis of the lower amplification prescribed for low frequencies, which are the main spectral components of the phoneme /m/. ACAEPs with speech tokens were also recorded by Vanaja et al. who observed an improvement in the aided conditions in 8 out of 9 SNHL patients for the /ma/ sound, in 6 for /ga/ and in 4 for /ta/; ACAEP latencies were longer than those obtained for persons with normal hearing. Sensitivity to different speech tokens may vary: aided CAEPs showed reliable differences between the syllables 'see' and 'shee' (Tremblay et al., 2006), but did not distinguish between the syllables /ma/, /ga/ and /ta/ (Munro et al., 2011).

Different methods have been proposed for recording ACAEPs. The simplest is recording in the free-field while the patient wears his/her hearing aids; obviously monoaural testing needs to reduce the contribution of the non-test ear with an earplug. The second method involves recording the hearing aid output offline, either in a coupler or a mannequin, and then delivering it through insert earphones to the participant. In the third approach, the stimulus is presented using direct audio input through the hearing aid worn by the patient (Glista et al., 2012; Easwar et al., 2012; Billings et al., 2013).

To sum up, the differences that emerge between CAEPs in unaided and aided conditions mean that the principles underlying electrophysiological recording cannot be directly applied when the testing stimulus is processed by a hearing aid device; the latency and amplitude of ACAEP waves are the product of a complex interaction between the aforementioned hearing aid-related parameters and factors that are not yet known. The interpretation of ACAEP tracks, particularly when comparing aided conditions with different gains, cannot be definitely related to behavioural thresholds until each of the factors involved in hearing aid electrophysiology have been discovered.

Of course, the presence of ACAEP waves in aided versus unaided conditions may suggest to the clinician the detectability of the incoming signal by the patient, but an adequate fitting needs to relate the gain to aided thresholds, which means understanding how much of the sound is effectively amplified and listened to by the patient, and whether this information can be inferred from ACAEP morphology.

1.4: Hearing aid and speech perception outcome over time

1.4.1 Speech perception in hearing aid users

Speech perception may be defined as the ability to perceive linguistic structure in the acoustic speech signal (McRoberts, 2008) and is usually tested using speech sounds (e.g., vowels or syllables), spoken words or connected speech (Poeppel, 2015). This ability, particularly in noisy environments, tends to decline with age, with a mean deterioration in speech recognition in noisy conditions of 1.37 and 1.69 dB SNR over 10 years among 51–60 and 61–70 year-old patients, respectively (corresponding to a 27% and 34% decrease in speech understanding) (Goderie et al., 2020).

Speech perception requires a listener to find an acceptable match between the incoming acoustic signal generated by the talker and a linguistic structure likely to be similar to the one intended by the talker. The process of speech perception appears to be automatic and effortless every time the sensory input provided by a talker is audible and uncorrupted with a message that is not unexpected or cognitively difficult. The corruption of sensory input may slow the process of speech recognition, increasing the dependence on inferences based on partial sensory information, the listener's knowledge and understanding of the topic and other communication circumstances. The greater the corruption of the speech signal, the greater the effort needed to arrive at a plausible hypothesis about the message (Miller et al., 2013).

Even when wearing hearing aids, patients suffering from SNHL do not acquire complete information from the acoustic signal, at least not to the extent of the redundant information usually available to normal-hearing people. Missed information may be filled in through top-down pathways requiring more listening effort from hearing-impaired listeners (Hällgren et al., 2001). Cognitive resources, such as working memory capacity, may partially account for individual differences in speech perception outcomes between hearing aid users with similar pure-tone thresholds (Besser et al., 2013).

Various investigations have reported an association between cognitive abilities and speech perception outcomes. Gatehouse et al. (2003) found that better cognitive ability in experienced hearing aid users, measured using visual digit and letter-monitoring tasks, was associated with better speech recognition in noisy conditions. Lunner et al. (2003)

also observed better speech recognition performance in both aided and unaided conditions among hearing aid users with good cognitive abilities. Other authors have reported that speech perception performance may be influenced by general processing speed, lexical access speed and phonological processing skills (Hällgrenet al., 2001; Larsby et al., 2005; Lunner, 2003; Rönnberg et al., 2008). In particular, degraded phonological representation, which is commonly found in patients with severe hearing impairment, may make the process of listening in noise challenging. In fact, when the incoming speech signal is masked by noise, a mismatch condition between the incoming signal and the phonological representation may arise. This condition, also from distortion of the incoming signal due to cochlear damage, may create an important source of mismatch, which may explain why SNHL patients can experience a disproportionate difficulty listening in noise. Hearing aids may generate further side-effects, such as generating unwanted artifacts in the auditory scene or distorting the waveform of the speech signal (Lunner et al., 2009; Wang, 2008). Consequently, the new hearing aid user may not find congruency between aided incoming signals and nonaided phonological representations in long-term memory. After becoming accustomed to the hearing aid amplification and setting, the degree of mismatch may be reduced because new phonological representations that are congruent with the processed speech input may become established in the lexicon over time (Ng et al., 2014). It has been reported that a familiarisation period of between 4 and 9 weeks may be required to reduce cognitive load (Rudner et al., 2011).

The bilateral superior and middle temporal gyri, left prefrontal and premotor cortex, and left inferior temporal cortex are the main circuitries that support speech comprehension. The correct codification of two acoustic components of speech, the envelope (the slowly modulating aspect of speech) and the temporal fine structure (the rapidly modulating aspect of the signal that carries the envelope) may account for a patient's ability to understand speech in quiet and noisy environments (Henry, 2012).

Sensory declines such as presbycusis and impaired cognitive function may negatively influence speech perception during aging, making the auditory processing of speech cues more challenging and less speedy (Wingfield, 2005). From a pathophysiological perspective, the disruption of speech intelligibility may be a consequence of prolonged

neural refractory times, loss of myelin integrity, decreased brain connectivity and increased variability in neural firing (Lu et al., 2011; Forstmann et al., 2011).

The altered neural activity related to hearing loss can influence not only the perception of the speech signal but also the resources required to perform higher-level cognitive operations. In this context, a crucial role is played by the thalamus, which supports speech comprehension by transferring ascending auditory information to the prefrontal and premotor cortices. In older adults, difficulty in discriminating speech sounds was also revealed by CAEPs which showed an abnormal P1–N1–P2 complex neural response (Harkrider et al., 2005).

1.4.2 The acclimatization effect

In patients who are affected by SNHL, speech perception may change over time with a progressive reduction of the ability to recognise words which could be reversed by wearing a hearing aid (Hurley, 1998; Hurley, 1999). This phenomenon was previously studied in patients with bilateral symmetrical SNHL and late-onset auditory deprivation after a period of monoaural hearing aid use; the non-rehabilitated ear showed degraded suprathreshold speech recognition performance when compared to the aided ear (Silman et al., 1984). The deprivation effect was recognised mainly in patients with at least a moderate degree of bilateral SNHL after several years of monaural hearing aid use, and the degraded speech-recognition performance in the unaided ear was similar to that seen in people with asymmetric SNHL (Silvermann & Emmer, 1993). It is possible that asymmetric auditory deprivation may induce a neuroplastic process in favour of the auditory cortex ipsilateral to the aided ear, leaving the unaided ear less receptive to the incoming stimuli.

At the same time, an acclimatization effect was observed in the aided ear; its original definition, from the Eriksholm Workshop on auditory deprivation and acclimatization, is “a systematic change in auditory performance with time that is linked to a change in the acoustic information available to the listener. It involves an improvement in performance that cannot be attributed purely to task, procedural, or training effects” (Arlinger et al., 1996). Acclimatization should not be confused with the improvement in speech perception that can be observed immediately after providing a hearing aid to a new

hearing aid user. For this reason, the patient should be informed about the variable time that he/she needs wait before receiving the maximum benefit from the hearing aid; on the other hand, the audiologist should be guided by the progressive improvement of the patient when optimising the fitting of the hearing device.

Some authors have reported that the process of acclimatization is either very fast or, perhaps, does not exist at all because speech perception outcomes immediately after fitting (or at least within a day or two) were similar to those measured after months of experience with hearing aids (Cox & Alexander, 1992; Bentler et al., 1993; Bentler et al., 1996; humes et al., 1996; Flynn et al., 2004). Others studies have instead found continuing improvement in speech measurements after 10 to 18 weeks of experience with new hearing aids (Gatehouse, 1992; Horwitz & Turner, 1997; Kuk et al., 2003; Munro et al., 2003; Silman et al., 1993). This wide variability between results should be read in terms of methodological differences between studies. In particular, the following kinds of factors may influence the final outcome after a period of follow-up with hearing aids: age, degree of hearing impairment, previous hearing aid experience; factors related to the hearing aid itself, such as the prescription formula for fitting; measurement factors such as the questionnaires and/or speech perception tests, the time schedule of the measurements, and the reference (or control) conditions against which performance changes were analysed (Yund et al., 2006).

After introducing a hearing aid into the non-aided ear, an increase in speech performance using headphones was seen in some patients (Boothroyd, 1993; Gelfand, 1995). It might be interpreted as a reversal of the auditory deprivation effects, driven by a secondary plasticity process.

However, the time needed to observe an improvement and the main predictors of speech recognition performance improvement have not yet been defined. According to Gatehouse et al. (1992), a patient affected by SNHL who starts wearing a hearing aid may need time to learn how to use the new incoming signal to improve auditory performance. Some authors have reported that an improvement in speech perception may be recorded after a period of weeks or months, while other studies showed a stable performance following the time of hearing aid fitting, over months and even years (Cox et al., 1992; Arlinger et al., 1999; Saunders & Cienkowski, 1997; Humes & Wilson, 2003). Some factors may mask the demonstration of an acclimatization effect, such as speech-

recognition tests that lack sensitivity, hearing aid fittings that do not provide sufficiently new information to require acclimatization and subjects with inadequate hearing loss. In addition, acclimatization may only occur at certain aided listening levels and may differ when investigated in quiet or noisy conditions. Furthermore, the subjective ability of perceptual learning may also be a factor in acclimatization. People who wear hearing aids may show different abilities to adapt to amplified speech; for this reason, differences in perceptual learning might justify the wide variability in improved aided speech perception over time (Gatehouse, 1993; Robinson & Summerfield, 1996). A factor that should be taken into account when evaluating auditory learning capability is the maladaptive changes that may occur in the central auditory system with aging (Irvine et al., 2001). In fact, even when hearing aids are optimally fitted, users often show difficulty with word recognition and speech understanding, particularly in background noise (Gordon-Salant, 2005) or in reverberant conditions (Van Tasell, 1993). These deficits may be the result of degraded temporal auditory processing, with auditory neural circuitries being affected by impaired neural synchrony (Sergeyenko et al., 2013), delayed neural recovery and reduced phase locking (Parthasarathy et al., 2014). In addition, hearing aids significantly change the physical characteristics of incoming stimuli, which may explain why adjusting to new hearing aids requires time and practice (Tyler & Summerfield, 1996).

Few longitudinal studies have assessed long-term speech perception improvement with hearing aids. In their longitudinal study, Humes and Wilson (2003) tracked changes in hearing aid performance and benefit in 9 binaural hearing-aid users over a three-year period following the hearing aid fitting. Little evidence of systematic improvement in aided performance or benefit was observed. Dawes et al., in a study involving patients with unilateral and bilateral hearing aids, found small gains in speech recognition across the three groups that were consistent with a practice effect.

Karawani et al. (2018), following a group of new hearing aid users for 6 months, analysed their outcomes through speech-in-noise measures and self-assessment questionnaires. Even though they observed an improvement in speech intelligibility in noise, it was attributed, similarly to Dawes et al., more to a practice effect than to an acclimatization effect. However, the self-perception of hearing aid benefit assessed through the Abbreviated Profile of Hearing Aid Benefit (APHAB) and the Speech, Spatial and Qualities of Hearing Scale (SSQ) questionnaires evidenced an improvement between the

beginning and the end of the follow-up. In contrast, in a study conducted on three groups of hearing aid users fitted with three different protocols, Reber & Kompis (2005) reported, an acclimatization effect over a period of six months with an improvement of speech understanding in noise.

The acclimatization process may be influenced by daily hearing aid use as well as the motivation for wearing hearing aids (Vestergaard, 2006). An acclimatization effect was also associated with the type of amplification, as reported by Yund et al. (2006), who monitored changes in nonsense syllable perception in speech-spectrum noise in a group of SNHL patients with no previous hearing aid experience. Based on their previous study which had reported that wide dynamic range multichannel compression (WDRMCC) signal processing provided consistent high-frequency speech cues as SNR decreased or as speech intensity decreased in constant noise, these authors studied hearing aid users with WDRMCC and linear amplification (LA) outcomes after 32 weeks of experience. The former group exhibited a 4.6% improvement in syllable recognition over the first 8 weeks while the latter showed a 2.2% improvement that was complete in 2 to 4 weeks. The authors concluded that the difference in auditory experience may be attributed to the more consistent encoding of intensity across frequency and intensity in WDRMCC versus LA processing.

1.5: CAEPs in monitoring neuroplasticity

1.5.1 Monitoring CAEPs in childhood hearing loss

Providing appropriate stimulation is the key to guaranteeing normal auditory cortex development in children as well as to maintaining correct functioning among adults who suffer from hearing loss. CAEPs may allow the clinician to non-invasively follow the maturation of the auditory cortex using various biomarkers. Understanding the different CAEP pattern in SNHL children may help in the decision of whether to continue with hearing aids or to recommend cochlear implantation.

First of all, monitoring activity means tracking changes in latency and amplitude of the main waves that characterise CAEPs. For example, the P1 latency, which is a positive-going peak reflecting the sum of the accumulated synaptic delays and neural conduction times as an auditory signal travels from the ear to the primary auditory cortex, decreases with age in normal-hearing children (Eggermont, 1988; Eggermont et al., 1997; Liegeois-Chauvel et al., 1994; Sharma et al., 1997, 2002b).

Among infants and young children, the P1 wave is typically identified as a broad positivity that may remain the only CAEP sign of auditory reception in cases of abnormal maturation processes (see, for example, Ceponiene et al., 2002; Liegeois-Chauvel et al., 1994; Ponton et al., 1996a,b, 2000b, 2002; Sharma et al., 1997). In new-borns and infants with normal hearing, it usually presents a latency of around 300 ms post-auditory stimulation. At two years of age, it usually undergoes a rapid decrease to approximately 100 ms, and then a more gradual decrease in latency to 50–70 ms in adulthood. Concerning N1, it is recognisable in younger children as a bifurcation of the P1 waveform; afterwards, it can be seen as a different wave represented by a separate negative peak that follows the P1 wave. N1 arises from the stimulation of the secondary auditory cortex as well as planum temporale and cortico-cortical connections.

Being independent from attention, both P1 and N1 are considered useful biomarkers for tracking the development of primary and higher-order auditory cortices and neuroplastic changes following auditory deprivation.

CAEPs recorded in congenitally SNHL children describe a limited period in early childhood when developmental plasticity of the central auditory system is at its

maximum. Studies conducted by Ponton et al. compared CAEP waveform morphologies and latencies from deaf children to those from normal-hearing peers and showed that deafness essentially stops central auditory development, resulting in an immature auditory cortex (Eggermont, 1988; Eggermont & Ponton, 2003; Ponton et al., 2002). This immaturity is the consequence of a lack of the extrinsic driving factors necessary to generate and stabilise neural connections. After cochlear implantation surgery, maturation can restart and proceed at a normal rate. For this reason, P1 latency may reflect the 'time in sound' experienced by the child. Despite years of sensory deprivation, the potential for normal auditory cortex development is kept intact in deaf children within the "sensitive period". For example, Sharma et al. (2002), evaluating the P1 latency of 245 children with profound congenital SNHL and fitted with cochlear implants, reported that patients who received stimulation via an implant early in childhood (<age 3.5 years) showed normal P1 morphology and latency, while children who were implanted later in childhood (>age 7 years) had abnormal cortical response latency and morphology. Patients who received implants between 3.5 and 7 years of age showed a normal P1 latency only half of the time, regardless of age of implantation within that 3.5–7 year age-range. In a subsequent study, the same authors examined individual developmental trajectories for the P1 wave after cochlear implantation surgery among 231 SNHL children (Sharma et al., 2007). Even though all patients exhibited a delayed P1 latency prior to implantation, children implanted under 3.5 years of age showed a normalisation of P1 wave latency within 6–8 months after surgery. A progressive decrease of P1 latency was also observed in children who were implanted after age 7 but, differently from those who were operated on earlier, they showed an abnormal developmental maturation with P1 latencies never catching up with their earlier-implanted peers, even after years of cochlear implant use. On the basis of their studies, Sharma et al. (2007) identified a sensitive period of 3.5 years in childhood during which sensory stimulation must be provided to achieve normal central auditory system development.

Monitoring N1 waves may also be useful for assessing the long-term development of the central auditory cortex in children suffering from SNHL and referred for hearing rehabilitation. In particular, the modification of N1 morphology may reflect the structural refinements in auditory cortical maturation, such as increased cortico-cortical coupling and enhanced auditory processing and language abilities (Eggermont & Ponton, 2003;

Moore & Guan, 2001). As reported by Sharma et al. in a study conducted among 41 normal-hearing children who were followed until the age of 15, N1 elicited by the speech syllable /ba/ began to emerge in the normal-hearing children at around 3–6 years of age. N1 detectability was 18% in children aged 0–3 years, increased to 60% among patients aged 3–6 years, and to 71% in the 6–9 year-old group; after 9 years of age, N1 was recognised in all patients tested, demonstrating that the percentage of its detectability is correlated with age. Conversely, when the same authors monitored N1 development among 80 SNHL children with cochlear implants, they observed that only in early implanted patients did the N1 component catch up to their peers at 9–12 years of age. In fact, in the mid-implanted group, 33% of subjects in the 0–3-year-old group presented with N1, increasing to 40% of subjects in the 6–9 year-old group and to 75% in the 9–12 year-old group. The late-implanted group showed poorer results, with 0% of children aged 9–12 years having N1, 30% in the 12–15-year group, and none among patients within 15–20 years of age.

As reported by the aforementioned study and also confirmed by Eggermont and Ponton (2003), the N1 wave recorded in cochlear implanted children show that most children who are implanted after 7 years of age never develop it. Instead, children implanted before a sensitive period of 3.5 years developed an N1 component that is similar in morphology and latency to that usually identified in children who have normal hearing (Sharma et al., 2007). The missing N1 wave in late-implanted children might be interpreted as an improper activation of higher-order areas, likely due to partial or total decoupling of higher-order areas from the primary auditory cortex (Sharma et al., 2015). However, the few cases of late-implanted children who developed an N1 response (consistent with Gordon et al., 2008) suggested that, despite less than optimal timing of implant fitting, other factors (e.g., early period of normal hearing, good aided hearing, and intensive auditory rehabilitation) may drive complete cortico-cortical and intra-hemispheric decoupling in long-term deafness (Dinces et al., 2009; Gordon et al., 2008; Waltzman et al., 2002).

An interesting insight about the acclimatization effect among children comes from Hutchinson and McGill's (1997) study. The authors used P300 to investigate auditory deprivation in ten unilaterally aided children with a mean age of 13.1 years. These patients suffered from bilateral congenital severe-to-profound SNHL and had a minimum

experience of 8 years with their hearing aids. Stimuli were presented at a level varying between 80 and 118 dB nHL for each subject. The results showed that P300 amplitude was significantly higher in the aided ear compared to the unaided ear, suggesting an acclimatization effect for the aided ear with respect to the unfitted ear. As reported by Ghiselli et al. (2020), long-term hearing rehabilitation in cochlear implant users was associated with close to normal P300 cortical activation only in early implanted patients. P300 latency instead, when comparing cochlear implant users and normal hearing subjects, tended to keep higher values in the former group. This study, using the P300 as an objective measurement of cognitive processes induced by auditory stimulation, underlined the importance of an adequate timing of rehabilitation to restore higher cognitive functions.

1.5.2 Monitoring CAEPs in adult-onset hearing loss

Differently from SNHL children who are at risk of abnormal development of the auditory cortex and, consequently, delayed or absent language, adults who experience hearing impairment present structured central auditory pathways. For this reason, monitoring CAEPs in adults who wear hearing aids or use cochlear implants has a different meaning and aims to identify an acclimatization effect through changes in wave morphology, latency and/or amplitude that can be correlated to speech perception improvement.

Few studies have identified asymmetrical CAEPs in experienced unilateral hearing aid users, and the methodologies and designs did not allow for definitive conclusions to be made about an acclimatization effect. Gatehouse and Robinson (1996) studied CAEP recordings in response to 500 and 2000 Hz tones at 65, 80, and 95 dB sound pressure level (SPL) in a 69-year-old long-term unilateral hearing aid user; the patient had been aided in the right ear for 4 years with an average daily use of 8 h. For the 500 Hz frequency there was no difference in N1 and P2 amplitude between the ears at all levels, but for the 2000-Hz stimulus, the aided ear had a larger amplitude for the 95 dB SPL presentation level. The authors concluded that these results supported a potential acclimatization effect and were the first to suggest a possible use of CAEPs to investigate auditory electrophysiological changes after rehabilitation.

Munro et al. (2007) studied ear asymmetry in the auditory brainstem response (ABR) of a group of hearing aid users with a minimum experience of 2 years and a self-reported daily use >5 h, which was compared with a group of patents with symmetric high-frequency SNHL prior to hearing aid fitting. Clicks were presented unilaterally at 70, 80 and 90 dB HL. The analysis of wave V morphology revealed a higher amplitude at 70 and 80 dB HL levels in the aided ear compared to the unaided ear, which was interpreted as an acclimatization effect at the level of the brainstem.

Bertoli et al. (2011) investigated CAEPs in 30 patients, ten experienced unilateral hearing aid users, ten experienced bilateral hearing aid users and ten normal-hearing subjects. The hypothesis tested was that fitted ears may show higher CAEP amplitudes and shorter latency compared to non-fitted ears. Stimuli of 500, 1000, and 2000 Hz at 55, 70, and 85 dB SPL were presented monaurally to both ears. Data analysis did not reveal any interaction between ear, frequency, and level observed for either latency or amplitude, with the exception of the unilateral group; specifically, an increased P2 amplitude for the 2000 Hz stimulus in the fitted ear of unilateral users was found. The authors hypothesised that larger P2 amplitude in the fitted ear of the unilateral group may reflect a more strenuous auditory processing, perhaps as a result of asymmetric amplification. Speech recognition testing did not show any significant difference between the unilateral and bilateral hearing aid user groups, although the recognition threshold was significantly better in the aided ear compared to the non-aided ear of unilateral users.

Dawes et al. (2014) investigated the relationship between CAEPs and speech recognition in noise following for 12 weeks a group of patients with a mild-to-moderate sloping high frequency SNHL who were unilaterally and bilaterally fitted. The N1 and P2 were recorded at 500 and 3000 Hz tones presented at 65, 75, and 85 dB SPL to both ears. They did not report any changes in CAEPs with a statistically significant 2% improvement in aided speech recognition over time, which was consistent with a general test–retest effect. They concluded that an acclimatization effect was not demonstrated after 12 weeks of hearing aid use.

A study conducted by Rao et al. (2017) among 22 patients with mild-to-moderate SNHL who were first-time hearing aid users tried to find a relationship between the P300 wave and speech perception through a Hearing in Noise Test (HINT) after 4 weeks of an

auditory training programme. Physiological changes, such as significant P3a amplitude reduction, were observed, while perceptual benefits assessed by HINT were not found.

Finally, Giroud et al. (2017) monitored behavioural and electrophysiological auditory and cognitive-related plasticity in older adults aged between 60 and 77 years who were moderately hearing-impaired and who were hearing aids users fitted with different protocols. All patients were tested 5 times across three months, and EEG measurements were recorded after stimulation with naturally high-pitched fricative (/sh/, /s/, and /f/) syllables. The authors observed longer latencies in the P1 and N1 peak in hearing aid users and, as expected, higher processing effort with respect to the normal-hearing control group. Using global field power (GFP) as a measure of processing effort, a decrease of the GFP of cognitive-related CAEPs was demonstrated among hearing-impaired patients after three months, suggesting that a minimum of twelve weeks is required to observe an acclimatization effect. Furthermore, a significant lowering of GFP in the P3b of the group who was fitted with nonlinear frequency compression (NLFC) was found compared to the group with NLFC off.

2. AIM OF THE PROJECT

The main goal of this project was to investigate the relationship between ACAEPs and speech perception capability over time in adult post-lingual SNHL patients who were first-time hearing aid users. In particular, the aim was to understand whether the electrophysiological parameters of ACAEPs might vary according to speech perception improvement. We hypothesised that, in patients with better speech understanding, a modification of the P1-N1-P2 complex could be expected as a result of neuroplastic changes due to hearing aid amplification. Identifying the ACAEP components which are more susceptible to variation may guide clinicians, audiologists and hearing aid professionals in optimising the hearing aid fitting of noncompliant patients.

To achieve this goal, we monitored the CAEPs of a sample of normal hearing patients before starting the study. Since we did not observe any significant fluctuations in the CAEP parameters, nor, as expected, any speech audiometry score variations, we proceeded with the main objective of the project.

To test the main study's hypothesis, we decided to follow a group of patients with a limited age range who were new hearing aid users; they were monitored from the first month of amplification to one year of hearing aid experience. The assessment was performed using ACAEP measurements, speech audiometry tests and hearing aid benefit questionnaires. We did not use a physiologic detection approach as we did not aim at comparing unaided and aided measurements because, besides the controversy still present in scientific literature regarding this issue, it was simply beyond the scope of this project. Including individuals with stable hearing loss and with a constant hearing aid gain, without altering the fitting algorithm during the follow-up period, may reduce its influence on cortical recordings and patient performance between appointments.

3. MATERIALS AND METHODS

3.1. Participants

A prospective longitudinal clinical study was conducted by enrolling a total of 77 patients, 44 male and 33 females, suffering from symmetrical, sloping SNHL. Out of 77 patients, 72 were ultimately included in the study because 5 were lost during follow-up. After ethical committee approval, all participants were recruited at the Audiology Section of the University of Palermo in the period from March 2018 to July 2019.

Inclusion criteria were: (1) age between 50 and 70 years; (2) having bilateral, sloping, moderate SNHL (calculated as the pure-tone average hearing loss at 500-4000 Hz); (3) being a first-time hearing aid user. Patients were chosen according to their absolute thresholds, and symmetrical absolute thresholds between the two ears were sought.

Patients suffering from mixed, conductive and unilateral hearing loss, fluctuating or recent changes in hearing, asymmetry in air conduction thresholds greater than 15 dB at two or more frequencies, an air-bone gap greater than 15 dB at any test frequency, neurological and psychiatric disorders, auditory neuropathy, acoustic neuroma, inner ear malformation and chronic otitis media, or who were undergoing therapy with central nervous system drugs were excluded from the study.

The full protocol was explained to each participant and written informed consent was obtained. All patients were first-time hearing aids users and were checked at our clinic after one-month of hearing aid use. The hearing aid fitting was kept the same at every appointment to avoid influencing behavioural and electrophysiological testing. We asked the daily duration of hearing aid use and checked that all patients wore their hearing aids for at least 8 hours per day.

Patients were assessed at three different time points: baseline (T0), 6 months after the initial assessment (T6), and 12 months after the initial assessment (T12). All the participants went through the same evaluation protocol, which is shown in Figure 2.

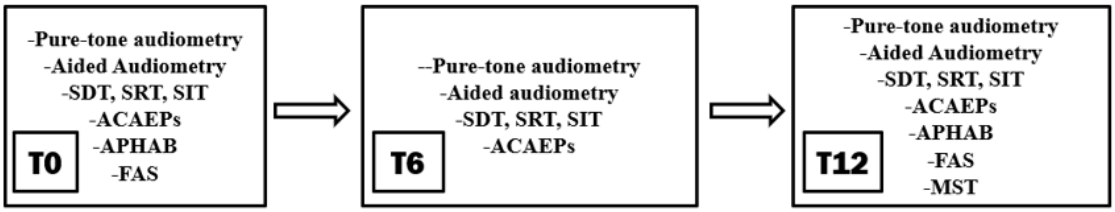

Figure 2: Timeline of the study protocol.

Each patient wore a digitally programmable, behind-the-ear hearing aid, fitted by professional hearing-aid dispensers, with nonlinear signal processing features according to NAL-NL1 prescription targets and set for omnidirectional amplification.

After a careful anamnesis, patients underwent micro-otoscopy to rule out middle ear pathologies and/or active infections. Pure tone audiometry (PTA) with and without hearing aids was performed by a trained audiologist with an Amplaid 309 audiometer in a soundproof audiometric room. Air conduction was measured without hearing aids using on-ear TDH-49 headphones set for 250-8000 Hz and in free-field with hearing aids testing at 250-4000 Hz; bone conduction was measured using a calibrated bone transducer for 250–4000 Hz.

To ensure stability of middle ear function, tympanometry was performed using an Amplaid 766, with a probe frequency of 226 Hz and an air pressure range of -400 to -100 mm H2O with automatic recording.

3.2. Fatigue Assessment Scale

The Fatigue Assessment Scale (FAS) is a validated scale consisting of 10 short items (Michielsen et al., 2004). Answers are provided on a five-point Likert scale with one point for “never” and five points for “always”. Five questions reflect physical fatigue and five questions regard mental fatigue. We instructed the patients as follows: “The following 10 statements refer to how you usually feel on a daily basis. For each statement, choose one out of the five answers. Please give an answer to each statement, even if you do not have any complaints at the moment.”

The total FAS score is calculated by summing the responses given by each participant to every single question. The overall FAS score ranges from 10 to 50, with higher scores indicating more fatigue.

3.3. Abbreviated Profile of Hearing Aid Benefit

The “Abbreviated Profile of Hearing Aid Benefit” (APHAB) is a 24-item hearing aid assessment questionnaire which is answered from the perspective of hearing aids users (Cox et al., 1995). It is a helpful tool for evaluating an individual’s experience using hearing aids and to quantify everyday life problems associated with hearing loss. The survey was originally developed to determine the difference between the responses given with and without hearing aids. Because the scope of the study was to monitor the advantages of wearing hearing aids over time, we did not administer the questionnaire to patients while they were not wearing them.

Participants were asked to fill in the questionnaire themselves. During this process, the researchers gave detailed information to those who participated in the questionnaire.

The APHAB consists of four subscales and reliably measures user satisfaction in different situations. Subscales of the questionnaire are Ease of Communication, Reverberation, Background Noise and Adoption of Voice. Each of the 24 items of the APHAB is a statement. The patient must decide how often the statement is true for his or her daily life. The patient chooses the best response from a list of seven descriptors, each associated with a percentage to help the patient to interpret the word.

The Ease of Communication score may be strictly related to measures describing mid-frequency sensitivity and/or objective clinical tests of speech understanding in quiet conditions. Measures of high-frequency sensitivity and objective clinical tests of speech understanding in noise may be reflected by the Background Noise subscale. The Reverberation score is closely related to objective measures of speech understanding in noise and to high-frequency sensitivity and concerns communication when speech is masked by reverberation. The Adoption of Voice subscale concerns reactions to sounds that can be at or near the level of discomfort.

The APHAB global score, which consists of responses on the subscales, was used as a summary measure in the present study. For the global score, which ranges from 0 to 100, lower scores indicate better performance, and higher scores indicate poorer performance.

3.4. Speech audiometry in quiet

Speech recognition with hearing aids was studied under quiet conditions using standard clinical protocols. Speech recognition in quiet conditions was administered using an open-set, phonemically balanced word test. Ten meaningful disyllabic words were presented via free-field loudspeaker at different intensities; the loudspeaker was placed approximately 1 m in front of the participant's head. The percentage of correct answers was calculated to determine three different levels of their speech recognition score: (1) the minimum hearing level (dB HL) for speech at which an individual can just detect the presence of speech material 0% of the time (Speech Detection Threshold, SDT); (2) the minimum hearing level (dB HL) for speech at which an individual can recognise 50% of the speech material (Speech Reception Threshold, SRT); (3) the lowest intensity (dB HL) at which the patient can recognise the 100% of words, also called "Speech Intellection Threshold" (SIT) in Italy.

3.5. Italian Matrix Sentence Test

Speech recognition in a noisy environment was administered using the Italian Matrix Sentence Test (MST). This test is the Italian version of the Oldenburg Sentence Test, a versatile examination composed of 20 randomised lists of five-word, semantically unpredictable sentences (Houben et al., 2014). The test is preceded by a training session to minimise the learning curve. The matrix sentences, structured as "name-verb-numeral-adjective-object" (e.g., "Andrea-dipinge-cinque-scatole-nere"), were presented against a noisy background via free-field loudspeaker at 65 dB SPL, placed approximately 1.2 m in front of the participant's head. The signal-to-noise ratio (SNR) was adaptively adjusted in order to determine a predefined percentage of correct word recognition.

The duration of a typical track of 20 sentences is about 4 minutes. The patient's task was to repeat the sentence he/she heard, or at least the separate words if the patient found it difficult to repeat the sentence completely.

The test yields three main measurements: (1) the SNR, in dB, at which the subject recognises 50% of the presented words (SRT), even if it occurs in different sentences (SNR-SRT); (2) the slope of the discrimination function at SRT (Slope) in percentage

(%/dB); and (3) the intelligibility percentage score, in terms of estimated accuracy in understanding whole sentences.

3.6. ACAEPs recording

Figure 3 illustrates the setting of the recording. The participant was seated in a reclining chair in the centre of a soundproof room (4.3 m × 2.3 m double-walled), 1 meter from the speaker at 0° azimuth. Each patient was instructed to ignore the stimuli, minimise head

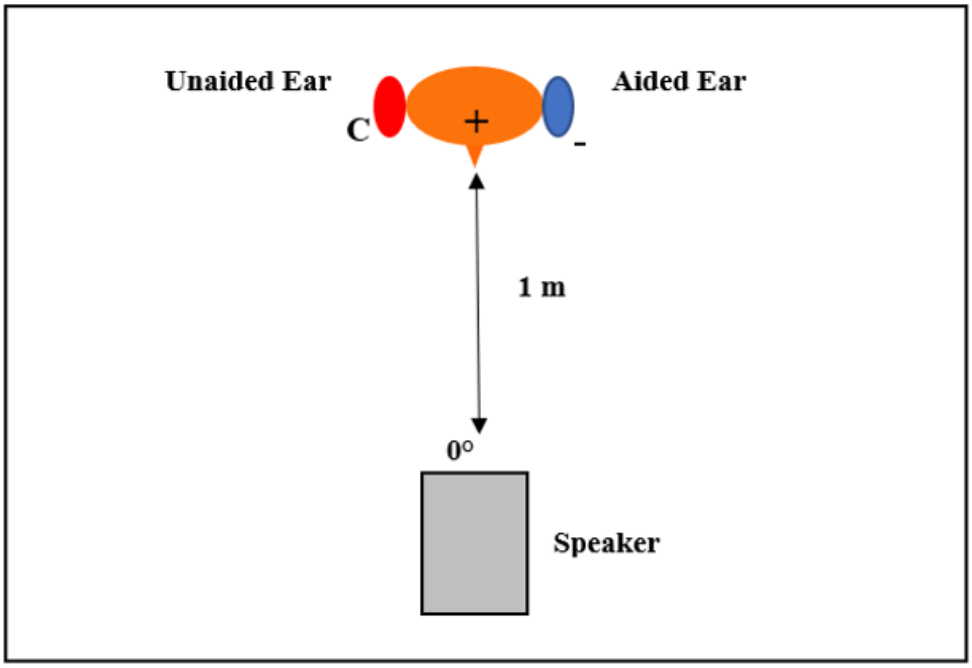

Figure 3: ACAEPs recording setting.
(+)=Positive electrode; (-)=Negative electrode; (C)= Common electrode.

and eye movement during the recording session and watch a silent, close-captioned movie. Distance measurements were repeated during and between each condition to ensure minimal movement. We decided to test one ear for each patient, choosing the one with the better hearing threshold for the 1000 and 2000 Hz frequencies and recording ACAEPs for the same ear at each time point. For all conditions, the non-investigated ear was plugged with a foam ear plug. The left ear was studied in 31 cases, while the right was examined in 41 subjects. The hearing aid gain fitting was the same at each recording. The stimuli were 1000 Hz and 2000 Hz tone-bursts with rise/fall times of 20 ms and a duration of 340 ms. Although CAEP stimuli need not be longer than 50 ms, a longer

stimulus was used for two reasons: (1) there is a movement toward using ecologically relevant speech sounds for CAEP research (Ostroff et al., 1998; Martin et al., 2007), and a longer stimulus more closely approximates syllables and words; and (2) this duration was used in our previous research (Billings et al., 2007, 2009), which enables us to compare our results to previously published findings.

The signal was delivered at 70 dB SPL through a speaker (JBL Professional LSR25P). Each stimulus was presented in a homogeneous train for a total of 60 stimulus presentations for each recording; the duration of one test block was about 20 minutes. A five-minute listening break was given between the first and second block. An inter-stimulus interval (offset to onset) of 2 s was used.

ACAEPs were recorded with a single channel protocol using the AMPLAID mk22 auditory evoked potentials system. The skin was cleaned with abrasive paste, and the silver recording electrodes were attached to the skin with electrolytic paste on the upper forehead (positive electrode), the ipsilateral mastoid process (negative electrode) and contralateral mastoid process (common electrode).

The latency (ms) and amplitude (μV) of P1-N1-P2 waves were obtained by identifying the waves at highest peak amplitude. Tracks were analysed by a trained audiologist with experience in hearing electrophysiology. The analysis time was 750 ms, and waves were band-pass filtered at 1-20 Hz.

3.7. Statistical analysis

Quantitative variables were summarised as means (95% confidence intervals) and medians (interquartile range, IQR) and categorical variables as percentages. N1 amplitude values were reported as positive numbers. "Δ" was used to report percentage change.

Linear regression was used for univariate analysis in order to evaluate the relationship between the variables. The Z test and non-parametric Mann-Whitney U test were used when appropriate.

The Wilcoxon signed-rank test was performed to test differences between patient-reported outcome measure scores at T0 and T12.

Differences between ACAEPs parameters and speech audiometry at T0, T6 and T12 were evaluated using one-way repeated measures ANOVA followed by Tukey's post hoc test or Friedman test followed by Nemeneyi's post hoc test, depending on the distribution of the data.

Correlation between speech audiometry tests and questionnaire scores was assessed using Spearman's rank-order correlation analysis. A two-tailed $p<0.05$ was considered statistically significant.

Stata Statistical Software 2016, Release14 (Stata-Corp, College-Station, TX, USA) was used for database management and all analyses.

4. RESULTS

The final cohort was composed of 72 new bilateral hearing aid users, 43 male and 29 female (Sex ratio=1.48), with a mean age of 62.52±5.87 years. There were 69.44% of the enrolled subjects in the 61-70 year-old age range, with the remaining 30.56% being in the 50-60 year age range. Hearing aid use was ≥ 12 hours per day in 59.72% of cases, while 40.28% of patients wore hearing aids for 8-11 hours per day (Fig. 4).

As shown in Figure 5, the mean hearing threshold for each frequency studied was in the range between 30 and 90 dB HL, with the low frequencies characterised by a better threshold than the higher frequencies; in particular, there was a mean $PTA_{(0.25\text{-}8kHz)}$ of 58.83±7.49 dB HL for the left ear and 59.53±7.15 dB HL for the right ear (p=0.56). The morphology of the mean audiometric curves for both ears showed symmetric, downward-sloping moderate SNHL. All patients showed a type "A" tympanogram.

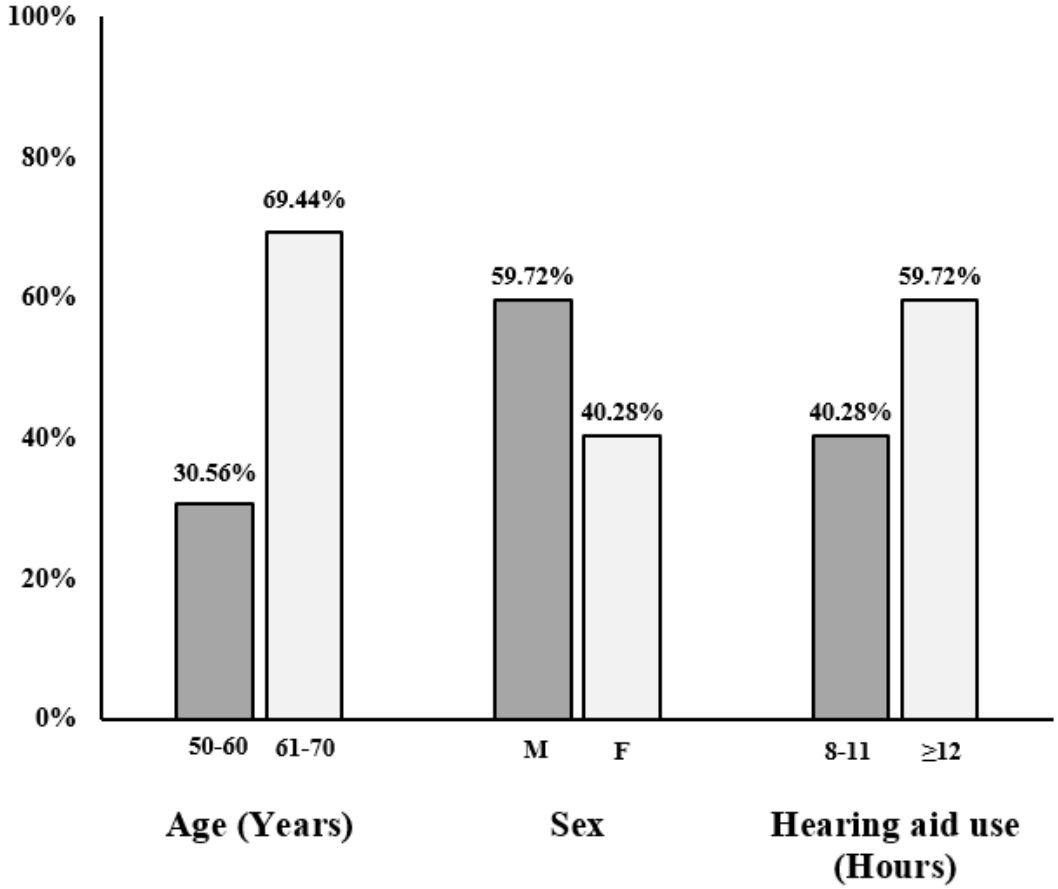

Figure 4: Characteristics of the cohort.

Aided hearing $PTA_{0.25\text{-}4kHz}$ (Fig. 5), measured wearing both hearing aids, had mean values of 21.8±3.38, 27.43±5.62, 31.8±5.53, 39.9±6.41 and 60.2±12.93 dB HL for the

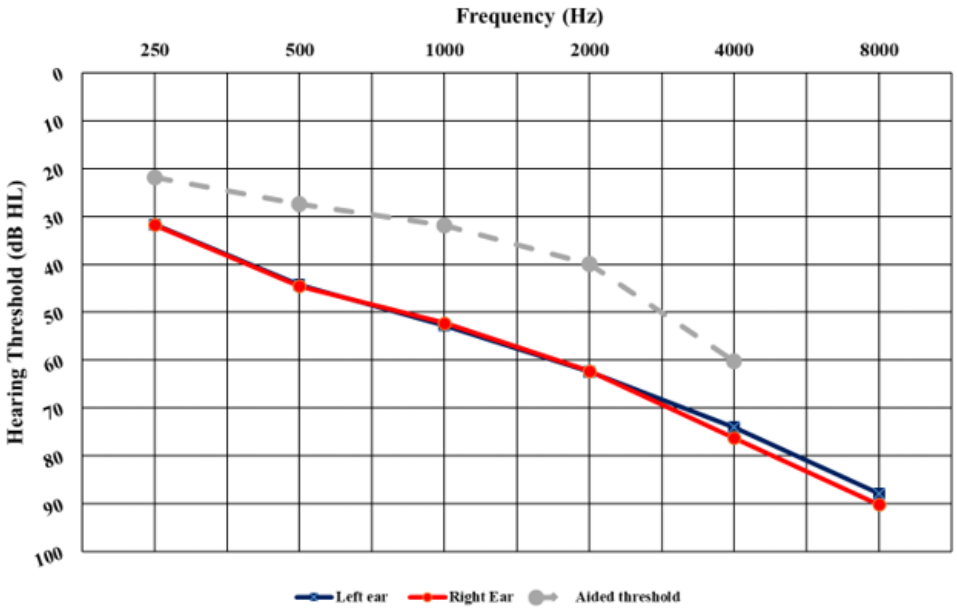

Figure 5: Mean $PTA_{0.25\text{-}8kHz}$ and mean aided threshold of the patients.

0.25, 0.5, 1, 2 and 4 kHz frequencies, respectively.

In terms of hearing aid gain (Fig. 6), its mean value (calculated as the average for 0.25-4 kHz frequencies) was 16.98±4.94 dB HL, with a mean gain < 10 dB HL for the 0.25 kHz frequency and > 20 dB HL for the 1 and 2 kHz frequencies. The mean hearing aid gain curve presented a peak centred on the 2 kHz frequency, where the highest hearing aid gain was provided.

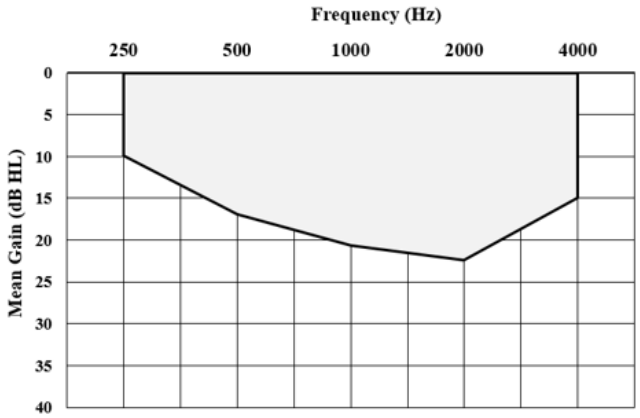

Figure 6: Mean hearing aid gain.

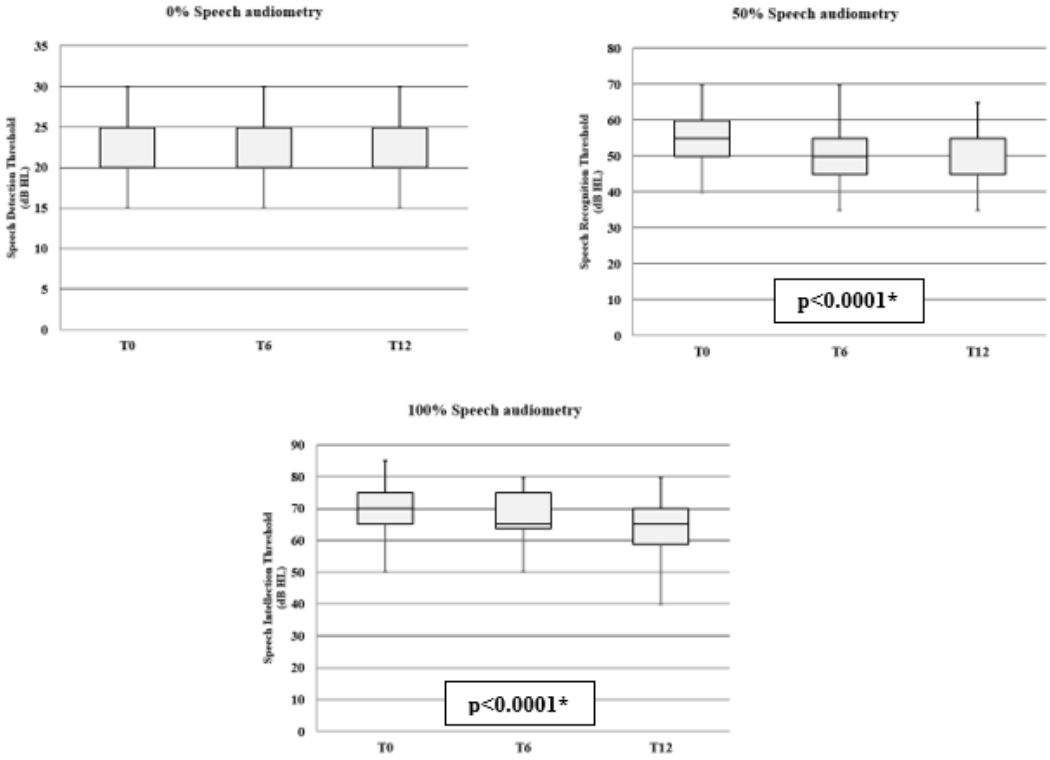

Figure 7: Distribution of SDT, SRT and SIT at three different time points.
***p-value refers to the difference between T0-T6-T12.**

Figure 7 depicts the distribution of speech audiometry data at each time interval. Out of 72 patients, 12 patients did not recognise 100% of words at any time point. SDT assessment indicated that 50% of patients had a threshold between 20-25 dB HL. For SRT, there was a higher variability with respect to SDT. In particular, 50% of patients had SRT between 50-60 dB HL at T0, while the same patients showed SRT between 45-55 dB HL at T6-T12, with a median SRT of 50 dB HL at T6 (IQR=45-55 dB HL) and 45 dB HL (IQR=45-55 dB HL) at T12. Distribution analysis of the SIT data showed a higher median value at T0 (70 dB HL, IQR=65-75 dB HL) with respect to T6 (70 dB HL, IQR=63.75-75 dB HL) and T12 (65 dB HL, IQR=58.75-70 dB HL), with 50% of patients showing SIT values between 65-75 dB HL at T0 and between 58.75-70 dB HL at T12 ($p<0.0001$). Post hoc analysis revealed a significant SRT and SIT decrease between T0-T6, T6-12 and T0-T12 ($p<0.0001$).

From the examination of Figure 8, which represents mean SDT, SRT and SIT tendencies through the three different time points, a lowering of the threshold emerged only for SRT

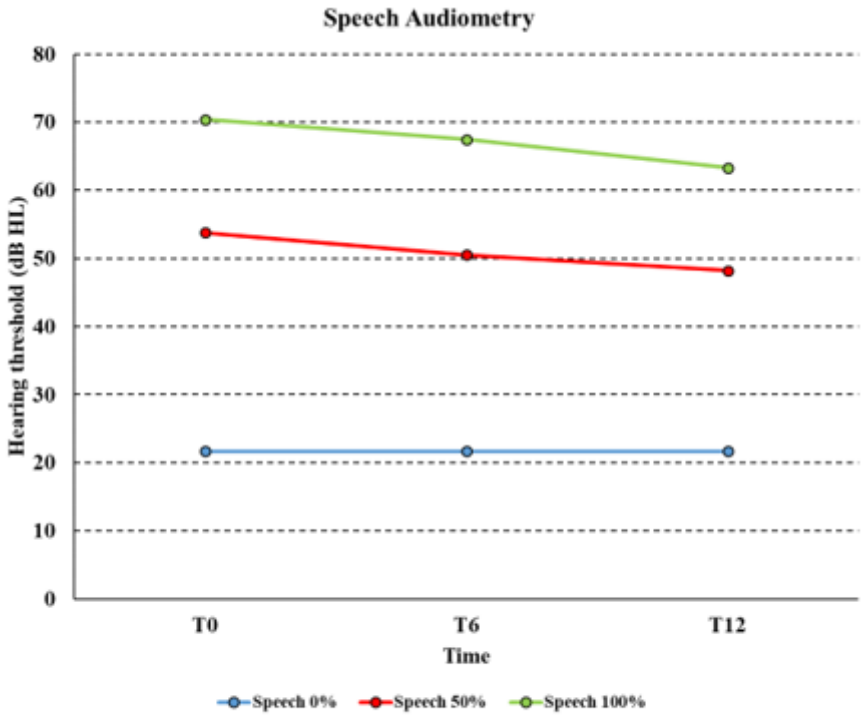

Figure 8: Mean speech audiometry scores at three different time points.

and SIT, with a mean threshold reduction between T0 and T12 of 5.6 dB HL and 7.1 dB HL, for SRT and SIT respectively. The variation of SRT from the beginning to the end of the follow-up was 10.2%, while for SIT it was 10.1%. No patients presented a reduction of SDT at T6 and T12. Twelve (16.66%) and 6 (8.33%) subjects showed no improvement of SRT and SIT, respectively. A SRT reduction of 5 dB HL was observed in 42 patients (58.33%), while the same improvement in SIT was detected in 27 hearing aid users (37.5%).

Speech audiometry at T12 was correlated to MST values (Fig. 9). No relationship was found between SDT and MST (ρ=0.07, p=0.54), while a moderate correlation was found between SRT and SIT and MST (ρ=0.62, and 0.68 respectively, p<0.0001, respectively). However, it was evident that, in the cases of SRT and SIT, an increase in their values was related to higher MST scores, suggesting a relationship between speech performance in quiet and in noise.

Linear regression analysis detected a moderate increase in APHAB variation and a reduction of the aided hearing threshold at 4000 Hz when ΔSIT_{T0-T12} increased (p<0.001). The APHAB score was measured when wearing hearing aids at T0 and T12, and it revealed a slight reduction in values from the beginning to the end of the follow-up, with

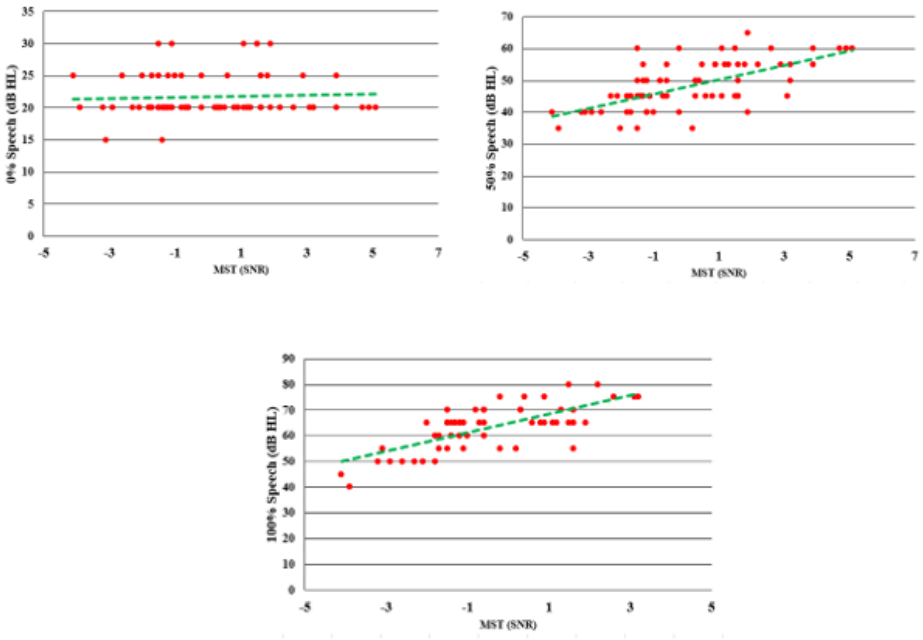

Figure 9: Scatter plot. Correlation analysis of speech audiometry and MST.

a median score of 37.85 (IQR=33.97-41.32) at T0 compared to 34 (IQR=26.3-38.57) at T12 ($p<0.0001$); the box plot (Fig. 10) clearly shows that, at T0, 31.94% of patients had an APHAB score <35, while the same results were found in 50% of subjects at T12. After dividing patients between those who wore hearing aids <12 hours/day and those who used them ≥12 hours/day, the difference between APHAB at T0 and T12 was not statistically significant ($p>0.05$). No significant variation was also detected in relation to sex and age

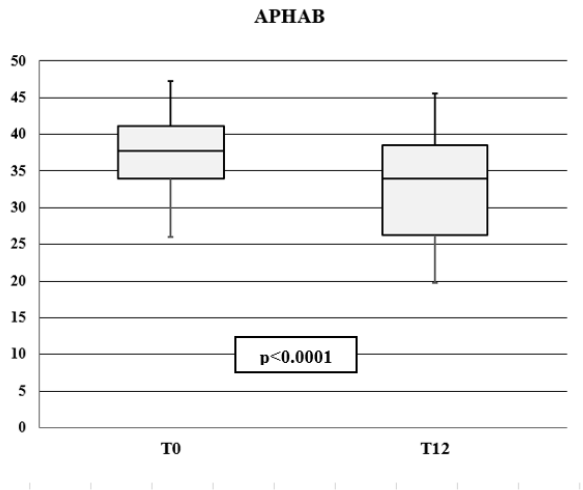

Figure 10: Distribution of APHAB scores at T0 and T12.
p-value refers to the difference between T0 and T12 (Wilcoxon signed-rank test).

(50- 60 years vs 61-70 years). A weak correlation was found between SIT and APHAP scores at T0 (ρ=0.26, p=0.04), while a moderate relationship was found at T12 (ρ=0.57, p< 0.0001).

The FAS test, performed at T0 and T12, showed a similar median score (p>0.05) between appointments (26 with IQR=22-29.5 and 25 with IQR=22-29.5, respectively). After dividing patients between those who wore hearing aids <12 hours/day and those who used them ≥12 hours/day, the difference between FAS at the beginning and end of the follow

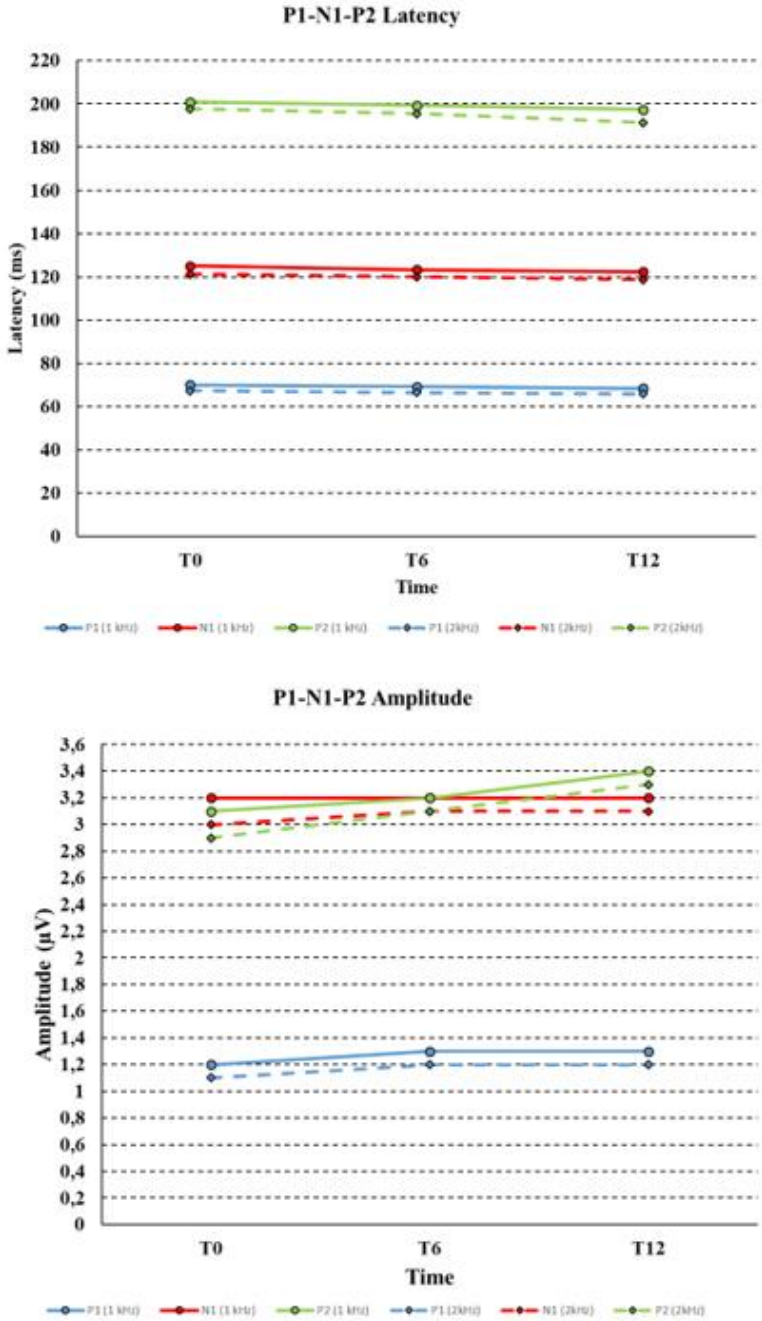

Figure 11: P1-N1-P2 Latency and Amplitude mean values at three different time points.

up period was not statistically significant ($p>0.05$). A weak correlation was detected between APHAB and FAS examined at T0 ($\rho=0.36$, $p=0.001$), while a moderate was found at T12 ($\rho=0.55$, $p<0.0001$). When testing the relationship between FAS and SIT, a moderate correlation was evidenced at T0 and T12 ($\rho=0.44$, $p=0.0003$).

Linear regression analysis showed a reduction of MST values and SIT at T12, when APHAB increased ($p<0.001$).

	Experimental condition					
	1000 Hz			**2000 Hz**		
	T0	***T6***	***T12***	***T0***	***T6***	***12***
Latency (ms)						
P1	70.01	69.27	68.47	67.30	66.61	65.94
N1	125.15	123.43	122.37	121.22	120.06	118.75
P2	200.94	199.22	194.13	197.43	195.59	194.13
Amplitude (μV)						
P1	1.27	1.33	1.31	1.17	1.24	1.25
N1	3.2	3.27	3.27	3.05	3.12	3.14
P2	3.17	3.28	3.42	2.99	3.18	3.35

Table 1: Mean latency and amplitude of P1-N1-P2 waves.

The study of amplitude mean values at the three different time points (Fig. 11, Table 1) revealed an increasing tendency for all waves in both experimental conditions. Latencies seemed to become shorter from T0 to T12 for each wave and in the case of 1 kHz and 2 kHz stimuli.

From the comparison of P1-N1-P2 in both experimental conditions, a slight difference emerged in terms of latency (2-3 ms) and amplitude (0.1-0.5 μV). Concerning amplitude variation, an increase ≥ 0.5 μV between T0 and T12 was observed only in case of P2 in 20 patients when stimulated with 1000 Hz tone burst and in 23 patients when using the 2000 Hz cue.

Analysis of the data relative to the latency and amplitude of P1-N1-P2 elicited by 1 kHz tone (Fig. 12) showed a mean latency $\Delta_{T0\text{-}T12}$ <1% for all waves with respect to a mean amplitude $\Delta_{T0\text{-}T12}$ of 4.7% in the case of P1, 2.1% in the case of N1 and 7.5% in the case of P2. As for amplitude, a higher variation was observed in the T0-T6 time interval for P1 and N1 (6.1% and 2.4%), while similar values were found for $\Delta_{T0\text{-}T6}$ and $\Delta_{T6\text{-}T12}$ in case

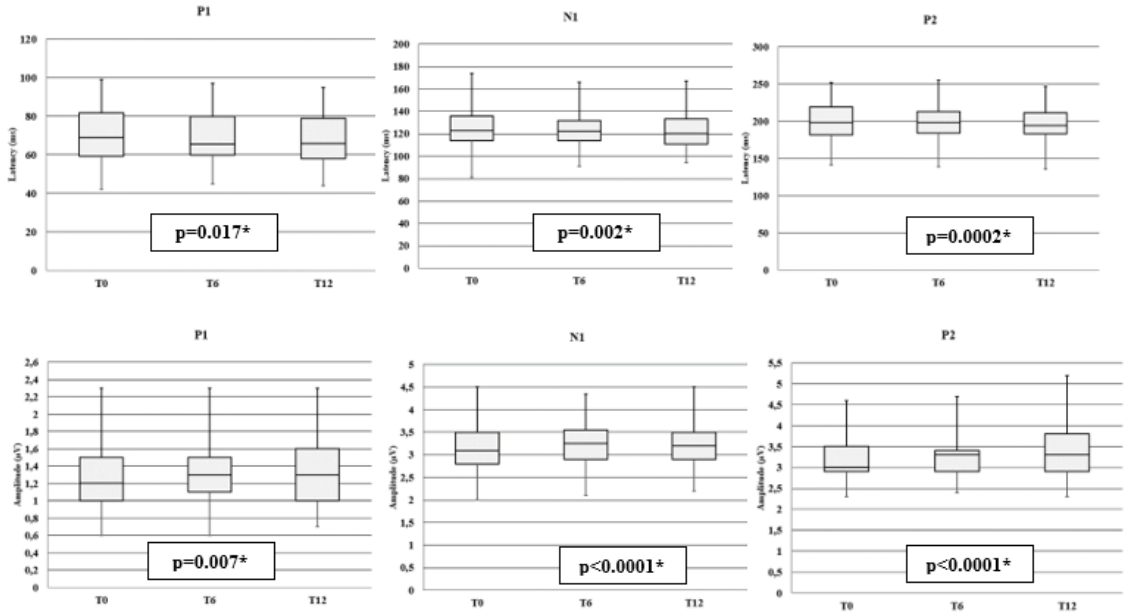

Figure 12: Distribution of P1-N1-P2 amplitude and latency elicited by 1000 Hz stimulus at three different time points.
***p-value refers to the difference between T0-T6-T12.**

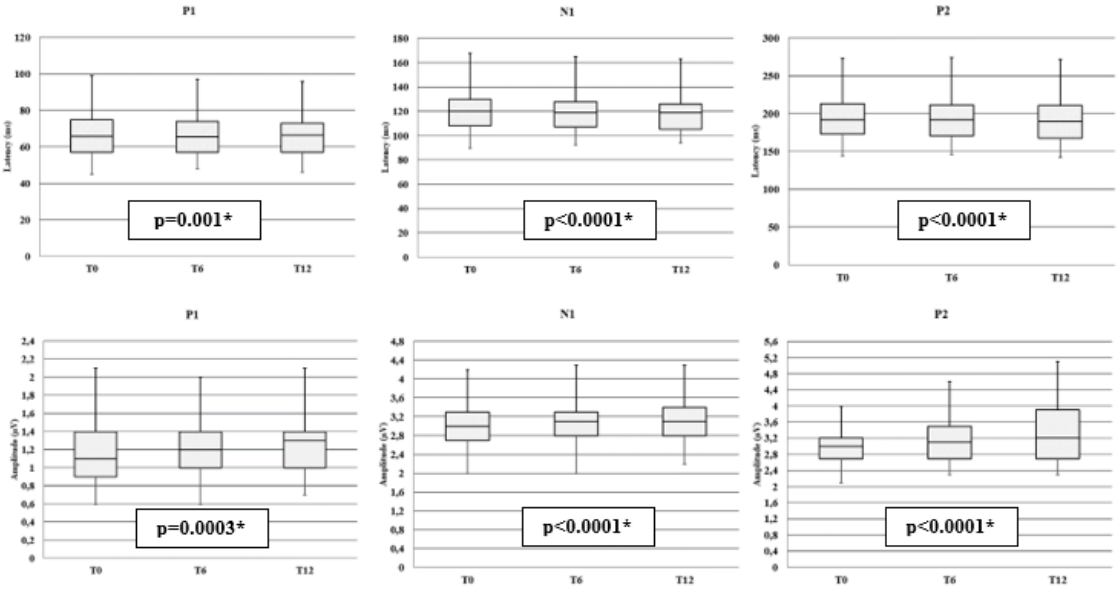

Figure 13: Distribution of P1-N1-P2 amplitude and latency elicited by 2000 Hz stimulus at three different time points.
***p-value refers to the difference between T0-T6-T12.**

of P2 (3.5% and 3.6%, respectively). Figure 13 shows the distribution of latency and amplitude of P1-N1-P2 with a 2 kHz stimulus. A mean latency $\Delta_{T0\text{-}T12}$ <2% was recognised for P1 and N1, while P2 showed a mean latency $\Delta_{T0\text{-}T12}$ of 2.4%. Differently from latency, wave amplitudes presented a higher mean $\Delta_{T0\text{-}T12}$ in case of P1 and P2, with a variation of 9% and 11.4%, respectively. Post hoc analysis (Table 2) showed that

amplitude increased significantly between T0 and T6 ($p<0.05$) and, with the exception of $P1_{1000Hz}$, between T0 and T12 ($p<0.01$); P1-N1-P2 latency decreased significantly between T0 and T12 in both experimental conditions ($p<0.05$).

ACAEPs	TIME INTERVAL		
Amplitude	**T0-T6**	**T6-T12**	**T0-T12**
$P1_{1000Hz}$	<0.01	ns	ns
$N1_{1000Hz}$	<0.01	ns	<0.01
$P2_{1000Hz}$	0.03	ns	<0.01
$P1_{2000Hz}$	<0.01	ns	<0.01
$N1_{2000Hz}$	<0.01	ns	<0.01
$P2_{2000Hz}$	<0.01	ns	<0.01
Latency			
$P1_{1000Hz}$	ns	ns	0.016
$N1_{1000Hz}$	ns	ns	<0.01
$P2_{1000Hz}$	ns	ns	<0.01
$P1_{2000Hz}$	ns	ns	<0.01
$N1_{2000Hz}$	ns	<0.01	<0.01
$P2_{2000Hz}$	<0.05	<0.01	<0.01

Table 2: Post hoc analysis of ACAEPs at T0-T6-T12: p-value.

	MST		SIT_{T0-T12}	
$Amplitude_{T0-T12}$	**Coeff.**	**p**	**Coeff.**	**p**
$P1_{1000Hz}$	-0.0231348	0.014	0.0102661	0.050
$N1_{1000Hz}$	-0.0064136	0.011	0.0017199	0.216
$P2_{1000Hz}$	-0.0348801	<0.001	0.0112759	0.002
$P1_{2000Hz}$	-2.98008	0.014	0.0064259	0.315
$N1_{2000Hz}$	-8.032371	0.099	0.0002676	0.864
$P2_{2000Hz}$	-0.0459165	<0.001	0.01027	0.041
$Latency_{T0-T12}$				
$P1_{1000Hz}$	-0.0124903	0.006	0.0026223	0.236
$N1_{1000Hz}$	-0.017151	<0.001	0.0049786	0.008
$P2_{1000Hz}$	-0.0020805	0.594	0.0030755	0.013
$P1_{2000Hz}$	-0.0064106	0.048	0.0039257	0.029
$N1_{2000Hz}$	-0.003316	0.137	0.002505	0.037
$P2_{2000Hz}$	-0.0031916	0.594	0.0019644	0.013

Table 3: Linear regression analysis between ACAEPs parameters and speech perception outcome.

Table 3 describes the linear regression analysis between latency and amplitude Δ_{T0-T12} and MST and ΔSIT_{T0-T12}. For amplitude, only P2 showed a statistically significant increase in its variation, whereas MST and SIT decreased in both experimental conditions, even when the analysis was adjusted for age and daily hearing aid use.

Latency Δ_{T0-T12} was significantly correlated to MST and SIT only for P1 under 2 kHz stimulation and N1 elicited by 1 kHz tone.

5. DISCUSSION

5.1. General considerations

In the last decade, ACAEPs have continued to be a focus of interest due to the lack of appropriate tools for objectively assessing cortical auditory activity in response to amplified stimuli. Still now, a number of controversies have emerged from electrophysiological recording at near-threshold and suprathreshold levels in hearing aid users.

The majority of authors have investigated the direct relationship between behavioural thresholds and ACAEPs and the evolution of ACAEP waves among SNHL children undergoing rehabilitation; in contrast, scarce data are available regarding changes in ACAEPs over time in adult hearing aid users, particularly when related to speech perception outcomes. In addition, because of the heterogeneous protocols used for assessing and monitoring hearing aid users, data are difficult to compare.

However, the main aim of this study was to understand whether ACAEPs can change over time after first amplification and whether there is a relationship between changing wave parameters and speech perception outcomes. Even though recording ACAEPs is more time-consuming compared to auditory brainstem response (ABR) testing, they reflect auditory neuronal activity at higher levels and are more frequency-specific. For this reason, they may better indicate plastic changes following auditory amplification and may indirectly reveal cortical improvement in speech perception in the follow-up period. Understanding the relationship between changing ACAEPs and speech recognition may impact clinical practice by helping to fit hard-to-test patients, allowing them to perceive the best sound environment. In other words, identifying how electrophysiological parameters may vary with respect to speech recognition could guide clinicians, audiologists and hearing aid dispensers in achieving optimal hearing aid fittings. In fact, patients who cannot cooperate because of age, mental or neurological disorders, syndromes and other disabling conditions make hearing aid fitting challenging and, consequently, are at risk of worsening their depression, anxiety and cognitive decline because of the isolation derived from auditory deprivation and inadequate hearing rehabilitation.

To summarise, we can divide the project's results into three parts. In the first, concerning the variation of electrophysiological parameters during the follow-up, it was clearly evidenced that P2 was associated with the higher percentage increase between T0 and T12 ($p<0.0001$) in both experimental conditions (7.5% for 1000 Hz and 11.4% for 2000 Hz) when compared to P1 and N1. Latency instead showed a smaller although statistically significant ($p<0.05$) variation toward the decrease for all waves from the beginning to the end of the follow-up (<1% for 1000 Hz and <2.5% for 2000 Hz).

In the second part, where the electrophysiological measurements were correlated to speech recognition tests, an interesting finding emerged when analysing the relationship between amplitude $\Delta_{T0\text{-}T12}$ and speech perception outcome. The only parameter that was significantly related to MST and $\Delta SIT_{T0\text{-}T12}$ when elicited by 1000 and 2000 Hz stimuli was P2 amplitude ($p<0.05$). In particular, it was observed that, as MST score and the SIT values decreased, P2 amplitude increased significantly; patients who had a higher improvement in their ability to recognise words in quiet and in noise exhibited larger amplitudes at the end of the follow-up compared to patients with poorer speech recognition performance. In other words, hearing aid users who showed a more negative S/N on the MST and recognised 100% of the words in quiet with the softest intensity were the ones whose P2 amplitude increased more. Patients with better speech performance were also those with better aided thresholds at 4000 Hz, as demonstrated by the fact that, as the $\Delta SIT_{T0\text{-}T12}$ increased, the aided PTA at 4000 Hz decreased ($p<0.001$). This result is not surprising, considering that high frequencies are crucial for speech discrimination of certain phonemes such as /s/, /f/ and /k/.

In the third part, studying the data on hearing aid benefit through the APHAB questionnaire, a negative relationship between APHAB variation and MST and SIT at T12 ($p<0.001$) emerged. APHAB score differences between T0 and T12 were not influenced by sex, age and the number of hours of hearing aid use ($p>0.05$); this result might be read in light of the strict inclusion criteria that required a minimum of 8 hours/day (which may guarantee appropriate hearing stimulation) and the relatively narrow age interval of the patients recruited (which may show similar habits and hearing complaints in everyday life). No difference was found in the case of FAS scores either, and a weak correlation with APHAB was reported; this result might be expected considering the questionnaire's low specificity relative to hearing disability and the

multiple factors that can influence the perception of fatigue in older patients. In line with previous investigations (Alhanbali et al, 2018; Dornhoffer et al, 2020), a strong correlation between patient-reported outcome measures and speech perception was found neither in case of FAS nor in case of APHAB.

5.2. Monitoring electrophysiological parameters in hearing aid users

Similarly to our study, Philibert et al. (2005) followed 8 patients with symmetrical SNHL who wore hearing aids at least 8 hours per day with greater amplification at 2000 Hz over a period of six months; through electrophysiological recording of ABR with 300 ms tone bursts, they demonstrated an increase in the amplitude and a shortening of the latency of wave V in the right ear, which might indicate an increase in neural synchronisation over the hearing aid fitting time-course.

McCullagh (2009), in his doctoral thesis, found a statistically significant change in the latency of N1 among a group of 10 new hearing aid users compared to 10 non-hearing aid users after a six to eight week monitoring period. No significant changes in speech recognition, N1 amplitude, P2 amplitude, or P2 latency were reported. He concluded that changes in N1 latency may be an indirect sign of cortical plasticity following hearing aid amplification.

A study conducted by Bertoli et al. (2011), who investigated acclimatisation effects through CAEP recordings of SNHL patients with a mean PTA similar to the one of our sample, showed larger P2 amplitude with 2000 Hz pure tone when testing the aided ear with respect to the non-aided ear in unilateral hearing aided users. An inverted finding was revealed when testing both ears with 500 and 1000 Hz stimuli. Even though the authors suggested that changes in P2 amplitude may be related to an acclimatisation effect, the study was not based on a follow-up of patients and included unilateral and bilateral hearing aid users who had a significant difference in terms of the duration of their hearing aid use. For this reason, no effects of time on P2 amplitude changes could be considered. CAEPs were recorded by delivering pure tones with insert earphones, so amplitude data cannot be compared to the ones collected in our study.

Dawes et al. (2014), analysed CAEPs and speech-in-noise audiometry data relative to 24 new hearing aid users (11 unilateral and 13 bilateral users) who were followed for 3

months. The authors did not find any significant correlation between changes in speech recognition and changes in N1/P2 latency and amplitude. A little improvement (2%) in speech perception outcomes was attained by the end of the follow-up period, but it was consistent with a test-retest effect rather than an acclimatisation effect. Differently from our study, the stimuli used in the testing protocol, though of the same duration, had different frequencies (500 Hz and 3000 Hz). The monitoring period was shorter than our time-interval, and the minimum daily hearing aid use required was 6 hours per day instead of 8.

Leite et al. (2017), in a 9-month follow-up study investigating ACAEPs in 32 children aged between 7 and 12 years, did not find any significant differences between the beginning and the end of the observation period for P1-N1 and P2-N2 amplitudes. However, data regarding amplitude were calculated as the summation of two peaks (e.g., P1+N1), so we cannot determine the contribution of each wave. In addition, patients were younger compared to our sample and are not suitable for comparison because, as reported by Wunderlich et al. (2006), CAEPs during childhood and adolescence undergo maturation processes.

Finally, Giroud et al. (2017), who studied ACAEPs in three groups of healthy older adults over three months, observed an increase in P1 and N1 amplitude among patients who used non-linear frequency compression (NLFC) hearing aids; the same group was characterised by a progressive decrease of the global field power (GFP) of the P3b-like microstate, suggesting a decreased processing effort due to an improved audibility of the fricatives provided by the NLFC algorithm.

5.3. Monitoring speech perception outcomes and hearing aid benefits

Our study, reporting an improvement of 10.2% for SRT and 10.1% for SIT over twelve months, falls within the 0-10% interval of benefit over time reported by Arlinger et al. (1996) and support the evidence of an acclimatisation process where progress can be seen even after one year of hearing aid use. Interestingly, although a decrease in APHAB scores was shown from the beginning to the end of the follow-up ($p<0.0001$), the subjective benefit change was not statistically significant after dividing patients between those who wore hearing aids <12 hours/day and those who used them ≥12 hours/day.

Cunningham et al. (2001) followed 18 new hearing aid users for 5 months; these were divided into two groups, one whose electroacoustic settings were maintained throughout the research project and one whose settings were not. No significant differences in speech in noise scores nor in subjective hearing aid benefit were reported between the groups; in addition, no acclimatisation effect emerged following the post-fitting period.

In one of the largest longitudinal studies assessing subjective and objective benefits with hearing aids, Humes et al. (2002) analysed data of 134 elderly hearing-aid wearers during the first year of hearing aid usage. With the exception of the Connected Speech Test (CST), when performed at an overall level of 65 dB SPL and with an SNR of +8 dB, all the other measures of aided speech recognition and subjective benefit tended to worsen over one year. In particular, the authors highlighted that, although some patients presented improved performance over time, they were offset by as many or more patients who experienced declines in performance. The overall data suggested that the objective and subjective benefit measures used did not change for most hearing aid wearers over the follow-up period, and that little evidence of acclimatisation was found in either the group or the individual data. An acclimatisation effect was suggested by Reber & Kompis (2005) in their 6 month follow-up study; comparing three hearing aid fitting protocols tested on 23 SNHL patients, the authors found improvements in the speech in noise score without significant changes in the insertion gain in all groups, irrespective of the fitting protocol used.

Vestergaard (2006) conducted a follow-up investigation of 25 patients with steeply-sloping SNHL who were assessed at 1, 4 and 13 weeks post fitting with different subjective questionnaires regarding hearing aid benefit. First-time users who used their hearing aids more than four hours per day reported improved outcomes over time. This result was restricted only to questionnaires which addressed general aspects of hearing-aid benefit and satisfaction, while no evidence of significant changes over time were demonstrated for those which addressed hearing-aid performance in specific situations.

Yund et al. (2006) identified the fitting algorithm as a possible factor influencing speech perception improvement over time in new hearing aid users. In particular, among 39 individuals affected by sloping, bilateral symmetrical SNHL and divided into two groups with respect to hearing aid fitting technology, those with the WDRMCC system showed significantly better syllable recognition scores compared to those using the linear

amplification system. The authors concluded that only WDRMCC processing, with many independent frequency channels and short time constants, could consistently encode virtually the entire normal-hearing frequency-intensity space, giving the patient a more consistent encoding of their everyday sound environment.

Ng et al. (2014), in a study conducted on 27 first-time hearing aid users, showed a statistically significant improvement in the SRT in noise after 6 months post-fitting ($p<0.05$); interestingly, the speech perception outcomes were predicted by a reading span test, which is a measure of working memory capacity. The authors suggested that, at the beginning, working memory recognises unfamiliar processed speech signals because their phonological forms cannot be automatically matched to phonological representations in long-term memory. As familiarisation proceeds, the mismatch effect is alleviated, and the engagement of working memory capacity is reduced.

An investigation carried out by Dawes et al. (2017) on 35 new hearing aid users, who completed a test of speech recognition in noise, demonstrated a significant improvement after 30 days post-fitting in the subgroup with mean PTA >40 dB HL and daily hearing aid use >6 hr/day compared with a control group of experienced hearing aid users ($p<0.01$). The improvement of 4.1 dB in the former group with respect to the 0.8 of the latter group suggested that, in the case of more consistent hearing aids use and more severe hearing loss, an acclimatisation process is more likely to occur.

Karawani et al. (2018), in a study investigating behavioural and electrophysiological variations among 35 older SNHL adults with no history of hearing aid use, observed better speech recognition in noise after 6 months of hearing aid use. However, a similar improvement over time was also recognised among hearing impaired patients who did not wear hearing aids, suggesting a practice effect rather than an acclimatisation effect.

From the aforementioned data emerges a controversial view of how, and to what extent, speech recognition improvement occurs in addition to subjective benefits after wearing hearing aids. However, some aspects should be pointed out: first of all, these authors reported samples of different sizes (usually small) which were characterised by various age ranges and mean hearing thresholds; it is clear that age may influence the acceptance of hearing aids, reducing the hours per day of hearing aid usage, that neuroplasticity may be less functional in people beyond a certain age, and that acclimatisation may be more hidden in cases of initial presbycusis compared to more severe SNHL forms.

Secondly, the duration of follow-up tended to be less than one year; thus, results may be related to the immediate benefit of the first amplification and cannot be read in light of a longer period of exposure to everyday sounds and hearing aid adaptation.
Third, it is possible that the type of fitting algorithm may influence the improvement of speech perception outcomes, while the number of fine tunings may not. The speech perception tests as well as questionnaires regarding hearing aid benefits were heterogeneous and, being influenced by many sample variables, showed different sensitivities in identifying objective and subjective improvements; globally, there was a trend toward an amelioration in many speech measurements, although often they were not statistically significant.

5.4. Limitations

The study presented the following limitations that will be further discussed. To begin with, the sample size was not large, but the strict inclusion criteria and the need to complete at least one year of follow-up limited the patient recruitment process. Secondly, the decision to start comparing data beginning from "month one" of the year of amplification might be criticised because the majority of hearing aid benefit is commonly observed within the first month of hearing aid use. However, I underline that, even though an immediate benefit can be detected after wearing hearing aids for the first time, the first month is typically characterised by frequent appointments with audiologists to better fit hearing aids according to the patients' needs. This implies making adjustments to the hearing device that can alter ACAEP recordings. For this reason, we verified that hearing aid parameters were kept constant during ACAEP recordings at T6 and T12. The choice to use 1000 and 2000 Hz stimuli was in line with other studies which investigated ACAEPs (Bertoli et al., 2011; Oppitz et al., 2015; Chun et al., 2016; Leite et al., 2018) and was preferred to speech syllables because, even though the latter present more complex sounds that better reflect everyday language, we do not really know to what extent they are perceived because of the processing effect of hearing aids. However, the use of tone-bursts with a duration of 340 ms kept the loudness constant during the recording and may approximate the time length of speech syllables used in previously published investigations.

Thirdly, even though P300 and mismatch negativity (MMN) better reflect speech discrimination, the choice to limit electrophysiological recording to exogenous evoked potentials was influenced by two reasons. Firstly, the P300 recording is not reproducible on hard-to-test patients because it requires active cooperation, and so it was beyond the scope of this investigation. In addition, the recording of MMN did not show reliable data in hearing aid users, making it ineligible for patient follow-up.

Fourthly, the lack of a control group might raise concerns about the possibility that similar improvements in terms of electrophysiological parameters and speech perception outcomes could be observed in normal hearing and SNHL patents who are not hearing aid users. Concerning normal listeners, before starting this study we followed a group of 20 normal hearing volunteers for one year, and they did not show significant fluctuation in ACAEPs nor, obviously, any speech audiometry improvement because it was within the normal range from the beginning of the study. Regarding SNHL patients who opt not to use hearing aids, it is difficult to recruit patients with similar audiometric curves without providing hearing aid rehabilitation, but, as shown by other authors, the effect of auditory deprivation may induce detrimental effects on speech recognition performance over time when compared to aided hearing.

Finally, the MST was inserted in the experimental design of the study only in the last part of the follow-up because it was available only in the final part of the investigation; unfortunately, it did not allow us to compare any score improvements between T0 and T12 but, differently from speech audiometry in quiet, revealed the speech sentence perception ability in noise environments, simulating the most challenging listening conditions which patient might have to deal with.

6. CONCLUSIONS AND FUTURE DIRECTIONS

The data collected in this study provide new evidence about the relationship between ACAEPs and the speech recognition capability of adult new hearing aid users. This is the first one-year follow-up study in which hearing aided patients were monitored not only through electrophysiologic measurements or behavioural tests, but with a combination of both. In line with previous investigations reporting a gain in P2 amplitude following various types of auditory training experiences (including music and speech-sound training) (Shahin et al., 2003; Kuriki et al., 2007; Seppänen et al., 2012; Kühnis et al., 2013), we observed, in both experimental conditions, larger P2 amplitude in patients with better speech perception outcomes. It should be underlined that, even though P2 may reflect auditory processing beyond sensation (Crowley and Colrain, 2004), its increase may be an expression of neural activity associated with the acquisition process driven by exposure to sounds and speech (Tremblay et al., 2014). It could be hypothesised that neuroplastic changes in the planum temporale and the associated cortices may underlie new hearing aid users' speech improvement over time.

Our study did not allow us to speculate about certain acclimatisation processes because we did not include a control group, for the aforementioned reasons; however, a tendency towards greater P2 amplitude and overall better speech perception scores from T0 to T12 was recognised ($p<0.0001$). The observation that P2 amplitude tended to improve as SIT and MST scores decreased might be, in the future, a further object of investigation to assess its reliability as a marker of speech perception improvement; its use may assist hearing aid dispensers and audiologists as a source of feedback in the evaluation of listening benefits in hard-to-test patients. We underline that the relationship between P2 and speech recognition tests was not influenced by patient age and/or the number of hours per day of hearing aid use; it seems that the age interval (50-70 years) and the minimum number of hours (8 h/day) that we used as inclusion criteria may not interfere with the electrophysiological and behavioural changes recorded. In addition, it should be considered that, as suggested by Dawes et al. (2017), the increase in speech recognition ability may have better emerged because of the audiogram configuration and the mean $PTA_{0.5\text{-}4kHz} > 40$ dB HL of the sample.

The use of the APHAB questionnaire to evaluate hearing aid benefits did not show any statistically significant improvement in relation to sex, age and daily use of hearing aids but, interestingly, its variation was significantly related to SIT and MST at the end of the follow-up period. As expected, APHAB seemed to provide its most useful data when evaluating the differences between unaided and aided conditions, but it could be a valuable tool for monitoring hearing aid users because it may predict speech perception outcomes.

In the future, we expect to study new electrophysiological parameters to objectively demonstrate what the neural and cortical consequences of amplification are and how they relate to hearing aid benefit. Discovering these factors may play a crucial role in providing the best fitting and reducing hearing aid drop-outs, particularly in noncompliant patients.

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