

## ORIGINAL PAPER

# Auditory cortical responses in patients with cochlear implants

## Potenziali uditivi corticali in pazienti con impianto cocleare

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## Key words

Cochlear implant • Auditory cortical responses • Maturation

## Parole chiave

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## Summary

Currently, the most commonly used electrophysiological tests for cochlear implant evaluation are Averaged Electrical Voltages (AEV), Electrical Advisory Brainstem Responses (EABR) and Neural Response Telemetry (NRT). The present paper focuses on the study of acoustic auditory cortical responses, or slow vertex responses, which are not widely used due to the difficulty in recording, especially in young children. Aims of this study were validation of slow vertex responses and their possible applications in monitoring postimplant results, particularly restoration of hearing and auditory maturation. In practice, the use of tone-bursts, also through hearing aids or cochlear implants, as in slow vertex responses, allows many more frequencies to be investigated and louder intensities to be reached than with other tests based on a click as stimulus. Study design focused on latencies of N1 and P2 slow vertex response peaks in cochlear implants. The study population comprised 45 implant recipients (aged 2 to 70 years), divided into 5 different homogeneous groups according to chronological age, age at onset of deafness, and age at implantation. For each subject, slow vertex responses and free-field auditory responses (PTAs) were recorded for tone-bursts at 500 and 2000 Hz before cochlear implant surgery (using hearing aid amplification) and during scheduled sessions at 3<sup>rd</sup> and 12<sup>th</sup> month after implant activation. Results showed that N1 and P2 latencies decreased in all groups starting from 3<sup>rd</sup> through 12<sup>th</sup> month after activation. Subjects implanted before school age or at least before age 8 yrs showed the widest latency changes. All subjects showed a reduction in the gap between subjective thresholds (obtained with free field auditory responses) and objective thresholds (obtained with slow vertex responses), obtained in presurgery stage and after cochlear implant. In conclusion, a natural evolution of neurophysiological cortical activities of the auditory pathway, over time, was found especially in young children with prelingual deafness and implanted in preschool age. Cochlear implantation appears to provide hearing restoration, demonstrated by the sharp reduction of the gap between subjective free field auditory responses and slow vertex responses threshold obtained with hearing aids vs. cochlear implant.

## Riassunto

*I tests elettrofisiologici attualmente più usati nella valutazione dei pazienti con impianto cocleare sono l'AEV, l'EABR e l'NRT. Gli Autori hanno studiato i potenziali elettrici corticali lenti (SVRs). Le SVRs non trovano di solito larga applicazione, soprattutto nei bambini, per la difficoltà di registrazione, ma permettono, anche in soggetti portatori di protesi acustiche, di valutare molte più frequenze e intensità maggiori rispetto agli altri tests che usano i clicks e non i tone-bursts come stimolo. Scopo dello studio è stato verificare il valore delle SVRs e le possibili applicazioni in soggetti portatori di impianto cocleare, in particolare per monitorare l'effettivo recupero delle capacità uditive e valutare la maturazione delle vie uditive nei bambini. Quarantacinque soggetti sottoposti ad intervento di impianto cocleare (2-70 anni) sono stati suddivisi in cinque gruppi omogenei per età cronologica, età di esordio della sordità ed età di impianto. In ciascun soggetto sono state registrate le SVRs con tone-bursts a 500 Hz e a 2000 Hz e le risposte all'audiometria soggettiva in campo libero (PTAs) rispettivamente prima dell'intervento di impianto cocleare (con protesi acustiche) e al 3° e 12° mese dopo l'attivazione dell'impianto cocleare. Per l'SVRs sono state considerate le latenze dei picchi N1 e P2. Le latenze di N1 e P2 al 12° mese sono risultate minori rispetto al 3° mese. La riduzione di latenza è risultata maggiore nei soggetti impiantati prima dell'età scolare o al massimo prima degli 8 anni di età. In tutti la differenza tra soglia soggettiva (descritta mediante PTAs) e soglia obiettiva all'SVRs misurata in fase pre-chirurgica si è ridotta dopo impianto cocleare. In conclusione è stata riscontrata una naturale evoluzione delle attività neurofisiologiche corticali delle vie uditive nel tempo in particolare nei bambini piccoli con sordità preverbale, impiantati in età prescolare. In tutti i casi inoltre l'impianto cocleare ha fornito un recupero uditivo che è stato evidenziato dal confronto del gap tra le soglie ottenute con PTAs e SVRs prima con protesi acustiche e poi con impianto cocleare.*

## Introduction

Cochlear implants encode sound electronically and then bypass a damaged inner ear in order to provide direct electrical stimulation to the auditory nerve. In individuals who are deaf and cannot benefit from conventional hearing aids, this electrical stimulation provides a sensation of hearing. Cochlear implants have become an accepted medical approach to treatment for subjects with profound bilateral sensorineural hearing loss. Cochlear implant recipients show great variability in the way in which they manage the information provided by the implant. Their speech perception abilities range from mere detection of sound to the ability to talk on the telephone. This variation in speech perception ability among users reflects the auditory cortex structural changes that follow the reintroduction of acoustic stimulation<sup>1</sup>.

The degree of further maturation is affected by different factors, first of all by the length of the auditory deprivation<sup>2</sup>. Therefore neural plasticity is, in some way, related to the length of the time during which the person has been deaf, to the age of onset, the type of noxa and to the occurrence before or after the acquisition of speech and language<sup>3</sup>. Developmental processes are also influenced by specific auditory experience<sup>4-6</sup>.

Other factors, such as the status of the cochlea<sup>7</sup>, the number of surviving nerve fibres<sup>8</sup>, basic psychophysical thresholds<sup>9</sup>, or the type of device implanted<sup>10</sup>, also affect implant outcome but cannot completely account for the variation in patient performance.

The wide range of speech perception abilities found in cochlear implant recipients may also depend in part, upon differences in the central auditory processing abilities of implant users. One way to evaluate central auditory function in these individuals is by measuring the evoked cortical potentials, which may provide insight into the central mechanisms underlying speech perception. From a theoretical standpoint, the presence of cortical potentials in cochlear implant users may provide a unique window for viewing the supratentorial auditory system. The late auditory response or slow vertex response (SVR) is a scalp recorded, averaged neurogenic field potential that appears in humans as a large positivity in the 90 to 200 msec latency range and reflects perceptive brain functions processing stimulus discrimination as sequential information.

The slow or long latency auditory evoked potentials are considered exogenous, referring to the characteristic of the response being related more to extrinsic or stimulus factors. The major components, in the long latency auditory evoked potential, include a positive component at about 60 msec, a negative component at about 100 msec and a positive component at about 160 msec.

The choice for recording SVRs is motivated by some interesting factors: the frequency specificity of the evoked response, the possibility of reaching higher stimulation intensities, and the not strongly disturbing effects due to the electrical artifacts which are very low from hearing aids and moderate from cochlear implants. The drawbacks consist in the high sensitivity of the response to the patient cortical maturation, and general conditions, including use of medication. These factors often hinder the recording and interpretation of data.

In the present investigation, the latencies of N1 and P2 SVR peaks were studied in order to establish whether cochlear implantation contributes to a more complete maturation of the auditory pathways.

A second issue consisted in evaluating the restoration of hearing provided by the cochlear implantation. To achieve this goal, cortical response thresholds and subjective free field tone audiometry responses, before surgery with hearing aids, were compared with those three and twelve months after implant switch on.

## Materials and methods

A series of 45 patients with clearly identified SVRs, evoked by acoustic stimulation, were selected from a group of 150 implantees. All patients underwent oralist rehabilitation before cochlear implantation. Patients were divided into 5 homogeneous groups according to their chronological age, age at onset of deafness, and age at implantation (Table I).

SVRs were recorded, in each subject, before cochlear implant surgery (using hearing aid amplification) and during scheduled sessions at the 3<sup>rd</sup> and 12<sup>th</sup> month after implant activation. SVRs were evoked and recorded using the Amplaid MK12 system for evoked potentials. Amplaid MK12 system standard headphones (TDH39) were acoustically coupled with the microphone of the hearing aid, lengthening the tube of the earmold during the SVR recording session performed before implantation, and directly to the microphone of the speech processor during the two recording sessions after implant activation. The electrode placement was made according to the International 10-20 Standard. A needle electrode was used for the vertex (Cz) as active derivation, surface gold electrode as reference (A1/A2) ipsilaterally to the side of stimulation and the ground electrode at Fpz. SVRs were evoked in response to tone bursts at 500 and 2000 Hz, with intensity decreasing in 10 dB steps from 120 to 60 dB HL at 2000 Hz and from 110 to 60 at 500 Hz. The stimulation rate was 1/sec. Responses were analogue bandpass filtered 1-20 Hz. The recording amplitude was 25µV/div. The morphology and the latencies of the major SVR compo-

Table 1. Group characteristics.

Group	Male	Female	Age at onset of deafness	Notes	Age (mean $\pm$ SD) at implantation (min-max)	Nucleus 22	Type of cochlear implant Nucleus 24	MXM
A	10	4	Prelingual total deafness	Implanted before school age	3.76 $\pm$ 1.08 (2.27-5.79)	9	5	
B	4	1	Prelingual total deafness	Implanted during school age	7.03 $\pm$ 0.81 (6.14 - 8.14)	1	4	
C	3	3	Profound congenital or prelingual deafness	Received hearing amplification before cochlear implantation	8.66 $\pm$ 1.75 (6.53-11.16)	6		
D	2	7	Profound prelingual deafness	Implanted in adult age and not receiving hearing amplification	25.39 $\pm$ 14.14 (12.11-58.37)		8	1
E	4	7	Profound acquired deafness	Implanted in adult age	51.47 $\pm$ 17.24 (21.4-70.45)	3	4	4

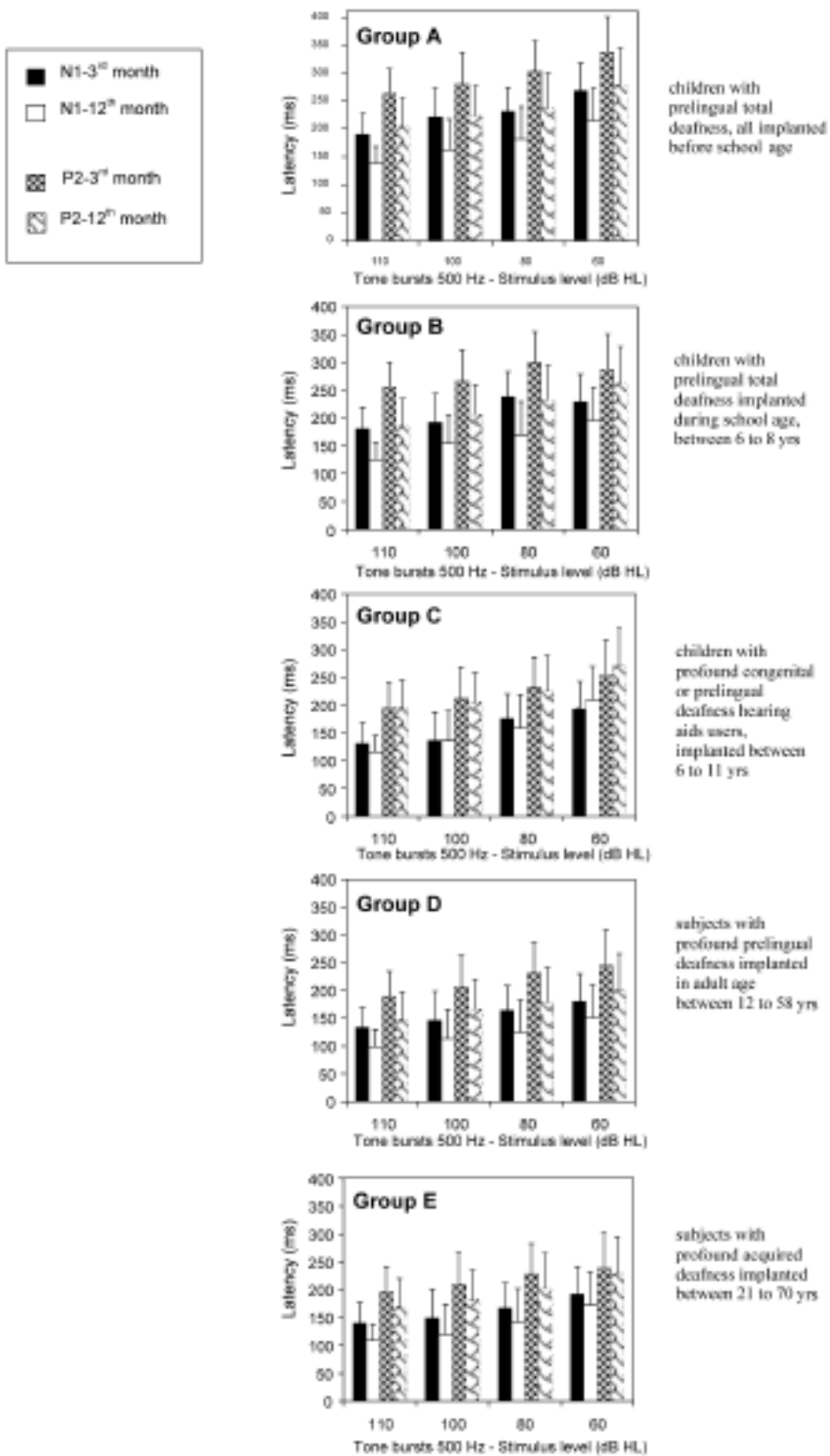


Fig. 1. N1 and P2 latencies over time at 3<sup>rd</sup> and 12<sup>th</sup> month from implant activation as a function of stimulus level (dB HL) for the five groups. SVR were evoked by tone bursts at 500 Hz.

nents, i.e., P60 (P1), N100 (N1), and P160 (P2), were evaluated by visual inspection of the recordings. Assuming that, unlike the early responses, late responses do not show graded responses in relation to the physical dimension of the stimulus, we considered the minimum stimulation level at which the three peaks were clearly recorded as the threshold of the response.

In addition to SVRs, subjective free field tone audiometry responses (PTA) were performed for each subject before surgery (using hearing aid amplification), and 3 and 12 months after implant switch on. For each recording session (i.e., pre-surgery, and at the 3<sup>rd</sup> and 12<sup>th</sup> month after implant activation) and both tested frequencies, thresholds obtained by PTA were compared to those obtained through SVRs. Differences in N1 and P2 latencies, SVR thresholds, and PTA thresholds between groups and recording sessions were tested using the analysis of variance (ANOVA) test. Values of  $p < 0.05$  were considered as statistically significant.

## Results

The latencies of N1 and P2, for the five groups, as a function of the stimulus intensity (dB HL) are shown in Figures 1 and 2, for SVRs evoked at 500 Hz and 2000 Hz, respectively; latencies were recorded at the 3<sup>rd</sup> and 12<sup>th</sup> month after implant activation.

Analyzing the data in Figures 1 and 2, a decrease in latency from the 3<sup>rd</sup> to the 12<sup>th</sup> month, both for N1 and P2, is observed in all groups and at all intensities. As expected, latency increased as the stimulus level decreased, in all groups and all recording sessions. A 2 (recording session)  $\times$  4 (stimulus level) ANOVA was performed on N1 and P2 latencies at 500 Hz (Fig. 1). In Groups A, B, D, and E, N1 and P2 latencies at the 12<sup>th</sup> month after activation were significantly different from those at the 3<sup>rd</sup> month ( $p < 0.00001$ ) and varied across stimulus levels ( $p < 0.0001$ ). In Group C, no significant differences were found in N1 and P2 latencies between the two recording sessions ( $p = 0.7625$ ), whereas significant differences were found across stimulus levels ( $p < 0.02$ ). Likewise, a 2 (recording session)  $\times$  4 (stimulus level) ANOVA was performed on N1 and P2 latencies at 2000 Hz (Fig. 2). In Groups A, B, D, and E, N1 and P2 latencies at the 12<sup>th</sup> month after activation were significantly different from those at the 3<sup>rd</sup> month ( $p < 0.00001$ ) and varied across stimulus levels ( $p < 0.0058$ ). In Group C, no significant differences were found either in N1 or P2 latencies between the two recording sessions ( $p > 0.1$ ), whereas significant differences were found across stimulus levels ( $p < 0.01$ ).

The trend of shorter latencies at the 12<sup>th</sup> month is clearly visible in Figure 3 where latencies at the 3<sup>rd</sup>

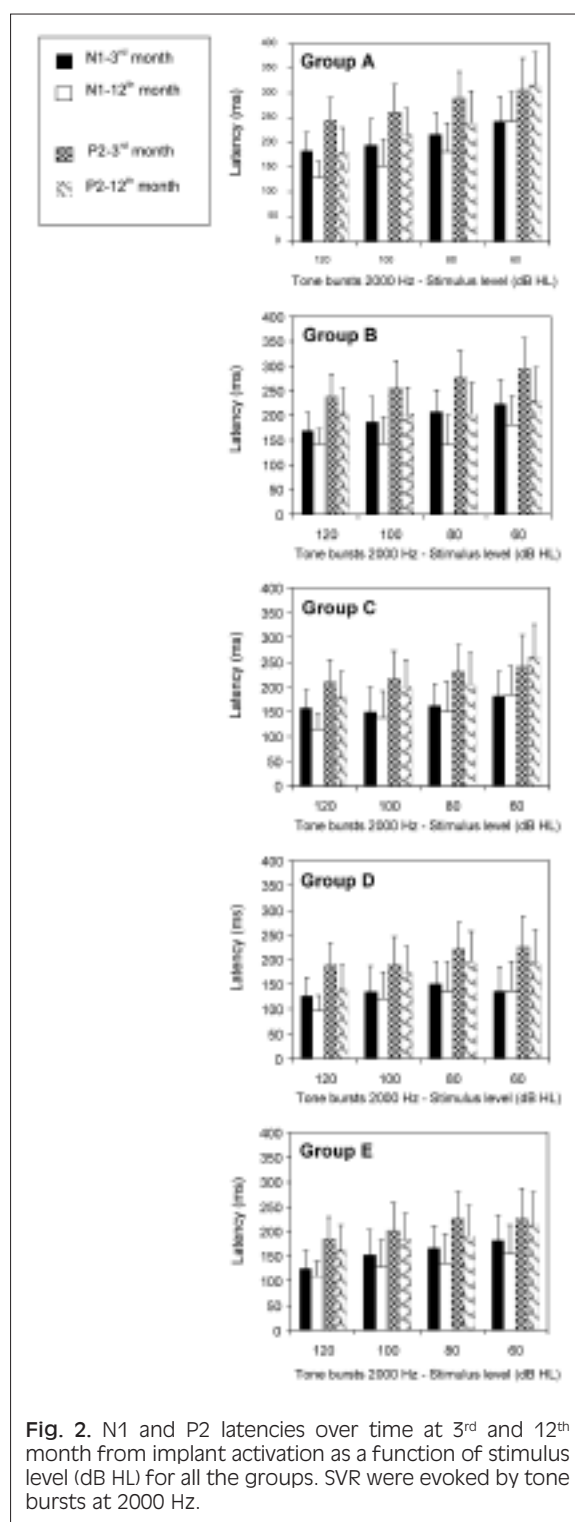


Fig. 2. N1 and P2 latencies over time at 3<sup>rd</sup> and 12<sup>th</sup> month from implant activation as a function of stimulus level (dB HL) for all the groups. SVR were evoked by tone bursts at 2000 Hz.

and 12<sup>th</sup> month are displayed at a fixed stimulation level of 100 dB HL in N1 and P2 at 500 Hz (Figs. 3a and 3b, respectively) and N1 and P2 at 2000 Hz

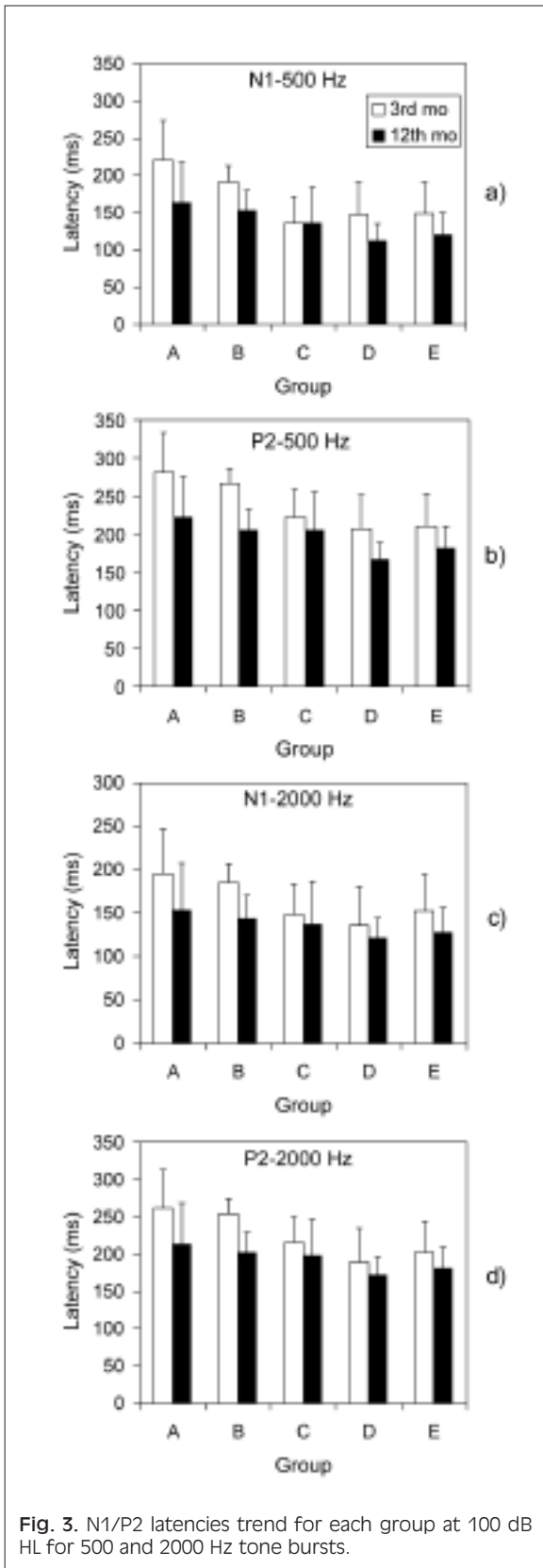


Fig. 3. N1/P2 latencies trend for each group at 100 dB HL for 500 and 2000 Hz tone bursts.

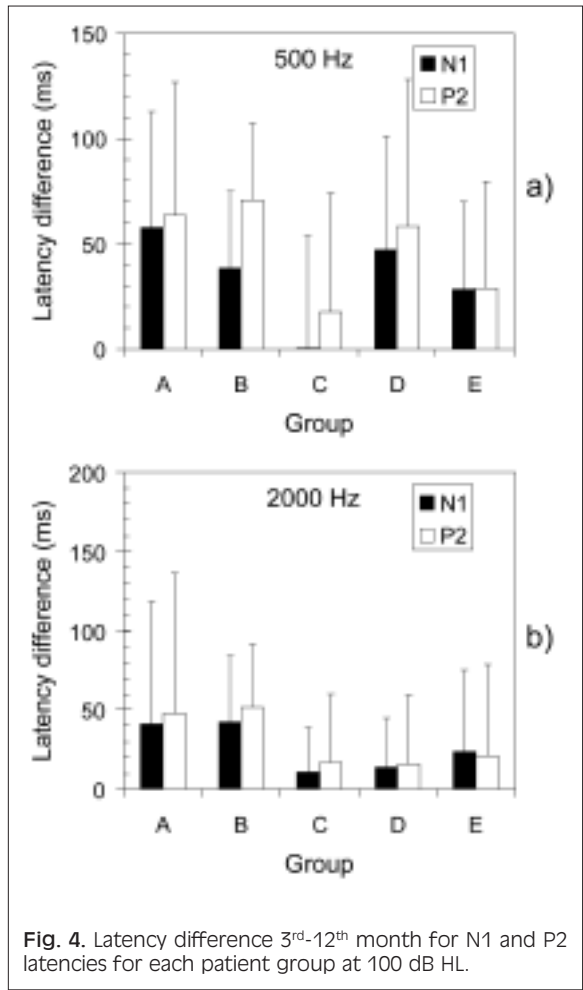


Fig. 4. Latency difference 3<sup>rd</sup>-12<sup>th</sup> month for N1 and P2 latencies for each patient group at 100 dB HL.

(Figs. 3c, 3d), in all groups. A 2 (recording session) x 5 (group) ANOVA was performed on N1 latencies at 500 Hz. Latencies of N1 peaks evoked by 500 Hz tone bursts at the 12<sup>th</sup> month after activation were significantly different from those at the 3<sup>rd</sup> month ( $p = 0.0014$ ); latency also varied across groups ( $p < 0.00001$ ). A 2 (recording session) x 5 (group) ANOVA was repeated separately for P2 latencies at 500 Hz and for N1 and P2 latencies at 2000 Hz. Like the N1 latencies at 500 Hz, also latencies of P2 at 500 Hz, N1 and P2 at 2000 Hz, at the 12<sup>th</sup> month after activation, were significantly different from those at the 3<sup>rd</sup> month ( $p < 0.005$ ). In all cases, latency differed significantly between groups ( $p < 0.0015$ ). Specifically, for SVR recorded at the 3<sup>rd</sup> month, N1 and P2 latencies at 500 and 2000 Hz in Groups A and B were significantly different from those in Groups C, D, E (Tukey's post-hoc multi-comparison test,  $p < 0.05$ ), whereas no significant differences were found between latencies in Groups A and B and between Groups C, D, E. For SVR recorded at the 12<sup>th</sup> month,



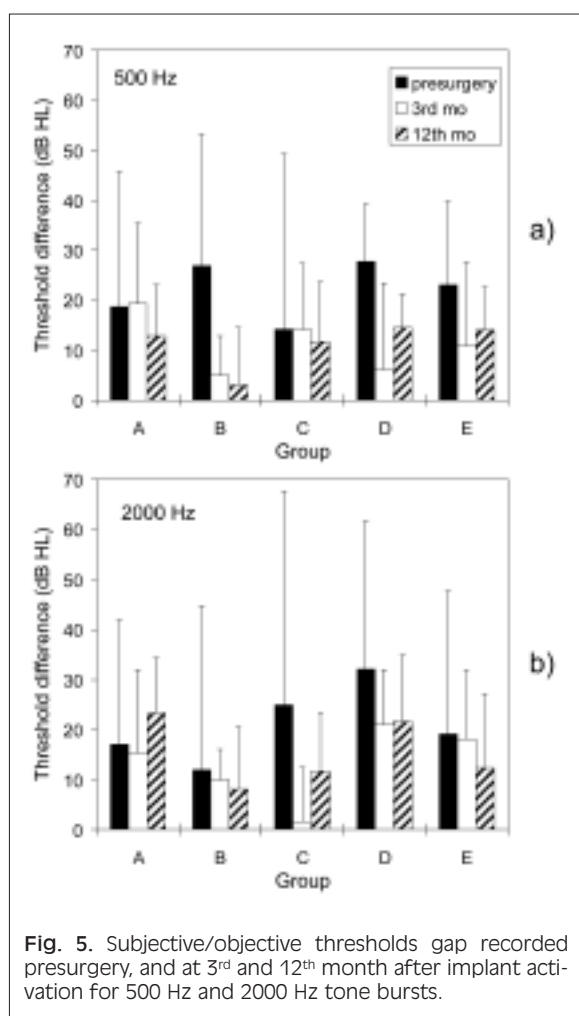


Fig. 5. Subjective/objective thresholds gap recorded presurgery, and at 3<sup>rd</sup> and 12<sup>th</sup> month after implant activation for 500 Hz and 2000 Hz tone bursts.

N1 and P2 latencies at 500 and 2000 Hz in Groups A, B, and C were significantly different from those in Groups D and E (Tukey's post-hoc multi-comparison test,  $p < 0.05$ ), whereas no significant differences were found between latencies in Groups A, B and C and between Groups D and E.

Results (Fig. 4) show the differences between N1 and P2 latencies recorded at the 3<sup>rd</sup> month and those recorded at the 12<sup>th</sup> month, for SVRs evoked by 500 Hz (Fig. 4a) and 2000 Hz (Fig. 4b) tone bursts. Clearly evident is the significant decrease in the latencies of SVR marker peaks especially for children with pre-lingual total deafness, implanted before school age (Group A) or implanted during school age (Group B) and in adult patients with profound pre-lingual deafness implanted in adult age (Group D), revealed only at 500 Hz. For Groups A and B, the latencies shortening repeats for both peaks and both frequencies investigated showed a minimum shift of 38 milliseconds, while in the other groups the gap are

less conspicuous and consistent.

As far as concerns our hypothesis of restoration of hearing provided by cochlear implants, some outstanding results have been obtained. The gap between subjective thresholds, measured by free field PTA and objective SVR thresholds from acoustic stimulus, was analyzed at three different stages: with hearing aids; 3 months after implant activation; 12 months after implant activation.

The results of these comparisons are shown in Figure 5 for subjective/objective thresholds at 500 Hz (Fig. 5a) and 2000 Hz (Fig. 5b). These results highlight the reduction of the subjective/objective threshold gap measured with cochlear implant in comparison to those obtained in the pre-surgery stage with hearing aids, especially for measurements at the 12<sup>th</sup> month after implant activation. What is most remarkable is that this trend has been found in each group. A 3 (recording session)  $\times$  5 (group) ANOVA revealed that subjective/objective threshold gaps measured at the 12<sup>th</sup> month after implant activation were significantly different from those measured in the pre-surgery stage ( $p < 0.01$ ) for both frequencies tested.

## Discussion

Acoustic auditory cortical responses are not widely used as a clinical test, especially in young children, due to the difficulty in recording. Indeed, the use of tone-bursts through hearing aids or cochlear implants, as in SVRs, offers the possibility to evaluate many more frequencies and louder intensities than with other tests based on a click as stimulus. In our experience, we observed that hearing aid users do not show variations in electrophysiological responses over time, whereas this occurs in cochlear implanted patients. These variations likely depend on a natural activation of the auditory pathway over time<sup>11</sup>, especially in young children with pre-lingual deafness and implanted in preschool age.

In our study, the latency of N1 and P2 peaks of SVRs was found to decrease from the 3<sup>rd</sup> to the 12<sup>th</sup> month after cochlear implant activation for all stimulus levels, both tested frequencies (but more evident at 500 Hz than at 2000 Hz), and all congenital groups, with the exception of Group C (i.e., children with profound congenital or pre-lingual deafness who received some benefits from hearing amplification before cochlear implantation). Specifically, in Group C, no changes were found for N1 latencies at 100 dB HL for SVRs evoked by 500 Hz tone bursts.

The decrease in N1 and P2 latency at the 12<sup>th</sup> month is not the same for all groups but seems to be influenced by age and the auditory memory. Indeed, comparing results from Groups B and C, which consisted of children with the same chronological age, type of

deafness, and age at implantation but different use of amplification before surgery (in fact, subjects in Group C were better hearing aid users as they had better residual hearing), it was observed that latencies at the 3<sup>rd</sup> month in Group C were shorter than in Group B. Instead, at the 12<sup>th</sup> month after implant activation, both groups showed the same latency. As a consequence, the latency difference between 3<sup>rd</sup>- and 12<sup>th</sup>-month recordings was greater for Group B than for Group C. Also for subjects implanted in adult age (i.e., Groups D and E) evaluation of the N1 and P2 latencies exhibited the auditory memory influence, since the latency variations in Group E (acquired deafness) were lower than for Group D (congenital deafness). This difference in latencies was more evident at 500 Hz than at 2000 Hz in Group D (congenital) compared to Group E (acquired).

As a general trend, the decrease of N1 and P2 latency was markedly greater for younger subjects (i.e., Groups A and B) than for older subjects (i.e., Groups D and E), confirming the role of neural plasticity. The present results are in agreement with previous studies on the development of cortical auditory evoked potentials after cochlear implantation. For example, Sharma et al.<sup>12,13</sup> observed that congenitally deaf children who were implanted before 3.5 yrs exhibited age-appropriated latency responses within 6 months of implant activation. Furthermore, the variation in cortical response latencies appeared earlier than in their normal-hearing age-matched peers. On the contrary, children who had experienced a period of auditory deprivation longer than 7 yrs had abnormal latencies. This was a strong indication that in

the absence of normal stimulation, there is a critical age during which the human central auditory system is maximally plastic. Moreover, according to Ponton et al.<sup>14</sup> and Eggermont and Ponton<sup>15</sup>, children with profound bilateral hearing loss and fitted with a cochlear implant exhibited an exponential decay of P1 latencies the same as normal-hearing children, revealing a progressive maturation of cortical auditory function. However, in implanted children, the overall maturation is delayed by the period of auditory deprivation prior to implantation. This suggested that the auditory system cannot completely mature without stimulation and that electrical stimulation of the auditory nerve provided by cochlear implants contributes to resuming an almost normal time course of maturation for at least some aspects of cortical auditory function. In conclusion, in the present investigation, the decrease of N1 and P2 latency was found to be more evident in the Groups without hearing memory (A, B and D) than in Groups C and E, thus confirming the immaturity of auditory cortical function in congenital deaf subjects without any hearing experience, and the role of electrical stimulation in restoring electrophysiological normality. It is impossible to record these effects, with acoustic amplification, in profoundly deaf individuals and this concept is confirmed by the objective functional gain with cochlear implant that is always better than results with a hearing aid. In other words, cochlear implant appears to provide not only normal maturation, but even hearing restoration, demonstrated by the sharp reduction in the gap between the tone free field audiometry threshold and the SVR response threshold.

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