P3 Cognitive Potential in Cochlear Implant Users

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Abstract

Introduction The P3 cognitive evoked potential is recorded when a subject correctly identifies, evaluates and processes two different auditory stimuli.

Objective to evaluate the latency and amplitude of the P3 evoked potential in 26 cochlear implant users with post-lingual deafness with good or poor speech recognition scores as compared with normal hearing subjects matched for age and educational level.

Methods In this prospective cohort study, auditory cortical responses were recorded from 26 post-lingual deaf adult cochlear implant users (19 with good and 7 with poor speech recognition scores) and 26 control subjects.

Results There was a significant difference in the P3 latency between cochlear implant users with poor speech recognition scores (G-) and their control group (CG) (p = 0.04), and between G- and cochlear implant users with good speech discrimination (G+) (p = 0.01). We found no significant difference in the P3 latency between the CG and G+. In this study, all G- patients had deafness due to meningitis, which suggests that higher auditory function was impaired too.

Conclusion Post-lingual deaf adult cochlear implant users in the G- group had prolonged P3 latencies as compared with the CG and the cochlear implant users in the G+ group. The amplitudes were similar between patients and controls. All G- subjects were deaf due to meningitis. These findings suggest that meningitis may have deleterious effects not only on the peripheral auditory system but on the central auditory processing as well.

Introduction

Cognitive and linguistic skills, as well as social and emotional behavior are influenced by hearing loss. According to the Brazilian Institute of Geography and Statistics (IBGE, in the Portuguese acronym), 344,200 people have profound hearing loss and may benefit from cochlear implantation. Even using careful selection criteria, not all cochlear implant (CI) recipients show the expected results of good speech and language skills. Results from CIs performed in 2002 at an institution in São Paulo, Brazil, indicate that among 10 implantees, 7 were able to have phone conversations. Sensory deprivation, cause of deafness, incomplete electrode insertion and even psychosocial and personality factors have been related to poor outcome in CI recipients.
All CI recipients go through postoperative speech tests that rely on subjective data. Objective testing of central nervous system (CNS) speech processing is not a routine procedure in postoperative CI protocols. The cognitive P3 potential is a powerful tool to evaluate auditory discrimination abilities and difficulties among CI recipients because it gives useful information about speech recognition, auditory maturation and functional integrity of the central auditory system as well as attention and memory status. Therefore, the plasticity of the central auditory system may be evaluated by the P3 cognitive potential in all CI recipients who understand the test conditions.\(^6,7\)

The P3 event-related late potential is recorded as a positive peak following the late potentials N1, P2 and N2 with a peak latency of ~300 to 350 milliseconds (ms) in young normal hearing subjects\(^6-10\) after presentation of two contrasting auditory stimuli (oddball paradigm). The rare or target stimulus is presented with frequency, intensity or variety of speech contrasts and must be identified by the proband. The subject must recognize, categorize and process the auditory stimulus to produce the cognitive potential. The latency depends on the age, attention and memory status of the subject, but no significant differences between genders have been observed.\(^8\) The P3 arises primarily from areas of the temporal lobe and hippocampus.\(^11,12\)

The aim of this study was to evaluate the latency and amplitude of the P3 potential in adult CI recipients with post-lingual deafness with poor and good speech recognition scores, as compared with normal hearing subjects, matched for age and educational level.

**Method**

One hundred and eleven adults with post-lingual deafness were implanted at the Hospital das Clínicas, Universidade de São Paulo, School of Medicine, Cochlear Implant Center between April 1999 and January 2006. The study was performed according to the guidelines of the Ethics Committee of the Universidade de São Paulo and was approved under the protocol number 1059/07.

The inclusion criteria were: age ≥18 years on the day of implantation, complete electrode insertion, post-lingual deafness, device activation of at least 3 months, pure tone thresholds of 35 dB HL or better at frequencies between 500 and 8,000 Hz, no hearing or tinnitus complaints and no history of otological diseases. Among the 26 controls, there were 15 females (mean age: 44.69 years, from 23–68 years, SD: 14.75). The exclusion criteria were the same as for the study group. All the participants were informed about the study and signed the informed consent form.

**Procedures**

Before testing, every subject completed a questionnaire about his or her medical history and had a complete ear, nose and throat examination. Pure tone thresholds and speech recognition scores were obtained from all the subjects.

The cortical auditory evoked responses were recorded with an Amplaid MK 12 equipment (Amplifon, Milan, Italy) in a sound treated, light attenuated room. The subjects were seated comfortably in a reclining chair. The stimulus was delivered by a loudspeaker placed at an angle of 45° on the side of the implant, at a distance of 4.26 feet. For the control subjects, the loudspeaker was placed at an angle of 45° on the right side. The loudspeaker was calibrated to deliver 70 dB HL tone bursts, generated by the Amplaid MK 12 equipment. All the subjects were asked to keep their eyes closed, to point out with the left hand index finger when they heard the rare stimulus and to count silently all the rare stimuli of each run.

Before testing, we explained the test session and introduced the stimuli to all the subjects, encouraging them to be attentive during the whole session and to count only the rare stimuli. Cochlear implant recipients were asked to use their usual device setting.

The subjects had to discriminate between two sounds with different frequencies. In the first test condition, the rare (target) stimulus was a 2,000 Hz tone burst, and the non-target (frequent) stimulus a 1,000 Hz tone burst. In the second condition, the target was a low-frequency tone burst at 1,000 Hz, and the non-target a 1,500 Hz tone burst. This condition is thought to be more difficult. At every test condition, 100 stimuli were presented at the rate of 0.5 per second, with 20 rare (target) stimuli randomly distributed among 80 frequent (non-target) ones, and every condition was run at least twice. The recordings were automatically suspended every time eye movements or other electrical sweeps of great amplitude (rejection level, 100 μV) interfered with the responses, and then a new run was started. Each test session took about 40 minutes.
For evaluation, we selected the best run at each test condition for each subject (waves with highest amplitudes). Only replicable responses were accepted.

The positive silver/silver chloride cup electrode was placed at Cz with reference at M1 or M2 and ground at Fpz. The reference electrode was placed on the non-implanted mastoid in CI recipients and on the right side in the case of controls. Evoked potentials for frequent and rare stimuli were averaged simultaneously, but separately.

The event-related potential P3 was identified at the rare stimulus recording from 230 to 750 ms after stimulus onset. The N1 potential was measured at 50 to 150 ms after stimulus onset and the P2 at 125 to 230 ms.

**Data Analysis**

Median latencies of N1, P2 and P3 of CI recipients were compared with those of controls (Wilcoxon non-parametric test). Cochlear implant recipients were further subdivided into two groups: G+ and G-. The results were considered significant if \( p < 0.05 \).

**Results**

The etiology and duration of deafness, age at implantation, duration of device activation and speech recognition scores in open-set sentences of G+ and G- are shown in Table 1.

Three control subjects were excluded because their recordings were contaminated by electrical artifacts and despite of filtering and subtraction, no reliable waves could be identified. One subject of G- showed inconsistent responses in both test conditions and was excluded for this reason. The remaining six poor performers completed successfully the test conditions with the exception of one subject, who was not able to discriminate between 1,000 and 1,500 Hz, the second test condition, but nonetheless remained in the G- group.

The median latencies of N1, P2 and P3 of G- (all were deaf due to meningitis) and their controls are shown in Table 2. The median P3 latencies were significantly prolonged among poor performers in both test conditions as compared with their controls (1,000/2,000 Hz \( p = 0.028 \), 1,500/1,000 Hz \( p = 0.042 \)).

All 19 subjects in the G+ group completed both test conditions. The results of median N1, P2 and P3 latencies for G+ and controls are presented in Table 3. There was no significant difference in median P3 latency between G+ and controls \( p > 0.05 \). On the other hand, median N1 and P2 latencies were significantly longer among G+ as compared with their controls in both test conditions (N1: \( p = 0.02 \) and \( p < 0.001 \), P2: \( p = 0.028 \) and \( p = 0.038 \)).

When we compared the CI recipients among themselves, G+ outperformed G- with shorter median P3 latencies in both test conditions \( p = 0.009 \) and \( p = 0.005 \) (Table 4).

The median amplitude of P3 showed no significant difference in either test condition between CI recipients and controls, or between G+ and G-.

The N1, P2 and P3 latencies of each subject are shown in Appendices 1 to 3.

### Table 1 Clinical data of 16 CI users with post-lingual deafness

|                         | G- (N = 7) | G+ (N = 9) |
|-------------------------|------------|------------|
| % of speech recognition in open-set sentences: Mean (Min–Max) | 8.6 (0–60) | 97.7 (80–100) |
| Male: N (%)             | 4 (66.7%)  | 9 (56.3%)  |
| Mean Age at CI surgery (years) | 38.8 (±10.1) | 42.8 (±13.1) |
| Duration of hearing loss (years): Median (Min–Max) | 18.8 (1–36) | 12.8 (1–43) |
| Cochlear implant activation (years): Median (percentile 25–75) | 2.7 (1.5–4.2) | 1.5 (0.8–3.3) |
| Nucleus 22 processing strategy: Speak | 4 | 10 |
| Nucleus 24 processing strategy: ACE | 3 | 8 |
| MED-EL Speech processing strategy: CIS | 0 | 1 |
| Etiology of deafness    |            |            |
| Meningitis              | 7          | 0          |
| Head trauma             | 0          | 3          |
| Otosclerosis            | 0          | 3          |
| Otoxicity               | 0          | 2          |
| Chronic otitis media    | 0          | 1          |
| Viral infection         | 0          | 1          |
| Unknown                 | 0          | 9          |

Abbreviations: %, percentage; ACE, Advanced Combination Encoder; CI, cochlear implant; CIS, continuous interleaved sampling; G-, cochlear implant users with poor hearing performance; G+, cochlear implant users with good hearing performance; Min-Max, minimum – maximum; N, sample size.

\( ^* p < 0.001 \).
Discussion

All CI recipients with poor speech recognition scores (G-) presented longer P3 latencies when compared with good performers (G+) and controls (CG), as shown in previous studies. Whereas G+ subjects scored mostly between 90 and 100% in open-set sentences (mean: 97.7%), G- subjects had a mean score of 8.6% of speech recognition with a wide distribution from 0 to 60%. Thus, their performance was significantly poorer. The cause of deafness was meningitis in all, whereas no G+ subject had this etiology. Remaining auditory neuron population is thought to be related to CI

Table 2 N1, P2 and P3 latencies of G- and CG

|       | G-          | CG          | p†     |
|-------|-------------|-------------|--------|
|       | Latency (ms)| Latency (ms)|        |
| 1,000/2,000 Hz |             |             |        |
| N1 (n = 4)   | 131 (119–224) | 132 (113–140) | 0.72   |
| P2 (n = 6)   | 266 (180–305) | 189 (174–255) | 0.17   |
| P3 (n = 6)   | 402 (387–449) | 353 (293–369) | 0.028† |
| 1,500/1,000 Hz |             |             |        |
| N1 (n = 3)   | 117 (114–228) | 135 (123–138) | 1      |
| P2 (n = 5)   | 288 (204–302) | 195 (180–227) | 0.14   |
| P3 (n = 5)   | 453 (431–482) | 363 (318–384) | 0.042† |

Median (percentile 25–75). † Wilcoxon rank sum test. *significant p value.

Table 3 N1, P2 and P3 latencies of G+ and CG

|       | G+          | CG          | p†     |
|-------|-------------|-------------|--------|
|       | Latencies (ms)| Latencies (ms)|        |
| 1,000/2,000 Hz |             |             |        |
| N1 (n = 15)  | 150 (138–174) | 126 (108–132) | 0.02*  |
| P2 (n = 16)  | 230 (205–249) | 203 (188–212) | 0.028* |
| P3 (n = 19)  | 360 (330–387) | 360 (336–387) | 0.67   |
| 1,500/1,000 Hz |             |             |        |
| N1 (n = 18)  | 146 (132–173) | 123 (108–133) | < 0.001*|
| P2 (n = 19)  | 228 (201–246) | 201 (195–213) | 0.038* |
| P3 (n = 19)  | 354 (333–396) | 384 (363–399) | 0.41   |

Median (percentile 25–75). † Wilcoxon rank sum test. *significant p value.

Table 4 N1, P2 and P3 latencies of G- and G+

|       | G-          | G+          | p†     |
|-------|-------------|-------------|--------|
|       | Latencies (ms)| Latencies (ms)|        |
| 1,000/2,000 Hz |             |             |        |
| N1 (n = 3)   | 123 (117–138) | 132 (123–138) | 0.32   |
| P2 (n = 4)   | 219 (174–271) | 170 (143–200) | 0.14   |
| P3 (n = 6)   | 402 (387–449) | 321 (300–340) | 0.027* |
| 1,500/1,000 Hz |             |             |        |
| N1 (n = 3)   | 117 (114–228) | 171 (123–183) | 0.59   |
| P2 (n = 5)   | 288 (204–302) | 204 (200–242) | 0.1    |
| P3 (n = 5)   | 453 (431–482) | 354 (335–386) | 0.043* |

Median (percentile 25–75). † Wilcoxon rank sum test. *significant p value.
performance. Most studies have found the cochlea to be the major site of hearing loss after bacterial meningitis, with support from histological studies due to hair cell destruction and decreased number of spiral ganglion cells. But audiological and neuropsychological assessment of meningitis survivors with valuable hearing suggests that lesions of the central auditory system may also be an important cause of hearing dysfunction, including abnormalities of auditory memory and poor short-term memory, which could be responsible for longer P3 latencies among our meningitis patients. These alterations may be subtle, not causing psychological or social problems, so they may be overlooked. The P3 test is a valuable tool to evaluate cognitive function and gives us an insight on how the subject processes auditory information.

The task to detect differences between tonal stimuli is rather simple and may be accomplished easily by CI recipients if the tones are detected by different electrodes. One subject amongst the poor performers did not discriminate between 1,000 and 1,500 Hz, as both frequencies were encoded by the same electrode. In this case the test condition could not be performed. In all other CI recipients P3 was recorded, so the individual speech processor settings or coding strategies did not interfere in the results, differing from Mühler et al.

The P3 potential elicited by this simple task correlated well with speech recognition scores, indicating, like other studies, that it reflects real cognitive activity, and is not just a function of perceived stimulus differences. Therefore, it is not surprising that post-meningitis subjects had a poorer outcome than those who became deaf due to other causes, suggesting discrete CNS dysfunction.

It is interesting, that three patients, deaf due to head trauma, also performed better than the post-meningitis deaf subjects. One possible explanation for that is that central bacterial infection is more devastating, or central nervous plasticity may be more effective to overcome traumatic injury. Recently, it was shown that postural recovery was reduced in CI recipients with poor hearing performance as compared with good CI recipients.

The N1–P2 waves indicate that all subjects detected either or both stimuli; in other words, sound had reached the auditory cortex. This finding suggests functional integrity of auditory pathways, including brainstem pathways up to cortical levels. Not sound perception, but auditory processing was affected, which is important for speech discrimination. We do not have an explanation for the longer N1 and P2 latencies among G+ as compared with normal subjects. Similar results were found by Beynon et al., probably an effect of our small sample size. The amplitudes of all waves were similar among CI recipients and controls, like in other studies.

Auditory deprivation is thought to be a cause of poor speech discrimination and prolonged P3 latencies among CI users. Although the mean duration of deafness was slightly longer among G- than G+, this difference was not significant. So it could not have accounted for prolonged P3 latencies among this group, contrasting with the findings of Blamey et al. Duration of deafness does not mean auditory deprivation, since all CI candidates at our institution use hearing aids prior to surgery and receive auditory rehabilitation. Furthermore, post-lingual individuals must have preserved speech abilities to be suitable for implantation.

The subjects in G+ had similar P3 latencies as normal hearing subjects, even after long duration of deafness, in agreement with the findings of Kubo et al. These results suggest that in deaf adults, auditory pathways may remain functional over a long period of time and plasticity of the central auditory system is preserved, even when hearing aids do not provide optimal auditory stimulation.

We carefully selected the control subjects, mainly among relatives or friends of the CI recipients, with similar social conditions and educational level to avoid other cognitive or linguistic skills to interfere with P3 results.

In our study, we found that the main variable for poor speech performance and prolonged P3 latencies of CI users was meningitis as cause of deafness. There were no subjects with auditory neuropathy spectrum disorder in our study. As P3 and speech perception scores measure auditory processing and cognitive abilities, these may be impaired in deaf meningitis survivors, even without evident clinical symptoms. We suggest including more specific psychological test batteries in preoperative evaluation of post-meningitis CI candidates to better estimate their performance after surgery. This could prevent them from having unrealistic expectations on the device. The P3 test has proven to be a useful test to evaluate the CI recipient who did not reach the expected speech performance and could be used, among other tests, to reconsider if this patient may benefit from bilateral CI or even a brainstem implant.

**Conclusion**

In this study, post-lingual deaf adult CI users in the G+ group had prolonged P3 latencies as compared with normal CG subjects and CI users in the G+ group. Amplitudes were similar among patients and controls. All CI users with poor recognition scores were deaf due to meningitis. These findings suggest that meningitis may have deleterious effects not only on the peripheral auditory system but on central auditory processing as well.

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Appendix 1 N1, P2, P3 latencies of G+ in both tests

| Patient | AGE | Latencies (ms) 1,000/2,000 | Latencies (ms) 1,500/1,000 |
|---------|-----|-----------------------------|-----------------------------|
|         |     | N1  P2  P3                  | N1  P2  P3                  |
| AJS     | 60  | 138 240 378                 | 135 237 378                 |
| AMFC    | 38  | 147 237 360                 | 120 249 324                 |
| AEN     | 45  | 150 207 330                 | 141 237 339                 |
| CLNL    | 53  | 123 222 450                 | 114 228 474                 |
| EGS     | 30  | 123 159 333                 | 150 201 342                 |
| EPC     | 50  | 195 222 327                 | 138 186 330                 |
| FJC     | 35  | 165 204 357                 | 132 192 378                 |
| FRCJ    | 39  | NA  NA  282                 | 183 246 396                 |
| GM      | 39  | NA  NA  360                 | 132 195 375                 |
| GRS     | 22  | 138 189 312                 | 171 204 330                 |
| JE      | 60  | 159 264 381                 | 132 237 348                 |
| LCM     | 47  | 132 180 306                 | 123 204 354                 |
| MHR     | 34  | NA  273 387                 | NA  351 486                 |
| MFF     | 19  | 174 249 405                 | 153 192 306                 |
| MFSA    | 63  | 126 288 423                 | 183 246 450                 |
| MFSP    | 49  | NA  NA  351                 | 180 225 333                 |
| RR      | 60  | 138 246 333                 | 150 252 345                 |
| FFC     | 67  | 177 249 390                 | 165 255 402                 |
| MRHRA   | 63  | 165 219 378                 | 177 228 381                 |

Abbreviation: NA, data not available (no reliable potential).
### Appendix 2 N1, P2, P3 latencies of G- in both tests

| Patient | AGE | N1 1,000/2,000 | P2 1,000/2,000 | P3 1,000/2,000 | N1 1,500/1,000 | P2 1,500/1,000 | P3 1,500/1,000 |
|---------|-----|----------------|----------------|----------------|----------------|----------------|----------------|
| AAS     | 42  | 252            | 312            | 492            | 228            | 297            | 501            |
| JGC     | 25  | 123            | 255            | 405            | NA             | NA             | NA             |
| LAF     | 44  | 177            | 276            | 369            | NA             | 288            | 447            |
| MFCA    | 42  | 117            | 171            | 393            | 117            | 177            | 414            |
| REC     | 36  | NA             | 303            | 435            | NA             | 306            | 453            |
| RMB (*) | 52  | NA             | NA             | NA             | NA             | NA             | NA             |
| VES     | 20  | 138            | 183            | 399            | 114            | 231            | 462            |

Abbreviation: NA, data not available (no reliable potential).

*patient excluded from analysis due to inconsistent responses in both tests.

### Appendix 3 Latencies of the CG in both tests

| Patient | AGE | N1 1,000/2,000 | P2 1,000/2,000 | P3 1,000/2,000 | N1 1,500/1,000 | P2 1,500/1,000 | P3 1,500/1,000 |
|---------|-----|----------------|----------------|----------------|----------------|----------------|----------------|
| AFAS    | 23  | 141            | 249            | 360            | 135            | 204            | 363            |
| NA      | 68  | 120            | 162            | 375            | 114            | 162            | 390            |
| BBS     | 49  | 129            | 213            | 360            | 132            | 195            | 393            |
| DC      | 51  | 132            | 198            | 375            | 117            | 255            | 375            |
| HZE     | 63  | 126            | 201            | 363            | 123            | 291            | 393            |
| IZS     | 42  | 108            | 177            | 300            | 123            | 195            | 378            |
| JSS     | 27  | 129            | 198            | 363            | 141            | 210            | 384            |
| LIJ     | 35  | 132            | 213            | 339            | 123            | 195            | 390            |
| LS      | 30  | 126            | 225            | 333            | 138            | 204            | 357            |
| MA      | 45  | 126            | 213            | 351            | 135            | 225            | 393            |
| MAF     | 61  | 129            | 213            | 390            | 111            | 228            | 369            |
| MAL     | 45  | 96             | 204            | 387            | 108            | 177            | 399            |
| MBC     | 41  | 150            | 273            | 387            | 105            | 165            | 330            |
| MHC     | 26  | 135            | 207            | 351            | 123            | 216            | 345            |
| MEG     | 49  | 126            | 180            | 345            | 126            | 195            | 390            |
| MAC     | 40  | 99             | 207            | 336            | 99             | 270            | 378            |
| NR      | 31  | 96             | 213            | 261            | 114            | 219            | 339            |
| OV      | 47  | 132            | 192            | 297            | 150            | 213            | 423            |
| RNC     | 67  | 117            | 204            | 339            | 168            | 240            | 351            |
| SRS     | 56  | 126            | 186            | 402            | 114            | 210            | 438            |
| IDN     | 65  | 120            | 186            | 351            | 126            | 180            | 345            |
| BR      | 24  | 156            | 195            | 303            | 141            | 204            | 303            |
| TPL     | 24  | 135            | 165            | 273            | 138            | 249            | 306            |