Normative findings of electrically evoked compound action potential measurements using the neural response telemetry of the Nucleus CI24M cochlear implant system

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Abstract: One hundred and forty-seven adult recipients of the Nucleus 24 cochlear implant system, from 13 different European countries, were tested using neural response telemetry to measure the electrically evoked compound action potential (ECAP), according to a standardised postoperative measurement procedure. Recordings were obtained in 96% of these subjects with this standardised procedure. The group results are presented in terms of peak amplitude and latency, slope of the amplitude growth function and ECAP threshold. The effects of aetiological factors and the duration of deafness on the ECAP were also studied. While large intersubject variability and intrasubject variability (across electrodes) were found, results fell within a consistent pattern and a normative range of peak amplitudes and latencies was established. The aetiological factors had little effect on the ECAP characteristics. However, age affected ECAP amplitude and slope of the amplitude growth function significantly; i.e., the amplitude is higher in the lowest age category (15-30 years). Principal component analysis of the ECAP thresholds shows that the thresholds across 5 electrodes can be described by two factors accounting for 92% of the total variance. The two factors represent the overall level of the threshold profiles ('shift') and their slopes across the electrode array ('tilt'). Correlation between these two factors and the same factors describing the T- and C-levels appeared to be moderate, in the range of 0.5-0.6.

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Normative Findings of Electrically Evoked Compound Action Potential Measurements Using the Neural Response Telemetry of the Nucleus CI24M Cochlear Implant System

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Key Words

Cochlear implant · Neural response telemetry · Electrically evoked compound action potential

Abstract

One hundred and forty-seven adult recipients of the Nucleus® 24 cochlear implant system, from 13 different European countries, were tested using neural response telemetry to measure the electrically evoked compound action potential (ECAP), according to a standardised postoperative measurement procedure. Recordings were obtained in 96% of these subjects with this standardised procedure. The group results are presented in terms of peak amplitude and latency, slope of the amplitude growth function and ECAP threshold. The effects of aetiological factors and the duration of deafness on the ECAP were also studied. While large intersubject variability and intrasubject variability (across electrodes) were found, results fell within a consistent pattern and a normative range of peak amplitudes and latencies was established. The aetiological factors had little effect on the ECAP characteristics. However, age affected ECAP amplitude and slope of the amplitude growth function significantly; i.e., the amplitude is higher in the lowest age category (15–30 years). Principal component analysis of the ECAP thresholds shows that the thresholds across 5 electrodes can be described by two factors accounting for 92% of the total variance. The two factors represent the overall level of the threshold profiles ('shift') and their slopes across the electrode array ('tilt'). Correlation between these two factors and the same factors describing the T- and C-levels appeared to be moderate, in the range of 0.5–0.6.

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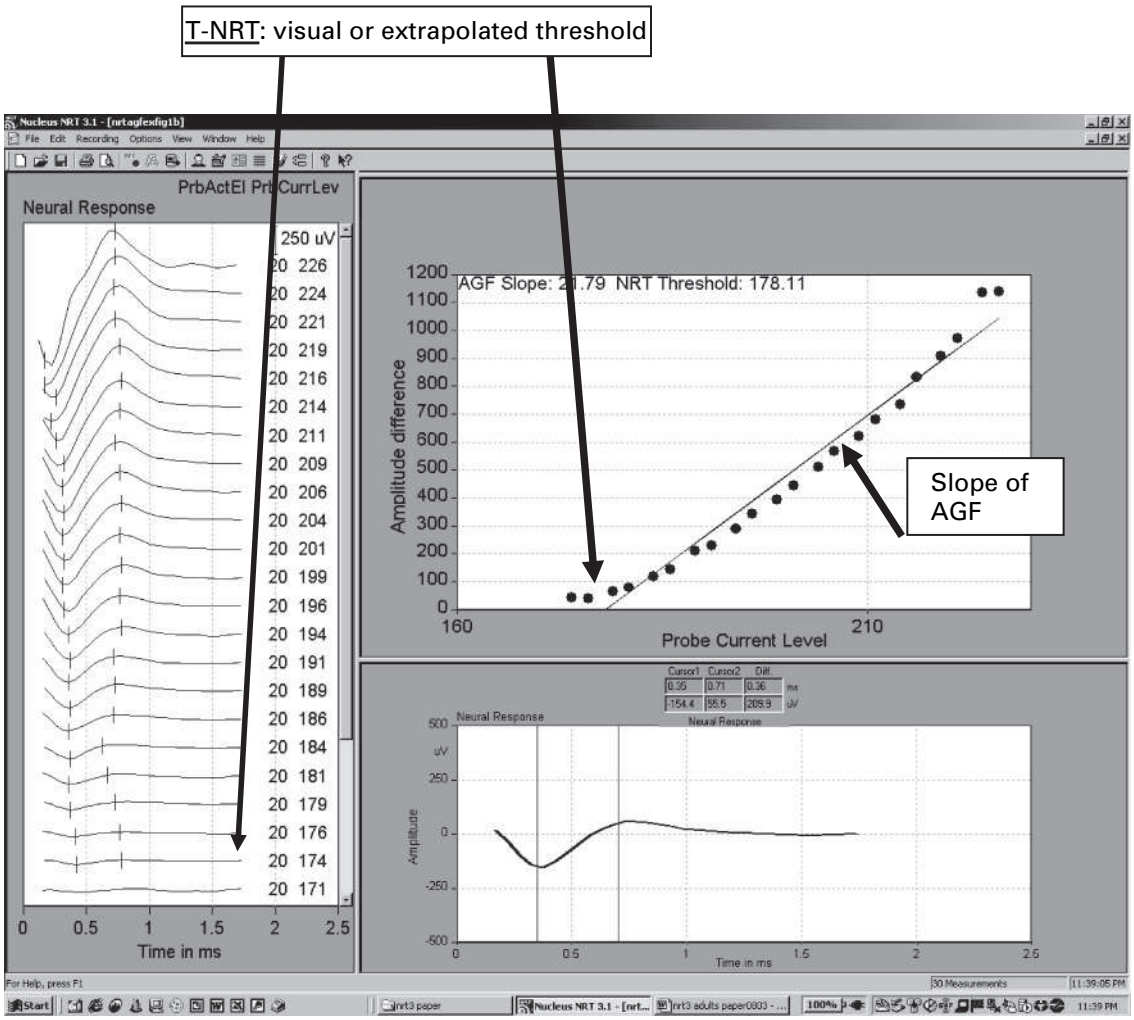


Fig. 1. Example of ECAP waveform, T-NRT, AGF and AGF slope.

Introduction

The electrically evoked compound action potential (ECAP) from the auditory nerve is characterised by a large negative peak (N1) with a very short latency (within a fraction of a millisecond), followed by a positive peak (P1)[1] as described by Killian et al. [1994] and illustrated in figure 1. Neural response telemetry [NRT™, 1999] is a feature of the Nucleus® 24 cochlear implant system combined with the Windows®-based NRT software developed by Dillier and Lai. It enables measurements of the ECAP via bidirectional telemetry using the electrodes of the implant without the need of external electrodes. Abbas et al. [1999] and Dillier et al. [2002] validated a simplified and reliable clinical procedure for ECAP measurements in adults. Several authors [Brown et al., 2000; Thai Van et al., 2001; Kiefer et al., 2001; Mason et al., 2001; Smoorenburg et al., 2002] have reported on possible clinical uses of NRT, such as confirmation of response to electrical stimulation from the cochlear implant and prediction of speech processor programming parameters (T-/C-levels) in adults and children. Few studies to date have been carried out in more than 1 or 2 centres and on a large variety of cochlear implant recipients. Therefore, these studies alone do not provide a representative 'normal range' of ECAP response characteristics as measured via NRT.

[1] As NRT is a near-field measurement, there is no positive peak prior to N1; thus, we have adopted the nomenclature of Killian et al. in 1994, since this more accurately describes the ECAP as measured with NRT.

Furthermore, the above procedural studies of Abbas et al. [1999] and Dillier et al. [2002] measuring the amplitude growth of the ECAP utilised a test procedure that presented one stimulus (the masker) at a fixed high level, while the presentation level of the target stimulus (the probe) was systematically reduced. Although these masker levels were not reported as unpleasant, postoperative NRT measurements may be more readily adopted if the persistent use of high-level stimuli is not required. Therefore, we preferred a test procedure, as described by Lai [1999], in which the masker stimulus is reduced in association with the probe stimulus. Such a test procedure also increases the possibility that longitudinal NRT measurements can be performed under similar test conditions both intraoperatively and postoperatively.

One of the main aims of this study was to establish a normative data set from a large group of subjects from several different centres under similar testing conditions. This involved the characterisation of the presence, morphology and amplitude growth function (AGF) of the ECAP (from a minimum of 3 electrodes placed in basal, medial and apical regions of the intracochlear electrode array) in adult cochlear implant users. The effects of aetiological factors and the duration of deafness were also studied as it is important to investigate the influence of such 'patient-related' factors on the peripheral neural response characteristics found. Comparisons between NRT results and psychophysical measurements were included to investigate possible clinical applications, such as programming and optimising the adjustment of the speech processor.

Methods

In previous publications, Abbas et al. [1999], Dillier et al. [2002] and Lai [1999] described the technique of using the Nucleus telemetry system to record the ECAP along the electrode array. In summary, the intracochlear electrodes of the Nucleus 24 implant system are used to stimulate and record the ECAP at discrete sites along the electrode array. No further specialised equipment was used, only each centre's own standard cochlear implant programming system consisting of a Sprint speech processor, processor control interface with programming cable, IF5 card and a PC running the NRT 2.04™ software. A method based on the subtraction paradigm described by Brown et al. [1990] was used to separate the small responses from the large stimulus artefact. Additionally, potential contamination from the amplifier switch-on artefact was excluded by the subtraction method [Lai, 1999; Dillier et al., 2002].

Subjects

One hundred and forty-seven subjects from 17 clinics in 13 countries were enrolled in this study. All subjects had to be at least 15 years old, postlingually deafened recipients of the Nucleus CI24M cochlear implant system, able to perform adult speech tests in their native language and willing to participate. Speech performance was noted for each subject. However, a minimum level of speech performance was not required in subject selection. One subject with neural adaptation of probably central origin was excluded from the study. Each subject had to be implanted with a minimum of 18 intracochlear electrodes so that a minimum range of stimulating/recording electrodes (electrodes 20/22, 10/12, and 5/7) could be tested. The electrode pairs 15/17 and 3/5 were optional and not attempted by all clinicians for all subjects. Data collection of NRT and psychophysical measurements started at a minimum of 1 month after initial tuning to ensure stability of behavioural threshold (T-levels) and maximum comfortable levels (C-levels).

Subject Characteristics: Age, Aetiology and Duration of Deafness

To investigate possible effects of the individual subject characteristics on the ECAP characteristics, gender, age, aetiology and duration of deafness were noted for all subjects. Age was categorized into four groups covering approximately 15 years each: (1) 15–30 years, (2) 31–45 years, (3) 46–60 years and (4) >61 years. Aetiology and/or mode of deafness was classified into 10 common categories in current use across the participating centres: (1) progressive, (2) meningitis, (3) congenital, (4) other/sudden deafness such as Ménière's syn-

Table 1. Test parameters

Stimulation rate	80 Hz
Pulse width	25–50 μs
Masker level	+5 CU above probe level
Masker probe interval	500 μs
Gain/number of sweeps	60 dB/100 or 40 dB/200
Delay	50–150 μs

Table 2. Distribution of aetiology for all 147 subjects and for the subset of 85 subjects with results from all 5 electrodes

Aetiology	All subjects		Subset with 5 electrodes	
	n	%	n	%
Progressive	42	29	23	27
Meningitis	21	14	13	15
Congenital	20	14	14	17
Sudden/other	20	14	9	11
Unknown	14	10	13	15
Infection/non-meningitis	11	7	5	6
Head trauma	9	6	5	6
Ototoxicity	4	3	2	2
Otosclerosis	4	3	1	1
Unspecified syndrome	2	1	0	0

drome or other causes of a sudden onset but not listed in any of the other categories, (5) unknown, (6) infection (not meningitis), (7) head trauma, (8) ototoxicity, (9) otosclerosis and (10) unspecified syndrome. The duration of profound deafness (defined as pure tone average, across 0.5, 1, 2 kHz ≥90 dB HL) was recorded for each subject. Duration was categorised into one of four groups as follows: (1) 0–1 year, (2) >1–5 years, (3) >5–15 years and (4) >15 years. A few (n = 4) subjects with hearing thresholds <90 dB HL were included in category 1.

The 147 subjects (81 females, 66 males) ranged in age from 15 to 79 years (median age, 44 years). Speech performance ranged from poor (closed set only) to excellent open-set speech recognition. The range and distribution of aetiologies across the subjects are listed in table 2. Half (53%) of the subjects were classified into large non-specific groups including the categories progressive, sudden/Ménière's syndrome or unknown causes.

Test Procedures

All NRT measurements in the 17 centres were made postoperatively using the Nucleus NRT 2.04 software, following a standardised test measurement protocol based on the findings of a previous stage of this project [Dillier et al., 2002] and outlined in table 1. A default stimulation rate of 80 Hz was used with an amplifier gain of 60 dB and 100 averaging sweeps. This provided the fastest test time without a significant difference in the repeated measurements of the neural responses [Dillier et al., 2002]. In some cases, a stimulation rate of 35 Hz or a gain of 40 dB was used. These parameters were found to be helpful where responses could not be obtained at the higher rate (80 Hz) or the higher gain (60 dB). The masker level was always set at 5 current units (CU) above the probe level. Thus, as the probe level was decreased at a constant step size to obtain the amplitude growth function, the masker level also decreased at the same step size. (The stimulus current level is expressed in current units; the relation between current units and electrical current is approximately logarithmic with 34 CU corresponding to a factor of 2 in electrical current or 6 dB. For further details, the reader is referred to the documentation of the Nucleus CI24M cochlear implant system.) The masker probe interval was set to 500 μs. The high-resolution measurement option in NRT, interleaving 2 recordings with a 10-kHz sampling rate each, provided a 20-kHz effective sampling rate and was selected as the default setting. Measurement delay refers to the time interval between the offset of the stimulus and the start of the recording (the moment the internal NRT amplifier was switched 'on'). It is important to adjust this parameter to ensure that the amplifier is in a linear operating mode when recording the ECAP. Non-linear amplifier behaviour, resulting in artefactual anomalies in the recorded response, is introduced when the recording of the neural response begins before the stimulus artefact has sufficiently been dissipated. To avoid this, while still attempting to capture the entire waveform, the default delay setting was 50 μs, but it could be adjusted through a range of 35–150 μs for each stimulus series recorded at a certain electrode.

Test Electrodes

A minimum of 3 electrodes (20, 10, 5) was chosen as the set of active stimulating electrodes and the reference electrode was the MP1 (ball) electrode. The active recording electrodes (22, 12 and 7, respectively) were separated from the active stimulating electrodes by 2 positions in the apical direction and the reference electrode was the MP2 (plate) electrode. Additionally, the electrode pairs 15/17 and/or 3/5 were tested in some cases (128 and 97 cases, respectively).

The subjective thresholds (T-levels) and loudest acceptable presentation levels (LAPLs) of each of the test electrodes were also measured. LAPLs were measured according to an agreed definition such that the LAPL was the highest stimulus level indicated as 'very loud' in 2 out of 3 trials but never indicated as 'too loud' on a loudness scale printed in the subjects' local language. Written subject instructions were also provided to ensure that the minimum and maximum stimulation levels were consistent across centres (Appendix). The purpose of the LAPL was to ensure that any test stimulus level (masker or probe) did not exceed the individual subjects' tolerance level for each electrode tested.

Morphology of ECAP Waveforms

Lai and Dillier [2000] have previously reported on the morphology of the ECAP waveforms recorded with NRT. They developed a simple 2-component mathematical model of the compound action potential based on the assumption that the recorded waveform represented a combination of dendritic and axonal processes as described by Stypulkowski and van den Honert [1984]. Two main categories of responses were found: type 1 representing a single positive peak response following a negative peak and type 2 describing a double positive peak response. Within type 1, 3 subcategories were found: (1) a large and distinct negative peak, N1, followed by a smaller but clearly visible positive peak, P1 (fig. 1), (2) a similar waveform, but N1 is not visible although the waveform clearly rises from below the baseline to a distinct positive peak and (3) N1 and the rising trajectory are visible; however, there is no clearly defined positive peak above the level of the baseline. Type 2 waveforms are comprised of a large rising trajectory with or without a clearly visible N1 and two clearly distinct positive peaks, P1 occurring at approximately 0.4–0.5 ms and P2 at approximately 0.6–0.7 ms after stimulus onset. For simplicity, the waveforms in this study were classified as either type 1 or type 2. Waveforms of type 1, subcategory 2 were not included in the data set.

Amplitude Growth Function

The AGF for the ECAP at each electrode pair was determined by the N1–P1 peak-to-peak amplitude measured at a minimum of 3 different current levels. Only those measurements with a clear N1 peak were included in the calculation of the AGF slope. In the few cases in which the maximum positive point did not occur above the baseline, the highest asymptotic point of the waveform occurring before 1 ms was selected as the positive peak. Peak-to-peak amplitudes less than 20 μV are considered to be likely within the noise floor. Unclear responses below 20 μV were therefore excluded from the AGF calculation, clear responses, however, were included.

The ECAP threshold measured by NRT, often referred to as 'T-NRT', was calculated from the linear portion of the AGF, taking the intercept point at the x-axis, as described by Dillier et al. [2002] (fig. 1).

Many persons performed the ECAP measurements. However, to ensure consistency in the interpretation of the responses, one clinician using the Nucleus NRT 3.0 software reviewed all NRT results. There appeared to be no consistency problems. STATISTICA-6 software was used for all descriptive statistics, correlation and principal component analyses.

The ECAP thresholds vary along the electrode array; this has been referred to as the 'profile'. Franck [2002] and Smoorenburg et

al. [2002] have investigated methods to use this profile in speech processor programming. They found that the profiles tend to follow the subjective thresholds (T-levels). Further, Smoorenburg et al. [2002] described a method to simplify comparisons between the ECAP profile and the subjectively measured profiles using principal component analysis. All profiles could be described by only two components, roughly corresponding to the overall level ('shift') and the slope ('tilt') of the profile. The present results are subjected to the same analysis.

Results

Success/Failure Rate

All subjects were tested using NRT as part of a postoperative out-patient session, without any severe restriction of movement or sedation of any kind. Once the test parameters were optimised for each electrode (primarily amplifier gain and onset delay, if necessary stimulus repetition rate), the AGFs could be completed in less than 1 min per electrode pair.

The success/failure rate of using this standardised test procedure was investigated in a number of different ways: the percentage of subjects in which a neural response could be measured at all, the percentage of test electrodes across all subjects in which a neural response could be recorded and the percentage of subjects in which neural responses were measured on 5 test electrodes. In the first instance, a reproducible and clear ECAP could be successfully measured in 96% of all subjects (141 out of 147). In other words, 6 subjects (4%) did not demonstrate a reproducible neural response with any of the 3 test electrode pairs, when using the default test procedure. Secondly, neural responses were measured in 96% of all electrodes tested in all subjects together (621 out of 647). To investigate the success in measuring an ECAP across the entire length of the electrode array, we investigated only those subjects where NRT was tried on 5 electrode pairs and counted the number of visual responses. The number of subjects totalled 85, of which in 5 cases (6%) no ECAP was recorded at all (on any of the 5 electrodes) and in 6 cases (7%) there was 1 out of 5 electrodes without ECAP response. Hence, in total, ECAP responses were obtained on all 5 attempted electrodes in 87% of the cases.

Effect of Duration of Deafness on Required Stimulation Rate

Duration of profound deafness (pure tone average >90 dB HL, sensorineural hearing loss) ranged from 0 years (for those subjects who were implanted with severe hearing loss) to 60 years. We found that, in general, subjects with a long duration of deafness (greater than 10 years) tended to have lower tolerance levels and required lower stimulation rates in order to achieve a sufficiently high stimulation level to produce a synchronous neural response in at least 1 electrode. Out of the 11 subjects requiring a stimulation rate less than 80 Hz, 8 subjects had been deaf for more than 10 years prior to implantation, whereas 67 out of all 147 subjects had been deaf for more than 10 years. Five out of these 11 subjects required a stimulation rate less than 35 Hz. These 5 subjects had been deaf for 15 years or longer, while this was true for 44 subjects out of the total population. However, these age fractions within subjects with lower stimulation rates did not differ significantly ($p = 0.08$ and $p = 0.28$ for rates <80 Hz and <35 Hz, respectively, χ^2 test) from the fractions in the total population.

Morphology of ECAP Waveforms

Some variation was observed in the morphology of the measured NRT results. Following the characterization of Lai and Dillier [2000], we found that type 1 (single positive peak) was the most commonly found, i.e. in 93% of responses. Type 2 (double positive peak), occurring in only 7% of the responses, was usually found on the more apical test electrodes, with only a few subjects demonstrating type 2 responses across 4 of the 5 test electrodes. Double positive peaks were not found on the basal test electrodes alone and none were recorded on electrode 3. Also, we found no correlation between the occurrence of double peaks and aetiology and between the occurrence of double peaks and the duration of deafness.

ECAP Characteristics

The minimum, maximum, mean, median and standard deviation of each ECAP characteristic, as measured by NRT, are listed in table 3. The analysis follows below:

ECAP Amplitude. Since the NRT thresholds vary considerably among subjects, we do not present the amplitude statistics across subjects at fixed current levels but at 10 CU above the ECAP threshold for each subject and each electrode individually. Even when the differences in individual thresholds are taken into account, we found that the amplitudes, calculated from the difference between the N1 and P1 peaks, cover a wide range, from 12 to 633 μV (table 3). Moreover, some individuals showed large differences in peak-to-peak amplitudes across the test electrode array, suggesting intrasubject variability in neural responsiveness in different regions of the cochlea. In order to quantify the intra-electrode amplitude variability, we calculated the standard deviation of the ampli-

Table 3. ECAP characteristics

	NRT data range (postoperative)					
	valid n	mean	median	minimum	maximum	SD
Peak-peak amplitude, μV						
El. 20	122	107	78	13	602	96
El. 15	125	119	83	12	544	112
El. 10	128	132	112	19	633	100
El. 05	116	112	93	12	490	85
El. 03	94	108	94	14	431	75
Latency N1, ms						
El. 20	123	0.32	0.32	0.23	0.49	0.05
El. 15	129	0.33	0.33	0.22	0.47	0.05
El. 10	133	0.34	0.33	0.24	0.62	0.04
El. 05	119	0.34	0.34	0.27	0.46	0.04
El. 03	98	0.34	0.34	0.26	0.43	0.04
Latency P1, ms						
El. 20	124	0.67	0.67	0.47	0.98	0.08
El. 15	127	0.66	0.67	0.49	0.91	0.08
El. 10	131	0.66	0.65	0.49	0.98	0.08
El. 05	119	0.66	0.64	0.49	0.91	0.08
El. 03	97	0.66	0.66	0.35	0.98	0.08
Peak-peak latency, ms						
El. 20	123	0.34	0.35	0.16	0.66	0.08
El. 15	128	0.33	0.33	0.16	0.59	0.08
El. 10	132	0.32	0.31	0.15	0.66	0.08
El. 05	118	0.32	0.31	0.15	0.56	0.08
El. 03	97	0.33	0.32	0.21	0.66	0.07
Slope of AGF, μV/CU						
El. 20	122	10.7	7.8	1.3	60.2	9.6
El. 15	125	11.9	8.3	1.2	54.4	11.2
El. 10	128	13.2	11.2	1.9	63.3	10.0
El. 05	116	11.2	9.3	1.2	49.0	8.5
El. 03	94	10.8	9.4	1.4	43.1	7.5
ECAP threshold (T-NRT)						
El. 20	125	176	178	104	218	16
El. 15	127	183	184	149	213	13
El. 10	132	188	187	157	218	12
El. 05	118	187	187	146	221	14
El. 03	96	187	186	156	228	14

El. = Electrode.

tudes measured per electrode at 10 CU above the ECAP threshold for the subset of 85 subjects with results from 5 electrodes. There appeared to be no correlation between the standard deviation relative to the mean value and the mean value itself (p = –0.17). Therefore, the relative standard deviation provides a good summary of this variability. Most subjects showed a variability of 20–40%. This variability may be due to a systematic trend across electrodes. However, the relative amplitudes per electrode, averaged across subjects, did not show a clear systematic trend: the amplitudes were 102, 96, 109, 96 and 94% at electrodes 20, 15, 10, 5 and 3, respectively.

Slope of the ECAP AGF. The slope of the AGF ranged from a minimum of 1.2 μV/CU to a maximum of 63.3 μV/CU. The distribution of the slopes across all electrodes of the subjects with results from 5 electrodes is presented in figure 2. Most AGFs had a slope of 5–20 μV/CU. The slopes depended significantly (p = 0.01) on the

electrode. The slopes, averaged across subjects, were 12, 14, 15, 13 and 11 μV/CU for electrodes 20, 15, 10, 5 and 3, respectively. Thus, the steepest slopes were found midway the electrode array, which is also reflected in table 3 for all measurements. The intra-electrode variability reported above for the ECAP amplitudes might also be reflected in the AGF slopes. Again looking at the relative standard deviation, we found the results shown in figure 3. Most subjects showed a variability of 30–40% across the electrode array, for a minor part due to the systematic effect of the steepest slopes midway the electrode array. The possible effects of age, duration of deafness, aetiology and gender on AGF were tested (ANOVA) for the subset of 106 subjects with results from 3 electrodes. In these analyses, the dependence on electrode location, as described in the previous paragraph, appeared to be a main effect at about $p = 0.01$. There were no interactions between the factor 'electrode' and any of the 4 variables: age, duration of deafness, aetiology and gender. A main effect of age was found at $p < 0.001$. The post hoc Tukey HSD test showed significant differences (at the $p = 0.01$ level and lower) between age category 1 (15–30 years) and categories 2, 3 and 4 (30 years and over; fig. 4). Another main effect was found for the aetiology factor; infections appeared to possess steeper AGFs ($p = 0.05$). Duration of deafness and gender had no effect on the AGF.

ECAP Latency. The latency of N1, measured at LAPL, ranged from 0.22 to 0.62 ms after stimulus onset and the latency of P1 from 0.35 to 0.98 ms, over all test electrodes. Thus, N1 was not recorded later than 0.6 ms and the first positive peak (P1) never extended beyond 1 ms. The interpeak latency or the time interval between the N1 and P1 peaks ranged from 0.15 to 0.66 ms with early P1 latencies tending to coincide with early N1 latencies. The possible effects of age, duration of deafness, aetiology and gender on N1 and P1 latency were tested, again for the subset of 106 subjects with results from 3 electrodes. No main effects ($p > 0.1$) on N1 and no interactions with electrode location were found. P1 latency showed a main effect of gender only ($p < 0.01$, 0.64 ms for males versus 0.68 ms for females). There was a clear main effect of electrode location on N1. This was investigated in more detail for the subset of 83 subjects with results from 5 electrodes. Although small, the effect was significant at $p < 0.01$. The

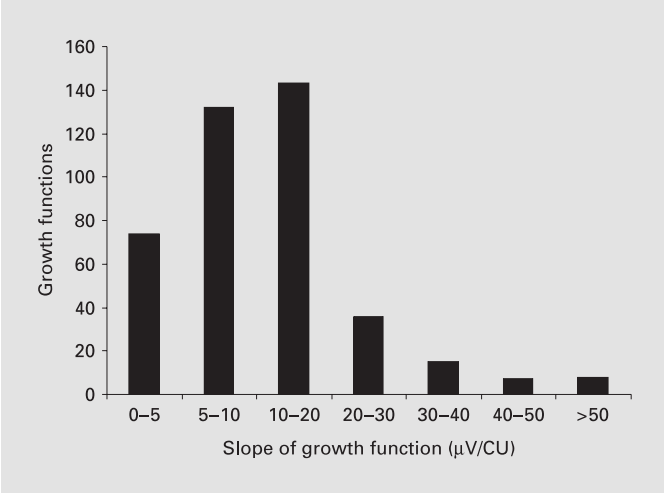


Fig. 2. Distribution of ECAP AGFs with a certain slope expressed in microvolts per current unit.

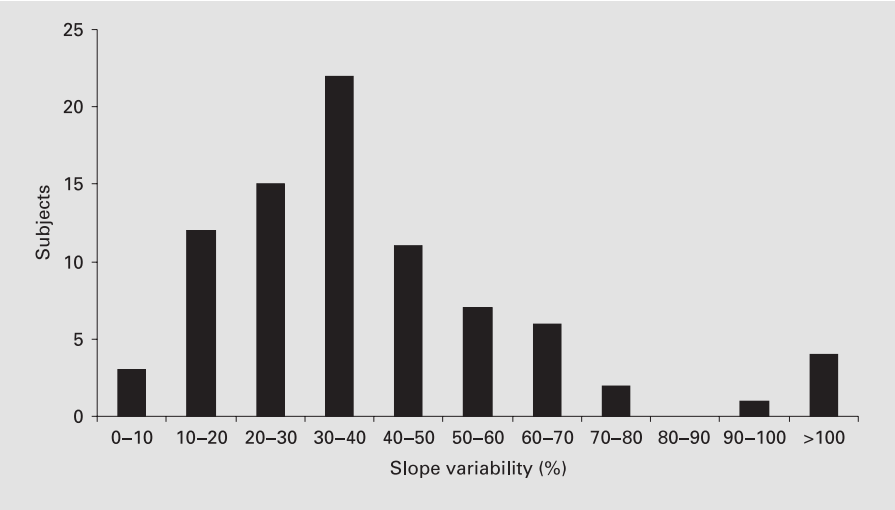
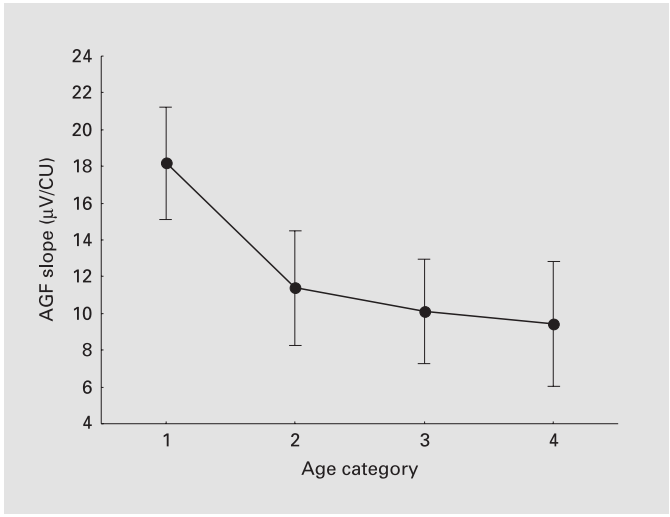


Fig. 3. Distribution of subjects with a certain relative variability in the slope of the AGFs across the electrodes 20, 15, 10, 5 and 3.

latencies for electrodes 20 and 15 were smaller (both 0.325 ms) than for electrodes 10, 5 and 3 (0.337–0.340). An interaction with the duration factor showed that the small latencies for electrodes 20 and 15 were mainly determined by small latencies in subjects with the shortest duration of deafness (0.305 ms).

ECAP Threshold. The ECAP thresholds, defined as the intercept of the linear part of the amplitude growth function and the base line at 0 CU, ranged from 104 to 228 CU, taking together the data from all subjects and all electrodes (table 3). The distribution of the ECAP thresholds for the subset of subjects with results from 5 electrodes is presented in figure 5 for each electrode individually. ANOVA showed a significant effect of electrode location on the mean threshold ($p < 0.001$). The ECAP threshold for electrode 20 was significantly lower than any other threshold; the threshold for electrode 15 was significantly lower than those for 10 and 3 (fig. 6, table 3). The possible effects of age, duration of deafness, aetiology and gender on ECAP threshold were tested, again for the subset of 106 subjects with results from 3 electrodes. There was a significant effect of gender ($p < 0.01$); 188 CU for males versus 182 CU for females. ECAP threshold did not depend on age, duration of deafness and aetiology. Also, there were no interactions between these 3 variables and gender on the one hand and location of electrode on the other.



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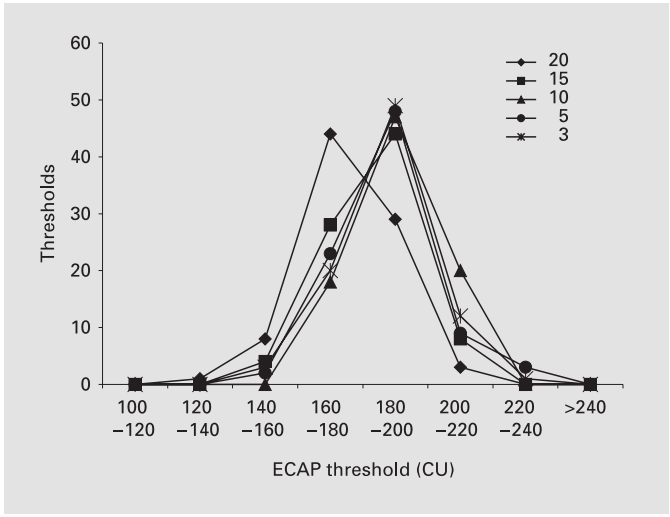

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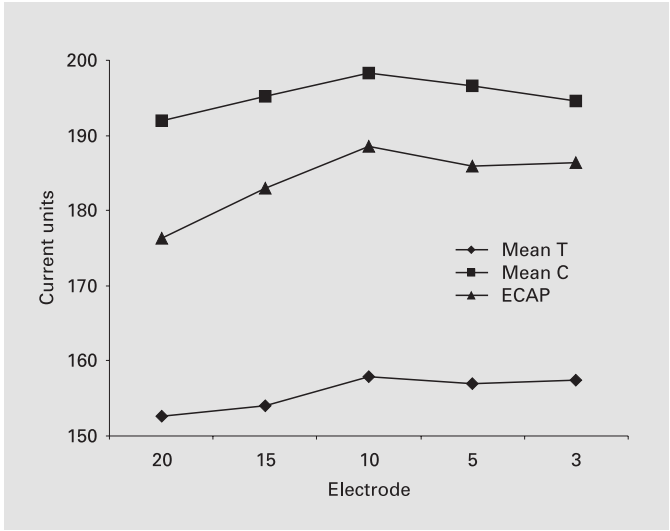

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Fig. 4. Effect of age on AGF slope: category 1, 15–30 years; category 2, 30–45 years; category 3, 45–60 years and category 4, >60 years.
Fig. 5. Distribution of the ECAP thresholds (T-NRT) in current units for each of the 5 electrodes, given in the legend.
Fig. 6. Comparison of the mean T-level, the mean C-level and the mean ECAP threshold (T-NRT). Standard deviations across all electrodes for the T- and C-levels and the ECAP thresholds are respectively: 18–19, 19–20 and 12–15 CU.

Comparison between ECAP Thresholds and T- and C-Levels

The ECAP thresholds are compared with the T- and C-levels (the maximum loudness comfort levels) in figure 6 for the subset of subjects with results from the 5 electrodes. Using the definition of ECAP threshold as given above, this threshold is found in between the T- and C-levels, on average 28 CU above T-level and 11 CU below C-level. The electrode dependence of the ECAP thresholds, reported before, appears to be reflected in the T- and C-levels, be it to a lesser extent. This suggested that the ECAP thresholds might be correlated with the T- and C-levels. However, the correlation coefficients ranged from only 0.40 to 0.51 for the 5 electrodes and both the T- and C-levels. The T- and C-levels were not all measured at the same stimulus rate. The standard rate was 250 Hz, but 12 measurements were performed at rates from 700 to 14,400 Hz. At these high rates, the T-levels tended to be 7–12 CU lower, while the C-levels tended to be 0–4 CU higher. Therefore, stimulus rate might have been a confounding factor in comparing the ECAP thresholds to the T- and C-levels. Excluding the high rate stimuli resulted, however, in only a slightly higher correlation between the ECAP thresholds and the T- and C-levels. The coefficients ranged from 0.44 to 0.58.

Applying principal component analysis, Smoorenburg et al. [2002] showed that ECAP thresholds and T- and C-levels across the full array of 22 electrodes can be described by only two factors, the major factor being related to the overall level (called 'shift'), the second factor roughly to the slope of the profile (called 'tilt'). Although the correlations per electrode were low, like reported above for the present data set, there appeared to be a high correlation between the tilts in the ECAP thresholds and T-levels of the study by Smoorenburg et al. (R = 0.82). Applying the same analysis to the present data set, restricted to only 5 electrodes, also yielded two factors corresponding to the shift and tilt parameters. They accounted for 92% of the variance considering the ECAP thresholds and for 96% considering the T- and C-levels. The correlation between the overall levels of the ECAP thresholds and the T- and C-levels appeared to be low (R = 0.60 and 0.56, respectively). This was expected because of the previous analysis [Smoorenburg et al., 2002] and because the low correlation per electrode is, for the major part, due to intersubject differences between overall level. However, the correlation between the tilts of the ECAP thresholds and the T- and C-levels was also low, R = 0.50 for both the T- and C-levels. Thus, although the mean profiles of figure 6 show the same trend, we found no clear correlation between the ECAP thresholds and the T- and C-levels, not per electrode nor for the principal components. The result from Smoorenburg et al. [2002] concerning the high correlation between the tilts of the ECAP threshold and the T-level has not been confirmed.

Predicting T- and C-Levels from ECAP Thresholds

Brown et al. [2000] have suggested a method to improve the prediction of T- and C-levels based upon ECAP thresholds. They suggested measuring the T- and C-level at one electrode position and then shifting the ECAP threshold such that the shifted threshold coincides with the T- and C-level at this electrode position. Following this procedure for the subset of subjects with results from the 5 electrodes and taking the subjective measurements found for electrode 10, we found root mean square (rms) errors in the prediction of the T- and C-levels at the other electrode positions of 15 and 14 CU, respectively. In view of clinical experience, this error is too large. Taking the population average of the T- and C-levels (fig. 6) rather than the ECAP threshold and applying the same shifting procedure based on an individual measurement at electrode 10, we found rms errors of 10 and 9 CU, in predicting the T- and C-levels, respectively. Although this average is based upon the same population, the markedly smaller errors suggest that an average behavioural profile provides as good a prediction of individual T- and C-levels as the individual ECAP thresholds.

Discussion and Conclusions

Success Rate

The present study aimed to establish a normative data set for recordings of ECAPs via NRT. The data set includes 147 subjects from 16 departments. All data pertain to the Nucleus CI24M cochlear implant, fully inserted. All measurements were performed with a masker level 5 CU above the probe level. This method, rather than a fixed high masker level, reduces the risk that the overall stimulus level required to collect all recordings becomes too loud. Therefore, this method is better suited for postoperative recordings. All other parameter settings complied with normal clinical practice.

At least one response was measured in 141 (96%) of the subjects. ECAP thresholds could be determined for electrodes 20, 10 and 5 in 106 (72%) of the subjects. These data were used to analyse the possible effects of age, duration of deafness, aetiology and gender on ECAP characteristics. The participating departments were asked to op-

tionally extend the measurements to electrodes 15 and 3. Data for 5 electrodes were collected for 85 (58%) subjects. These data were used to analyse possible effects of electrode location. Table 2 shows that the distribution of aetiologies does not differ markedly in the subsets of data.

The score of 96% responses compares favourably with other objective measures of cochlear implant performance, such as the scores for electrically evoked brainstem response of 71–91% [Kileny et al., 1994; van den Borne et al., 1994] and electrically evoked stapedius reflex threshold of 69–83% [Battmer et al., 1990; Mason et al., 1995]. This is only a rough comparison because it is not certain that responses could have been obtained in cases where no response was reported. In our case, 1 of the 6 subjects without responses had no subjective response with electrical stimulation at all. Subsequent investigations, including enhanced radiology, indicated a poorly developed auditory nerve. Two other subjects had acquired deafness from head trauma that might have caused peripheral neural impairment. However, these 2 individuals have been categorised as having moderate (2) and good (3) open-set speech performance by their clinic on a 4-point scale of speech perception. Formal speech performance test scores and other details of these subjects were not provided. A fourth subject had a long-standing deafness prior to implantation. Yet, another clinician obtained some poor responses at a slower stimulus rate of 15 Hz after data collection had been finished. We cannot exclude the possibility that responses might have been found after more extensive stimulus parameter exploration. Also, one should take into account that responses might have been found at stimulus levels higher than tolerated in these postoperative measurements. Thus, responses might have been found during anaesthesia.

Waveform Morphology

Double positive peak responses (type 2) were found in 7% of the responses, mainly on the apical electrodes. The origin of these responses might be related to dendrite survival [Lai and Dillier, 2000]. Stypulkowski and van den Honert [1984] recorded double positive peak responses in animals with intact dendritic and axonal sites. The second positive peak disappeared when the dendrites were selectively ablated, leaving only the axons. Our findings of double positive peak responses in only the apical electrode sites is consistent with the animal models of Stypulkowski and van den Honert [1984], as one may expect more neural degeneration in the basal than in the apical region of the cochlea. In addition, the spiral ganglion cells are more remote from the dendrites in the apical region, which may likely result in greater temporal separation between the responses from the two parts of the neuron. However, the appearance of the type 2 response is so rare that more subjects with similar double peak responses would be necessary to determine the significance of this possible link between morphology of the waveform and the neuronal degeneration pattern.

Aetiological Factors, Age, Duration of Deafness and Gender

The possible effects of age, duration of deafness, aetiology and gender on ECAP characteristics appeared to be very limited. An effect of age on the slope of the AGF (and thus implicitly on the ECAP amplitudes measured at 10 CU above ECAP threshold) appeared to be the most important one. Subjects between 15 and 30 years of age showed a considerably steeper slope, 18 μV/CU versus about 10 μV/CU for subjects above 30 years (fig. 6). Remarkably, there was no significant effect of duration of deafness on ECAP amplitude or the AGF. Also, there was no effect of age or duration of deafness on ECAP threshold. Lai et al. [2004] also found an effect of age on ECAP amplitude but not on ECAP threshold. Age rather than duration of deafness seems to determine the response amplitude. Duration of deafness appeared to have an effect on N1 latency. On average, latencies were smaller for electrodes 20 and 15 than for the other electrodes. This was related to an interaction between the factors electrode location and duration of deafness. The smaller latencies for electrodes 20 and 15 were solely due to smaller latencies in the group with the shortest duration of deafness (0–1 year).

In addition, there was a significant effect of gender on ECAP threshold (188 CU for males versus 182 CU for females). Also, gender had a significant effect on P1 latency (0.64 ms for males versus 0.68 for females). We offer no explanation for these findings. However, we checked whether or not the gender factor was confounded with the factor age; it was not. Finally, we found that within the aetiological factor there was a significantly (closely at $p = 0.05$) greater slope of the AGF for the category infections. However, this effect is probably confounded with the age factor. Five out of the 9 subjects, or 56%, with infections in the subset of subjects with results from 3 electrodes fell within age category 1, 15–30 years, whereas only 27% of the whole subset fell in this age category. In the previous paragraph, we mentioned the large effect of age, in particular of group 1, on the slope of the AGF.

Inter- and Intrasubject Variability

The variability in ECAP peak-to-peak amplitudes, measured 10 CU above ECAP threshold, and in the slope of the AGFs was large (12–633 μV and 1.2–63.3 μV/CU, respectively; table 3 and fig. 2). Most of this variability is due to intersubject differences in the amplitudes across all electrodes but the intrasubject variability from electrode to electrode was also considerable. Across the 5 electrodes, most subjects showed a variability of 20–40% in amplitudes at 10 CU above ECAP threshold and of 30–40% in the slope of the AGFs (fig. 3). The variability in AGFs was, for a minor part, due to a systematic effect across electrodes with the steepest slopes midway the electrode array. Abbas et al. [1999] also found large intrasubject variability in the slopes of the AGFs in their study concerning 23 subjects. The ECAP threshold depended highly significantly on electrode location ($p = 0.000$, means presented in figure 6). Thus, the variability in ECAP threshold across electrodes cannot be specified without taking this systematic effect into account. Principal component analysis showed that 78% of the variance was due to a component representing overall threshold and 14% to a second component representing differences with respect to the overall threshold. This second component reflects primarily changes in the slope of the profile (the tilt) across the electrodes, and thus it should be taken into account. Finally, we found that the variability in latency was very limited. It does not require any further discussion.

Relation between ECAP Thresholds and T- and C-Levels

Presently, T- and C-levels are the basis of the processor adjustment procedure. Since this procedure is rather time consuming, many workers in the field have asked the question of whether or not ECAP thresholds can be used to predict the T- and C-levels. The poor correlation between the ECAP thresholds and the T- and C-levels found by Brown et al. [2000] is too low to allow for individual predictions of the T- and C-levels. The present results are in agreement with this finding. The correlation coefficients, determined per electrode, ranged from 0.44 to 0.58, restricting us to measurements of the T- and C-level at 250 Hz stimulus rate. Brown et al. [2000] further showed that the correlation could be improved considerably by including a subjective measurement of the T- and C-level at a certain electrode and, subsequently shifting the ECAP threshold by equal amounts of current units per electrode such that the shifted profile coincides with the subjectively measured current level at that electrode. Applying their method to our data yielded predictions of the T- and C-levels with rms errors of 15 and 14 CU, respectively. In view of clinical experience (measurement accuracy), this error is too large. Taking the population average of the T- and C-levels and applying the same procedure yielded rms errors of 10 and 9 CU, respectively. Although these average profiles are derived from the same population, the large difference in rms error suggests that one might as well base the fitting procedure on the average T- and C-level profiles as on the ECAP threshold.

Rather than considering the results from individual electrodes, Smoorenburg et al. [2002] suggested that more insight in the data set can be obtained by first reducing the number of variables applying principal component analysis. They found that the second principal component, the tilt, in the ECAP threshold and the one in the T-level profile correlate highly ($R = 0.82$). However, the same approach in this study yielded a correlation of only $R = 0.50$. Also, the correlation between the tilt of the ECAP threshold and the tilt in the C-levels and the correlations between the first principal component (overall level or 'shift') of the ECAP thresholds and the T- and C-levels did not exceed $R = 0.60$. Thus, we have not been able to show how ECAP thresholds could contribute substantially to estimating the T- and C-levels. However, this does not necessarily imply that ECAP thresholds cannot contribute to signal processor adjustment. There is no proof that the T- and C-levels provide the best basis for individual processor adjustment either. On the contrary, Craddock et al. [2003] have found no significant difference in speech performance in adults between MAPs they had been wearing based on psychophysical T- and C-levels and MAPs created with a T/C offset of T-NRT as previously described by Brown et al. [2000]. Furthermore, Smoorenburg et al. [2002], for example, have shown that the lower limit of the dynamic range of the speech processor can be adjusted considerably lower than at the T-level, virtually without affecting word perception. The optimal procedure for processor adjustment has yet to be evaluated.

Appendix: Written Instructions and Prompts for Subjects in English and Translated into Local Languages for All Co-Investigator Sites

NRT Patient Instructions

Today we are going to record some measurements from your cochlear implant. You will hear some loud sounds, but you do not have to do anything except relax.

We will NOT change your MAP today and we will NOT be using your speech processor.

Do you have any questions?

We are going to start now.

You will hear some sounds. They will increase in loudness. Using the loudness scale, please indicate the point on the scale that corresponds to the loudness of the sound that you are hearing.

Please tell us to STOP when the sound becomes very loud.

Remember VERY LOUD is the level where the sound is as loud as possible without being uncomfortable. You should be able to listen to this sound for some time.

It is important that the sounds are not uncomfortable for you, but it is equally important that the sounds are as loud as possible so that we can obtain the best measurements.

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