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Sensitivity to across-electrode delays and electrode order in Cochlear Implant users

Ana Šodan¹, Sabine Meunier¹, Vincent Péan², Stéphane Roman³⁻⁴, Marion Montava⁵⁻⁶, Jean-Pierre Lavieille⁵⁻⁶, Olivier Macherey¹

¹Aix Marseille Univ, CNRS, Centrale Marseille, LMA, 4 impasse Nikola Tesla, 13453 Marseille Cedex 13,

France

²MED-EL France, Paris, France

³Institut de Neurosciences des systèmes, Inserm UMR1106, Aix-Marseille Univ., Marseille, France
 ⁴Dept. of Pediatric Otolaryngology and Neck Surgery, Aix-Marseille Univ., Marseille, France
 ⁵Laboratory of Applied Biomechanics, IFSSTAR, LBA, UMR-T 24, Aix Marseille Univ, Marseille, France.
 ⁶Dept of Otorhinolaryngology, Conception University Hospital, APHM, Marseille, France

sodan@lma.cnrs-mrs.fr

ABSTRACT

In normal hearing, cochlear filtering introduces a temporal delay between the firings of auditory nerve fibers coding for different frequencies. However, frequency components presented simultaneously are perceived as synchronous, suggesting this delay may be compensated more centrally. As cochlear implants (CIs) bypass the cochlea, it may be important to reintroduce this delay in the CI processor. However, little is known on the sensitivity of CI subjects to delays between widely-spaced electrodes.

Eight Med-El CI recipients took part in two experiments where they had to discriminate between stimuli consisting of pairs of electrical pulses presented on the most basal and most apical electrodes. Experiment 1 measured across-electrode delay discrimination in six conditions differing in electrode order (apical or basal first) and in reference delay (0.1, 10 or 20 ms). Experiment 2 measured electrode order discrimination for three reference delay conditions (0.1, 10 or 20 ms).

Preliminary results show that (i) delay discrimination thresholds increase when the reference delay increases, (ii) some subjects can discriminate between delays differing by less than 10 ms, showing they are sensitive to delays within the range of physiological cochlear delays, (iii) discrimination is not easier when the reference delay mimics the physiological cochlear delay.

1. INTRODUCTION

First observed by Von Békésy [1], the travelling wave propagates from the base to the apex of the cochlea and displays peaks at certain locations depending on the frequency content of the incoming sound. This phenomenon leads to a temporal delay between simultaneously-presented tones of different frequencies. Effectively, fibers located in the basal part of the cochlea are stimulated before those in the apical part (because of their distance to the oval window, where the sound wave enters the cochlea). This frequency-dependent motion has been measured in animals and post-mortem in humans. Due to the invasive aspect of measuring the travelling wave directly in a human cochlea, several non-invasive measures have also been performed and were shown to be consistent with this phenomenon. For example, the latencies of Auditory Brainstem Responses (ABRs) and of Tone burstevoked otoacoustic emissions [2] decrease with increases in stimulus frequency. Campdell et al. [3] also recently showed evidence for the existence of the travelling wave in humans by recording the cochlear microphonic from CI electrodes during their insertion in acoustically-stimulated ears.

However, it remains unclear how these across-channel cochlear delays are processed centrally. Dau et al. [4] used an optimized chirp stimulus (chirp with rising frequency) aimed to compensate the cochlear delay in an ABR experiment with normal-hearing (NH) subjects. They showed that this optimized chirp lead to higher wave V amplitudes compared to clicks or reverse chirps, suggesting there was more firing synchrony across the tonotopic regions of the brainstem responding to the optimized stimulus. Uppenkamp et al. [5] further used these same signals and measured their perceptual effects in NH subjects. Surprisingly, they found that the reversed chirp (decreasing frequency) sounded more "compact" than a click (the most compact sound can be viewed as the sound having the shortest perceived duration). In summary, the optimized signal probably lead to more synchrony between apical and basal fiber discharges at the level of the auditory nerve and of the brainstem but still sounded less compact than a click. Uppenkamp et al.[5] further proposed that a mechanism located beyond the inferior colliculus might compensate for this cochlear delay. Wojtczak et al.[6] found results compatible with this hypothesis in NH listeners, by measuring subjectively the perceived asynchrony between lowand high-frequency tone bursts in two conditions (low-frequency and high-frequency leading). However, studies in NH subjects are limited by spectral splatter (i.e., the spread of energy to adjacent frequencies) and by auditory filter ringing, thereby preventing short stimuli to be restricted in the spectral and temporal domains. Testing CI users in a similar task may partially avoid the temporal limitation and potentially highlights the existence of this mechanism at a higher stage of auditory processing.

In addition, a remaining question is whether this cochlear delay is important for sound perception in NH listeners. If this is the case, it would provide a strong rationale for introducing it in a CI where the cochlea is bypassed and where the traveling wave is absent. Some signal processing strategies happen to create delays between electrodes at the bandpass filtering stage of sound analysis. Zirn et al. [7] showed in 4 CI subjects that bandpass filtering produced eABR latencies of CI users more similar to those from NH subjects. In two other studies, Taft et al. [8-9] introduced different delays across the frequency channels of a CI speech processor. In one case [8] the delays were based on a pitch matching procedure: cochlear implantees with contralateral residual hearing had to match the pitch of each electrode to pure tones presented to their partially hearing ear. Using Greenwood function, they introduced individual delays associated to each electrode and showed an improvement in some speech tasks. In a companion study [9], using different delays, they also showed an improvement in the perception of words in quiet. However, the direction of the delay (Apical leading versus Basal leading) did not have any effect on the results. These two studies show that implementing across-channel delays in CI processors can lead to changes in speech perception but so far, no specific advantage has been obtained when the delays mimic the physiological NH delays. Apart from these speech studies, the sensitivity of CI users to electrode delays and electrode stimulation order has not been extensively investigated. To our knowledge, this was only studied by Carlyon et al. [10] who measured the discrimination abilities of CI listeners to small time differences between pulse trains presented to two widely-spaced channels. They showed that the subjects could discriminate between a stimulus with the two CI channels being nearly synchronous and a stimulus with a short delay between channels. Their range of delays was restricted to values below the assumed delays produced by the traveling wave in NH (ranging from 0.1 ms to 2 ms). Here, we extend these results by investigating the sensitivity of MED-EL CI users to a broader range of delays imposed between widely-separated electrodes. Based on previous estimations of electrode insertion angles using pitch matching procedures [11] or CT-Scans [12] the most apical electrode of the MED-EL device should have an insertion angle ranging from 454° to 720° [12]. Using these insertion data and estimates of the cochlear delay as a function of frequency [13] we may infer the value of the delay that should theoretically be present between fibers located near the most apical and near the most basal electrodes of CI subjects if they were normal hearing. This delay could range between 3 to 20 ms. Here, CI users implanted with a MED-EL device will be tested in different conditions including a condition roughly mimicking the cochlear delay.

In Experiment 1, we measure delay discrimination thresholds for different reference delays in a group of eight CI users. In Experiment 2, we investigate their sensitivity to electrode order.

Our hypothesis was that if there is a central mechanism compensating the cochlear delay, CI users should be better at discriminating between delays or electrode order when the delay imposed on the reference signal mimics the cochlear delay present in normal hearing. This hypothesis is based on the idea that for a reference signal mimicking the cochlear delay, two pulses presented on different electrodes should be perceived as more synchronous than other stimuli. If subjects base their judgements on duration cues, they should more easily detect an increment in duration for such a "compact" reference.

2. MATERIALS AND METHODS

2.1 Subjects

Experiments 1 and 2 were carried out with 8 CI users. At the time of testing, all had used their implant for at least one year and did not have any other known disabilities. All subjects were implanted with MED-EL CIs (MED-EL GmbH, Innsbruck, Austria) and were paid for their participation. Procedures were approved by the local ethics Committee "Sud-Méditerranée 2" (Eudract 2016-A00221-50) and subjects provided informed consent. Experiment 1 was split into two sessions lasting three hours each. Experiment 2 was completed in one session lasting three hours.

2.2 Stimuli

Electrical stimuli were designed through Matlab R2011a (Mathworks, Natick,MA,2010), using the Research Interface Box (RIB2) developed by Department of Ion Physics and Applied Physics at the University of Innsbruck (Innsbruck, Austria). This library of functions enables to generate electrical stimuli directly in the implant through the Med-EL Max Interface Box (MED-EL GmbH, Innsbruck, Austria) and the adequate coil.

Stimuli were composed of two cathodicfirst biphasic pulses having a 50-µs phase duration and presented in monopolar mode. Each pulse was presented to a different electrode. Thus, only two electrodes were stimulated: the most basal (electrode 12) and the most apical (electrode 1). When an electrode was deactivated in the clinical map, the closest neighboring electrode was selected. This was the case for subjects S2, S6 and S8 for whom the more basal electrodes were electrodes 9, 11 and 11, respectively.

2.3 Preliminary Loudness adjustment

Most comfortable loudness levels (MCLs) were first determined on each electrode separately by presenting a pulse train of 1.5-second duration at a rate of 2 Hz. Subjects indicated their perceived loudness using a loudness chart. The dual-electrode stimuli were then constructed by keeping the difference in MCL between the two electrodes fixed in dB. The MCLs of the dual-electrode stimuli were then measured for two different delays between the electrodes: 128 ms, which was the maximum delay used in the main task and 0.1 ms which was the minimum. Two estimations were obtained for each delay, resulting in four estimations of MCLs. The level chosen for the main task was the lowest of these four levels. It was, however, verified that individual electrodes were still audible at this level and that they provided a similar loudness percept when stimulated individually. If this was not the case, the overall level was increased without exceeding comfort. This procedure was sufficient to define the testing levels, and additional loudness adjustments across electrodes were not needed.

2.4 Experiments

2.4.1 Experiment 1: Across-electrode delay discrimination

Three stimuli were presented in each trial. The first one always was the reference. Among the second and third intervals, the stimulus was either identical to the reference or had a different acrosselectrode delay (c.f. Figure 1). The task of the subject was to find the odd-one-out in a 3-Interval, 2-Alternative Forced Choice (3I-2AFC) task. Visual feedback was provided for correct (virtual button highlighted in green) and incorrect (button highlighted in red) responses.



Figure 1: Example of a trial of Experiment 1. The reference condition is a basal-electrode leading stimulus with a reference delay d. The 3rd stimulus is the odd-one out with a test delay d(test).

A training phase was first provided before the main task. For this training, the method of constant stimuli was used with a test delay value fixed at 128 ms. Each block was composed of six runs, corresponding to the six conditions including 2 electrode orders (apical leading, AL or basal leading, BL) combined with 3 reference delays (0.1 ms, 10 ms and 20 ms). In total 30 trials composed a run. After each block, the scores were calculated for each condition. An entire block was repeated until the scores for all conditions reached more than 80% correct. On average, two to three blocks were necessary. Two subjects were excluded because they could not achieve this level of performance, after five training blocks.

The main task also consisted in 3I-2AFC trials combined with a 2-down, 1-up adaptive procedure. The delay difference between the test signal and the reference was the adapted parameter. Starting at a test delay of 128 ms, the adaptive procedure followed the exact same steps as those used in Experiment 2 of Wojtczak et al. [6]. The measure stopped after twelve reversals. An adaptive run was composed of all trials for one defined reference condition and leading electrode condition. The discrimination threshold within each run was obtained by geometrically averaging the last eight reversals. Delay discrimination thresholds were obtained for six conditions (3 reference delays * 2 electrodes order). A block was composed of six adaptive runs corresponding to each condition. Within a block, the runs were presented in randomized order. In total, six blocks were performed, thereby leading to six threshold estimations for each condition. The 1st block was considered as training. The threshold for one condition was therefore defined as the geometric average of the five ultimate thresholds collected.

2.4.2 Experiment 2: Electrode order discrimination task

To evaluate the sensitivity of CI users to electrode stimulation order, the same electrodes as in Experiment 1 were used. The stimuli were also presented in a 3I-2AFC task using the method of constant stimuli. Among the three stimuli presented in each trial, the odd-one-out only differed by the electrode order (i.e., the across-electrode delay was always kept fixed within trial.). Fig. 2 presents an example of one trial. Moreover, the order of the reference stimulus was arbitrarily chosen to be basalfirst.



Figure 2: Example of a trial of Experiment 2. The reference condition is the basal-electrode leading stimulus with a reference delay d.

A training block of 30 trials was first performed with the electrode delay fixed at 128 ms. This training block was repeated until the subjects obtained more than 80% of correct responses. For most subjects, one run was sufficient. Visual feedback was provided for correct and incorrect responses during the entire run.

The main task was carried out also using the method of constant stimuli, but the delays were set at different reference values (0.1, 10 ms and 20 ms). Similar to the training procedure, one run was composed of 30 trials; the first five trials counted as training and were not taken into account in the calculation of the final scores. Visual feedback was provided only for the first five trials. Each block was composed of three runs and each run corresponded to one reference delay condition. The runs within each block were presented in randomized order. Each block was repeated five times to complete a test session, leading to 125 responses in each condition. The 1st block was not taken into account in the final scores and was considered as training. Therefore, the percentage of success in one condition represents the average of 100 responses.

Moreover, in order to determine the minimum delay condition for which the subjects could discriminate between stimulation order, the same task was repeated in a 2 down-1 up adaptive procedure by varying the delay between pulses. Similar to Experiment 1, the initial test delay was 128 ms and adapted with the same up-down rule. In total, six runs were obtained. The 1st run was considered as training and was not taken into account in the average. To match the protocol of Experiment 1, visual feedback was provided all along the procedure to keep the subjects motivated. Threshold was defined as the geometric mean of the last five thresholds collected.

2.5 Statistical Analysis

All data were saved into an Excel spreadsheet (Microsoft Office 2016). The statistical analysis was carried out using Excel and R (R Foundation for Statistical Computing, Vienna, Austria). For Experiment 1, we used a two-way repeated measures ANOVA. The within subject factors were the reference delay and the leading electrode. Following theses analyses, post-hoc pairwise comparisons were performed. For Experiment 2, for each subject and condition, a binomial test was performed to evaluate which scores were above chance. The differences in performance between the different reference delay conditions was assessed by a repeated Wilcoxon test.

3. RESULTS

3.1 Experiment 1: Sensitivity to delay between electrodes

The geometric mean across all tested subjects are presented in Fig. 3. The blue lines with circle symbols represent the AL condition while the red lines with triangular symbols are for the BL condition. It appears that changing the leading electrode does not have a consistent effect across subjects. Furthermore, discrimination thresholds show an increase with increases in reference delay. These observations are confirmed by the results of the repeated-measures ANOVA. Reference delay has a significant effect on discrimination thresholds (F(2,14) = 7.1335, p=0.00731) whereas the leading electrode does not have any effect (F(1,7)=0.059), p=0.815). Finally, the interaction between reference delay and leading electrode is not significant (*F*(2,14)=0.287, *p*=0.458). A LSD post-hoc analysis show that discrimination thresholds significantly increase by 11.1 ms on average between the 0.1-ms and the 20-ms condition (p=0.0021), and by 5.9 ms on average between the 0.1-ms and the 10-ms condition (p=0.04021). However, there is no significant difference between the 10-ms and 20-ms conditions (p=0.1584).



Figure 3: Across-subject mean discrimination thresholds obtained in Experiment 1, as a function of reference delay.

3.2 Experiment 2: Sensitivity to electrode order

Up to now, seven subjects have completed Experiment 2. The results shown in Figure 4 represent the percentages of success over 100 trials, in each condition, except for Subject S2 who did not manage to perform the task. The results for this subject represent the average of 50 trials in each reference condition. Results from S2 remained at chance for all conditions and are not analyzed in the following, even though S2 performed above chance in the training phase (i.e. for a delay of 128 ms). Fig. 4 reveals that CI users are sensitive to electrode order for reference delays equal or higher than 10 ms. Wilcoxon tests show that discrimination of electrode order differed across electrode delay conditions and that scores increased on average by 35% between the and 20-ms conditions (Z=-2.1024,0.1-ms p=0.03552), by 27.5% between the 0.1-ms and 10ms conditions (Z=-2.1539, p=0.03125), and by 8% between the 10-ms and 20-ms conditions (Z= -2.1024, p=0.03552).

The adaptive procedure converges to the 70.7% point of the psychometric function.[14] Adaptive thresholds were consistent with the scores obtained using the method of constant stimuli in the different reference conditions. For example, the discrimination threshold for S1 was 17.96 ms while his scores were 69% and 79% in the 10-ms and 20-ms delay conditions, respectively.



Figure 4: Percentage of success in the electrode order discrimination task (Experiment 2) for different reference delays. The numbers below the subject labels at the bottom of the figure show the electrode order discrimination thresholds measured adaptively. The star symbols above the bars represent the significance level in response to a binomial test: (**) p < 0.01, (*) p < 0.05.

4. DISCUSSION

These two experiments show that CI subjects are sensitive to both electrode delay and electrode order for wide electrode separations. For a reference delay of 0.1 ms, their delay discrimination thresholds ranged from 3 to 30 ms (mean of 15 ms). They could

also discriminate between electrode order when the across-electrode delay was higher than 12.1 ms on average. Moreover, for some subjects, delay discrimination thresholds were within the range of expected cochlear delays. We initially assumed that if there is a central mechanism compensating the cochlear delay, an electrical stimulus consisting of two pulses with a delay mimicking the physiological cochlear delay should be perceived as shorter than other dual-pulse stimuli. We further hypothesized that if subjects use stimulus duration as a cue to discriminate between stimuli, their discrimination thresholds should be lowest when the acrosselectrode delay of the reference stimulus matches the physiological cochlear delay between the two fiber populations excited by each electrode. Due to a lack of precision of the post-op x-rays, it was not possible to determine the exact location of the most apical electrode of our subjects. It appears therefore difficult to infer, for each subject, the expected cochlear delay between the apical and basal fiber populations. Based on averaged electrode insertion angles from the literature and according to the rough estimation of cochlear delay previously mentioned, we may still expect the 10-ms delay, basal-leading stimulus to approach the natural cochlear delay, at least in subjects with deep insertions. In both experiments, however, discrimination thresholds were not lower for this condition than for others. This result, therefore, does not validate our hypothesis. Below we discuss the possible reasons for this and compare our data with previouslypublished results.

4.1 Potential cues used in the discrimination tasks

Due to the specific design of Experiments 1 and 2 (odd-one-out task), subjects could potentially use any cues available to perform the task and it is possible that the perceived duration was not the most salient cue. Additional potential cues encompass differences in loudness, the presence of electrode interactions and segregation cues.

First, it was observed in Experiment 1 that the small-delay stimuli sounded louder than the long-delay ones (up to 2 dB difference in MCL). Similarly, McKay et al. [15] showed in four subjects that longer delays between electrodes sound softer than smaller delays, even for small delay variations of 1 ms.

Second, it may be possible that the apical and basal electrodes excited overlapping neural populations and that subjects selectively attended to neurons responding to both electrodes. If this was the case, they could potentially base their judgments on the temporal delay between the firings of the *same* neural population instead of detecting a delay between the firings of *distinct* neural populations. In another study, McKay et al. [16] asked CI subjects to discriminate between several dual-channel pulse trains. The pulse trains were delivered to distinct electrodes and the stimuli differed in the temporal delay between each channel (delayed by 1 ms or by 5 ms). They showed that discrimination became impossible for electrode separations larger than 8 mm, suggesting that for such distances, the two channels excited different neural populations. In the present experiments, the apical and basal electrodes were separated by distances ranging from 14 to 26 mm (mean of 22.2 mm) so we may expect even less channel interactions than in the McKay et al.'s study [16]. This electrode interaction explanation cannot, however, be completely ruled out for two reasons. (i) we used monopolar stimulation whereas McKay et al. [16] used bipolar coupling which may be more spatially selective; (ii) we used single pulses instead of pulse trains and it is possible that the current levels needed to reach MCL were overall higher than if we had used pulse trains, thereby potentially yielding more current spread and more electrode interactions.

Note that the loudness and electrode interactions explanations may only hold for Experiment 1. In Experiment 2, the across-electrode delay was constant within trial. If loudness is determined by the integration of neural activity within a certain temporal window, it should not play a role in the electrode order experiment. Similarly, if subjects based their judgments by listening to neurons responding to both electrodes, they should be unable to use this strategy in Experiment 2 because the firing pattern of the "overlapping" population should be identical for all stimuli of a given trial. Given the delay discrimination thresholds were in the same range for both experiments, we argue that the loudness and electrode interactions were probably not the only cues that the subjects used.

This was also pointed out by Carlyon et al. [10] who investigated the sensitivity of CI users to electrode stimulation order. In their experiment, electrode interactions were controlled by stimulating an electrode in the middle of the array to mask the response of neurons to both electrodes. Carlyon et al. [10] showed that among five cochlear implantees, three of them were not able to discriminate between electrode stimulation order when the inter-electrode delay was 2 ms, which is consistent with our result since delay discrimination threshold was 12.1 ms in average. However, Carlyon et al. [10] also reported that their subjects could distinguish between acrosselectrode order for a delay of 0.1 ms. In contrast, the results of Experiment 2 showed that only two subjects among seven scored above chance in the 0.1-ms condition. This difference between studies may be explained by electrode distance: the average distance between our electrodes was 22.2 mm whereas it was 11.1 mm in their population. Also, Carlyon et al. [10] reported that for their subjects, one of the 0.1-ms delay stimulus sounded "special"

and was easily distinguishable from other stimuli. None of our subjects reported such differences.

Finally, it is also possible that the subjects perceived the two pulses as distinct auditory objects and did not perceive differences in overall duration between the stimuli but rather differences in onset time between the two (very short) objects. Using an irregular rhythm detection task, Tejani et al. [17] measured the ability of CI users to segregate between two 60-ms pulse trains presented on widely separated electrodes. For their largest electrode separation, the time delay needed to produce segregation averaged 12 ms. This value is close to both the average threshold obtained in the 0.1-ms condition of Experiment 1 (15 ms) and to the threshold for electrode order discrimination obtained in Experiment 2 (12.1 ms). It is possible that our CI subjects could perform both experiments only when the two pulses were segregated.

4.2 Central compensation of the cochlear delay

Experiment 1 showed that delay discrimination improved with increases in reference delay but did not show any difference between the apical and basal leading conditions. Based on the hypothesis of central compensation of cochlear delay mentioned previously, we were expecting the delay condition presumably similar to the physiological cochlear delay (10-ms, basal-leading) to yield the best performance. However, this was not the case. As we do not have information on the insertion depth of the electrode array of our subjects, it may be possible that they had relatively shallow insertions and that the two populations of fibers excited by the apical and basal electrodes were closer than expected. This would imply that the cochlear delay between these two populations would have been smaller than 10 ms.

It is also interesting to compare the results of Experiment 1 to those obtained by Wojtczak et al. in NH [6] and hearing impaired subjects for the same paradigm [18]. In these studies, they presented two 40-ms tone bursts of different frequencies separated by various delays in the presence of background noise to mask possible overlapping excitation. Consistent with Uppenkamp et al. [5], they found that the maximum of perceived synchrony was obtained when presenting the two tone bursts simultaneously, even if this presentation resulted from an asynchronous recruitment of the two neural populations within the cochlea. They further measured delay discrimination thresholds for two tone bursts as a function of reference delay (0 ms, 10 ms, 20 ms and 40 ms). They found that increasing the reference delay yielded higher thresholds for both low-frequency and high-frequency leading conditions. This result is similar to our observations. They also observed an effect of leading frequency only for the smallest reference delay (0 ms) for which threshold was lower when the 250-Hz tone was leading. Although this observation differs from the results of Experiment 1, it is important to note that for our subjects, there is no cochlear delay. This means that to adequately compare these two studies, our data need to be shifted in time. Assuming that the theoretical cochlear delay of our subjects is 10 ms, this means that our basal-leading, 10-ms delay condition should be similar to the 0-ms reference delay condition of Wojtczak et al. [6]. Fig. 5 shows the data of Wojtczak et al. obtained for the largest tone separation (250 Hz and 6 kHz) [6, 18] together with our averaged data shifted in time. Despite several differences between studies (stimulus duration, presence of background noise), the similarity between the different data sets is striking and it is possible that these different subject groups used the same cues to perform the task.



Figure 5: CI threshold of Experiment 1 replotted as a function of transposed delay to make them comparable to acoustic hearing experiments. Data from Wojctzak et al. studies [6,18] obtained in NH and hearing impaired subjects are also shown by dotted and dashed lines.

To conclude, our results do not provide evidence for the existence of a central compensating mechanism of the cochlear delay but do not disprove it either. Furthermore, the similarity between CI and NH delay discrimination data suggest that similar mechanisms may be at play in both subject groups. This observation is potentially important because it may suggest that CI subjects remain sensitive to across-channel delays several years after implantation despite the fact that the stimulation patterns they hear everyday do not encode information in these across-electrode delays and do not intend to match them to physiological cochlear delays. Given cortical reorganization has been

shown to occur during the first months postimplantation [19], it may be possible that this acrosschannel sensitivity is overall preserved over time.

5. CONCLUSION

The ability of CI listeners to discriminate between electrode delay and electrode stimulation order for widely-spaced electrodes was investigated in two experiments.

Our results show that CI listeners are sensitive to both electrode delay and electrode order with discrimination threshold averaging 15 ms and 12.1 ms, which is in the upper range of the delays produced by the traveling wave in normal hearing. The level of performance achieved in the delay discrimination experiment was similar to that observed in a previous experiment performed in normal hearing subjects.

Given the nature of the task, however, subjects could potentially use different cues to achieve this level of performance, including stimulus duration cues, loudness cues, electrode interaction cues and segregation cues.

We are currently focusing our effort on designing a task where only stimulus duration cues would be present in order to more directly test the existence of a central mechanism compensating cochlear delay.

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