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Pulse-rate discrimination deficit in cochlear implant users: is the upper limit of pitch peripheral or central?

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Abstract

Cochlear implant (CI) users do not reliably associate increases in pulse rate above 300 pulses per second (pps) with an increase in pitch. The locus of this upper limit of pitch remains unknown. The present study tested the hypothesis that this deficit resides at least initially at the auditory nerve. The hypothesis was tested by comparing pulse rate discrimination in different neural excitation pattern, in which a large versus small population of auditory nerve fibers was activated. If poorer pulse rate discrimination was found under conditions where narrower spread of neural excitation (SOE) was anticipated where a relatively small neural population was activated, then it would support the hypothesis that the rate processing deficit found in CI users is related to peripheral neural degeneration. Nine listeners (12 ears) implanted with the Cochlear Americas Nucleus® devices participated in the study. Different SOE conditions were created by (1) selecting electrodes that showed narrow versus broad forward-masked psychophysical spatial tuning curves, and (2) by measuring these electrodes in monopolar (MP) and narrow bipolar (BP0) electrode configurations. Rate discrimination difference limen (DL) were measured at the selected electrodes in two electrode configurations at three base rates (200, 300 and 500 pps). Consistent with the prediction, group mean DL was better (1) at stimulation sites measured with broader tuning, and (2) in MP relative to BP stimulation. These effects were more salient at the more challenging base rates. There was a weak relationship between rate discrimination (above thresholds) and the effect of rate on detection thresholds. Finally, rate discrimination at rates above the known upper limit (i.e., 500 pps) was correlated with duration of deafness and highly predicted the subjects' speech recognition performance in noise. These findings support that pulse rate discrimination depends, at least partially, on neural conditions at the auditory periphery and this peripheral limit predicts speech recognition outcomes with a CI.

Keywords

spread of excitation; multipulse integration; speech recognition; temporal processing

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1. Introduction

Pitch perception remains one of the biggest challenges for electrical hearing with a cochlear implant (CI). Pitch information coded via place of excitation, i.e., differential excitation of the auditory nerve fibers of different characteristic frequencies, is limited (Moore, 2003). CI listeners rely also on temporal processing of the repetition rate of electrical pulses to perceive pitch (Bahmer and Baumann, 2013; Baumann and Nobbe, 2004; Carlyon et al., 2010; Venter and Hanekom, 2014; Gaudrain et al., 2017). Previous studies show that CI listeners are able to identify musical intervals and even recognize melodies by varying the rate of stimulation delivered on a single electrode (Pijl and Schwarz, 1995; McDermott and McKay, 1997). However, the perception of pitch usually only changes with pulse rate up to 300 pulses per second (pps). Beyond, an increase in rate does not reliably elicit percept of an increased pitch (McDermott and McKay, 1997; Venter and Hanekom, 2014; Zeng, 2002). The ability to discriminate pulse rates has been shown to have marked individual variability, with performance typically steeply deteriorating as pulse rate becomes higher than 300 pps), consistent with the “upper limit of pitch” (Bahmer and Baumann, 2013; Baumann and Nobbe, 2004; Carlyon et al., 2010; McKay et al., 2000; Kong et al., 2009; Kong and Carlyon, 2010).

Using just temporal information, normal-hearing listeners are able to estimate pitch of pure tones up to several thousand Hz (Moore, 1973; Moore and Ernest, 2012) and detect rate changes in filtered pulse trains similar to those provided by CIs up to 700 pps (Carlyon and Deeks, 2002; Macherey and Carlyon, 2014). Compared to normal-hearing listeners, CI listeners’ ability to process temporal pitch shows a remarkable deficit. These findings seemed to be consistent with the idea that the deficit in CI listeners is due to the degenerated auditory periphery in deafened ears. However, there is limited evidence supporting a peripheral origin of this limit.

Previous research has tested the hypothesis that the rate processing deficit was related to the auditory nerve (AN) refractory and adaptation behavior. Physiological studies have shown that the AN responses to electrical stimulation, unlike in acoustic stimulation, are highly synchronized (Wilson et al., 1997), and show more adaptation (bursting then silence) to dense stimulation compared to those in non-deafened systems (Shepherd and Javel, 1997). As pulse rate increases, AN response often becomes amplitude modulated, reflecting a synchronized onset response in the evoked compound action potential (ECAP), a reduced response due to refractoriness, and then recovery (Wilson et al., 1997). This refractory and adaptation behavior would limit the accuracy in the AN representation of high-rate stimuli, and the modulation pattern may even result in an octave drop in the perceived pitch relative to the stimulus frequency (Carlyon et al., 2010; Kong and Carlyon, 2010). Studies however have shown that manipulation of the pulse trains that would reduce the effect of adaptation and disrupt AN response synchronization, thus greatly changing the AN response pattern, did not result in expected changes in rate discrimination (Carlyon et al., 2010; Kong et al., 2009; Litvak et al., 2003; Rubinstein et al., 1999; Zeng, 2002). Carlyon and Deeks (2015) further showed that although deteriorated rate discrimination at high rates is accompanied by an increased ECAP amplitude modulation, the modulation was not enough to account for the

observed psychophysical data. These data support the idea that the deficit of rate discrimination with CIs is not specific to any AN response pattern.

There is also only circumstantial evidence to suggest that the upper limit of rate processing resides at a location central to the AN. Oxenham et al. (2004) argued that for rate information to be processed efficiently in the brainstem and above, the information must be represented in AN fibers innervating the corresponding frequency regions of the cochlea, i.e., matching place and rate. Most of the psychophysical studies that compared rate discrimination at different electrodes nonetheless showed no effect of stimulation site (Baumann and Nobbe, 2004; Gaudrain et al., 2017). As an exception, one study showed that MED-EL CI subjects, implanted with the deeply inserted electrodes that potentially access the low-frequency fibers, were able to discriminate rate better at the apical electrode with less place-rate mismatch than the high-frequency basal electrode (Stahl et al., 2016). These results were consistent with a specialized apical temporal processing pathway (Middlebrooks and Snyder, 2009), although such effect was not observed in a different group of MED-EL subjects similarly implanted with the deeply inserted electrodes (Baumann and Nobbe, 2004). Some evidence to support a central origin comes from studies that show the rate processing deficit in electrical hearing is not specific to pitch perception but also occurs in binaural tasks that involve detecting stimulus timing differences at sites central to the AN. Localization studies have shown that bilaterally implanted CI listeners' ability to detect interaural time differences (ITD) in pulse trains arriving at the two ears also deteriorates as rate increases (Van Hoesel and Clark, 1997; Van Hoesel and Tyler, 2003; Ihlefeld et al., 2015). The ITD deficit however could very well be due to poor monaural representations of the high-rate stimuli at any location prior to the inferior colliculus including the AN.

Whether the rate processing deficit with CIs arises at a central or peripheral site remains unknown, and, thus solutions to extend such limit have also been few and unsuccessful. Our recent studies, however, provided evidence that motivated the current study to further investigate whether the rate processing deficit is related to the AN response pattern resulting from peripheral degeneration. Results of our recent studies showed that rate processing at the threshold level, that is how steeply threshold improves with increasing stimulation rate, is related to changes in the spatial activation patterns of the AN (Zhou and Pfingst, 2016; Zhou and Dong, 2017; Zhou et al., 2018a). These studies demonstrated that as the psychophysically estimated neural excitation pattern becomes narrower, achieved by stimulating perimodiolar electrodes or using narrow electrode configurations, the effect of stimulation rate on threshold reduces. These findings suggest that neural representation of changes in stimulation rate depends on the size of the neural population activated to process this information. The idea is that a small number of neurons would need to operate at a relatively high firing probability to achieve the same number of spikes, compared to a scenario where a large number of neurons are excited. With narrow spread of neural excitation (SOE), and thus a small number of activated neurons, moderate stimulation density would drive the sparse nerve fibers close to their maximum firing capacity. Further stimulation (higher rate) would produce small changes in neural responses. Conversely, a large population of neurons would operate with a relatively low firing probability allowing faster stimulation to evoke an increased response. Thus a larger neural population would

yield better neural representation of rate differences. If rate processing at threshold level is limited by the number of participating neurons, the mechanism may similarly explain why rate processing at the suprathreshold levels, e.g., rate discrimination and associated temporal pitch perception, is worse in the degenerated auditory systems compared to normal hearing. It may also explain why there is such a high individual variability in rate discrimination across CI subjects, since the number of the surviving spiral ganglion cells in deafened human ears can widely vary from 4% to 70% of the normal complement of 35,000 to 40,000 cell counts (e.g., Nadol et al., 2001).

In this study, we tested the hypothesis that the upper limit of pitch is related, at least partially, to the condition of the auditory periphery. We measured rate discrimination using similar manipulations that result in different SOE, as those adopted in previous studies (Zhou and Pfingst, 2016; Zhou and Dong, 2017; Zhou et al., 2018a). Specifically, we measured rate discrimination at stimulation sites with considerably different steepness of psychophysical spatial tuning curves (PTCs) and in stimulation modes expected to produce narrow versus wide activating patterns. If the effect of rate on thresholds and rate discrimination at suprathreshold levels indeed share a common mechanism, the two measures should correlate across the experimental conditions within subjects or across subjects, which was also examined in the study. Lastly, if rate processing is limited by the physiological factors, and if we assume these physiological factors are important for implant function, then a subject's rate processing deficit should also predict the subject's overall speech recognition performance. To test this hypothesis, subjects' speech recognition performance was evaluated and compared to their rate processing abilities.

2. Methods

2.1. Subjects and Hardware

Nine adult listeners implanted with the Cochlear Nucleus® devices (Cochlear Corporation, Englewood, CO) participated in the study. Three subjects were bilaterally implanted and both ears were tested, one ear at a time. This resulted in a total of twelve ears. All subjects had used the implant for at least one year at the time of the experiment. The use of human subjects was approved by the East Carolina University Institutional Review Board. All psychophysical testing was conducted using a Nucleus Freedom® processor (Cochlear Corporation, Englewood, CO). The experiments were designed and controlled by MATLAB (The Mathworks, Nattick), interfaced with the NIC (Nucleus Implant Communicator) II research software. Stimuli used in the psychophysical experiments were all biphasic pulse trains with a phase duration of 25 μ s and an interphase interval of 8 μ s. Speech recognition was measured using the subject's own processors (CP810 or CP910) with the subject's everyday-use program. For all subjects, the everyday-use program utilized an ACE speech processing strategy at a stimulation rate of 900 pps. Details of the subject information are provided in Table 1.

2.2. Choosing Stimulation Sites

For each implanted ear, two stimulation sites were selected. The sites were estimated to produce relatively narrow versus broad neural excitation. The sites were selected based on

their thresholds for detecting low-rate stimuli (pulse rate: 80 pps; duration: 300 ms), with lower threshold predicting narrower psychophysically estimated neural excitation (for details see Zhou, 2016). The selected sites and their low-rate thresholds (low threshold corresponding to narrow SOE) are shown in Table 1. Forward-masked psychophysical spatial tuning curves (PTCs) were measured, in MP stimulation mode, at the two sites (probe locations) to confirm the expected differences in spatial spread of neural excitation. In the forward-masking paradigm, the amount of current needed for a masker stimulus to just mask a low-level stimulus on the probe location was measured, as a function of masker-probe separation. The greater the spatial separation between the masker and the probe, and thus presumably the less overlap between the neuron populations excited by the masker and the probe, the higher the current would be required for masking to occur. A steeply-sloped masker level versus masker-probe separation function would suggest narrow SOE at the probe location. Both the masker and the probe stimuli used a rate of 900 pps. The maskers were 300 ms long and were placed on the 3 electrodes basal to the probe, on the same electrode as the probe, and on the 3 electrodes apical to the probe (7 masker locations when spatially allowed). The probe was 20 ms long, and was separated by a 10 ms gap from the masker presented forward in time. The dynamic ranges (DRs) of the masker (7 maskers per probe) and probe stimuli were estimated using method of adjustment (MOA), where the subject was asked to adjust the current level up and down to find the level that was just detectable (T level), and then increase the current to a level that was maximum comfortable (C level). Different step sizes of current adjustment (25, 5, and 1 clinical unit level; CL) were made available, but the subjects were encouraged to be cautious in using large step sizes to avoid over stimulation and were encouraged to use small step sizes when finding the T levels. The unmasked threshold of the probe was obtained using a 3-interval 3-alternative forced-choice paradigm (3I3AFC), where the stimulus was initially presented at 50% of its DR and adapted based on the subject's response following a 2-down 1-up rule. The step size was 10 CL for the 1st reversal, 5 CL for the 2nd, 2 CL for the 3rd, and 1 CL for the remainder of the 12 reversals. Threshold was taken as the average of the levels at the last 6 reversals. To measure PTC, the level of the probe was fixed at 2 dB above its unmasked threshold and the level of the masker started at 20% of its DR and adapted. The masker level at masked probe threshold was determined for each masker location, using the 3I3AFC paradigm described above. Since the probe level was set at a certain dB value above its unmasked threshold, rather than a certain % DR, the masker levels were also quantified in dB re mA rather than in % DR. Both the basal and apical sides of the PTC function were fit with a linear slope (dB/electrode), and the average of the two slopes was taken. Missing data in the PTCs were due to either the probe location being close to the apical or basal end of the electrode array or that the masker level exceeded its C limit before it could mask the probe. Note that some of the subjects tested here took part in the Zhou et al. (2018b) study, where their tuning curves had already been measured and reported, but those data were quantified in % DR. Also note that some subjects from Zhou et al. (2018b) were not included in the current study as they were unavailable at the time of the experiments.

2.3. Measuring pulse rate discrimination

Pulse rate discrimination was measured at the two selected sites for each ear, at three base rates (200, 300, and 500 pps) and in two stimulation modes (monopolar, MP; bipolar, BP0,

reference apical to the active). This resulted in 12 experimental conditions per ear (2 sites $\times$ 3 rates $\times$ 2 stimulation modes). DRs of the 12 stimuli were first estimated using MOA. The level corresponding to 50% DR of the 200-pps MP stimulus at the broadly-tuned stimulation site was determined and all other stimuli were loudness balanced to this reference. The subject was instructed to adjust the level of the stimulus within its DR and compare the loudness to that of the reference for as many times as needed, until the stimulus and the reference were perceived as equally loud. Subjects were instructed to listen for loudness rather than any other aspects of the stimuli. Then pulse rate discrimination was measured for the 12 conditions using the loudness balanced levels. For each condition, a 3-interval 2-alternative forced-choice paradigm (3I2AFC) was used, where the first interval always contained the reference stimulus, and the second or the third interval, chosen at random, contained the target stimulus (Baumann and Nobbe 2004). The subject was asked to ignore loudness, and to choose the one interval (either 2 or 3) that had a stimulus different in pitch than that in the first interval. No feedback was given. For a given base rate, the rate difference in the reference and the target stimuli, defined as R , started at 100% of the base rate and adapted, following the subject's responses. R adapted in a factor of 1.41 following the 2-down 1-up rule. The factor reduced to 1.19 starting with the 4th reversal of a total of 10 reversals. The arithmetic mean pulse rate of the reference and the target always equaled the base rate, while the reference stimulus could have a pulse rate either higher or lower by $R/2$ than the base rate. Pulse rate difference limen (DL) was quantified as the minimum R (mean R at the last 6 reversals) required to detect a pitch difference between the reference and the target stimuli, expressed in a percentage relative to the base rate. DL was unmeasurable when R exceeded twice the base rate such that the low-rate stimulus became smaller than zero.

2.4. Measuring effects of rate on threshold

The effect of stimulation rate on detection threshold was examined on the same stimulation sites that were evaluated for rate discrimination described above, in MP and BP0 stimulation (2 sites $\times$ 2 stimulation modes). The effect of the stimulation rate was referred to as multipulse integration (MPI) and was quantified as threshold decrease in dB per doubling of stimulation rate. Thresholds were measured using the 3I3AFC procedure described above, for 300-ms long pulse trains that varied in two stimulation rates: 160 and 640 pps. Stimuli were first estimated for their DRs using MOA. For each condition, the level of the stimulus started at 50% DR and adapted based on subjects' response using a 2-down 1-up rule. Some of the MPI data were published in Zhou et al. (2018a). MPIs were not measured for S19L and S25R due to time constraint.

2.5. Speech reception threshold

The subjects were then evaluated for speech recognition in noise, by lab members blind to the subjects' rate discrimination performance. The speech signal and noise were co-located and were delivered via a loud speaker positioned 1 meter away from the subject at 0° azimuth. The lowest signal to noise ratio (SNR) the subject needed to recognize speech with 50% accuracy was quantified as the speech reception threshold (SRT). SRT was measured with CUNY sentences presented in a white noise that was 100% sinusoidally amplitude modulated at a rate of 4 Hz. The noise was presented for 1.5 seconds alone before the

sentence, overlapping with the sentence, then alone again for 0.5 seconds after the sentence. SNR was calculated for the timeframe when the sentence and the noise overlapped. The level of the sentence was kept at 65 dB (A) SPL and the level of the noise was adapted to ensure that the sentence was audible at low SNRs. SNR started at 20 dB and adapted with a step size of 2 dB based on the subject's response following a 1-down 1-up rule. The subject was instructed to repeat the sentence she/he heard. The response was counted as a correct one if all key words were repeated correctly. The average SNR at the last 6 reversals of a total of 12 was taken as the SRT. Four sentence lists were used to measure one threshold, and the lists were chosen at random without replacement for each subject.

3. Results

Figure 1 shows PTCs measured for the two stimulation sites selected from each ear. As mentioned above, a part of the data, analyzed differently, were published in Zhou et al. (2018b). The two groups of selected stimulation sites (red circles versus blue squares) were estimated to contrast in the width of neural excitation. The mean PTC slopes for the low- and high-threshold electrodes were 2.66 and 0.46 dB/electrode, respectively, and the difference was statistically significant [Shapiro-Wilk test for normality, $p > 0.05$; paired samples t-test: $t(11) = 6.52$, $p < 0.001$]. There were few instances where the two electrodes did not show marked differences in PTC slope, such as the apical sides of the two functions from S16R.

Figure 2 shows pulse rate DLs for individual subjects, as a function of base rate (i.e., the mean pulse rate of the two stimuli in comparison), measured at the two sites in MP and BP stimulation modes. Note that although relative DL in percentage of base rate was used for all analyses, for better visual illustration of the data, DL was plotted here and in Figure 3, in absolute rate (pps) against $\log_2$ base rate. A Mixed Linear Model was used to analyze the effect of base rate, stimulation site, and stimulation mode on DLs, as well as the interactions among the three variables. Results showed that DLs were significantly different across base rates [$F(2, 66.44) = 49.17$, $p < 0.001$]. Paired comparisons showed that DLs were significantly better at the 200-pps base rate, compared to those at 300 pps [$t(11) = -3.99$, $p = 0.002$] and 500 pps [$t(10) = -7.24$, $p < 0.001$]. DLs were also significantly better at the 300-pps base rate compared to those at 500 pps [$t(10) = -5.63$, $p < 0.001$]. Note that these comparisons remained significant after Bonferroni corrections to control for Type I errors. DLs were better at stimulation sites estimated to produce broader neural excitation [$F(1, 56.37) = 30.61$, $p < 0.001$] and better in MP stimulation relative to BP stimulation [$F(1, 43.55) = 50.99$, $p < 0.001$]. Missing data were cases where DLs exceeded the possible rate range and were not measurable. Note that unmeasurable DLs were also often found at high base rates, at sharply tuned sites, or in BP stimulation. To include the unmeasurable thresholds in the analysis such that the main effects would not be underestimated, a non-parametric test was used where the numeric DL data were rank ordered, and the unmeasurable thresholds were assigned with the highest rankings. The Friedman's analysis of variance by ranking confirmed that DL was better in MP than in BP stimulation ($p = 0.001$), better at the broad excitation than the narrow excitation sites ($p = 0.002$), and the effect of base rate was also highly significant ($p < 0.001$). Wilcoxon matched-pair signed-rank tests showed that all 3 comparisons between the base rate conditions were significant (p

< 0.001). After removing S16R, whose electrodes did not show apparent difference in tuning, analyses of the results returned the same conclusions.

Group mean data are summarized in Figure 3. It can be seen that the DL differences between stimulation sites and those between stimulation modes were more prominent at the higher base rates (e.g., 500 pps). Significant interaction terms confirmed that the effect of stimulation site was larger at higher base rates [$F(2, 37.80) = 16.13, p < 0.001$], and similarly, the effect of stimulation mode was larger at higher base rates [$F(2, 70.69) = 10.33, p < 0.001$]. At the base rates of 200 and 300 pps, DLs were not significantly different across conditions, after Bonferroni corrections for multiple comparisons. At 500 pps, the trend of the data evidenced better DLs at the broadly tuned sites in MP stimulation, relative to those at the sharply tuned sites in MP stimulation, followed by the broadly tuned sites in BP stimulation, and finally the sharply tuned sites in BP stimulation. After Bonferroni corrections, paired comparisons showed that for DLs measured at both the sharply and broadly tuned sites, discrimination was significantly better in MP than in BP stimulation [broad: $t(8) = -2.77, p < 0.025$; sharp: $t(9) = -3.07, p < 0.025$].

The relationship between MPI (effect of rate on threshold) and rate DL was examined across subjects and across conditions within subject. As mentioned earlier, some of the MPI data were published in Zhou et al. (2018a). Considering the within- and between-subject variances in one Univariate General Linear Model, results indicated that for all base rates, rate DL was correlated with the steepness of the MPI function [base rate 200 pps: $r^2 = 0.58, p = 0.001$; base rate 300 pps: $r^2 = 0.83, p < 0.001$; base rate 500 pps: $r^2 = 0.59, p = 0.003$]. Note that r^2 was adjusted (lowered) for accounting for both the within- and between-subject variances. Next, the relationship between MPI and rate DL was analyzed again to separate the within- and between-subject variances. That is, analyses were performed to examine whether subjects who generally did better on rate discrimination also showed steeper MPI (between-subject correlation), and whether rate discrimination and MPI varied in an associated pattern across the within-subject stimulation site and mode conditions. To remove within-subject variances and examine the between-subject effects only, MPI and rate DL were averaged across conditions within each subject. The subject mean MPI slope and DL were normally distributed as indicated by the Shapiro-Wilk test for normality ($p > 0.05$), and the relationship between the two variables was examined using Pearson's correlation for each base rate. The results are shown in Figure 4. To remove between-subject variances and examine the within-subject effects only, the MPI slopes were normalized by subtracting the mean MPI measured from a given subject from that subject's data. The same normalization was applied to the DL data. Because the normalized rate DL at 300 pps was not normally distributed (Shapiro-Wilk test for normality, $p = 0.007$), the nonparametric Spearman's rho was used for these correlations. The results are shown in Figure 5. Note that each subject had four data points representing the four within-subject conditions: 2 sites and 2 stimulation modes. A significant correlation was found between MPI and DL at the 300-pps base rate [$r = 0.33, p = 0.03$]. The correlation indicated that at the base rate of 300 pps, better rate DLs, which were associated with broader tuning and MP stimulation, predicted steeper MPI.

Figure 6 shows the relationship between rate DLs averaged across stimulation site and mode conditions and subjects' SRTs. The general trend of the data was that better pulse rate

discrimination was associated with better speech recognition performance in noise. The correlation between the high-rate DLs (i.e., 500 pps) and SRTs remained significant after controlling for Type I errors ($p < 0.0125$), while correlations at 200 and 300 pps did not survive the correction.

The relationship between rate DLs and subjects' demographic variables was also examined. Results showed that rate DLs at 200 pps and 500 pps were correlated with subjects' chronological age, but the correlations were not significant after Bonferroni correction ($p > 0.016$). It is interesting to observe that duration of deafness was correlated with rate DLs at 500 pps, the more challenging rate ($r = 0.68$, $p < 0.016$), but not at 200 or 300 pps. The correlation showed that longer duration of deafness predicted poorer rate discrimination. Duration of implant use did not predict rate discrimination performance.

4. Discussion

Pitch perception remains to be a major disability for deafened individuals with CIs. This disability results in great challenges for CI listeners to use pitch information to segregate competing auditory objects in noisy listening environments (Bird and Darwin, 1998), understand lexical tones in tonal languages (Zhou and Xu, 2008), and appreciate music (Gfeller and Lansing, 1991). CI listeners are only able to detect pitch differences well in the temporal repetition patterns of the stimulus when this repetition rate remains under 300 pps (e.g., Carlyon et al., 2010). More importantly, the origin of this limit was unknown. In the present study, we tested the hypothesis that the rate processing deficit and the accompanying upper limit of pitch with CIs resides, at least initially, at the level of the auditory nerve.

The existing pulse rate discrimination data suggest that the upper limit of pitch is not specific to any AN response patterns. First, CI users have similar difficulty discriminating the rate of AM modulation applied on a high-rate carrier as discriminating pulse rates, although AN response to the modulated high-rate stimulus and the unmodulated low-rate stimulus can be substantially different (Kong et al., 2009). Reducing synchronization and adaption in the AN response pattern, for example by introducing ramping in a long pulse train or adding a conditioning background high-rate stimulus (Rubinstein et al., 1999), did not improve performance (Carlyon et al., 2010). Findings of the present study support the idea that rate discrimination indeed depends on how the AN responds to stimulation. The favorable response pattern is one that is spatially broad. The possible mechanism is that, with broader neural activation, single fibers in the large number of activated neurons may not need to respond to each pulse in a low-rate pulse train, thus as rate increases, these neurons would be able to increase their firing rate to respond to an increase in the density of stimulation, producing a better representation of a high-rate stimulus. If the activated neurons are small in quantity, a low-rate stimulus may already have driven these neurons to a high point on their DR, thus leaving little room for further increase in response to an increase in rate. This idea is supported by current data that showed better rate discrimination in MP stimulation and at stimulation sites estimated to produce broad spatial neural activation patterns (i.e., flat PTCs). More interestingly, such differences were not apparent at the low base rates (200 and 300 pps), which were rates that were at or below the known "upper limit." Remarkable differences were seen at 500 pps, where in MP stimulation at the

broadly tuned sites, the subjects on average needed a ~75% rate difference between two pulse trains to detect a pitch difference, compared with a ~140% rate difference in BP stimulation at the sharply tuned sites. The interactions suggest that the differences in the number of activated neurons created by varying stimulation site and mode were more likely to have an effect on rate discrimination at higher rates. It is important to point out that given an equal number of neurons available to respond to stimulus, the limit in rate processing certainly also depends on the inherent temporal responsiveness of the activated neurons determined by their biophysical properties (Boulet et al., 2016), or the degree to which the fidelity of the surviving neurons, such as refractoriness, has degraded (Zhou et al., 1995).

If broad stimulation results in better rate discrimination, then simultaneous stimulation of multiple electrodes should produce better rate discrimination compared to that with single electrodes. This was indeed demonstrated by Bahmer and Baumann (2013). They showed that, with the MED-EL devices, rate discrimination in simultaneous multichannel stimulation was better than that in the single channel condition for base rates higher than 500 pps, as was reported here, than for lower rates. Bahmer and Baumann (2013) attributed the benefit of broad stimulation to the fact that onset neurons in the cochlear nucleus that are sensitive to stimulus periodicity integrate over a broad frequency range thus require a broad input. The summation effect via cross correlation across channels may also reduce noise in the neural response to the stimulus. These alternative mechanisms are certainly also plausible. They however would predict better performance with broader stimulation across all base rates, and thus cannot explain why broad activation was particularly helpful at or beyond the known rate limit.

One may argue that the spatially restricting electrode configurations may not necessarily result in narrow neural excitation (e.g., Kwon and van den Honert, 2006; Srinivasan et al., 2013), if the required loudness cannot be achieved by exciting the neurons just local to the electrode. To achieve equal loudness, current levels required by BP stimulation are typically higher than MP stimulation, and the spread of current might result in a spread of neural excitation. Worse rate discrimination seen in BP stimulation, relative to MP stimulation, then may not necessarily be attributed to the differences in the number of activated neurons. The worse performance could alternatively be due to the unnatural bimodal excitation peaks resulting from the return electrode being immediately adjacent to the active electrode. If this were true, the effect would again, have occurred at all base rates, but our results indicated that performance in BP stimulation was worse than that in MP stimulation only when base rate was high enough that perhaps the differences in the number of activated neurons by the two electrode configurations started to play a role.

Our previous studies showed similar effects of stimulation site and mode on rate processing at the threshold level (Zhou and Pfingst, 2016; Zhou and Dong, 2017; Zhou et al., 2018a). That is, a greater reduction in threshold current level with increasing stimulation rate (steeper MPI) was associated with MP stimulation and with stimulation sites estimated to produce broad neural excitation. The present study measured both effects in the same subjects and conditions. Considering the mixed between- and within-subject variances in both variables, there was a strong relationship between discrimination of pulse rates at suprathreshold levels and the effect of increasing rate on lowering thresholds. These

correlations suggest that subjects who performed on average well on pulse rate discrimination also showed a large average effect of rate on lowering thresholds, and that rate discrimination varied in correlated pattern with MPI across stimulation site and mode conditions within subjects. When considering the two sources of variance separately, a weak within-subject relationship was found, where rate discrimination at a base rate of 300 pps varied in correlated pattern with MPI across within-subject stimulation site and mode conditions. These findings overall suggest that rate processing at and above threshold levels might share a common mechanism. That is, they both depend on the size of the activated neurons processing a change in pulse rate.

During the task of rate discrimination, subjects were asked to judge whether the target and reference stimuli had the same pitch. When pulse rate difference between the two stimuli adapted and the current level remained constant, the higher-rate stimulus could be perceived as louder than the lower-rate stimulus, even though the loudness versus pulse rate functions at super-threshold levels is relatively shallow (McKay and McDermott, 1998; Zhou and Pfingst, 2012; Venter and Hanekom, 2014). However, if the subjects did perceive a loudness difference between the high- and low-rate stimuli in comparison, it would at least indicate that there was indeed a difference in neural response to the stimuli, i.e., an increase in neural spikes. Whether such increase in neural activity is accurate enough in its timing to follow the inter-pulse interval of the stimulus to support pitch coding, however, is unknown. This was consistent with several previous studies that reported an improvement in pulse rate discrimination does not necessarily lead to an improvement in pitch ranking (e.g., Venter and Hanekom, 2014).

Since the “narrow” experimental condition that activated fewer auditory fibers resulted in poorer rate processing, it supports the idea that the overall poor rate processing ability in implant subjects is due to a reduction in spiral ganglion cells resulted from neural degeneration. It may also explain why there is such a wide individual variability in rate processing abilities across CI subjects (e.g., Goldsworthy and Shannon, 2014), since neural degeneration is highly subject dependent, the pattern and time course of which vary with etiology, duration of deafness, and age at deafening (Nadol et al., 2001). Our results in fact showed that the subjects who were deaf for a longer period of time and had probably suffered from more severe nerve loss, tended to perform more poorly on the rate discrimination tasks. It is interesting that duration of deafness was only a factor for rate discrimination performance at 500 pps, suggesting that the nerve condition in implant subjects, although highly variable, may have been generally sufficient for processing the lower rates. This agrees with the result reported earlier that the benefit of broad stimulation was also only salient at 500 pps. Our results also indicated that the subjects who had longer duration of deafness and performed more poorly on rate discrimination, were those who had more difficulties understanding speech in noise. These results were consistent with the idea that rate discrimination performance reflects implant subjects’ nerve condition, which in turn predicts the subjects’ outcome with the CI (Seyyedi et al., 2014; Kenway et al., 2015). The fact that strongest correlation between rate discrimination and speech recognition was also found at the most challenging rate, i.e., 500 pps, suggests that individual differences in neural health condition may be better captured by rate processing above 300 pps, the average upper limit. Although the current data support that the rate processing deficits of implant

subjects reside initially at the AN, they cannot prove that the deficits are only in the periphery.

5. Conclusions

In summary, the results of the current study indicate:

- Broader stimulation of the auditory nerve facilitates rate discrimination by activating a larger number of neurons
- There was a weak relationship between suprathreshold rate discrimination and the effect of stimulation rate on detection threshold
- Rate discrimination at high rates was correlated with duration of deafness with longer duration of deafness predicting poorer performance
- Rate discrimination at high rates may reflect implant subjects' neural health condition at the periphery, which in turn predicted subjects' speech recognition performance

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Abbreviations:

CI	cochlear implants
pps	pulses per second
DL	difference limen
MP	monopolar
BP	bipolar
SOE	spread of excitation
AN	auditory nerve
ECAP	evoked compound action potential
ITD	interaural time differences
PTCs	psychophysical spatial tuning curves
DRs	dynamic ranges
MOA	method of adjustment
3I3AFC	3-interval 3-alternative forced-choice
3I2AFC	three-interval two-alternative forced-choice

SNR	signal to noise ratio
SRT	speech reception threshold
SPL	sound pressure level
T	threshold
C	maximum comfortable level
CL	clinical unit level
MPI	multipulse integration

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- Rate discrimination with cochlear implants is better in broader neural activation
- Rate discrimination beyond the upper limit (500 pps) is correlated with duration of deafness and predicts speech recognition in noise across subjects
- The upper limit of pitch resides initially at the auditory nerve

Figure 1.

Forward-masked psychophysical spatial tuning curves (PTCs). The masker level required to just mask a low-level probe stimulus is shown as a function of masker-probe separation in number of electrodes. Negative separation indicates that the masker location was basal to the probe electrode and zero separation indicates that the masker was on the same electrode as the probe. Two probe sites, one estimated to produce relatively broad (blue square) and the other relatively sharp (red circle) neural excitation patterns, were measured for each ear. The probe electrode numbers in the order of sharper/broader are shown in the upper corner of each panel.

Figure 2.

Individual pulse rate difference limen (DL). DL, the smallest pulse rate difference (pps) required to discriminate pitch differences in electrical stimuli, is plotted as a function of three base pulse rates. Red functions with circle symbols show DLs measured at the sharply tuned sites, while blue functions with square symbols show DLs measured at the broadly tuned sites. Filled symbols represent MP and unfilled symbols represent BP conditions.

Figure 3.

Group mean pulse rate DL. DL (pps) averaged across subjects is plotted as a function of base rate for the various conditions indicated by legend, shown in the upper left corner of the figure. Error bars represent standard errors.

Figure 4.

Between-subject correlations (Pearson's) between MPI (multipulse integration: effect of rate on threshold) and pulse rate DL. DL averaged across stimulation mode and site conditions, for each base rate, is plotted as a function of MPI averaged across stimulation mode and site conditions. Each data point represents one ear of a subject. Lines represent linear fit to the data.

Figure 5. Within-subject correlations (Spearman's rho) between normalized MPI (multipulse integration: effect of rate on threshold) and normalized pulse rate DL. Symbols represent the ears as indicated by the legend. Each subject had four data points from the four within-subject conditions: 2 rates $\times$ 2 stimulation modes.

Figure 6.

Correlations between speech reception thresholds (SRTs) and DLs. SRT is plotted as a function of DL averaged across the four experimental conditions (2 sites and 2 modes) at a given base rate in panels A-C. Panel D shows SRT plotted as a function of DL averaged across all conditions (2 sites, 2 modes, and 3 base rates). Each data point represents an ear, as indicated by the legend. Correlation coefficient, p value, and the number of independent samples in the correlation are shown in the upper left corner of each panel. Note that S22R did not have DL data at 500 pps, thus n was 11.

Table 1.

Subject demographic information.

Subject	Gender	Age (Yrs)	Duration of Implant (yrs)	Duration of Deafness (yrs)	Device Type	Speech recognition in quiet (TIMITs %)	Tested sites/electrodes (sharp/broad)	Low-rate T level on tested sites (CL)
S1L	M	77	13.8	0.1	CI24R (CS)	86.3	4/11	155/191
S1R	M	77	7.8	6.0	CI24RE (CA)	89.3	8/14	138/166
S3L	F	67	11.3	3.4	CI24RE (CA)	93.1	3/10	67/95
S3R	F	67	12.8	1.8	CI24RE (CA)	95	3/14	54/74
S4L	F	57	5.3	0.4	CI24RE (CS)	50.8	21/6	124/154
S10R	F	66	2.7	12.4	CI24RE (CS)	69.91	4/13	52/102
S16L	M	56	10.9	45.1	CI24RE (CA)	22.6	4/9	79/103
S16R	M	56	9.0	47.0	CI24RE (CA)	12	18/6	79/116
S17R	F	72	1.0	0.3	CI422	50.8	7/10	132/174
S19L	F	69	1.0	6.0	CI24RE (CA)	30	20/7	134/168
S22R	F	71	3.1	0.4	CI24RE (CA)	48.7	22/9	127/168