A COMPARISON OF INFERIOR COLLICULUS RESPONSES TO BAND PASSED NOISE IN YOUNG AND AGED RATS USING SINGLE UNIT RECORDINGS

by

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To my family and friends who have supported me along the way.

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LIST OF ABREVIATIONS

A1	Primary Auditory Cortex
ARHL	Age Related Hearing Loss
BPN	Band Passed Noise
CF	Center Frequency
F344	Fischer 344 Rats
IC	Inferior Colliculus
ICC	Central Nucleus of IC
MGB	Medial Geniculate Body
MGV	Ventral Division of MGB

ABSTRACT

Half of people over 75 in the United States suffer from age related hearing loss and have trouble understanding speech in a noisy background. Even older adults who have normal pure tone audiograms can have trouble understanding speech in a noisy background. Speech is a complex sound and therefore sounds more complex than pure tones are required to understand the differences in processing noisy speech in young and aged individuals. Band passed noise is easily controlled and is more complex than pure tones making it better stimulus for testing. The first place in the ascending auditory pathway that does complex processing is the inferior colliculus. Single unit recordings from the inferior colliculus of young and aged F344 rats were preformed using half octave band passed noise and pure tones. Firing rates, first spike latencies, the number of tuning peaks, normalized peak slope, bandwidth, and Q factors were all evaluated for each unit in response to band passed noise. For 54 of the units their responses to pure tones were also collected. Out of 286 units recorded from young animals, 218 were responsive and 178 of them had a band passed response. Out of 193 aged units, 145 were responsive and 134 had a band passed response. Young units had a significantly higher total firing rate ($p = 0.008$) and bandwidth ($p = 0.004$). The normalized peak slopes and Q factors were significantly lower in young units indicating sharper tuning in the aged units. Pure tones elicited a stronger response than band passed noise however, for many units the best frequency was similar for both stimuli. These results show that aged units are less responsive to stimuli containing multiple frequencies which may help explain why older adults have trouble understanding noisy speech.

1. INTRODUCTION

Age related hearing loss (ARHL) affects 1/3rd of people over 65 in the United States and half of people over 75 [1]. One of the largest problems associated with hearing and aging is the ability to understand speech, especially in noisy environments [2]. Even older adults who do not have ARHL experience issues with understanding speech in noisy backgrounds [3, 4]. Due to this, pure tone audiograms are not able to accurately predict whether an older adult will have trouble understanding speech [5]. The fact that these adults have normal audiograms suggests that they do not have a deficit in the periphery auditory system. Instead there is most likely a deficit in the processing of speech in the central auditory system. The first area in the central auditory system that does complex processing is the inferior colliculus (IC). Therefore, it is important to understand the differences in speech processing in the IC in young and aged mammals. Bandwidth is an important part of understanding noisy speech [6], since it is a good representation of the background noise. Thus, band passed noise is a good choice of stimulus and will be used here.

1.1 Auditory System Overview

The auditory system is comprised of multiple parts and can be broken down into the ascending and descending pathway. Sound identification and localization are mostly controlled by the ascending pathway with the descending pathway modulating attention and behavior [7]. Both pathways innervate nuclei from the cochlear nucleus (CN) to the core auditory cortex (A1), with the ascending pathway leading from the cochlea to A1 and the descending pathway leading from A1 to the CN.

In the ascending pathway sound waves initially enter the ear where they contact the tympanic membrane which in turn transmits the vibrations to the cochlea via the three bones of the middle ear [8]. Hair cells within the cochlea convert the mechanical vibrations into an electrical signal that is sent to the auditory nerve [8]. Processing of the sound wave begins in the cochlea due to its tonotopic organization. The frequency of the sound wave determines which area of the cochlea is activated and therefore what electrical signal is sent to the auditory nerve. From the auditory nerve, the electrical signal is passed to the central nervous system via the CN. Each CN then sends projections to both the left and right superior olivary nucleus. The inferior colliculus receives inputs from the superior olivary nucleus and is the first location in the ascending pathway where sound localization and identification occur [7]. Further processing then occurs in the medial geniculate body (MGB) and A1. Figure 1A depicts the ascending pathway and includes further inputs to the IC which will be discussed later.

After processing the information from the ascending pathway, A1 sends information back to the MGB, IC, superior olivary nucleus, and CN. This information is used to modulate processing, attention and control the behavioral response [9]. Figure 1B shows the connections of the descending pathway. Given that these experiments do not involve attention or behavior the descending pathway will not be described in much detail.

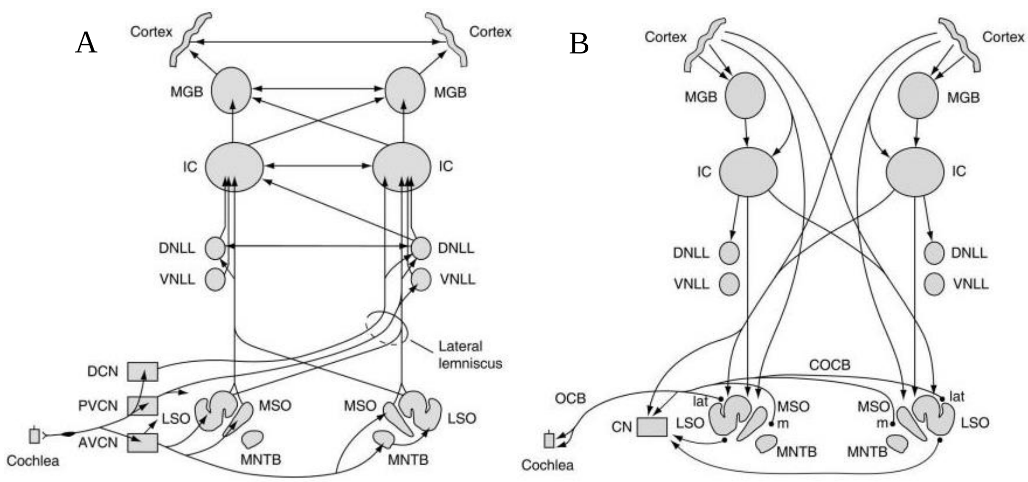

Figure 1.1. Views of the A) ascending and B) descending auditory pathways [7].

1.2 Inferior Colliculus

The IC is located in the midbrain is an integrative auditory center where sound localization and identification occur [7]. It is divided into three sections, the central nucleus (ICC), the dorsal cortex, and the external cortex. The ICC makes up the largest portion of IC and receives only auditory inputs, whereas the dorsal cortex and external cortex also receive non-auditory inputs [9].

Similar to the cochlea, ICC also has a tonotopic organization although in a different manner than the cochlea. Instead of a continuous frequency representation, ICC has a discontinuous pattern of frequency representation. Each lamina has a range of frequencies that it best responds to creating a step-like frequency representation when plotting the best frequencies of each lamina [10]. The frequency range of each lamina is around 0.3 octaves and is broader than those of areas lower in the ascending auditory pathway [10, 11]. As 0.3 octaves is not large, many of the neurons in ICC exhibit sharp tuning curves in anesthetized animals [7]. However, ICC neurons also respond well to frequency modulated stimuli and not just pure tones. Poon et al. found that 75% of ICC units responses to frequency modulated stimuli were not able to be predicted by pure tones [12]. This result helps explain why the ICC is able to pick specific sounds out of a group of sounds, an important part of understanding noisy speech [7].

1.3 Band Passed Noise

Band passed noise (BPN) is created by using a band pass filter with varying cutoffs on random noise [13]. The center frequency can be changed by changing the center frequency of the random noise and the bandwidth can be changed by changing the filter cutoffs on either side. The further apart the cutoffs are, the larger the bandwidth. Figure 1.2 shows a pure tone, multiple bandwidths at the same CF and white noise, all with the same center frequency. Pure tones, as the name suggests, consist of a single frequency whereas white noise contains frequencies across the entire spectrum. In the middle is BPN in which the frequencies within it can be easily controlled making it a useful stimulus.

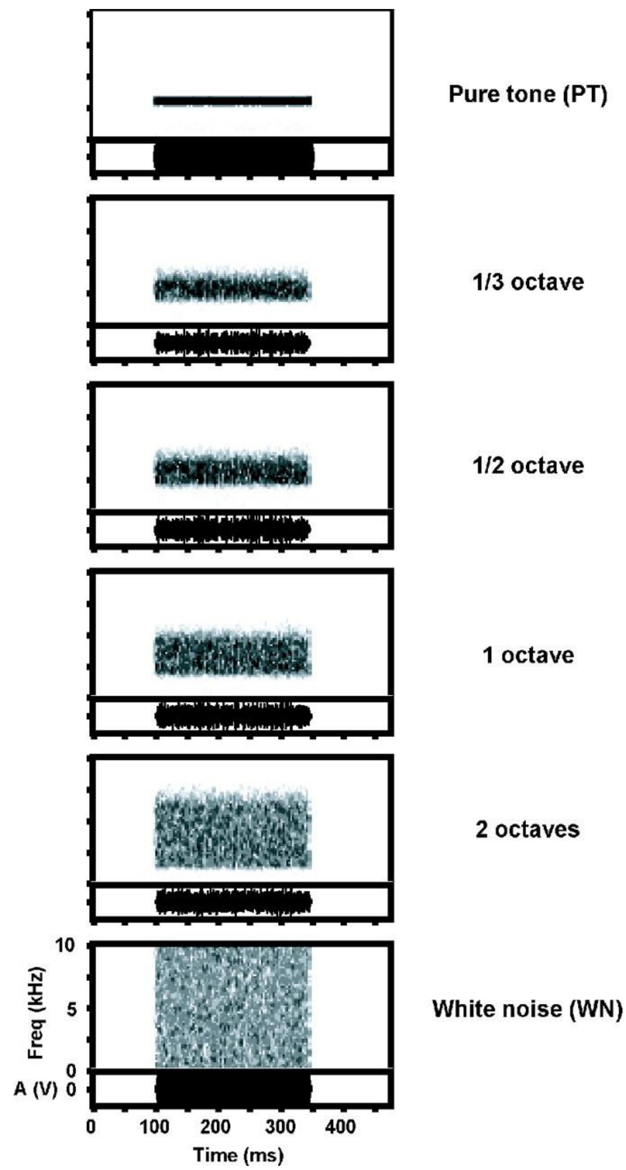

Figure 1.2. Spectrograms for stimuli with the same CF but varying bandwidths [13].

Responses to BPN have been well studied in various animals in IC, MGB, and A1. Most of these studies compare responses to BPN and pure tones. When comparing responses multiple parameters are used including the response bandwidth, the number of tuning peaks, first spike latencies and firing rates.

1.3.1 Responses in Auditory Cortex

Historically, it had been thought that A1 neurons preferred pure tone or narrow band stimuli [14, 15]. However, as BPN becomes more widely used, there is increasing evidence that there are many neurons in A1 that prefer broad-band stimuli. O'Connor et al. found that in rhesus monkeys, 85% of the neurons in A1 they tested responded to BPN and 40% of those responsive neurons had a wide bandwidth [14]. In a study in marmoset monkeys, BPN of 1/3rd and 2/3rd octaves produced shorter latencies, greater responses, and lower thresholds than pure tones with the same CF [14, 15]. Ehret et al. 1997 found that the bandwidth and frequency tuning of A1 units were similar to those of IC [16]. They also concluded that tuning curves created using pure tones were unable to accurately predict responses to complex sounds such as BPN [16].

1.3.2 Responses in Thalamus

The core part of the MGB is the ventral division (MGV) which receives input from ICC [7]. It is important to note the responses of MGV to BPN to determine if the responses could in part be inherited from ICC. Single unit recordings in the MGV of marmoset monkeys showed that MGV responded to both pure tones and BPN, however it preferred narrow bandwidths [17]. Most of the MGV units also had only a single peak in their frequency tuning curves [17]. This idea is further supported by the large quality factors or Q factors for MGV in various species. For mice and guinea pigs, Q factors for the MGV range from 2 – 3, indicating sharp tuning [18, 19].

1.3.3 Responses in Inferior Colliculus

Many studies that use single unit recordings in the IC do not use BPN, however they do evaluate the response bandwidths. In a study with mice that recorded responses in the IC to pure tones masked with narrow band noise, the response bandwidth at a CF of 10 kHz was around 2.5 kHz [11]. Whereas in the cat IC, the response bandwidth at 10 kHz was 3.5 kHz [20], indicating there may be some species differences. Both studies mentioned here showed that as the CF increased the bandwidth also increased [11, 20]. Similar to pure tone studies, IC units in mice had bandwidths between 3/8 - 1/3 of an octave when pure tones were masked by narrow band noise [11]. Q factors in the IC also increased as CF increased. At 1 kHz the Q factor was 4 versus 8 at 20 kHz in cats [20]. Given that these results are from cats they may not be comparable to rats.

1.4 Fischer 344 Rats as an Auditory Aging Model

Presbycusis, or the loss of hearing with age, occurs as adults age and is often a gradual decline caused by the loss of hair cells in the inner ear. Fischer 344 (F344) rats are commonly used as an animal model for presbycusis due to their similarities to human aging. Anatomically, in F344 rats there is a loss of GABAergic neurons in the IC of aged rats leading to less inhibition [21-23]. While this would seem to cause more firing in aged animals, it is more likely a compensation mechanism for the degraded inputs to the IC that has been shown with local field potentials [21].

Physiologically, both older humans and aged F344 rats have higher auditory brainstem response (ABR) thresholds and lower ABR amplitudes, figure 1.3 [24]. Lower envelope following response (EFR) amplitudes and higher thresholds in both humans and rats indicates that there may be a loss of synapses in the cochlea referred to as cochlear synaptopathy [21]. Aged F344 rats also have lower endocochlear potentials, that may results from cochlear synaptopahy, however endocochlear potentials have not been well studied in humans [25]. Distortion product otoacoustic emission (DPOAE) amplitudes are lower and thresholds are higher as well for both aged humans and aged F344 rats [26].

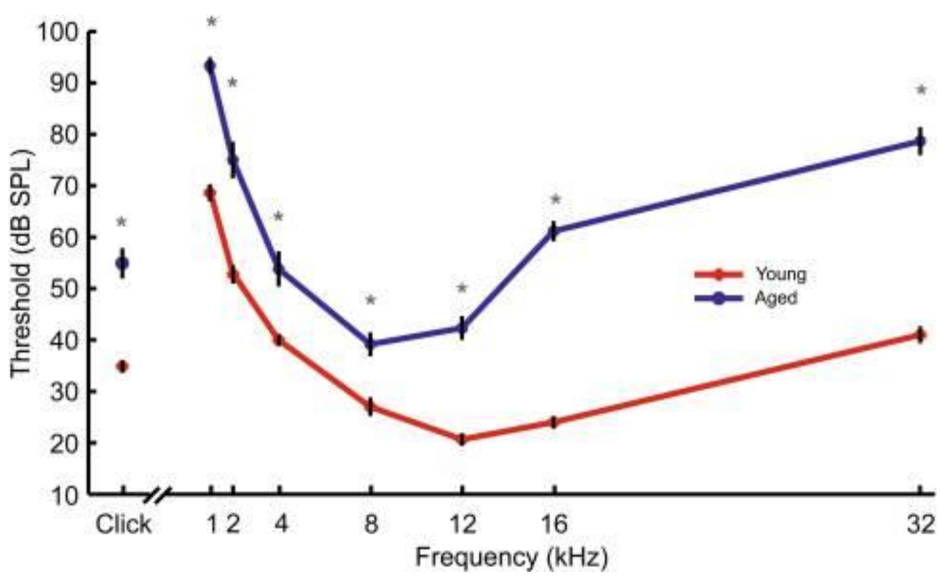

Figure 1.3. Audiograms for young and aged F344 rats in response to clicks and pure tones [24].

Although they do not use BPN, many studies have compared the responses of IC in young and aged animals using single unit recordings. As expected, young units were more responsive and had significantly higher firing rates [27] [28]. Aged units also had a significantly narrower bandwidth [29]. A common observation among both single unit recording studies and those that employ other methods is that aged animals have much higher hearing thresholds [27-31]. Younger animals are also better at responding to noise [28, 30], however, in Shadduck et al. firing rates in response to white noise were lower than those in response to pure tones [27].

1.5 Research Questions

Does the IC of young animals respond differently than the IC of aged animals when presented with BPN stimuli? Considering that the response to other stimuli is vastly different for young versus aged animals, it is expected that young units will have a significantly larger response to BPN than aged units, not only in firing rates but also in bandwidth.

Is there a difference in IC response to BPN and pure tones? Multiple previous studies have shown that pure tones are unable to accurately predict responses to BPN [16]. In A1, BPN has produced larger responses than pure tones [14]. So, the responses to BPN should be significantly different than the responses to pure tones.

2. MATERIALS AND METHODS ANIMALS

2.1 Electrophysiology

All experiments were previously conducted by the Bartlett lab; however, the data had not been analyzed yet.

2.1.1 Stimulus Creation

BPN stimuli consisted of center frequencies from 1 – 36 kHz in 0.25 octave steps and were created with SigGenRP. Overall, there were 22 stimuli, each with a 0.5 octave bandwidth. During recordings, stimuli were presented by a speaker 0 degree azimuth and 0 degree elevation to the rat.

Pure tone stimuli included frequencies from 0.5-40 kHz in 0.1 octave steps and were presented in the same way as BPN stimuli.

2.1.2 Single Unit Recordings

Single unit recording methods were previously described in Rabang et al. 2012 [32] and will only be briefly explained here. Sixteen young (4 – 6 months old) and 10 aged (22 – 24 months old) Fischer-344 rats were used for this experiment. Animals were anesthetized with a combination of ketamine and medetomidine for surgery. To secure the head for recording a stainless steel headpost was attached to the skull anterior to bregma and three screws were drilled into the skull to serve as ground. To reach the IC a craniotomy was created posterior to lambda and 1 mm lateral from midline.

Recordings were performed in a 9’ x 9’ sound-proof chamber. A micro-drive was used to advance an electrode into the craniotomy and locate IC. Once ICC was located, recording started with the stimuli as specified above. For each stimulus 5 - 8 trials were conducted. Each trial began with 200 ms of silence to obtain a baseline of spontaneous activity. Following the initial 200 ms of silence, the stimulus was presented for 200 ms. After stimulus presentation was over there was 300 ms of silence to allow the unit to recover. A visual representation of the trial timeline can be seen in figure 2.1. For most young animals, stimuli were presented at 55 dB SL and for most aged animals the stimuli were presented at 65 dB SL. Recorded units were then filtered from 300 to 5000 Hz.

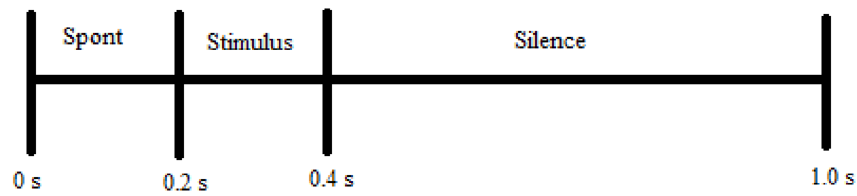

Figure 2.1. A timeline of each trial that consists of measuring spontaneous activity, the response to the stimulus and recovery.

Parameters that were recorded and used for analysis include onset, sustained and total firing rates, raster data, and spontaneous activity. From these recorded parameters other important parameters such as the first spike latency, number of tuning peaks, Q factor, and bandwidth could be calculated.

2.2 Data Analysis

2.2.1 Determining Parameters

2.2.1.1 Unit Responsiveness

To ensure that all responsive units were captured three measures were used; the onset, sustained and total firing rates. The mean spontaneous rate was recorded for each unit and used to determine if the three above mentioned firing rates were significantly higher than the spontaneous activity. A threshold was set at the mean spontaneous rate plus two standard deviations of the mean spontaneous activity. If the median firing rate across any of the 22 stimuli was higher than the threshold the unit was considered responsive. This comparison was done for each of the three firing rates and if one of the three indicated responsiveness the unit was treated as responsive. All further analysis only included responsive units.

2.2.1.2 Best Stimulus

Total firing rate was used to determine which stimulus each unit responded to best. The total mean firing rate for each stimulus across the number of trials conducted was calculated. The stimulus that resulted in the highest total mean firing rate was considered the best stimulus for that unit.

2.2.1.3 Filtering Type

If the best stimulus for a unit was the first or second stimulus the unit was considered to have low pass filtering. If the best stimulus was the second to last or last stimulus it was considered to have high pass filtering.

2.2.1.4 First Spike Latency

Since the stimulus was presented 200 ms into each trial, spikes in response to the stimulus are not expected until 206 ms into the trial. Using this information, the first spike that was recorded in the raster data for each trial at each stimulus that occurred at or past 206 ms was pulled out. The median first spike across trials for each stimulus was considered the first spike latency for that unit in response to each stimulus. From the first spike latencies, the first spike latency at the best stimulus for that unit was considered the overall first spike latency.

2.2.1.5 Bandwidth

From the calculations used to determine if a unit was responsive, each stimulus for each unit was assigned a 1 or a 0 based on whether it was responsive using the total firing rate. A 1 indicated that the unit responded to that stimulus, whereas a 0 indicated it was not significantly responsive.

2.2.1.5.1 Number of Tuning Peaks

The vector that indicated responsiveness based on the total firing rate was then run through the MATLAB function *numpeaks* to determine the number of tuning peaks present.

2.2.1.5.2 Peak Slope

Total firing rate at the best stimulus was used as the peak. The total firing rate for the stimuli on either side of the peak was then found. Using these values, the slope up to and down from the peak were calculated. The higher slope was considered the peak slope.

To ensure a valid comparison between units, peak slopes were normalized to the total firing rate at the peak. A normalized value of 1 indicates the peak stimulus was the only stimulus that elicited a response and a normalized value of 0 indicates the stimuli on either side of the peak stimulus had similar firing rates and were also responsive.

2.2.1.5.3 Longest Peak Length

Before being able to determine the bandwidth of each unit the longest continuous range of responsive stimuli needed to be calculated. A function was created to go through the binary vector indicating responsiveness to find the longest continuous string of ones. To begin the MATLAB *find* function was used to find the first instance of a 1 in the vector. The location of the first one was recorded as the start stimulus. A custom function then went through the vector and continued until a 0 was found. The last consecutive stimulus with a value of 1 was considered the last stimulus in the peak. The difference between the last and first stimulus was used as the bandwidth.

2.2.1.5.4 Q Factor

To further evaluate the sharpness of the tuning curve, the Q factor was calculated by dividing the best CF of each unit by its bandwidth. The higher the Q factor the sharper the peak of the tuning curve [33] [34].

2.2.2 Young Versus Aged Comparisons

Given that there is not an equal sample size for the young versus aged units both a two-sample t-test and a traditional one-way ANOVA are not applicable. Instead two alternatives were used: the Wilcoxon rank-sum and the Kruskal Wallis test of medians. Both are non-parametric tests, do not require equal sample sizes, and do not assume a normal distribution [35, 36].

2.2.3 Band Passed Noise and Pure Tones

2.2.3.1 Determining Common Responsive Units

For both the BPN and pure tone experiments the animal number, track number and track depth were recorded. These three identifiers were used to determine which units were responsive to both the BPN and the pure tone stimuli.

2.2.3.2 Comparing BPN and Pure Tone Units

Total firing rate, the onset sustained ratio and the best CF for the same unit in response to BPN and pure tones were evaluated. For firing rate comparisons, the firing rate at the best CF for that type of stimulus was used. Scatterplots of the parameter value in response to the pure tones versus the response to BPN were created. Each dot represents one unit. A line that shows where the parameters for each stimulus type are equal is included on the scatterplot. Mathematical comparisons were performed by calculating the correlation values between the responses to pure tones and responses to BPN. The closer to 1 the correlation value is the more similar the parameter values are.

3. RESULTS

3.1 Young versus Aged Units

3.1.1 Responsiveness

Out of 479 recorded units, 363 were responsive with 218 being from young animals and 145 from aged animals. Only 68 and 48 units were unresponsive from the young and aged animals respectively. The units came from 16 young and 10 aged animals. For both the young and aged animal, most units were classified as bandpass. Young animals had 32 low pass units versus 1 for aged animals, whereas for high pass responses there were more aged units. A summary of the breakdown of units by age and response can be seen in table 3.1.1. Figure 3.1A shows an example unit that had a low pass response as seen by the fact that only the beginning stimuli are above the threshold and therefore responsive. The opposite is seen in figure 3.1B which shows a high pass response. A bandpass response is shown in figure 3.1C and is clearly defined with multiple consecutive responsive stimuli. Stimulus 4, which has a CF of 1.68 kHz, us the first responsive stimulus and the last consecutive responsive stimulus is 13 which has a CF of 8 kHz. Therefore, the bandwidth of the unit is 6.4 kHz.

Table 3.1. Classifications of responsive units for young and aged animals.

	Low Pass	**High Pass**	**Bandpass**	**Total**
Young	32	8	178	218
Aged	1	10	134	145

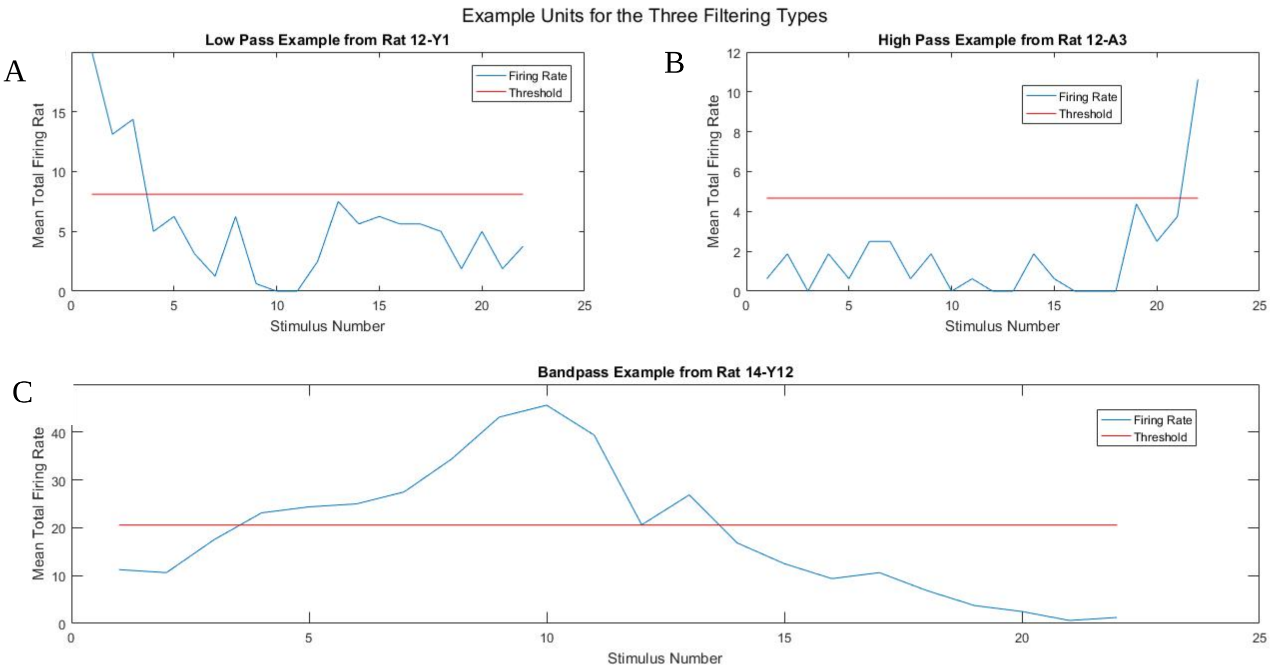

Figure 3.1. Graphs of stimulus number versus mean total firing rate. A) low pass response B) high pass response C) bandpass response.

3.1.2 Firing Rate

The only firing rate parameter than was not significantly higher in the young units was the sustained firing rate. Table 3.2 summarizes the findings on firing rate. Of note is the fact that although there was not a significant difference for the sustained firing rate, the ratio of onset to sustained was still significant due to the large difference in onset firing rate. The distributions of firing rates for young and aged animals for all four firing rate parameters can be seen in figures 3.2 – 3.5.

Table 3.2. p values for comparison of firing rates in young versus aged animals.

Parameter	**P value**	**Higher Age**
Total Firing Rate	0.008	Young
Onset Firing Rate	< 0.001	Young
Sustained Firing Rate	0.07	N/A
Onset, Sustained Ratio	< 0.001	Young

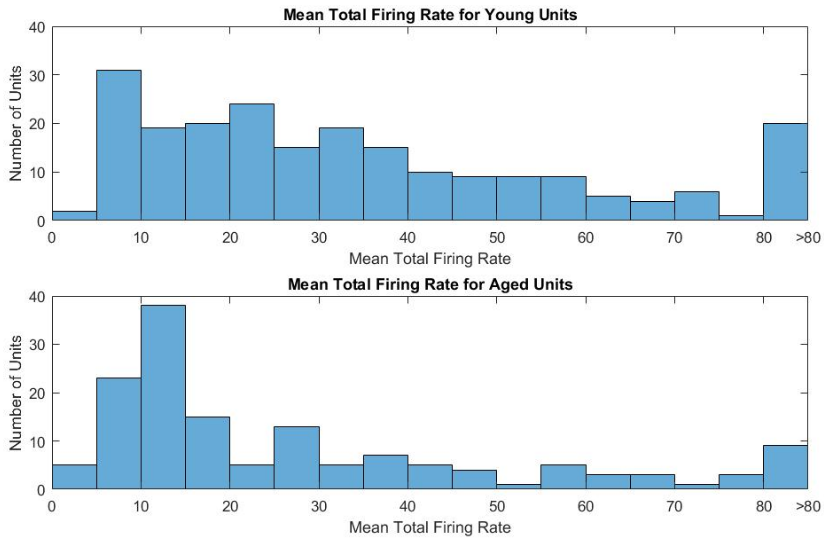

Figure 3.2. Distribution of the total firing rates for young and aged units.

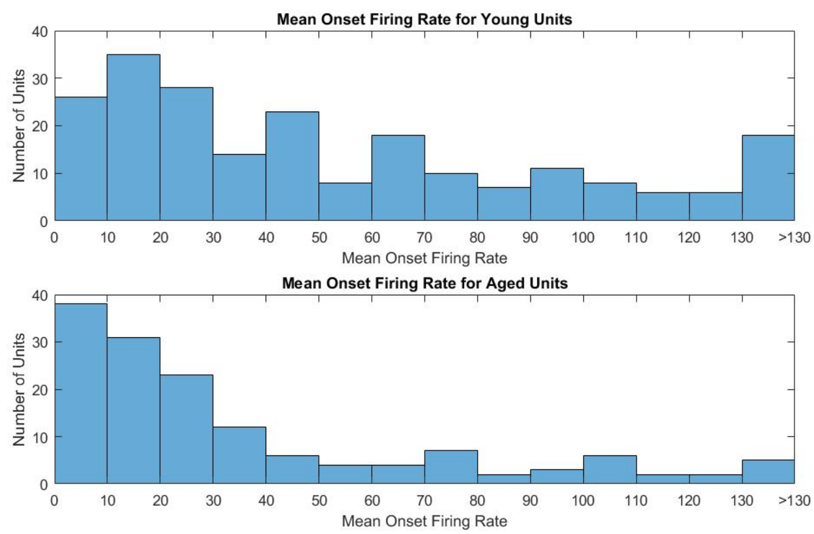

Figure 3.3. Distribution of the onset firing rates for young and aged units.

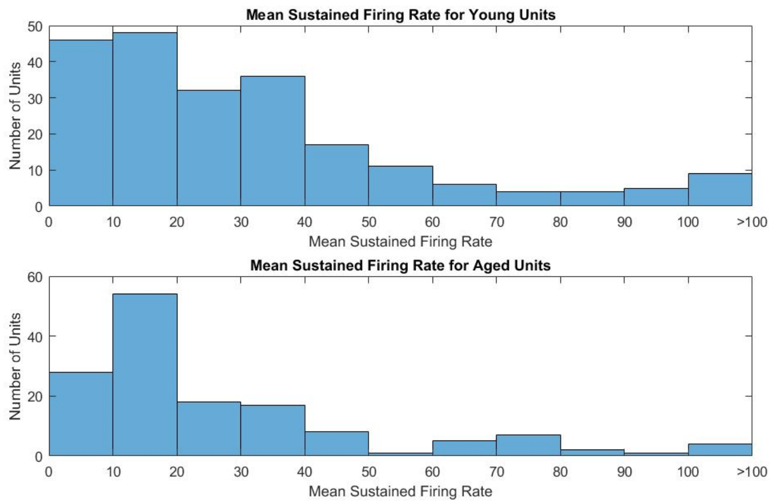

Figure 3.4. Distribution of the sustained firing rates for young and aged units.

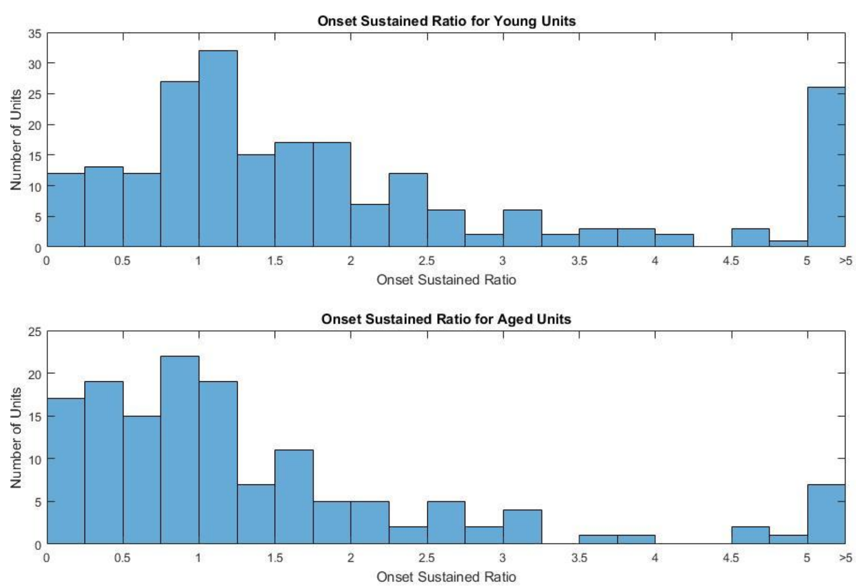

Figure 3.5. Distribution of the ratio of onset to sustained firing rates for young and aged units.

3.1.3 First Spike Latency

There was not a significant difference in first spike latencies between young and aged units ($p > 0.05$, Wilcoxon rank-sum test). For both young and aged units the majority of first spike latencies were under 30 ms.

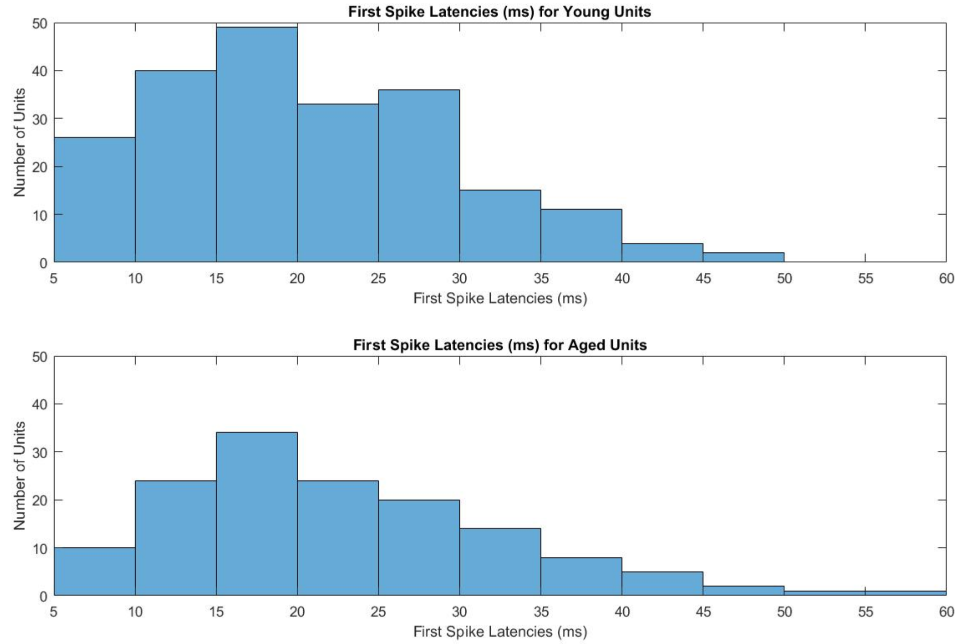

Figure 3.6. Distribution of first spike latencies for young and aged units.

3.1.4 Number of Tuning Peaks

Many of the recorded units responded to the BPN stimuli in a way that created multiple peaks that are referred to as tuning peaks. As can be seen in figure 3.7, most units only had one peak for both the young and aged units. Only a small percentage of units had more than 3 peaks; 8.7% of young units and 9.6% of aged units. When compared using the Wilcoxon rank-sum test the p value was 0.15, indicating that there is not a significant difference in the number of tuning peaks between young and aged units.

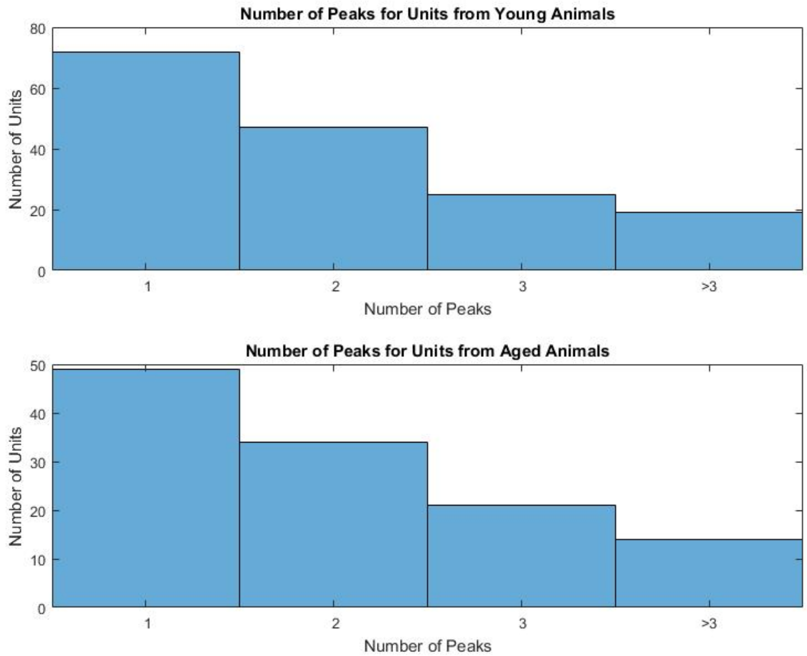

Figure 3.7. Histograms for the distributions of the number of tuning peaks for young and aged units.

3.1.5 Best Stimulus

Young units preferred the 15th stimulus (11 kHz) more than any other stimulus, whereas there was not a clear preference for aged units shown in figure 3.8. Surprisingly, aged units had a best CF that was significantly higher than that of young units ($p = 0.001$, Wilcoxon rank-sum test).

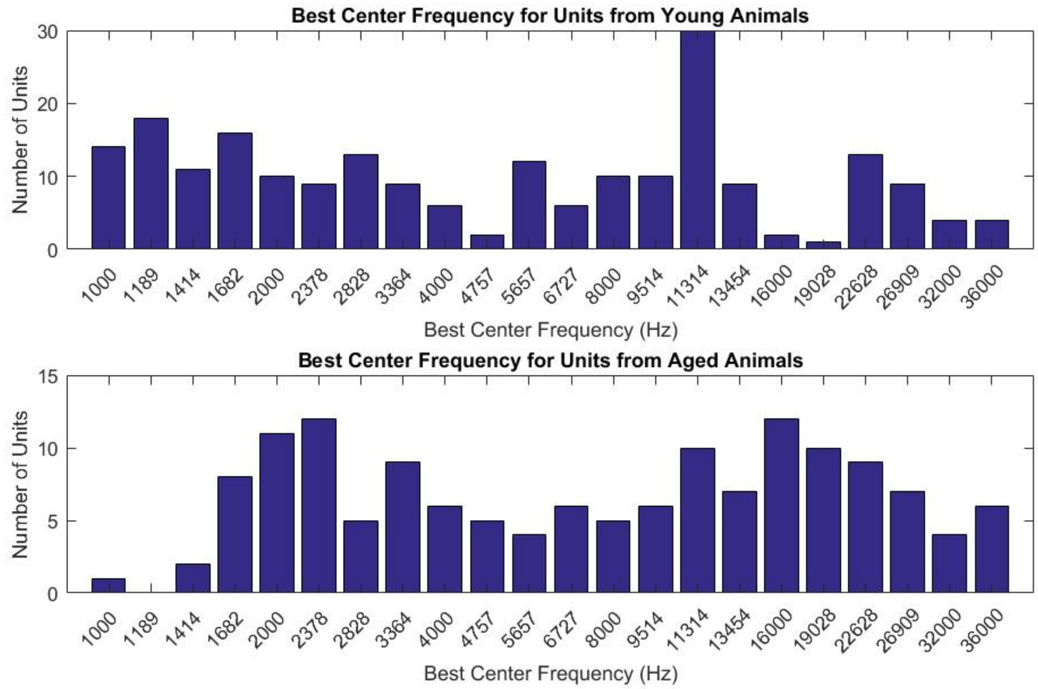

Figure 3.8. Best center frequencies for young and aged units across all 22 stimuli.

3.1.6 Bandwidth

After calculating the bandwidths for each unit, the distribution of bandwidths was plotted for both groups and can be seen in figure 3.9. Most units from each group have a bandwidth below 1.5 kHz, however, there were some young units that have very large bandwidths of 35 kHz meaning they responded to almost all the stimuli. The Wilcoxon rank-sum test produced a p value of 0.004 where young units had the higher rank. Therefore, the bandwidth of young units is significantly larger than those of aged units.

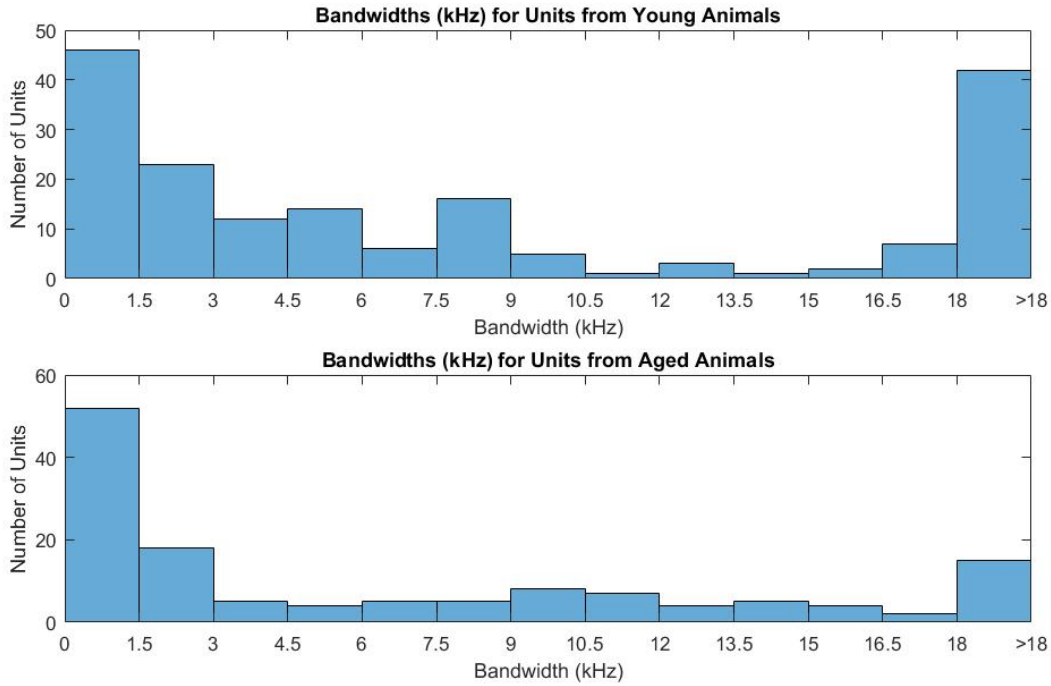

Figure 3.9. Distribution of bandwidths for young and aged units.

3.1.7 Normalized Peak Slope

The normalized peak slope is significantly higher for aged units compared to young units. For aged units, the most common normalized peak slope was between 0.7 and 0.8 whereas for young units the most common normalized peak slope was between 0.5 and 0.6 as seen in figure 3.10. A comparison using the Wilcoxon rank-sum test resulted in a p value of 0.0075 with aged units having a significantly higher peak slope.

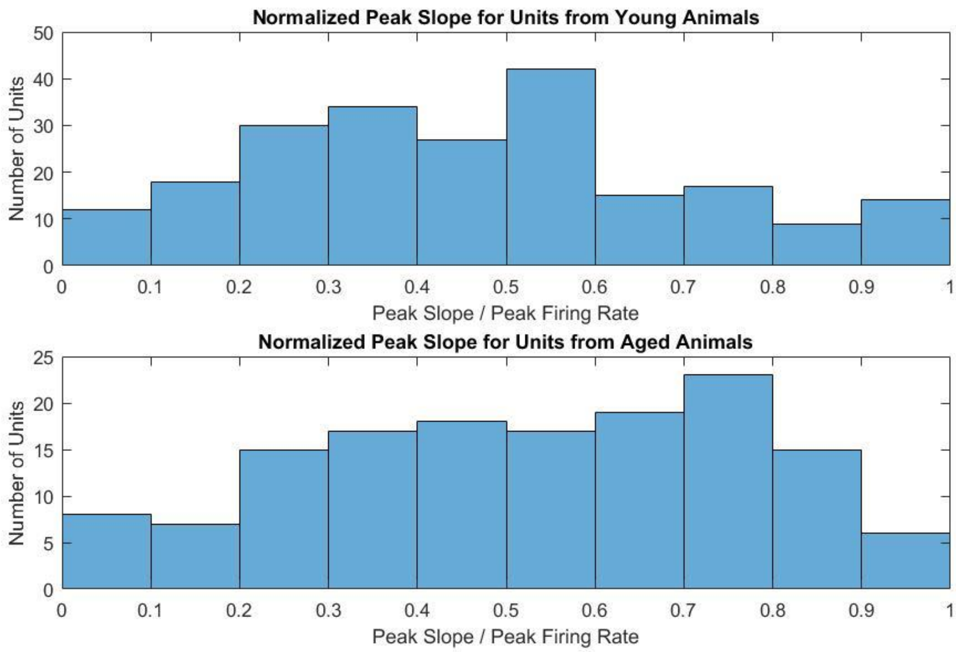

Figure 3.10. Distribution of normalized peak slopes for young and aged units.

3.1.8 Q factor

In young units, most Q factors were below 1.5 indicating relatively spread out tuning curves (figure 3.11). Many of the aged units also had Q factors below 1.5 but the Q factors for aged units were significantly higher than those of young units ($p = 0.0002$, Wilcoxon rank-sum test). This is further evidenced by the fact that 77% of young units had a Q factor below 5 versus only 62% of aged units. Therefore, the tuning peaks of aged units were much sharper.

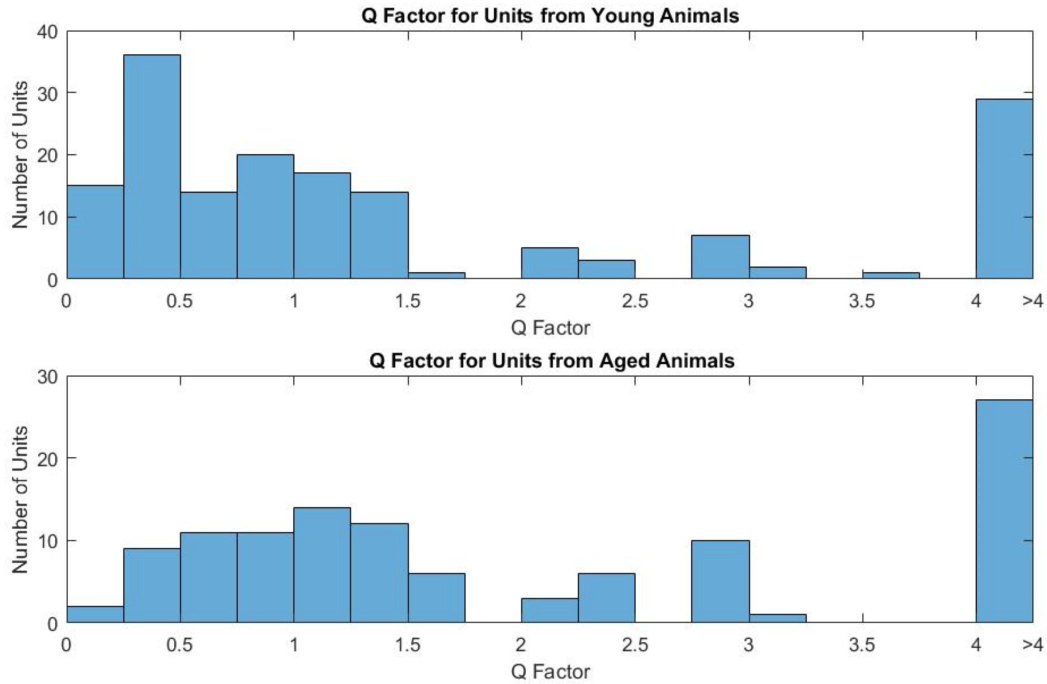

Figure 3.11. Distribution of Q factors for young and aged units.

3.2 Band Passed Noise versus Pure Tones

Out of the 363 units that responded to BPN, only 54 of those were also tested with pure tones. Of those 54 units, 31 were from young animals and 23 were from aged animals.

3.2.1 Best Stimulus

Many of the units that responded to both BPN and pure tones preferred similar center frequencies as can be seen by many of the units being on or near the equality line in figure 3.12. There was a significant correlation between the best frequencies for BPN and pure tones at $R = 0.48$ ($p = 0.003$).

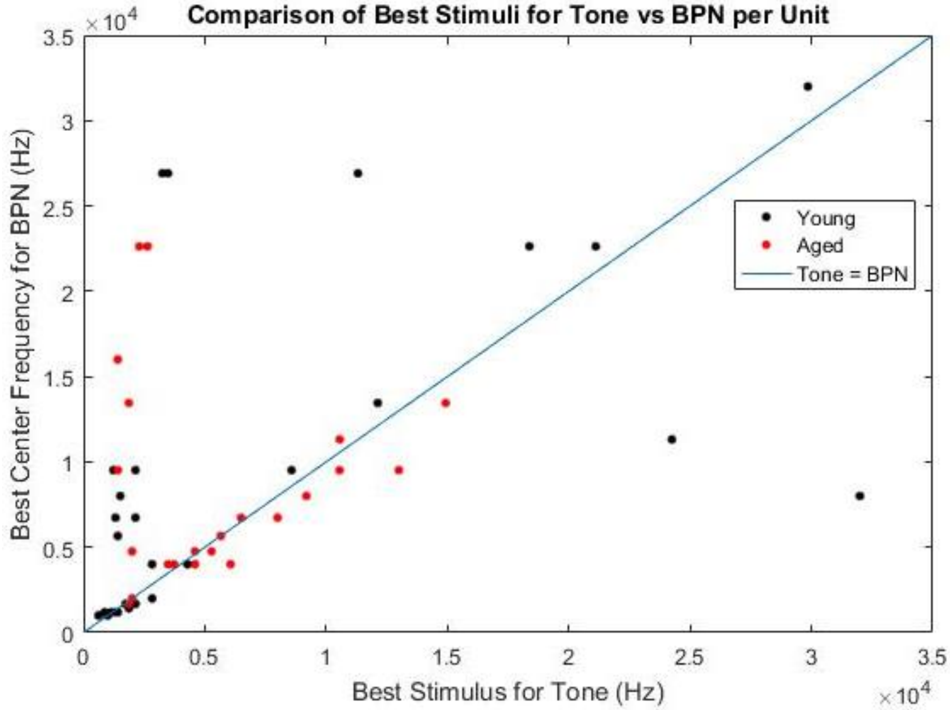

Figure 3.12. Best frequencies for units that responded to both BPN and tones. Each point represents one unit with the blue line being the equality line where the best frequency for pure tones is equal to the best center frequency for BPN.

3.2.2 Firing Rates

While the total, onset and sustained firing rates are all significantly higher for pure tones, the ratio between the onset and sustained firing rates is not significantly different (figure 3.13). Table 3.3 shows the correlation coefficient between the firing rates in response to pure tones at the best stimulus versus the firing rates in response to BPN at its best stimulus. It also includes the p values that are produced when using the *corrcoef* function in MATLAB and indicates if the correlation is significant.

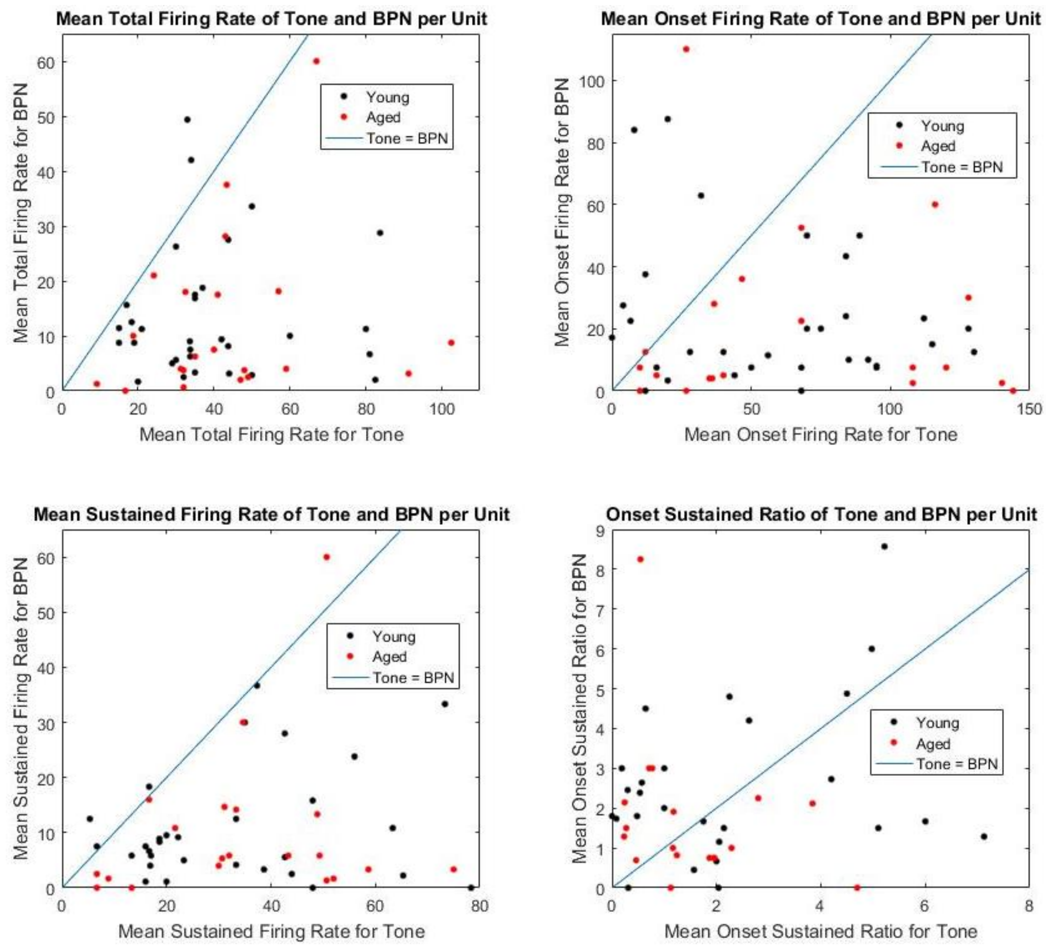

Figure 3.13. Comparison of firing rates of units in response to pure tones and BPN. Each point represents one unit. The blue line represents where the firing rates for pure tones and BPN are equal.

Table 3.3 Correlation and probability values for the best stimulus and firing rates in response to pure tones and BPN.

Parameter	**R**	**p**
Best Stimulus	0.48	0.003
Total Firing Rate	0.09	0.51
Onset Firing Rate	-0.12	0.39
Sustained Firing Rate	0.17	0.23
Onset, Sustained Ratio	0.09	0.5

4. DISCUSSION

4.1 Young versus Aged

4.1.1 Firing Rates

All firing rates except the sustained firing rate were significantly higher for young which is consistent with previous studies [27] [28]. This result confirms that the F344 rat aging model used here works and is valid when using BPN as a stimulus based on the similar results of previous studies using pure tones [21, 22]. The ratio of the onset to sustained firing rate was significantly higher in young units even though there was not a difference in sustained firing rates. Not only did the young units have a higher onset firing rate, which has been seen in previous studies [31], it was more dominant than in aged units. Part of this may be due to the rats being under anesthesia during recording. Onset responses dominate in anesthetized animals. However, unlike in the A1, IC responses are not strongly affected by anesthesia [37].

4.1.2 First Spike Latency

Although previous studies have shown that aged units have shorter first spike latencies [31], that was not the case here. Instead there was not a significant difference in first spike latencies. For both groups, the first spike latencies were within the range of 10 – 30 ms seen by other studies [31].

4.1.3 Number of peaks

There was no significant difference in the number of tuning peaks with most units from both groups only having one tuning peak. Many neurons throughout the central auditory system have only single peaked responses.

4.1.4 Best Stimulus

In aged animals as well as humans the ability to hear high frequencies if often diminished making it unusual that here the aged units had a significantly higher best CF. Given that the IC is tonotopically organized it is possible that the multiple units for the young animals were from areas that prefer lower frequencies whereas aged units were not leading to a large sample bias.

4.1.5 Bandwidth

Perhaps one of the most important results is that young units had a significantly wider bandwidth. Even though aged units had a higher best CF they did not have a wider bandwidth. Multiple studies in A1, MGB, and IC have shown that as the CF increases so does bandwidth [15] [11] [20]. However, none of these studies were performed on aged animals. One study preformed on both young and aged units from IC also found that aged units had narrower bandwidths [29]. Although this seems counter intuitive, aged animals tend to have hearing loss at multiple frequencies so although they may respond to a particular frequency it is possible that they may be unable to hear the surrounding frequencies resulting in narrower bandwidths. Here, 76% of young and 75% of aged units responded to BPN. Almost 30% of young units had a bandwidth of at least 18 kHz whereas only 14% of aged units had bandwidths at or above 18 kHz.

To determine if sound level had an effect on response bandwidth, rate level tuning and bandwidths were compared for 74 units from both young and aged animals (figure 4.1). Across the different rate responses there are multiple bandwidths. There is not a clear trend in rate versus bandwidth indicating that sound level did not have a large impact.

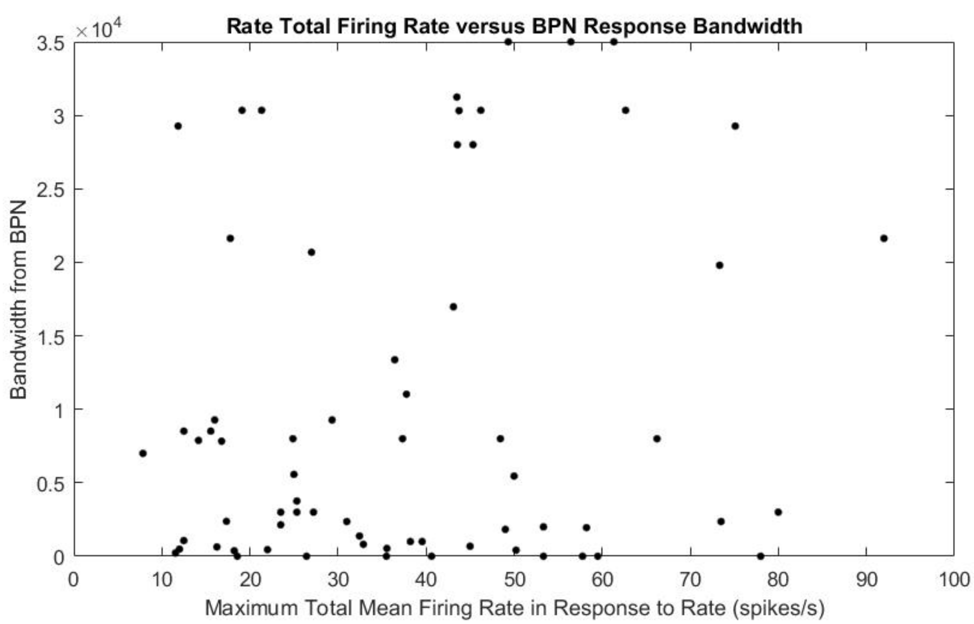

Figure 4.1. Rate tuning versus BPN bandwidth response.

4.1.6 Normalized Peak slope

Since young units had a wider bandwidth the slope of their tuning peak was also significantly smaller. Peak slopes will be lower when the stimuli around the peak are also responsive. The stimuli on either side of the peak stimulus in young animals were more likely to be responsive leading to the wider bandwidth and smaller peak slopes. Responses for young units tended to reduce in amplitude more gradually than aged units where they were often not responsive to the frequencies on either side of the CF resulting in high slopes for aged units.

4.1.7 Q factor

As with peak slopes, the Q factors for young units were significantly smaller both of which support the finding that aged units have much sharper tuning. Q factors are calculated by dividing the CF by the bandwidth and given that not only are the bandwidths much larger for young units the CFs are also lower it is expected that young units have the lower Q factors. Studies in the MGB of other rodents have resulted in average Q factors of 2 – 3 [18, 19]. Here almost 60% of young units had a Q factor below 2 meaning MGB has sharper tuning. Although not in response to BPN, in the A1 of rats, the highest Q factor was 3 [38]. Therefore, MGB has the sharpest tuning followed by A1 and IC. Aged units have a higher average Q factor (~ 2.6) than A1 suggests they are missing a large portion of the information in the BPN and may have trouble interpreting it. When the information is then passed to MGB they may lose even more information about the stimulus. Similarly, to figure 4.1, a plot comparing rate tuning and the Q factors in response to BPN was created to determine if sound level of the stimulus had a significant impact (figure 4.2). As with the bandwidth, there is not a clear trend between rate level and Q factors.

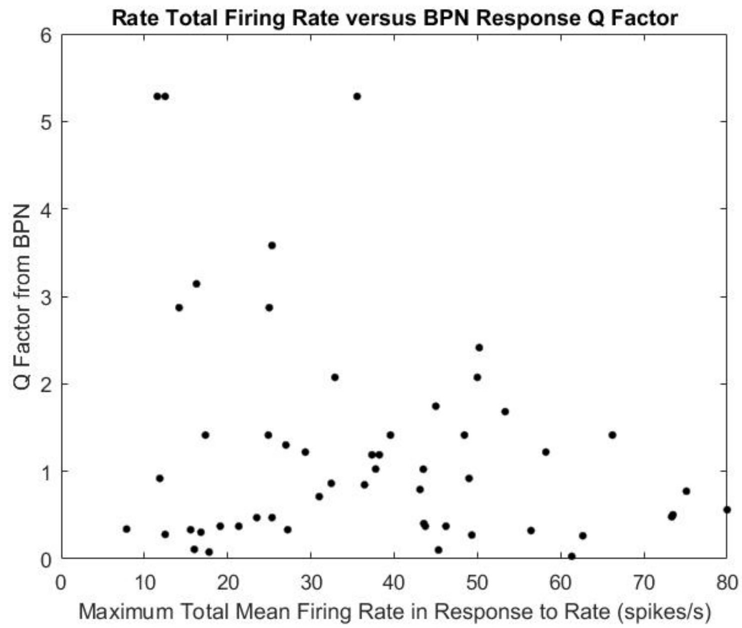

Figure 4.2. Rate tuning versus Q factor in response to BPN.

4.2 BPN versus Pure Tones

4.2.1 Best Stimulus

Many units preferred a similar CF as evidenced by the significant correlation value of R = 0.48. In the majority of studies comparing BPN and pure tones, the CF for both was very close no matter what area was being studied (A1, thalamus, or IC) [14]. Of note is the large variation in preferred BPN CF when the preferred tone frequency was low. On the left side of the graph there are multiple units who prefer tones under 5 kHz, but they respond best to BPN frequencies from 1 kHz to 30 kHz. One explanation for this may be that there is an overlap of multiple areas that respond to BPN and a specific area that responds to low frequency tones.

4.2.2 Firing Rates

In A1 BPN elicited stronger responses than pure tone stimuli [14, 15], however, in this study with units from IC, pure tones produced much stronger responses. This result is not unique and has been seen in other studies involving IC units and noise stimuli [27], indicating a potential difference in the way A1 and IC process BPN. Ratios of onset to sustained firing rates are not different between pure tones and BPN suggesting IC responds to pure tones and BPN in the same manner.

5. CONCLUSION

Here single unit recordings in the IC of young and aged animals in response to BPN and pure tones were performed. Young units had higher firing rates to BPN, longer bandwidths and smaller Q factors all indicating they responded much better to BPN than aged units. Sharper tuning was present in the aged units which may help explain why older adults have trouble processing sounds with frequencies that are close together. Although the IC in the aged units was able to respond to the center frequencies of the BPN it was often unable to respond to the surrounding frequencies. To understand how these responses from IC are then processed in MGB and A1 further studies using single unit recordings in those areas are needed.

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