Neural Correlates of Phantom Auditory Perception

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NEURAL CORRELATES OF PHANTOM AUDITORY PERCEPTION

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DEDICATION

To my parents
ACKNOWLEDGEMENTS

I would first like to thank Professor Lucas C. Parra for giving me the opportunity to do my master’s thesis research in his lab. He gave me the freedom to work on a topic of interest to me, while providing the necessary guidance, advice, and help to complete each step of the way. The skills and knowledge I have learned over the last few years have opened new doors of opportunity.

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Abstract

Tinnitus is the perception of sound in the absence of an external stimulus, also known as a phantom percept. There are various types of tinnitus, but people most often describe it as a “constant ringing in the ear.” While there has been an effort to find objective measures to diagnose tinnitus, neural correlates are still somewhat elusive.

In this study, we sought to find EEG correlates of the perception of the Zwicker tone and also investigated the role of prestimulus oscillations. The Zwicker tone is an auditory illusion where a transient phantom tone may be perceived during the silence following the presentation of a notched noise. Both the Zwicker tone and tinnitus are thought to be a result of neuronal gain adaptation, where peripheral deficits lead to increased hyperactivity in the auditory ascending pathway, ultimately leading to a phantom percept. Human subjects without tinnitus were recruited for this study and were presented (randomly with equal probability) two different types of notched noise: one with a center frequency that was most likely to elicit the Zwicker tone, and one with a different center frequency that did not elicit the Zwicker tone. The subject was instructed to indicated whether or not a tone was perceived after each stimulus was played.

Three subsets of subjects were identified: those that consistently perceived the Zwicker tone (ZT subjects), those that did not (non-ZT subjects) and those whose response results were at threshold (Threshold subjects). ERP results revealed, for ZT subjects only, a negativity in the fronto-central sites at 140 ms and a broad central positivity around 340 ms when taking the difference between when a subject reported hearing the tone versus when no tone was heard. Neural oscillatory results did not reveal any alpha power activity differences (hearing the tone
versus not hearing the tone) during the one second prior to notched-noise offset for the ZT subjects subset. However, in the same time period for non-ZT subjects, increased alpha was present when the subjects reported hearing a tone versus when they did not.

The negativity seen at 140 ms may be a result of adaptation, resulting in a change in the N1 response or may possibly be a mismatch negativity (MMN), which is an automatic brain process that detects stimulus change. The positivity at 340 ms resembles a P300 response, which is a component associated with conscious detection of a target/stimulus. Analysis of the alpha activity suggests that, for non-ZT subjects, where detection is not obvious, more attention and processing is required. The increased alpha power seen may be the result of inhibition of sensory systems not sensitive to the Zwicker tone, for example, the visual system. In the case of ZT subjects, no difference is observed because the tone was very easily detected.

The findings of this study opens doors for further analysis of ERP components and oscillatory activity, with the ultimate goal of developing objective diagnosis and treatment of tinnitus.
1 Introduction

Tinnitus is the perception of a sound in the absence of a detectable physical stimulus. It affects 6-20% of the population, of which about 1-3% of the cases are considered severe enough to interfere with daily activities. In extreme cases tinnitus can lead to depression and even suicide (Axelsson and Ringdahl, 1989). In recent years, the increased popularity of personal music devices (iPods, MP3 players, etc) and veterans returning from the wars in Iraq and Afghanistan have led to rapid increases in those affected by tinnitus.

Various methods have attempted to treat tinnitus, including tinnitus maskers, hearing aids, brain stimulation, and neurofeedback therapies (Fregni et al, 2006; De Ridder et al, 2010; Davis et al, 2008; Viirre et al, 2011). Unfortunately, these treatments generally yield inconsistent results. Because tinnitus comes in many forms (ringing, hissing, buzzing, etc), it is not surprising that there is not one solution that works for all tinnitus sufferers. A better approach is to develop patient specific customized therapies based on objective criteria. However, before moving forward with device development, it is important to take a step back and better understand the basic science.

In the last decade, researchers have shown that an impaired cochlea leads to the increased spontaneous activity (hyperactivity) in central auditory nuclei. This hyperactivity is thought to be involved in the generation of tinnitus. This has been demonstrated in a wide range of animals models using either mechanically, acoustically, or drug induced cochlear lesions (Kaltenbach et al., 2000; Seki and Eggermont 2003; Kaltenbach et al., 2004; Brozoski et al.,
While improvements have been made over the last several years in characterizing various aspects of tinnitus, neural correlates of tinnitus in humans has remained elusive over the last few decades. A common limitation with all these studies (with the exception of Hoke et al., 1996), is that no ideal control groups can be recruited. Because of the wide variety of hearing loss, types of tinnitus, and many other factors, it is nearly impossible to perfectly match subjects. In a study by Hoke et al. (1996), a solution to this issue was to use the same subjects for the control and test groups. They took advantage of an auditory illusion known as the Zwicker tone, where a phantom tone can be perceived in the period of silence following the presentation of a notched noise (Zwicker, 1964). A more recent study by Parra and Pearlmutter (2007) empirically linked the Zwicker tone to tinnitus. They showed that in both cases, illusory phantom perception is a result of neuronal gain adaptation. In other words, neural populations become more sensitive to sounds that fall within the range of the notch (in the case of the Zwicker tone) or where peripheral hearing deficits occur (tinnitus).

In the first part of this study we investigated ERPs related to the Zwicker tone, using the same subject for control and test conditions. Previous studies have characterized the obligatory components in EEG and MEG, such as the N1 and P2 in subjects with tinnitus (Hoke et al., 1996; Kadner et al., 2002; Jacobson and McCaslin, 2003; Delb et al., 2008; Filah and Matas, 2010). Others have looked at other responses such as the Mismatch Negativity (MMN) and P3 (Attias et al., 1995; Weisz et al, 2004). Since the present study is similar to that of Hoke (1996), we verify if our results support their claims and well as compare results to studies of those with tinnitus.
Second, a preliminary oscillatory analysis will be performed. More recently, there has been a growing number of reports that describe neural oscillatory activity in subjects with tinnitus (Weisz et al 2005, Kahlbrock, 2008; Lorenz, 2009; Schlee et al, 2009; Vanneste et al, 2011). This study, in particular will investigate the role of prestimulus alpha on the perception of the Zwicker tone.

In summary, the present study seeks to determine whether or not correlates of phantom tone perception can be found while making use of the Zwicker tone phenomenon. Results are then compared to previous tinnitus studies in hopes to strengthen the link between tinnitus and the Zwicker tone. Once the perception of the Zwicker tone is more fully characterized, we can proceed with developing objective tinnitus diagnosis tools and treatments.
2 Methods

2.1 Subjects and procedures

Twenty-five subjects without tinnitus were volunteered for this study. Prior to the start of the experiments, all subjects gave informed consent and signed a consent form approved by the Institutional Review Board of the City College of New York. First, the perceptual thresholds for each subject were measured. A preliminary test was then conducted to determine whether or not the subject could reliably hear the Zwicker tone. For the main experiment, EEG was recorded while presenting stimuli which were based on the results of the preliminary test. One subject was excluded due to an event triggering issue found in this specific dataset, leaving twenty-four subjects for analysis. The mean age of these subjects was 27 ± 4 yrs; 16 were male and 8 were female.

2.2 Perceptual thresholds

Subjects were seated in a sound-attenuating and RF shielded room. MATLAB (Mathworks, Natick, MA) was used to generate all stimuli, which were played using a 24-bit M-Audio USB sound card (Fast Track Pro) at a sampling rate of 44.1 kHz. The stimuli passed through a headphone buffer (Tucker-Davis Technologies HB7) before being delivered to the subjects using Sony MDR-7506 headphones. The specific pair of headphones was equalized to obtain a flat frequency response at the ear drum. Equalization filters were obtained by recording a white noise signal emitted by the headphones with a calibrated microphone (Bruel & Kjaer model 2218) inside a KEMAR head and torso simulator. Filter coefficients were computed from
these using linear prediction coefficients of order 100.

Bekesy tracking was used to obtain absolute thresholds for both ears (procedure modified from Zhou et al., 2011). The frequency range was from 250 to 1375 kHz with 2 points per octave (12 different frequencies). Absolute thresholds were determined with 1000 Hz tones. Repeated pure tone pulses lasted 250 ms with 250 ms silent gaps, and the amplitude onset and offset ramps followed a 25 ms Hanning half window. The initial level of the tones pulses was set to 50 dB sound pressure level (SPL), which was audible in most instances. However, subjects were instructed to increase or decrease the starting level of the pulses to an audible and comfortable level. During Bekesy tracking, subjects pressed a button as long as the pulses were audible. Keeping the button pressed reduced the level of the pulses by 2 dB per pulse (4 dB/s). Subjects were instructed to release the button when they no longer heard the pulses. When this occurred, the level of the pulses was increased by 2 dB per pulse. The tracking procedure terminated after 8 reversals. The thresholds reported here are the average level of the last 6 reversals.

2.3 Experimental paradigm and data acquisition

A preliminary test was conducted to determine whether or not the subject could reliably perceive the Zwicker tone. The same acoustical setup described in the previous section was used. Five different noise conditions (white noise and four notched-noise with 4-ERB bandwidth, centered at 500, 1000, 2000, 4000 Hz) were binaurally presented 4 times each, at a 50 dB sound pressure level (SPL), in random order. Equivalent rectangular bandwidth (ERB) was calculated according to the following formula: $\text{ERB}(f) = 0.108f + 24.7$ at center frequency.
f. In all conditions, the total duration of the stimulus (including onset/offset ramps) was 3000 ms. The amplitude of the noise onset rose linearly for 500 ms while the offset had a 25 ms Hanning window ramp. A period of silence for 3000 ms followed the noise. The subject then indicated whether or not he/she heard a ringing sound during the silence after the offset of the noise. See Figure 1 for a schematic of the presentation paradigm. The response was given via an on-screen visual analogue scale (VAS), ranging from “Definitely did not hear the tone” to “Definitely heard the tone,” with “Unsure” at the midpoint. Corresponding numerical positional values (not visible to the subject) were -250, 0, and 250, respectively. Using the left and right directional arrows on the keyboard, the subject was able to adjust the position of the marker to the desired location. Positive-valued responses were considered as “Yes” (i.e., yes the tone was heard) and negative values were considered to be “No.” Subjects that consistently reported a percept for the same notched-noise and not for the white noise were considered to have reliably heard the Zwicker tone. Those that gave inconsistent answers were considered to be unable to perceive the Zwicker tone.

For the main experiment, a test stimulus and a control stimulus were chosen based on the preliminary results. For those subjects that reliably heard the tone, the test stimulus was the notched-noise that most consistently elicited the phantom tone. The control was a notched-noise that did not produce the percept. For subjects that did not respond consistently, the notch that was most likely to elicit the tone was used as the test stimulus, while the notch that was most likely not to elicit the tones was the control. Equal total sound-pressure level was maintained for all stimuli (constant power-density).

The experiment consisted of two sets of 100 trials (200 trials total in random order: 100
test condition, 100 control). Within each of the 100 trial sets, the subject was offered a short break every 25 trials. An extended break was taken after the first 100 trials. A trial began with the appearance of a cross-hair at the center of the screen for 2000 ms. The subject was instructed to fixate on this cross-hair for the entire duration of the trial to minimize eye movements. Like in the preliminary testing, the noise was then played for 3000 ms, followed by 3000 ms of silence (the cross-hair remained unchanged on the screen). The subject then gave a response using the on-screen VAS. The right hand was used to control the directional arrows and the left hand for the spacebar to continue to the next trial. The subject was also instructed to maintain the hands fixed over the keys during the trial, and only move when making a response.

**Figure 1. Presentation Paradigm**
The subjects were prompted with an on-screen cross-hair that remained unchanged until a response from the subject was required. The auditory stimulus consisted of a 4 ERB notched-noise with a duration of 3000 ms, followed by a 3000 ms period of silence. The subject was free to give a response at any point after the period of silence.
The EEG was recorded during the experiment from 64 electrodes in the standard 10/10 International placement system, with a BioSemi Active Two system (BioSemi, Amsterdam, Netherlands) at a sampling rate of 1024 Hz. The electrooculogram (EOG) was also recorded from 4 sites (2 below and 2 to the outer sides of each eye). Headphones were carefully placed over the electrode cap, avoiding contact with the electrodes. To minimize head movements, the subject's head was restrained with a head mount placed about 0.5 m away from the screen.

2.4 Data analysis

All data analysis was performed offline using MATLAB. Three subsets of subjects were identified, based on the behavioral results of the main experiment: those that consistently heard the tone (ZT subjects), those that did not (non-ZT subjects), and those whose responses were in between consistent and random (threshold subjects). The following analyses will be made for all three subsets.

2.4.1 Preprocessing

For each subject, 2000 ms epochs were extracted from the EEG/EOG records (±1000 ms relative to noise onset and offset). A 4th order Butterworth high-pass filter with a cutoff frequency of 0.5 Hz and a 4th order Butterworth notch filter centered at 60 Hz were applied to the signal in the forward and backward directions. Eye movement/blink artifacts were then removed by linearly regressing out the EOG channels from the EEG channels. Next, the signals were downsampled to 256 Hz. Finally, channel rejection was performed. Any channels whose
powers exceeded the median power averaged across all trials by 4 standard deviations, were zeroed. This procedure was repeated three times, recomputing the average median channel power for each iteration.

2.4.2 Event related potentials analysis

The epochs for each subject were first separated by response: “Yes” and “No”. A response of “Yes” was defined as when the subject reported hearing the ZT ( > 0 on the VAS). A “No” corresponds to when the subject indicated not hearing the ZT ( < 0 on the VAS). Response values of 0 were not included. The terms Yes and No will be used for the remainder of this paper.

For each response, Yes and No, the mean over all trials for each channel was computed. The difference of the No from the Yes responses were then taken.

Significance was established by randomly shuffling the response labels 200 times and computing the 99.5 percentile of the amplitude for each time sample and each channel. Any time sample in the original data whose amplitude is greater than the 99.5 percentile of the amplitude in the randomized labels is considered significant (p < 0.005).

2.4.3 Oscillatory power analysis

Prestimulus alpha band power was analyzed in this study. The Zwicker tone was
considered as the stimulus alpha power was therefore calculated for 1 second prior to the noise offset. The EEG was band-passed filtered using a complex Morlet wavelet filter, which had a center frequency of 10 Hz and a 5 Hz bandwidth (7.5 to 12.5 Hz). The difference between the No from the Yes (i.e. Yes minus No) responses were taken. The mean alpha power over the 1 second prestimulus interval was then calculated for each channel.

Significance was calculated in a similar manner as the ERPs, employing a permutation test by randomly shuffling the response labels 200 times. In this case, any mean alpha power difference whose value exceeds the 99.5 percentile of the randomized labels' alpha power distribution was considered significant where \( p < 0.005 \).
3 Results

3.1 Perceptual thresholds

The average pure tone audiogram across all subjects is shown in Figure 2. For all frequencies, the average audiogram fell within the normal range (< 25 dB HL). When inspecting individual audiograms (not shown) a few subjects had thresholds that exceeded this normal range (thresholds in moderate loss range), for a few specific frequencies.

![Figure 2. Audiogram](image)

On the left, the mean absolute thresholds for twelve different frequencies, across all subjects, are shown. The blue and red lines represent the left and right ears, respectively. The black dashed line represents the absolute thresholds for normal, young individuals. On the right, the corresponding hearing level is shown. Hearing thresholds below the gray area (< 25 dB HL) are considered normal.
3.2 Behavioral Results

The test and control stimuli were based on the preliminary testing session. Subjects that were able consistently perceive the Zwicker tone in these preliminary tests were generally also able to perceive the tone during the main experiment. Similarly, those that did could not consistently hear the tone or consistently did not hear the tone performed similarly in the experiment. Table 1 shows the percentage of each possible response for each subject to the notched noises presented. Due to the subjective nature of this experiment, there is no notion of “true positives” or “true negatives,” defined as responding Yes to the test condition and No to the control condition, respectively. However, it was possible to gain a sense of whether or not the subject actually perceived a Zwicker tone. This was done by calculating the response accuracy (true positive + true negative / (true positive + true negative + false positive + false negative), which is effectively a measure of how consistently a subject responded. Using these accuracy values allowed subjects to be assigned to certain subsets. Those subjects whose accuracy scores were above 0.85 were considered to have consistently heard the Zwicker tone, and were placed in the subset called Zwicker tone subjects (ZT subjects). Subjects whose accuracy fell between 0.35 and 0.65 were considered to be unable to reliably perceive the Zwicker tone (either effectively responded randomly or did not hear the tone at all), and were placed in the non-Zwicker tone (non-ZT subjects) subset. There were some subjects with accuracies between 0.65 and 0.85 and were categorized as “Threshold subjects.”
Table 1. Behavioral Responses

The Test and Control stimuli were equally presented. However, percentages may exceed 50% because “Maybe” responses were excluded. Subsets of subjects were classified based on their accuracy score.

* Note that Subject 16 completed only the first of two blocks of 100 trials

<table>
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<tr>
<th>Subject ID</th>
<th>Test Yes (%)</th>
<th>Test No (%)</th>
<th>Control Yes (%)</th>
<th>Control No (%)</th>
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</table>
3.3 Electrophysiological Results

For each subset of subjects, the mean ERPs for Yes and No responses were shown, and their differences taken. Scalp distributions were shown for latencies where significant differences occurred.

3.3.1 ERPs to Notched Noise Offset

Figure 3 shows the ERPs of the ZT subjects. In the top row, the mean ERP for when the subjects responded Yes to hearing a tone during the silence following the notched-noise. Here, we see a typical auditory N1 response at a sound offset: central negativity occurring 100 ms after onset (also referred to as the N1b), followed by a right-lateralized negative temporal component at 140 ms, known as the N1c (Naatanen et al, 1987). In addition, a central positivity from 200 to 300 ms and a broad centro-temporal positivity with some right lateralization from about 300 to 450 ms are seen. The middle row of Figure 3 shows the mean ERP when the subjects responded No. In this case, the N1b and N1c is also seen, but a central positivity occurs from about 130 to 250 ms.

To isolate common components not presumed to be related to Zwicker tone perception, the difference was taken. When taking the difference, a fronto-central negativity at 140 ms and a central-parietal positivity at 340 ms occur as shown in bottom row of Figure 3. Only electrodes with significant positivity or negativity are shown (p < 0.005). Electrodes not considered significant have been zeroed. The corresponding scalp distributions for the Yes and
No responses, and their Difference are shown to the right of the ERP image plots.

**Figure 4** shows the ERPs for non-ZT subjects. Like in the ZT subjects, non-ZT subjects also showed an N1b and N1c for both the Yes and No responses with latencies at 100 and 140 ms, respectively. However, a central positivity from 130 to 250 ms is seen for both responses, whereas this component was only seen in the NO response of the ZT subjects. There also is a slight central positive deflection which occurs from about 330 to 420 ms. For comparison, scalp distributions taken at 140 ms and 340 ms are shown. Taking the difference of the Yes and No responses reveal few significant pixels that fell above chance with no obvious spatio-temporal distributions.

Finally, Threshold subjects' ERPs (Figure 5) had an N1b/N1c response consistent with the previous two subsets of subjects. When subjects responded Yes, a central positive deflection was seen from 130 to 250 ms, as well as a broad right-lateralized positivity from 340 to 500 ms. For No responses, a similar positivity from 130 to 200 ms appeared, along with an occipital negativity from 220 to 300 ms and frontal negativity from 300 to 400 ms. It is interesting to note that there seems to be a slight frontal positivity difference at 140 ms, which is the reversed polarity seen for the ZT subjects. The difference between the two responses for any components, however, is not significant.
Figure 3. ERP Difference of Noise Offset for ZT Subjects
The top row, left column is the ERP for when the subject responded Yes. The electrode channels are on the y-axis and the latency are on the x-axis. The corresponding scalp plots to the right are taken at 140 ms (mean from 130 to 150 ms) and 340 ms (mean from 330 to 350 ms). A right-lateralized N1c component is seen at 140 ms, while a broad central temporal positivity is seen at 340 ms.

The middle row shows the ERP for when the subject responded No, along with its corresponding scalp plots on the right. Here, the N1c component is seen at the temporal sites.

The bottom row shows the significant difference ($p < 0.005$) between the Yes and No conditions (Yes minus No). At 140 ms, a fronto-central negativity is found at 140 ms, while a central-parietal positivity is shown at 340 ms.
Figure 4. ERP Difference of Noise Offset for non-ZT Subjects
The top row, left column is the ERP for when the subject responded Yes. The electrode channels are on the y-axis and the latency are on the x-axis. The corresponding scalp plots to the right are taken at 140 ms (mean from 130 to 150 ms) and 340 ms (mean from 330 to 350 ms). An N1c component is seen at 140 ms, while a slight broad positivity is seen at 340 ms.

The middle row shows the ERP for when the subject responded No, along with its corresponding scalp plots on the right. Here, the N1c component is seen at the temporal sites.

The bottom row shows the no significant difference between the Yes and No conditions.
Figure 5. ERP Difference of Noise Offset for Threshold Subjects
The top row, left column is the ERP for when the subject responded Yes. The electrode channels are on the y-axis and the latency are on the x-axis. The corresponding scalp plots to the right are taken at 140 ms (mean from 130 to 150 ms) and 340 ms (mean from 330 to 350 ms). An N1c component is seen at 140 ms.
The middle row shows the ERP for when the subject responded No, along with its corresponding scalp plots on the right. Here, the N1c component is seen.
The bottom row shows the no significant difference between the Yes and No conditions, however, there seems to be an increased positivity for the Yes response compared to the no.
3.3.2 ERPs to Notched Noise Onset

For comparison, the onset responses are also analyzed. Figure 6 shows the ERPs to the onset of the notched-noise for ZT subjects. For both the Yes and No responses, clear obligatory responses: central negativity (from 130 to 200 ms), right-lateralized temporal negativity at 200 ms, and central positivity from 200 to 300 ms. While no significant differences are seen between the Yes and No responses, it can be seen that the ERP latencies have been delayed. Using the N1c component as an index, the delay was calculated to be 60 ms (N1c latencies, onset: 200 ms, offset 140 ms). Similarly, the corresponding delayed positivity found at 340 ms for the offset response is not present in the onset response (here, 400 ms). Scalp plots taken at 200 ms and 400 ms are shown to the right.

The ERPs of the Yes and No responses were also similar for the non-ZT subjects (Figure 7). The same delayed central negativity at 200 ms is seen for both responses, as is the central positivity from 200 to 300 ms. There may also be another fronto-central component from about 300 to 400 ms present, or may be a continuation of the previous component. The difference between Yes and No responses show few sites with significant left-lateralized negativity, however this is more likely to be an artifact resulting from differing signal-to-noise ratio between the two conditions.

In Figure 8, the N1b, N1c, and central positivity from 200 to 300 ms are seen. For the Yes responses, a slight broad positivity is shown around 400 ms, while a frontal negativity is seen when the subject responded No. A few frontal sites show significance, but is also likely to be an artifact.
Figure 6. ERP Difference of Noise Onset for ZT Subjects

The top row, left column is the ERP for when the subject responded Yes. The electrode channels are on the y-axis and the latency are on the x-axis. The corresponding scalp plots to the right are taken at 140 ms (mean from 130 to 150 ms) and 340 ms (mean from 330 to 350 ms). An N1c component is seen at 140 ms.

The middle row shows the ERP for when the subject responded No, along with its corresponding scalp plots on the right. Here, the N1c component is seen at the temporal sites.

The bottom row shows the no significant difference between the Yes and No conditions.
Figure 7. ERP Difference of Noise Onset for non-ZT Subjects
The top row, left column is the ERP for when the subject responded Yes. The electrode channels are on the y-axis and the latency are on the x-axis. The corresponding scalp plots to the right are taken at 140 ms (mean from 130 to 150 ms) and 340 ms (mean from 330 to 350 ms). An N1c component is seen at 140 ms.
The middle row shows the ERP for when the subject responded No, along with its corresponding scalp plots on the right. Here, the N1c component is seen at the temporal sites. The bottom row shows the no significant difference between the Yes and No conditions.
Figure 8. ERP Difference of Noise Onset for Threshold Subjects
The top row, left column is the ERP for when the subject responded Yes. The electrode channels are on the y-axis and the latency are on the x-axis. The corresponding scalp plots to the right are taken at 140 ms (mean from 130 to 150 ms) and 340 ms (mean from 330 to 350 ms). An N1c component is seen at 140 ms.

The middle row shows the ERP for when the subject responded No, along with its corresponding scalp plots on the right. Here, the N1c component is seen at the temporal sites.

The bottom row shows the no significant difference between the Yes and No conditions.
3.4 Prestimulus Alpha Power

3.4.1 Noise offset

The prestimulus alpha power difference between the Yes and No responses for each subset were calculated, see Figure 9. In this case, the Zwicker tone was considered to be the stimulus and alpha power was therefore calculated for 1 second prior to the noise offset. Surprisingly, no significant prestimulus alpha power difference between the Yes and No conditions was found for ZT subjects. Threshold subjects showed significance in three occipital sites, but effectively is insignificant. A rather peculiar result is a very broad front-central alpha power increase for non-ZT subjects when they responded Yes. The increase is roughly 5 dB, with a significance of $p < 0.005$.

![Figure 9. Prestimulus Alpha Power Difference Offset](image)

No significant alpha power difference is seen for the ZT or Threshold subjects. Non-ZT subjects, however, show a broad alpha increase difference (increased alpha when subject responds Yes).
4 Discussion

The goal of the study was to find any neural correlates related to the perception of the Zwicker tone. Here we find some consistency with previous studies and also encounter some new and/or unanticipated results.

4.1 Behavioral Results

Based on the responses of the subjects, subjects could be placed into one of the subsets. It is fair to say that the ZT subjects could, more or less, clearly perceive the Zwicker tone. They could discriminate between the test and control stimuli, as shown by their high accuracy scores. Therefore, any neural correlate found can likely be attributed to the perception of the phantom tone. Non-ZT subjects responded either randomly or did not perceive any tone at all and, as a result, responded No to nearly all trials. While neither of the two types of non-ZT subjects could hear the tone, it would be more appropriate to divide the non-ZT subset. By doing this, we may be able to uncover correlates related to the “random guessing” as opposed to no perception. However, the design of the experiment prevented this analysis from being properly performed as the assumption was that subjects that do not hear the tone will answer randomly. In the case of those subjects that do not hear the tone at all, the electrophysiological responses are expected to be the same for both the test and control stimuli. Finally, the third subset of subjects were Threshold subjects. The hope was to find correlates that may explain why these subjects seem to hear the tone somewhat consistently above chance, but below a level of easy perception.
4.2 N1-P3 Complex to Noise Offset in ZT Subjects

As stated in the previous section, the high accuracy/consistency of the ZT subjects' responses are important to the main finding of this study. For these subjects, a very clear and significant negativity is found in fronto-central electrodes when the subject responded Yes when compared to No. Alternatively stated: when the subject perceives the Zwicker tone, there is a decrease in amplitude for these fronto-central sites. When comparing tinnitus subjects to controls, previous studies have mostly found a reduced N1 amplitude and decreased latency (Jacobsen et al, 1991; Attias, 1993; Kadner et al., 2002; Jacobson and McCaslin, 2003). These studies, however, analyzed the peak of the N1 component whereas in the present study, no change in N1 peak amplitude was observed. The general interpretation of these results were a result of adaptive brain processes that occur for tinnitus subjects. It has been suggested that continuous perception of a tone, in this case tinnitus, may place the N1 into a relative refractory state where a complete response to a stimulus change may not occur. While this is a possible explanation of the Zwicker tone perception, there are some differences compared to the previous studies. The ZT is a short, transient percept, unlike the constant ringing of tinnitus and therefore the N1 would not be expected to be a result of adaptation to the tone. However, during presentation of the notched-noise, it is thought that a gain adaptation occurs (Parra and Pearlmutter, 2007), which may explain the reduction in the N1-like component. Also, the fronto-central negativity seen occurred after the peak of the N1, and is coincident with temporal N1c component.
There is a possibility that the negativity at 140 ms is the polarity inversion of the N1c, but may also be explained by a separate process - the mismatch negativity (MMN). Although typically elicited by an oddball paradigm where one stimulus is presented more frequently than another, the MMN represents a pre-perceptual automatic brain process for detecting change (Naatanen et al., 1987, Picton et al.; 2000). In the present study, specifically for ZT subjects, there are two different types of change: 1) from noise to a phantom tone (test condition) or 2) from noise to silence (control). Because discrimination between the two cases is simple for ZT subjects, as well as being a simple tone, the amplitude of the MMN is smaller and shorter in latency than if a more difficult task was presented.

Additionally, the broad central-temporal, with slight right lateralization resembling a P300-like response when the subject reported hearing the ZT. As stated previously, in this experiment, the stimuli were presented with equal probabilities. Generally the P300 has its strongest response in an oddball paradigm, but can still be elicited with conscious detection of a target. The P300 amplitude is known to decrease when presented with increasing probability (Polich 2007). It is also common for a P300 component to follow a MMN, but unlike the MMN, the P300 requires active input from the subject.

Finally, the present study was not in agreement with the similar neuromagnetic study done by Hoke et al. (1996). Instead of using two different notches, they compared a notched noise to white noise. For both stimuli, an N1m-P2m complex were seen. However, taking the difference revealed no N1-P3 complex as in the present study. Instead, they found a broad deflection after noise offset from 200 to 1000 ms, peaking around 500 to 600 ms. After performing source localization, the authors concluded that this was a sustained response to the
notched-noise condition over the supratemporal auditory cortex. This response is also found when a subject perceives a real tone (non-phantom) and therefore the auditory system is not able to distinguish whether or not a sound originates from external or internal sources. This issue was not addressed in the present study, so a comparison of the phantom percept to a real tone would need to be performed.

### 4.3 ERP offset responses in non-ZT and Threshold Subjects

There were less conclusive results from the non-ZT and threshold subjects. In both subsets, there essentially were no significant difference between the Yes and No responses. This is not surprising since the Zwicker tone cannot be reliably perceived. In the case of non-ZT subjects, regardless of if the subjects exhibited random responses or consistent No responses to either conditions, the ERPs are expected to be the same. The analysis could benefit from more non-ZT subject data to support this claim, but it is still likely that an N1-P3 complex would not be seen. There were a few subjects whose responses were “at threshold,” but no significant differences were seen. There are even fewer Threshold subjects here so statistical power is weak, but more data may be able to give more insight into why subjects can or cannot hear the Zwicker tone using ERPs.

### 4.4 ERP onset responses

For comparison, the ERPs to the onset of the stimulus were analyzed. In all cases, no significant difference was seen. This was expected since in both conditions, the change is from
silence to noise. The adaptive processes are likely to occur after the obligatory N1-P2 responses seen. A study by Davis, 1939 described the onset and offset responses to be “similar.” It is interesting, however, to see a delay in the N1-P2 components of the onset compared to the offset. The noise linearly increased in amplitude over the first 500 ms, but the N1 responses have been shown to increase in amplitude and not in latency (Kodera et al, 1978). It is possible that the noise cannot be perceived until after some tens of milliseconds when the stimulus level exceeds the absolute threshold.

4.5 Prestimulus Alpha

ERPs are important in analyzing EEG data, but isolating specific frequency bands may uncover more information underlying phantom tone perception. In this study we did a preliminary investigation of the role of prestimulus alpha on Zwicker tone perception. In the visual modality, prestimulus alpha has been shown to modulate perception of a target (van Dijk et al., 2008). However, much less is known about the functional significance of alpha activity in the auditory domain. To our surprise, the only significant alpha activity was found for non-ZT subjects and not in ZT subjects (or Threshold subjects).

Previous studies have shown a decrease in overall resting-state alpha activity for tinnitus subjects compared to normal subjects (Weisz et al., 2005; Weisz et al., 2007). Similarly, processing of real, external sound has shown an alpha decrease (Lehtela et al., 1997, Klimesch et al, 2007). A similar result was expected for ZT subjects when comparing the conditions when they heard a tone versus when they did not. However, this was not the case. In another
study by Ortmann et al. (2011), they compared the alpha power prior to and after loud exposure sound experienced during the subjects rock band practices. Here they also found no alpha power difference, and suggested that the reduced alpha activity evolves over time. The only significant increased activity in the gamma band was found, but the authors attributed this to other factors and not the temporary tinnitus experienced after exposure to loud noise.

For non-ZT subjects, an increased alpha power was found when the subjects responded Yes as opposed to the No response. This is especially peculiar since we previously suggested through behavioral and ERP results, that a response of Yes is essentially the same as a response of No. Often, alpha activity is related to attention (Foxe et al., 1998, Rihs et al., 2007), but it is not clear why attention would be different for one response versus another. One possible explanation could be that the alpha activity acts to inhibit sensory systems not sensitive to nor required in processing of the Zwicker tone, for example, inhibition of the visual system while accessing memory (Jokisch and Jensen, 2007; Haegens et al., 2010). Non-ZT subjects, for whom detection is not obvious, may require an increase in processing. In the case of ZT subjects, the lack of difference observed may be due to the easy detection of the Zwicker tone.
5 Summary and Recommendations

The search for objective criteria by which to diagnose tinnitus has continued to be elusive over the past few decades. Since the Zwicker tone was empirically linked to tinnitus by Parra and Pearlmutter (2007), using this auditory illusion may lead to an objective method of diagnosis. In this study, we have shown a neural correlate in phantom perception of the Zwicker tone for subjects that can clearly discriminate the stimulus that elicits the ZT from the one that does not. This N1-P3 complex is not present for subjects that cannot reliably hear the tone. It has been shown that about half of non-tinnitus subjects can perceive the ZT, while almost all subjects with tinnitus are able to perceive it (Parra and Pearlmutter, 2007). Therefore, one of the next steps is to conduct these experiments on tinnitus subjects. It would be interesting to see whether or not the N1-P3 complex also exists for tinnitus subjects, and how the properties may be changed (amplitudes, latencies, etc). It would also be useful to identify any differences between active and passive responses. To further classify tinnitus subjects, investigation of oscillatory activity related to the Zwicker tone could yield interesting results. First, for normal subjects, the alpha power and other frequency bands must be more precisely characterized. Then a comparison of the results between subjects with and without tinnitus can be made. These comparisons may reveal further sub classifications of subjects and can be used to ultimately develop customized treatments for tinnitus, and as a result, lead to more effective treatments.
6 References


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