Increment and decrement tone frequency effects in English-speaking adults

Cummings, Alycia ¹ and Seddoh, Amebu ²

¹ Idaho State University

² University of North Dakota

Contact Author:

Alycia Cummings
Communication Sciences & Disorders – Meridian
Idaho State University
1311 E. Central Drive
Meridian, ID 83642
Phone: 858.245.7222

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ABSTRACT

Mismatch negativity (MMN) has been shown to vary in amplitude and latency depending on deviance magnitude. However, how tone deviance direction affects its generation is poorly understood due to paucity of data. The present study sought to determine whether increment and decrement frequencies with deviance magnitudes of 20, 40, and 50 Hz yield differential MMN responses. English-speaking adults were presented two sets of standard and deviant pure tones in a passive event-related potential (ERP) oddball paradigm. Both stimulus sets had the same standard tone of 200 Hz. Each standard tone was accompanied by a set of either increment or decrement deviant tones. The increment tones were 220, 240, and 250 Hz, and the decrement tones were 180, 160, and 150 Hz. Thus, regardless of direction, deviance magnitudes were kept the same at 20 Hz, 40 Hz, and 50 Hz across each stimulus set. Results showed that ERP amplitudes varied according to deviance direction. Decrement stimuli of 160 Hz and 150 Hz elicited larger MMN responses than their corresponding increment stimuli (240 Hz and 150 Hz). These outcomes are consistent with data that indicate that the perception of low and high pitch is mediated by differential discrimination thresholds.

Keywords

ERP; MMN; pure tone; adults; pitch; auditory perception

1. INTRODUCTION

Mismatch negativity (MMN) is a neurophysiological response of the brain to an acoustically deviant sound presented among a series of homogenous (standard) other acoustic stimuli (Näätänen, 1995; Näätänen, Gaillard, & Mäntysalo, 1978; Näätänen, Paavilainen, Rinne, & Alho, 2007; Näätänen & Winkler, 1999; Picton, Alain, Otten, Ritter, & Achim, 2000). It is an automatic or attention-independent phenomenon that is believed to reflect sensory memory (Sams, Paavilainen, Alho, & Näätänen, 1985). Studies indicate that variations in MMN amplitude depend on deviant tone characteristics. The deviant stimulus may differ from the standard in magnitude, intensity, duration, and location (Koistinen, Rinne, Cederström, & Alho, 2012; Näätänen, Paavilainen, Alho, Reinikainen, & Sams, 1989; Peter, McArthur, & Thompson, 2010; Sams et al., 1985). As it becomes more different from the standard in these regards, MMN amplitude increases and latency decreases.

Apart from these differences, deviant tones are also distinguishable from the standard in terms of directionality: they are either higher or lower in frequency than the standard. Although this difference also has a potential to influence MMN size and/or latency, it is often ignored. Early studies such as Sams et al. (1985) have led to the generalization that a large enough (at least 16 Hz) frequency difference is necessary to elicit measurable MMN responses. However, deviant stimuli used in this study were increments only (1004 Hz, 1008 Hz, 1016 Hz, and 1032 Hz) with a standard of 1000 Hz. The first two deviant tones (1004 Hz and 1008 Hz), which were only 4 Hz and 8 Hz above the standard, respectively, elicited little or no MMN response. By contrast, the last two deviant tones (1016 Hz and 1032 Hz), which differed from the standard by 16 Hz and 32 Hz, respectively, elicited large and early responses. It is possible that in addition to magnitude, directionality played a role in these findings.

This possibility implies that increment and decrement tones of the same magnitude might elicit different MMN responses. The findings of studies that used increment and decrement frequencies are, however, mixed and difficult to interpret. Whereas some indicate that adults have differential discrimination thresholds for perceiving low and high pitch (Kishon-Rabin, Roth, Van Dijk, Yinon, & Amir, 2004), others found no evidence in support of this possibility. Peter, McArthur and Thompson (2010) who used 250 Hz and 350 Hz both as standards and deviants in opposing stimulus conditions reported greater sensitivity to increment compared to decrement frequency. Ruusuvirta and Astikainen (2012) also found a similar pattern of results when they presented a standard tone of 400 Hz and two deviants of 420 Hz (increment) and 380 Hz (decrement) to their participants. By contrast, Jacobsen and Schröger's report (2001), who used two sets of pure tones—(1) 1072 Hz (standard) and 1179 Hz (deviant), (2) 550 Hz (standard) and 500 Hz (deviant)—found similar amplitudes for their increment and decrement stimuli, suggesting that deviance direction has no effect on MMN.

The source of the differential findings is unclear. However, the possibility that deviance direction might play a role in MMN generation is also consistent with markedness theory (see Andersen, 1989; Chomsky & Halle, 1968). According to this theory, members of a language category are distinguishable based on their opposing features. The more distinct member of the category is usually complex, uncommon or irregular, or sparsely distributed relative to the opposing element, which tends to be dominant, regular, or frequently occurring. The two elements are considered to be marked and unmarked, respectively. Marked items are also difficult to process in comparison to the unmarked.

High and low phonological tones are marked and unmarked, respectively (Hyman, 2012; Pulleyblank, 2004). Similar to pure tones, phonological tones consist of acoustic information that

is processed at pre-attentive stage (Luo et al., 2006; Xi et al., 2010; Yu, Wang, Li and Li, 2014). If high and low tones are marked and unmarked, respectively, then it may be that the auditory system has a preference for lower frequency compared to higher frequency tones. Studies of MMN responses to deviant pure tones with the same frequency above and below the standard might provide evidence for or against this possibility. They might also indicate whether deviance direction has the same or differential effect on MMN generation.

We explored the latter possibility by comparing ERP data for two stimulus sets with the same standard tones but different deviants that were either increments or decrements. Deviance magnitudes in both conditions were kept the same at 20 Hz, 40 Hz, and 50 Hz. This design allowed for examination of comparative responses to increment and decrement frequencies. The goal was to determine whether deviant tones of the same magnitude above and below the standard have similar or differential effects on MMN generation.

2. MATERIALS AND METHODS

2.1 Participants.

Twelve right handed native speakers of (American) English aged 19 to 26 (mean = 22.08) years participated in the study. They were 4 males and 8 females with normal or corrected-to-normal vision and no history of speech, language, and/or hearing deficit. All of them were undergraduate students; each signed informed consent in accordance with the university's human research subject protection program.

2.2 Stimuli.

Seven pure tones of 200 Hz, 150 Hz, 160 Hz, 180 Hz, 220 Hz, 240 Hz, and 250 Hz were synthesized using Adobe Audition®. They had normalized average intensity of 70 dB SPL and

duration of 300 ms including a 5 ms rise/fall time each. They were used to generate two sets of stimuli for increment or decrement frequency analyses. One stimulus set consisted of a standard of 200 Hz and three increment frequencies-of 220 Hz, 240 Hz and 250 Hz. The other set was made up of a standard of 200 Hz and three decrement frequencies of 180 Hz, 160 Hz, and 150 Hz. Multiples of each stimulus set formed a block of 300 stimuli that consisted of 237 standards and 63 deviants. The total number of each deviant in each block was 21.

2.3 Stimulus Presentation.

The stimuli were presented to participants in blocks using an oddball paradigm. They were delivered by Presentation Software (www.neurobs.com) in a pseudorandom order via two loudspeakers situated 120 cm and 30 degrees to the right and left from the midline in front of participants. This arrangement made it possible for the sounds to be perceived as appearing from the midline space. Based on the oddball paradigm, probability of presenting the three deviant stimuli with a standard was 7% (it was 79% in the case of the standard). Intensity of the stimuli was maintained at 70 dB SPL throughout the presentation. By contrast, the onset-to-onset inter-stimulus interval varied randomly between 600 and 800 ms. Participants sat in a sound-treated room and watched a silent cartoon video of their choice during the presentation. Each was presented at least 4 stimulus blocks or a maximum of 6 that lasted approximately 6 minutes each. Whenever necessary, 2-3 breaks were given between blocks in order to avoid participant fatigue. ERP recording time was approximately 1 hour.

2.4 EEG Recording and Averaging.

Sixty-four channels of continuous EEG (DC-128 Hz) was recorded using ActiveTwo data acquisition system (Biosemi, Inc, Amsterdam, Netherlands) at a sampling rate of 256 Hz. This system provides “active” EEG amplification at the scalp that substantially minimizes movement

artifacts. The amplifier gain on this system is fixed, allowing ample input range (-264 to 264 mV) on a wide dynamic range (110 dB) Delta- Sigma ($\Delta\Sigma$) 24-bit AD converter. Scalp data were recorded using electrodes mounted in a stretchy cap according to the International 10-20 system. Eye movements were monitored using FP1/FP2 (blinks) and F7/F8 channels (lateral movements, saccades). During data acquisition, all channels were referred to the system's internal loop (CMS/DRL sensors located in the centro-parietal region), which drives the average potential of a subject (the Common Mode voltage) as close as possible to the Analog-Digital Converter reference voltage (the amplifier "zero"). The DC offsets were kept below 25 microvolts at all channels. Off-line, data were re-referenced to a common average reference.

Prior to data averaging, sporadic artifact rejection of the continuous EEG was completed using EEGLAB (Delorme & Makeig, 2004). This involved marking and rejecting the time periods during which sporadic artifacts occurred. Sources of the artifacts included random head movements, muscle movements related to speaking, excessive electrode activation stemming from pressing the head into the back of the chair, etc. After sporadic artifact rejection, independent-component analysis (ICA) (Jung et al., 2000) was completed so that the experimenters could identify eye blink and saccadic movement effects. These components were then deleted from the continuous EEG. The remaining artifactual trials due to amplifier blocking as well as muscle and overall body movements were rejected from further analyses using the simple voltage threshold measure in ERPLAB (Luck & Lopez-Calderon, 2012). Voltage limits were set at -100 to 100 microvolts. Participants were excluded from the study if more than 25% of their data exceeded this threshold.

Epochs containing 100 ms pre-auditory stimulus and 800 ms stimulus time were baseline-corrected with respect to the pre-stimulus interval and averaged by stimulus type. The data were

low-pass filtered at 30 Hz and high-pass filtered at 0.05 Hz, using 2-way least squares FIR filters. For the 200 Hz standard increment oddball set, the remaining individual data contained on average 738 (SD = 58) standard tone trials, 88 (SD = 7) trials for the 220 Hz deviant stimuli, 88 (SD = 8) trials for the 240 Hz deviant stimuli, and 91 (SD = 8) trials for the 250 Hz deviant stimuli. For the 200 Hz standard decrement oddball set, the remaining individual data contained on average 762 (SD = 68) standard tone trials, 90 (SD = 10) trials for the 180 Hz deviant stimuli, 93 (SD = 11) trials for the 160 Hz deviant stimuli, and 91 (SD = 10) trials for the 150 Hz deviant stimuli.

2.5 ERP Measurements.

2.5.1 Standard and deviant ERPs. Visual inspection of the standard and deviant grand average waveforms suggested that the auditory N1 appeared between approximately 100 and 150 ms, the P2 appeared between 150 and 200 ms, and the N2 appeared between 200 and 300 ms (Figure 1).

<Insert Figure 1 about here>

The ERP responses elicited by the standard and deviant tone stimuli were examined over four time periods encompassing the auditory N1 (100-150 ms), P2 (150-200 ms), and N2 (200-250 ms and 250-300 ms). Ten electrodes were selected for all peak amplitude analyses: F3/F4, F1/F2, Fz, FC3/FC4, FC1/FC2, and FCz. They were separated into two levels of anterior-posterior position and five levels of scalp laterality. ERPLAB Toolbox (Luck & Lopez-Calderon, 2012) was used to calculate mean amplitudes of both the standard and deviant ERPs for each of the ten electrodes across the four 50 ms windows: 100-150 ms, 150-200 ms, 200-250 ms, and 250-300 ms. Differences in mean amplitude were compared separately for each time window using deviance direction (increment, decrement) x deviance magnitude (200 Hz standard, 20 Hz

deviant, 40 Hz deviant, 50 Hz deviant) x anterior-posterior (F, FC) x laterality (3, 1, z, 2, 4) repeated measure ANOVAs. Peak latency of the N1 was also measured in the 100 to 150 ms time window. The most negative peak within the window was automatically selected by ERPLAB Toolbox using the criterion of a +/- 20 ms maximum. Differences in N1 peak latency were compared separately using a deviance direction (increment, decrement) x deviance magnitude (200 Hz standard, 20 Hz deviant, 40 Hz deviant, 50 Hz deviant) x anterior-posterior (F, FC) x laterality (3, 1, z, 2, 4) repeated measure ANOVA.

Repeated measure two-tailed cluster-based permutation tests were also conducted using a family-wise alpha level of 0.05 (Bullmore et al., 1999; Groppe, Urbach, & Kutas, 2011). Separate tests were conducted on the ERPs elicited by each of the deviance magnitude conditions: 20 Hz, 40 Hz, and 50 Hz. This was in order to determine whether there were reliable differences between the ERPs for deviant tones that were higher or lower than a standard. Thus, three deviant ERP comparisons were conducted: 220 vs. 180 Hz, 240 vs. 160 Hz, and 250 vs. 150 Hz. All time points between 0 and 350 ms at 10 scalp electrodes (F3/F4, F1/F2, Fz, FC3/FC4, FC1/FC2, and FCz) were included in the test (i.e., 910 total comparisons). T-tests were performed for each comparison using the original data and 2500 random within-participant permutations of the data, which was more than twice the number recommended for a family-wise alpha level of 0.05 (Manly, 2006). For each permutation, all t-scores corresponding to uncorrected p-values of 0.05 or less were formed into clusters.

Electrodes within about 5.44 cm of one another were considered spatial neighbors, and adjacent time points were considered temporal neighbors. The sum of the t-scores in each cluster was the "mass" of that cluster. The most extreme cluster mass in each of the 2501 sets of tests was recorded and used to estimate the distribution of the null hypothesis (i.e., no difference

between conditions). The permutation cluster mass percentile ranking of each cluster from the observed data was used to derive p-values assigned to each member of the cluster. T-scores that were not included in a cluster were given a p-value of 1.

2.5.2 Difference waves. In an oddball paradigm, the MMN is calculated in difference waves that are created by subtracting the standard ERP response from the deviant response in the same condition. Thus, in the increment deviance direction condition, the lower standard of 200 Hz was subtracted from the three deviants of 220 Hz, 240 Hz and 250 Hz. Conversely, in the decrement deviance direction condition, the higher standard of 200 Hz was subtracted from the three deviants of 180 Hz, 160 Hz, and 250 Hz. Thus, three sets of difference waves were created for both the increment and the decrement conditions.

Visual inspection of the difference waves identified a large negative deflection occurring between approximately 100 and 250 ms post-tone onset (Figure 1). Within this large deflection, two distinct peaks were observed, with the earlier peak regarded as an index of the N1 Difference (indicating refractoriness of frequency-specific neurons) while the later peak was hypothesized to be the true MMN (representing the automatic comparison mechanism of auditory sensory memory) (Horváth et al., 2008; Jacobsen, Schröger, Horenkamp, & Winkler, 2003; Maess, Jacobsen, Schröger, & Friederici, 2007). In addition, the P3a appeared as a positive deflection in the difference waves occurring between 200 and 300 ms post-tone onset.

As with the standard/deviant analysis, ten electrodes were selected for difference wave peak amplitude analyses: F3/F4, F1/F2, Fz, FC3/FC4, FC1/FC2, and FCz. ERPLAB Toolbox (Luck & Lopez-Calderon, 2012) was used to calculate mean amplitudes of the differences waves at each of the ten electrodes across four 50 ms windows: 100-150 ms, 150-200 ms, 200-250 ms, and 250-300 ms. Variations in difference wave mean amplitude were compared separately for each

time window using deviance direction (increment, decrement) x deviance magnitude (20 Hz, 40 Hz, 50 Hz) x anterior-posterior (F, FC) x laterality (3, 1, z, 2, 4) repeated measure ANOVAs.

Similar to the standard and deviant ERP analyses, the difference wave cluster permutation analyses focused on the increment/decrement comparison at each of the three frequencies between 0 and 350 ms post-tone onset. Thus, three difference wave comparisons were subjected to separate repeated measure two-tailed cluster-based permutation tests using a family-wise alpha level of 0.05 (Bullmore et al., 1999; Groppe et al., 2011): 20 Hz Increment vs. 20 Hz Decrement, 40 Hz Increment vs. 40 Hz Decrement, and 50 Hz Increment vs. 50 Hz Decrement. All time points between 0 and 350 ms at 10 scalp electrodes (F3/F4, F1/F2, Fz, FC3/FC4, FC1/FC2, and FCz) were included in the test (i.e., 910 total comparisons).

3. RESULTS

3.1 Standard and deviant ERP results

3.1.1 Deviance Direction

The decrement stimuli elicited a larger negative response than did the increment stimuli during both the 150 to 200 ms ($F(1,11) = 7.281$, $p < .03$, $\eta^2 = .398$) and 200-250 ms time windows ($F(1,11) = 10.980$, $p < .008$, $\eta^2 = .500$) (Table 1).

3.1.2 Deviance Magnitude

A deviance magnitude effect was observed during the 100-150 ms window ($F(3,33) = 7.657$, $p < .002$, $\eta^2 = .410$). Post-hoc pairwise comparisons revealed that the responses elicited by both the 40 Hz deviants ($p < .03$) and the 50 Hz deviants ($p < .002$) differed significantly from the 200 Hz standards, regardless of deviance direction (Tables 1 & 2). Similarly, a deviance magnitude effect was found during the 150-200 ms window ($F(3,33) = 7.913$, $p < .003$, $\eta^2 = .418$). Post-hoc

pairwise comparisons revealed that regardless of deviance direction, the 40 Hz deviants differed significantly from the 200 Hz standards ($p < .003$).

3.1.3 Deviance Direction x Deviance Magnitude

A deviance direction x deviance magnitude interaction was observed during the 200-250 ms window ($F(3,33) = 7.023$, $p < .005$, $\eta^2 = .390$). Post-hoc ANOVAs showed that this interaction was driven by differences between the 40 Hz and 50 Hz deviants. The 160 Hz deviants elicited a significantly larger negativity than did the 240 Hz deviants ($F(1,11) = 12.394$, $p < .006$, $\eta^2 = .530$). Similarly, the 150 Hz deviants elicited a larger negativity than did the 250 Hz deviants ($F(1,11) = 13.238$, $p < .005$, $\eta^2 = .546$). No differences for 20 Hz.

<Insert Table 1 about here>

<Insert Table 2 about here>

A deviance direction x deviance magnitude interaction was found for the N1 peak latency ($F(3,33) = 3.641$, $p < .04$, $\eta^2 = .249$). Post-hoc comparisons showed that this interaction was driven by differences between the 40 Hz deviants (Table 3). The 240 Hz deviants elicited a significantly earlier N1 response than did the 160 Hz deviants ($F(1,11) = 8.312$, $p < .02$, $\eta^2 = .430$).

<Insert Table 3 about here>

3.1.2 Cluster permutation analyses.

20 Hz Increment vs. Decrement Deviance Magnitude. No significant clusters were identified.

40 Hz Increment vs. Decrement Deviance Magnitude. The results of this test are displayed in a raster diagram in Figure 2. There was one significant cluster that began at 180 ms and ended at 250 ms. The smallest significant t-score was: $t(11) = 2.2042$, $p < .02$, which had a test-wise alpha level of 0.0497. The decrement tone (160 Hz) elicited a larger and earlier N2 response than did

the increment tone (240 Hz), with differences being larger across the left hemisphere electrode locations (Figure 3).

<Insert Figure 2 about here>

<Insert Figure 3 about here>

50 Hz Increment vs. Decrement Deviance Magnitude. The results of this test are displayed in a raster diagram in Figure 4. There was one significant cluster that began at 141 ms and ended at 250 ms. The smallest significant t-score was: $t(11) = 2.2053$, $p < .02$, which had a test-wise alpha level of 0.0496. The decrement tone (150 Hz) elicited a large N2 response while no apparent N2 response was obvious in the ERPs elicited by the increment tone (250 Hz). Tone frequency differences were fairly prominent across all 10 electrode locations (Figure 5).

<Insert Figure 4 about here>

<Insert Figure 5 about here>

3.2 MMN difference wave results

3.2.1 Deviance Direction

Opposing waveform morphology patterns were observed for the increment and decrement waveforms during the 200-250 ms window. The decrement stimuli elicited a large negativity, the MMN, while the increment stimuli elicited a moderate positivity, the P3a, ($F(1,11) = 10.919$, $p < .008$, $\eta^2 = .498$).

3.2.2. Deviance Magnitude

No significant effects were observed.

3.2.3 Deviance Direction x Deviance Magnitude

A deviance direction x deviance magnitude interaction was observed during the 200-250 window ($F(2, 22) = 6.064$, $p < .02$, $\eta^2 = .355$). As with the standard and deviant waveforms, this

interaction was driven by the differences elicited by the 40 Hz and 50 Hz stimuli. A significantly larger MMN was present in the 40 Hz decrement difference wave as compared to the 40 Hz increment difference wave ($F(1,11) = 11.800, p < .007, \eta^2 = .518$). Similarly, a larger MMN was seen in the 50 Hz decrement difference wave as compared to the positivity in the 50 Hz increment wave ($F(1,11) = 10.589, p < .009, \eta^2 = .490$).

3.2.2 Cluster permutation analyses.

20 Hz Deviance Magnitude Difference Waves. No significant clusters were identified.

40 Hz Deviance Magnitude Difference Waves. The results of this test are displayed in a raster diagram in Figure 6. There was one significant cluster that began at 187 ms and ended at 250 ms. The smallest significant t-score was: $t(11) = 2.2092, p < .05$, which had a test-wise alpha level of 0.0492. The decrement tone (160 Hz) elicited a larger MMN than did the increment tone (240 Hz), with differences being larger across the left hemisphere electrode locations (Figure 7).

<Insert Figure 6 about here>

<Insert Figure 7 about here>

50 Hz Deviance Magnitude Difference Waves. The results of this test are displayed in a raster diagram in Figure 8. There was one significant cluster that began at 187 ms and ended at 246 ms. The smallest significant t-score was: $t(11) = 2.2137, p < .05$, which had a test-wise alpha level of 0.0488. Consistent with the 40 Hz analysis, the decrement tone (150 Hz) elicited a larger MMN than did the increment tone (250 Hz). In this analysis, tone frequency differences were fairly prominent across all 10 electrode locations (i.e., they were not localized to one hemisphere or midline; Figure 9).

<Insert Figure 8 about here>

<Insert Figure 9 about here>

4. DISCUSSION

This study examined effects of increment and decrement deviance magnitudes of 20 Hz, 40 Hz, and 50 Hz on MMN response. Specifically, it sought to determine whether tone frequency changes of the same magnitude above and below a standard tone have similar or differential effects on generation of MMN. Decrement tones that deviated from the standard by 40 Hz and 50 Hz elicited larger responses than increment tones of the same magnitude during the period of approximately 190 to 250 ms post-tone onset.

These outcomes are consistent with data that indicate that the perception of low and high pitch is mediated by differential discrimination thresholds (Kishon-Rabin, Roth, Van Dijk, Yinon, & Amir, 2004), and that pitch raising is more difficult than pitch lowering (Ohala & Ewan, 1973; Sundberg, 1979). They are also in consonance with markedness theory. Data indicate that high and low tones in tonal languages are marked and unmarked, respectively (Hyman, 2012; Pulleyblank, 2004). Marked entities are irregular, infrequent and less common compared to unmarked ones.

Like pure tones, phonological tones consist of acoustic information that is processed at pre-attentive stage (e.g., Yu et al., 2014). If low tones are unmarked, they might be the default, and their processing might involve recruitment of more neuronal populations compared to the case for high tones. By comparison, the perception of high tones, which are marked, might involve activation of a selectively small number of neurons that are tuned to respond to only specific frequencies. Consequently, its ERP output might be small relative to that generated by the perception of low tones. This possibility is consistent with data that indicate that the auditory cortex has a tonotopic organization (Krishnan et al., 2017; Pantev et al., 1995) in the form of a

V-shape, with one low frequency mid-zone positioned laterally and two high frequency end points positioned medially (Gardumi, Ivanov, Havlicek, Formisano, & Uludağ, 2017; Saenz & Langers, 2014). It has also been observed that the auditory cortex has neurons that respond to specific phonetic features of speech sounds (e.g., place or manner of articulation) (Shamma, 2014). Further exploration of this issue is warranted.

Contrary to the present results, some reports suggest that listeners are more sensitive to increment than decrement tones (Peter, McArthur, & Thompson, 2010; Ruusuvirta, & Astikainen, 2012) or have equal ability to distinguish high and low pitch (Jacobsen & Schröger, 2001). The source of the discrepancy is unclear. However, the timing of mean amplitude measurements suggests one possibility. The cluster permutation analyses conducted in the present study (Bullmore et al., 1999; Groppe et al., 2011) involved a large time window (350 ms) and multiple electrodes. This time window may have eliminated the need for “peak picking” while allowing for individual variation in the timing of responses. It makes it possible to capture responses of individual participants accurately since most adults have distinguishable peaks with predictable ERP waveform morphology.

Traditional ERP measurements in previous studies, on the other hand, are calculated by determining an analysis window based on the timing of peaks present in the grand average waveforms. Given that MMN varies greatly across participants in terms of amplitude and latency (Bishop & Hardiman, 2010; Brandmeyer, Farquhar, McQueen, & Desain, 2013; Diesch & Luce, 1997; Pettigrew et al., 2004), there is a relatively high potential for error in this approach, especially since individual peaks may occur outside the designated analysis time window. It is also possible that deviance direction interacts with standard-deviant frequency difference. In the present study, no differences were observed between the 20 Hz increment and 20 Hz decrement

stimuli. The 40 Hz and 50 Hz decrement tones elicited larger responses than their increment counterparts. In addition, the 40 Hz stimuli elicited a greater number of significant effects than the 50 Hz stimuli. Thus, within the three frequency differential groups of the present study, deviants differing from standards by 40 Hz elicited more effects than deviants that differed by 20 Hz or 50 Hz.

In the present study, the 20 Hz deviants might have been too challenging to differentially perceive, resulting in the null results. This finding contrasts with Ruusuvirta and Astikainen (2012) who observed that their 20 Hz increment deviant elicited a larger MMN than their 20 Hz decrement deviant. The differences between the Ruusuvirta and Astikainen study and the present study could be explained by comparing the standard tone frequencies, as the present study used a 200 Hz standard while Ruusuvirta and Astikainen used a 400 Hz standard. With all acoustic properties controlled, higher frequency tones will also sound louder than lower frequency tones. Thus, it is likely that a deviant with smaller differential might be easier to detect at a higher frequency (e.g., 420 Hz in Ruusuvirta and Astikainen) than a lower frequency (e.g., 220 Hz in the present study).

On the other hand, the 50 Hz difference between the standards and deviants might have been so great that it was easy to perceive both the increment and decrement deviants, resulting in fewer effects. It is possible that too large of a frequency differential between standards and deviants will elicit small to null deviance direction effects. This possibility is supported by the null findings of Jacobsen and Schröger (2001), whose increment deviant was 179 Hz higher than the standard and decrement deviant was 50 Hz lower than the standard. In the present study, the 40 Hz deviants might have been at the right frequency differential to be adequately tease apart the effects of increasing and decreasing tone frequencies. Alternatively, the findings of the

present study are inconsistent with those of Peter et al. (2010), who found differential effects with deviants with a differential of 100 Hz. It is likely that Peter and colleagues' use of the same two tone frequencies (250 Hz and 350 Hz) for both the standard and deviant stimuli created a confound as their participants' experiences with the tones in one condition might have impacted their responses to the tones in the opposing condition. Future studies controlling using a variety of standard and deviant tone frequencies are needed to test the hypothesis that certain frequency differentials will elicit greater MMN effects than others.

Additional studies using a variety of tone frequencies are also needed because the highest frequency tone in the present study was 250 Hz, which was a lower frequency tone than any used in the other studies examining increment and decrement MMN effects (Jacobsen & Schröger, 2001; Peter et al., 2010; Ruusuvirta & Astikainen, 2012). Thus, within the large range of frequencies that humans can perceive, all of the tones in the present study could be considered "low" frequency. Future studies using a variety of [higher] frequency ranges are necessary to determine whether the results of the present study can be extended and considered a universal outcome, or whether the present results were due to stimulus-specific characteristics. That is, there might a frequency threshold that might elicit larger MMN responses than others.

DECLARATION OF CONFLICTING INTERESTS

The Authors declare that there is no conflict of interest.

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7. FIGURE CAPTIONS

Figure 1. ERP waveforms elicited by the 20 Hz deviants (top row), 40 Hz deviants (middle row), and 50 Hz deviants (bottom row) in the ERP study at electrode *FCz*. The left column contains the increment deviant responses (220 Hz, 240 Hz, 250 Hz); the right column contains the decrement deviant responses (180 Hz, 160 Hz, 150 Hz). Standard stimulus responses, deviant stimulus responses, and difference waves (deviant minus standard) are presented; negative is plotted up.

Figure 2. Raster diagram illustrating differences between ERP elicited by 40 Hz deviance magnitude increment and decrement tones. Red rectangles indicate electrodes/time points in which the ERPs for decrement tones are more negative than those for increment tones. The color scale indicates the size of the t-test result: The darker the color, the higher the level of significance. Note that the electrodes are organized along the y-axis somewhat topographically. Electrodes on the left and right sides of the head are grouped on the figure's top and bottom, respectively; midline electrodes are shown in the middle. Within those three groupings, y-axis top-to-bottom corresponds to scalp anterior-to-posterior. One outcome was apparent: A significant N2 response difference was observed in the ERPs from 180-250 ms, for a duration of 70 ms.

Figure 3. 40 Hz increment and decrement N1 and N2 responses elicited by the deviant tone stimuli.

Figure 4. Raster diagram showing a significant N2 response difference in the ERPs between the

50 Hz deviance magnitude increment and decrement tones from 140-250 ms, for a duration of 90 ms.

Figure 5. 50 Hz increment and decrement N1 and N2 responses elicited by the deviant tone stimuli.

Figure 6. Raster diagram illustrating differences between MMN responses elicited by 40 Hz increment and decrement tones. A broadly distributed effect was observed from 187-250 ms, signifying a 63 ms period of time during which 40 Hz deviance magnitude decrement tones elicited larger MMN responses than did 40 Hz deviance magnitude increment tones.

Figure 7. 40 Hz deviance magnitude increment and decrement MMN responses found in the difference waves across three scalp regions: Left Hemisphere (F3, F1, FC3, FC1), Central (Fz, FCz), and Right Hemisphere (F2, F4, FC2, FC4).

Figure 8. Raster diagram identifying a significant MMN effect between the 50 Hz deviance magnitude increment and decrement difference waves from 187-246 ms, for a duration of 59 ms.

Figure 9. 50 Hz deviance magnitude increment and decrement MMN responses.

Table 1. Averaged (across 10 electrodes) mean amplitude measurements in microvolts (SEM) for four time periods: 100-150, 150-200, 200-250, and 250-300 ms post-tone onset. The MMN was measured in the deviant minus standard difference waveforms.

Standard and Deviant ERP Mean Amplitudes

Condition	Stimulus	100-150 ms	150-200 ms	200-250 ms	250-300 ms
Increment	200 Hz standards	-0.158 (.085)	0.134 (.101)	-0.267 (.143)	-0.650 (.175)
	220 Hz deviants	-0.236 (.185)	-0.208 (.206)	-0.430 (.222)	-0.407 (.253)
	240 Hz deviants	-0.650 (.189)	-0.214 (.201)	-0.132 (.207)	-0.472 (.182)
	250 Hz deviants	-0.590 (.182)	-0.078 (.259)	-0.092 (.283)	-0.241 (.268)
	Overall Increment	-0.409 (.129)	-0.092 (.167)	-0.230 (.191)	-0.442 (.190)
Decrement	200 Hz standards	-0.037 (.091)	0.060 (.104)	-0.310 (.130)	-0.603 (.123)
	180 Hz deviants	-0.285 (.166)	-0.315 (.173)	-0.427 (.225)	-0.569 (.227)
	160 Hz deviants	-0.433 (.183)	-0.666 (.220)	-0.703 (.175)	-0.523 (.173)
	150 Hz deviants	-0.665 (.120)	-0.605 (.213)	-0.826 (.246)	-0.489 (.194)
	Overall Decrement	-0.355 (.113)	-0.381 (.164)	-0.567 (.174)	-0.546 (.153)

MMN Mean Amplitude

Condition	Difference Wave	100-150 ms	150-200 ms	200-250 ms	250-300 ms
Increment	20 Hz	-0.078 (.145)	-0.342 (.144)	-0.163 (.166)	0.242 (.211)
	40 Hz	-0.492 (.159)	-0.348 (.162)	0.135 (.128)	0.178 (.098)
	50 Hz	-0.432 (.146)	-0.212 (.201)	0.175 (.224)	0.408 (.221)
	Overall Increment	-0.334 (.101)	-0.301 (.132)	0.049 (.146)	0.276 (.146)
Decrement	20 Hz	-0.203 (.155)	-0.350 (.121)	-0.097 (.145)	0.018 (.153)
	40 Hz	-0.351 (.152)	-0.701 (.156)	-0.374 (.121)	0.063 (.145)
	50 Hz	-0.583 (.085)	-0.640 (.158)	-0.497 (.178)	0.098 (.159)
	Overall Decrement	-0.379 (.095)	-0.564 (.127)	-0.323 (.115)	0.059 (.116)

Table 2. Summary of significant mean amplitude main effects and interactions for standard, deviant, and difference waveforms.

Standard and Deviant ERP Mean Amplitudes

Effect	100-150 ms	150-200 ms	200-250 ms	250-300 ms
Deviance Direction		Decrement > Increment	Decrement > Increment	
Deviance Magnitude	40 Hz Deviants > Standards 50 Hz Deviants > Standards	40 Hz Deviants > Standards		
Deviance Direction x Deviance Magnitude			160 Hz Deviants > 240 Hz Deviants 150 Hz Deviants > 250 Hz Deviants	

Difference Wave Mean Amplitudes

Effect	100-150 ms	150-200 ms	200-250 ms	250-300 ms
Deviance Direction			Decrement > Increment	
Deviance Magnitude				
Deviance Direction x Deviance Magnitude			40 Hz: Decrement > Increment 50 Hz: Decrement > Increment	

Table 3. Averaged (across 10 electrodes) N1 peak latency measurements in milliseconds (SEM) during the 100-150 ms post-tone onset time window.

Condition	Stimulus	100-150 ms
Increment	200 Hz standards	129 (2.49)
	220 Hz deviants	130 (2.51)
	240 Hz deviants	129 (2.82)
	250 Hz deviants	131 (2.98)
	Overall Increment	130 (1.98)
Decrement	200 Hz standards	129 (3.13)
	180 Hz deviants	126 (2.84)
	160 Hz deviants	138 (2.21)
	150 Hz deviants	130 (2.79)
	Overall Decrement	131 (1.46)

Increment

Decrement