

Adaptation Patterns and Their Associations with Mismatch Negativity: A Roving Electroencephalogram Paradigm with Expectations Maintained

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Abstract

Adaptation is defined as reduced neural activation following repeated stimulus presentation. While numerous previous electroencephalogram studies used either one repetition or multiple repetitions to elicit adaptation in event-related potentials, the adaptation patterns under controlled expectations manifested in the two main auditory components, N1 and P2, are still largely unknown. In addition, multiple repetitions were used in mismatch negativity experiments to measure deviance detection, but how adaptation in different time points contributes to the mismatch negativity remains unclear. Therefore, in the present study, 37 healthy adults participated in an electroencephalogram experiment with a pure tone roving paradigm and a random stimulus arrangement to maintain expectations. The amplitudes were traced along with the first ten tones in the auditory event-related potentials components, N1 and P2, to examine the adaptation patterns. Results showed an L-shaped adaptation in the N1 with a large decrease after the first repetition (N1 initial adaptation), and a continuous, linear amplitude increase in the P2 even after the first repetition (P2 subsequent adaptation), possibly indicating memory trace formation. Regression results showed that the peak amplitudes of the N1 initial adaptation and the P2 subsequent adaptation significantly explained the variance in the mismatch negativity amplitude. The results indicate distinct adaptation patterns for multiple repetitions in different components and suggest that the mismatch negativity combines two processes as indicated by the initial adaptation in the N1 and a continuous memory trace effect in the P2. Separating the two processes may be relevant for models of cognitive processing and clinical disorders.

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Keywords : Adaptation, expectation, electroencephalogram (EEG), mismatch negativity (MMN), repetition positivity (RP)

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Adaptation is defined as reduced neural activation following repeated stimulus presentation. While numerous previous electroencephalogram studies used either one repetition or multiple repetitions to elicit adaptation in event-related potentials, the adaptation patterns under controlled expectations manifested in the two main auditory components, N1 and P2, are still largely unknown. In addition, multiple repetitions were used in mismatch negativity experiments to measure deviance detection, but how adaptation in different time points contributes to the mismatch negativity remains unclear. Therefore, in the present study, 37 healthy adults participated in an electroencephalogram experiment with a pure tone roving paradigm and a random stimulus arrangement to maintain expectations. The amplitudes were traced along with the first ten tones in the auditory event-related potentials components, N1 and P2, to examine the adaptation patterns. Results showed an L-shaped adaptation in the N1 with a large decrease after the first repetition (N1 initial adaptation), and a continuous, linear amplitude increase in the P2 even after the first repetition (P2 subsequent adaptation), possibly indicating memory trace formation. Regression results showed that the peak amplitudes of the N1 initial adaptation and the P2 subsequent adaptation significantly explained the variance in the mismatch negativity amplitude. The results indicate distinct adaptation patterns for multiple repetitions in different components and suggest that the mismatch negativity combines two processes as indicated by the initial adaptation in the N1 and a continuous memory trace effect in the P2. Separating the two processes may be relevant for models of cognitive processing and clinical disorders.

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1. Introduction

1.1 Adaptation

Repeated presentation of the same stimulus typically leads to reduced neural activation, which is called neural adaptation (Grill-Spector et al., 2006; Ringo, 1996), repetition suppression (Desimone, 1996; Grill-Spector et al., 2006), sensory gating (Boutros & Belger, 1999; Freedman et al., 1987), habituation (Bourbon et al., 1987; Loveless, 1983; c.f. Barry et al., 1992), refractoriness (Berry & Meister, 1998; Budd et al., 1998; Rosburg & Mager, 2021) and some other terms with varying usage across the literature. In the present study, we refer

it to adaptation. Adaptation can be observed across different stimuli in both visual and auditory modalities, for example, in the repetition of faces (see Schweinberger & Neumann, 2016 for a review), symbols (e.g., Soltész & Szűcs, 2014), and tones (e.g., Todorovic & de Lange, 2012).

Adaptation can be measured by an amplitude decrement of components of the event-related potential (ERP) that is recorded from the scalp using electroencephalography (EEG). In the auditory modality, ERP components, including N1 and P2, are typically measured at fronto-central electrodes. N1 is a negative component occurring between around 60–160 ms (Woods, 1995) and P2 is a positive component that peaks at around 150–250 ms (Crowley & Colrain, 2004). Distributed over fronto-central areas (Crowley & Colrain, 2004; Woods, 1995), these components typically have a polarity reversal over inferior posterior electrodes, when measured against an average reference, as their sources are mainly in the temporal lobe (Crowley & Colrain, 2004; Fogarty et al., 2020; Näätänen & Picton, 1987). The auditory N1 and P2 adaptations, as reflected by amplitude decrement, were found in a vast number of previous studies using pairs of tones or long trains of tones (e.g., N1: Bourbon et al., 1987; Boutros et al., 1999; Budd et al., 1998; Lagemann et al., 2012; Näätänen & Picton, 1987; Rosburg, 2004; Rosburg & Mager, 2021; Rosburg et al., 2006; N1 and P2: Hari et al., 1982; Herrmann et al., 2016; Peter et al., 2019; Polich, 1986; Rosburg et al., 2022; Rosburg et al., 2010; Sambeth et al., 2004). Regarding the adaptation pattern, most studies showed an N1 decrease stabilized after the 2nd or 3rd sound in a stimulus sequence but no further decrease for subsequent sounds (e.g., Barry et al., 1992; Bourbon et al., 1987; Boutros et al., 1999; Budd et al., 1998; Lagemann et al., 2012; Rosburg, 2004), although some studies found a gradual response decrease (e.g., Öhman & Lader, 1972). An initial amplitude decrease was shown in the P2 in some studies (Rosburg & Sörös, 2016; Rosburg et al., 2010). However, some studies also reported an increase of a slow positive wave from 50 to 250 ms post-stimulus onset along with stimulus repetition, which reflected “repetition positivity” (RP; Cooper et al., 2013; Recasens et al., 2015; more details of RP will be discussed below). Since the RP corresponds to an increase of P2 and a decrease of N1, it seems to be contradictory to the diminishing P2. Therefore, more research on this topic is necessary to understand the adaptation patterns.

1.2 Adaptation and MMN

Adaptation is related to a component formed by an ERP difference wave called mismatch negativity (MMN). First described by Näätänen et al. (1978), the MMN usually occurs when a stimulus with different properties (e.g., frequency, intensity, duration, etc.) called deviant presented in a sequence of repeated stimuli called standards. It has been studied extensively in the auditory modality, and it is measured by subtracting the ERP to standards that appear mostly near the end of a stimulus train from that to deviants (Garrido et al., 2009b). The MMN peaks at about 100–250 ms from the point of deviation (Kujala & Näätänen, 2001). For the scalp location, the MMN is usually maximal at fronto-central areas and reverses polarity at the mastoids (Kujala & Näätänen, 2001), while its source is in temporal and frontal areas (Alho, 1995). Attention is not required to trigger the MMN as it is associated with pre-attentive processing in the auditory modality (Näätänen et al., 2001).

Importantly, the formation of the MMN, which is measured by the amplitude from a difference waveform generated by subtracting the average response to standards from that to deviants, is not only due to the more negative amplitude in the deviant trials, but also more positive (or less negative) amplitudes caused by adaptation in the standard trials. For example, if the amplitudes of the N1 and P2 components become less negative or more positive along repetitions, the MMN will be larger assuming that the amplitude of the deviant is unchanged. However, the MMN will be smaller if the N1 and P2 amplitudes become more negative and less positive along repetitions. Indeed, the adaptation hypothesis (Jääskeläinen et al., 2004; May et al., 1999; May & Tiitinen, 2010) has been proposed to explain the mechanism of the MMN. The adaptation hypothesis emphasizes that MMN is induced by the attenuation and delay of the N1 due to adaptation to the repetitive standard stimuli (May et al., 1999; May & Tiitinen, 2010). Therefore, the MMN does not reflect any higher-level comparison processing or mismatch detection per se, but just a release from stimulus-specific adaptation (Fishman, 2014). On the contrary, the model-adjustment hypothesis (Näätänen & Alho, 1995; Näätänen et al., 2005; Näätänen & Winkler, 1999; Sussman & Winkler, 2001; Winkler et al., 1996) proposes

that the MMN represents the outcome of change detection between the deviants and the memory trace formed by standards. Originally, this hypothesis only applied to repeated sounds of the same standards, but later it was extended to include the detection of regularity violation to account for the existence of the MMN in some experiments using standard stimuli with predictable patterns, or regularities, such as a sequence of tones with increasing frequencies, and deviants which violate the regularities, for instance, a repeated or decreased tone (Winkler, 2007). The occurrence of the MMN in this type of experimental design supported the model-adjustment hypothesis but not the adaptation hypothesis because no repeated sound could cause adaptation in the regularities (Garrido et al., 2009b).

While the aforementioned studies attempted to discriminate the two postulations of MMN mechanisms, it is important to note that they are not mutually exclusive. Indeed, a predictive coding framework could explain the mechanisms of MMN by encompassing the adaptation hypothesis and the model-adjustment hypothesis (Carbajal & Malmierca, 2018; Friston, 2005; Garrido et al., 2009b; Winkler, 2007). It suggests that our brain extracts regularities in a sequence of stimuli and forms a hypothesis about upcoming stimuli based on the regularities. If a deviant happens, the MMN is elicited because a prediction error is generated due to a violation of the hypothesis about the stimulus and regularities by the deviant. The predictive coding framework incorporates the adaptation hypothesis by suggesting that when standard stimuli can be predicted more precisely by the top-down process, less weight is assigned to bottom-up influences, leading to a stronger adaptation shown by a weaker and later N1 (Garrido et al., 2009b). From the predictive coding perspective, adaptation and MMN can be considered as microscopic and macroscopic correlates of the same deviance-detection process when the repetition rule is involved (Carbajal & Malmierca, 2018). On the other hand, the predictive coding framework shares the same idea with the model-adjustment hypothesis that MMN is due to a comparison between the predicted inputs based on memory trace and the actual inputs. A mismatch between these two inputs leads to a prediction error, and the prediction model has to be adjusted. Therefore, in the predictive coding framework, the MMN represents a failure to predict bottom-up inputs and an ensuing failure to suppress prediction error (Garrido et al., 2009b).

Repetition positivity (RP) is a component that supports the predictive coding mechanism of MMN. RP is formed by subtracting the ERPs of fewer repetitions of standard stimuli from the ERPs with more repetitions. It may be pertinent to the phenomenon that an increase in standard stimulus repetition may lead to an increase in MMN (Sams et al., 1983). Crucially, the RP is not only limited to the N1 time window, and this is inconsistent with the adaptation hypothesis of MMN as it proposes that the N1 adaptation effect could explain the MMN completely (Haenschel et al., 2005). In the study by Haenschel et al. (2005), RP, which could account for a large proportion of the MMN, occurred early from the P1 time window, and it was larger when repetitions of standards increased. Based on these characteristics, they postulated that the RP is an ERP correlate of adaptation, a mechanism that underlies memory trace formation in the primary auditory cortex (A1). According to the predictive coding account, the RP is considered an index of prediction error suppression stemming from the congruence between sensory and predicted input (Baldeweg, 2007). Research studies that investigate the RP are relatively scarce compared with those examining MMN. Therefore, more studies need to be conducted before the relationship between RP, adaptation, and MMN can be firmly established.

1.3 Expectation Maintenance and the Present Study

Importantly, previous studies have suggested that stimulus expectations may affect the components related to adaptation and MMN. Specifically, the N1 amplitude of stimulus repetition was found to be enhanced by expectations of the stimuli (Hari et al., 1979), while the regular combination of standards and deviants might induce a pattern since grouping could happen pre-attentively even though the stimulus onset asynchrony (SOA) was as long as one second, which might affect the MMN amplitude (Herholz et al., 2009). In addition, explicit top-down expectations were found to diminish the MMN (Chennu et al., 2013; Costa-Faidella et al., 2011b; Lecaiguard et al., 2021). Recent findings have shown that stimulus expectations generated by participants may play a role in adaptation when attention is involved (e.g., Tang et al., 2018), or even not involved (e.g., Barbosa & Kouider, 2018; Kuravi & Vogels, 2017; Todorovic et al., 2011). Therefore, the top-down

processing may modulate the repetition effect. This underscores the importance of maintaining or controlling expectations when examining the adaptation effect. Nonetheless, restrictions imposed on stimulus arrangements could lead to expectations. For example, in typical MMN experiments, the consecutive occurrence of deviants is avoided, and the maximum tone repetition is set as a fixed number. These restrictions might induce participants to generate expectations regarding whether the next stimulus is a deviant or standard. These expectations may potentially affect components related to adaptation and the MMN. Therefore, in the present study, the expectations was maintained through a stable presentation probability of the stimuli to ensure a pure measurement of adaptation uninfluenced by expectation. Specifically, an experimental paradigm in which no restriction was imposed on the stimulus arrangement, besides an 85%-standard and 15%-deviant rule, and long trains of maximally 30 standards, was utilized.

In addition, a roving paradigm was adopted in the present study. In this paradigm, a deviant becomes the subsequent standard to ensure that the properties of the deviants and standards are the same. Therefore, the MMN must reflect the inherent differences between the standards and deviants, without being influenced by any other physical properties. Additionally, the memory trace of the standards needs to be re-established and strengthened during each train of standards (Cooper et al., 2013). This paradigm has been used in some previous studies (e.g., Costa-Faidella et al., 2011a; Cowan et al., 1993; Garrido et al., 2008; Haenschel et al., 2005; Recasens et al., 2015).

The present study used “initial adaptation” to represent the amplitude decrease from the 1st to the 2nd tones and “subsequent adaptation” to capture the following decrease from the 2nd to the final tones in each sequence of the same stimuli. Overall, using an auditory experimental paradigm with controlled expectations, the present study focuses on two research questions: 1) How are the initial and subsequent adaptation patterns manifested in N1 and P2? 2) To what extent can these adaptation patterns explain the MMN? These two research questions were examined using an EEG roving experiment in healthy adults, coupled with adaptation pattern, correlation, and regression analyses. Regarding the first research question, we predicted that the N1 and P2 components would show reduced amplitudes in the initial tones that signify adaptation based on previous studies (Budd et al., 1998; Rosburg & Sörös, 2016). However, increased amplitudes might be observed in P2 due to the RP, indicating a memory trace effect (Haenschel et al., 2005). Concerning the second research question, we hypothesized that the correlations of the MMN (negative values) and adaptation effects manifested by N1 (negative values) and P2 (positive values) would be positive and negative respectively. Moreover, the initial and subsequent adaptation effects might be important predictors of the MMN as the adaptation and the memory trace proposed by the model adjustment account may both play a role in the MMN.

2. Materials and Methods

2.1 Participants

We recruited 40 adults to participate in the experiment. Three participants were excluded due to excessive muscle movement or electric noise. Therefore, the data of the remaining 37 participants (*age range* : 19–26 years; *mean age* : 20.84 years; 19 females) were analyzed. Two of them were left-handed, while the others were right-handed. All participants were undergraduate students studying at the Chinese University of Hong Kong (CUHK). Written consent was obtained before the experiment started. They either received course credits or cash for compensation. This study was approved by The Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee (The Joint CUHK-NTEC CREC) (reference no.: 2019.048).

2.2 Stimuli and Procedure

The experiment was programmed using E-Prime 3.0 (Psychology Software Tools, Pittsburgh, PA). All stimuli were pure sinusoidal tones, with seven different frequencies (500 Hz, 550 Hz, 600 Hz, 650 Hz, 700 Hz, 750 Hz, and 800 Hz). The duration of each tone was 70 ms (with 5 ms rise and fall times), and the stimulus onset asynchrony (SOA) was fixed at 650 ms. All tones were presented at 70 dB. As a roving paradigm was used, deviants (the 1st tone in each sequence) would become subsequent standards.

EEG data were recorded using NetStation, with a Net Amps 300 amplifier and 128-channel Electrical Geodesics Incorporated (EGI) nets against a Cz reference. The sampling rate was 500 Hz, and the online filter setting was 0.1 Hz high-pass. The impedance was kept below 50 k Ω for each electrode. The data recording took place in a sound-attenuated laboratory. Before the experiment began, participants were told that some sounds would be played when they were watching a silent movie, but they should ignore the sounds. Also, they were instructed to limit body movements during the experiment to minimize muscle artifacts.

In the present experiment, the first tone was randomly played among the seven types of tones with different frequencies. After that, there was an 85% chance that the next tone would be the same as the first tone (standard) and a 15% chance that the next tone would be different from the first tone (deviant). This criterion was kept unchanged throughout the experiment. The only exception was that if 30 tones were played consecutively, the next tone must have been a deviant, which happened only 2.73 times on average ($SD = 1.59$ times; *range* : 0–5 times) among around 300 sequences for each participant. This restriction was to ensure that there were sufficient trials to be analyzed. The purpose of increasing the maximum stimulus number in each train (30) compared with previous studies (mostly 10 or fewer) and using a random stimulus arrangement was to maintain participants' expectations of the stimulus arrangement. Throughout the experiment, participants watched a silent movie, "Tom and Jerry", via a laptop during the experiment, when the tones were played by two speakers 80 cm away from them. The present experiment ended after 2,000 tones had been played, which were divided into two blocks with 1,000 tones each. There was a small pause between the two blocks for the experimenter to check the impedance of all the electrodes and lower it if needed. The duration of the experiment was around 20 minutes. Figure 1 shows the experimental paradigm.

After the EEG experiment, a tone discrimination task run by E-Prime 3.0 was conducted to confirm that participants were able to discriminate tones with a frequency difference of 50 Hz. In each trial, participants listened to a pair of tones. The task began with eight practice trials to ensure that participants understood the task, followed by 104 experimental trials. Among the 104 trials, the tone pairs were different in 48 trials and they were the same in 56 trials. The properties of the tones were the same as those in the EEG experiment, and they were played in a pseudorandomized sequence. All different tone pairs in the experimental trials had 50 Hz discrepancy, the least frequency difference that appeared in the EEG task, but tone pairs with larger frequency differences appeared in practice trials. Participants were told to press "f" on the keyboard when the two tones were the same and press "j" when they were different. Participants were emphasized that they should make the judgment as accurately and quickly as possible. In each trial, a fixation cross first appeared for one second, followed by a pair of tones (70 ms each), with an inter-tone interval of 280 ms. Then, a question mark appeared on the screen, which remained until participants had judged whether the two tones were the same or different by pressing the corresponding button. After that, the fixation cross reappeared as the next trial began. Accuracy and reaction time were shown immediately after the response in practice trials, but not in the main experiment. This task lasted for around five minutes. The average accuracy was 94.49% ($SD = 5.38\%$; $d' = 3.56$), indicating that participants were able to discriminate the tones used in the experiment. No participant was excluded based on their performance in this task.

2.3 EEG Preprocessing

Brain Vision Analyzer (version 2.2.1.8266; Brain Products, Gilching, Germany) was used for data preprocessing and waveform analyses. The data preprocessing steps for each participant began with segmentation, followed by filtering (0.3 Hz high-pass with a slope of 24 dB/oct and 30 Hz low-pass with a slope of 48 dB/oct), bad channel selection, raw data inspection, independent component analysis (ICA) for eye blink and lateral eye movement corrections based on a restricted Infomax algorithm, bad channel interpolation with spherical splines, re-referencing to the average signals recorded from all electrodes, and artifact rejection (if an extreme voltage ($>+80$ or <-80 μV) was detected, a segment before and after 200 ms of that detection point was excluded). Overall, an average of 24% of trials were rejected. The average remaining trial numbers in the three conditions related to the adaptation effects, namely the deviants (1st tones), the 2nd tones, and the final tones in the 3rd to 30th positions, were 230 (152–297), 197 (133–250), and 139 (98–172) respectively. The average remaining trial numbers for the 3rd to 10th tones, which are relevant to the adaptation pattern

analyses, are recorded in Table S1. We included only the final tones in the 4th to 30th positions for the adaptation and MMN analyses, rather than all the tones within these positions. This approach ensures a relatively balanced comparison between standards and deviants by maintaining a similar number of each. A fixed delay of 18 ms was corrected due to the anti-aliasing filter of the amplifier (see the advisory notice about the timing affected by anti-alias filter effects used in Net Amps 300 amplifiers, 26 November 2014, EGI for more details). The epoch was from 168 ms pre-stimulus to 632 ms post-stimulus. Baseline correction was conducted based on the data in the pre-stimulus period.

2.4 Data Analyses

Based on previous literature related to adaptation and MMN (e.g., Bühler et al., 2017; Jaffe-Dax et al., 2017; Jost et al., 2015), the following 25 frontocentral electrodes were pooled for analyses: E19, E11, E4, E20, E12, E5, E118, E13, E6, E112, E10, E16, E18, E30, E7, E106, E105, E37, E31, E129, E80, E87, E55, E36, E104 (see the top-left corner of Figure 3 for the electrode positions). The time window for the detection of the local peak amplitude of N1 was defined by the global field power (GFP) and global dissimilarity peaks of subsequent maps of the grand average data. GFP is the root mean square (RMS) across the average-referenced electrode values, or the standard deviation of all electrodes at a given time point (Murray et al., 2008), while global dissimilarity is an index of configuration differences between the maps, notwithstanding their strength (Lehmann & Skrandies, 1980; Murray et al., 2008). The GFP and global dissimilarity were generated from Brain Vision Analyzer and Cartool (Brunet et al., 2011). The N1 time windows of the deviants, the 2nd tones, and the final tones were 70–218 ms, 76–118 ms, and 76–140 ms respectively. On the other hand, since there were no clear GFP peaks in the P2, its time windows were defined by the peaks between N1 and N2. The P2 time windows of the corresponding conditions were 120–348 ms, 96–240 ms, and 98–254 ms respectively (see Figure S1 for the illustrations of how these P2 time windows were defined).

In addition, the MMN waveform was formed by subtracting the amplitudes of the final tones in the 4th to 30th positions from that of the deviants in the same frontocentral electrodes (deviants–final tones), and the time window based on the GFP and the global dissimilarity peaks was defined as 76–196 ms. Local peak MMN amplitude was identified automatically using Brain Vision Analyzer. Similarly, for the adaptation effects, the local peak amplitude in each tone position and time window was identified automatically using Brain Vision Analyzer. We defined the initial adaptation as the peak amplitude decrease between the deviants and the tones in the 2nd position in the frontocentral electrodes (deviants–2nd tones). On the other hand, the subsequent adaptation was defined as the subtraction of the peak amplitudes of the final tones in the 4th to 30th positions from that of the tones in the 2nd position in the same electrodes (2nd tones–final tones). Figure 1 illustrates the calculation methods of initial adaptation, subsequent adaptation, and MMN.

The adaptation curves of the first ten tones of N1 and P2 were first plotted based on the peak amplitudes in the corresponding time window, as after the tenth tone, the trial number (< 50 trials on average) might not be enough to generate reliable results. Then, a paired sample t-test between each consecutive tone pair with Holm-Bonferroni corrections (Holm, 1979) and a repeated-measures ANOVA on the amplitude based on an a priori linear trend analysis across the first ten tones in each stimulus train were conducted to understand the adaptation pattern manifested in N1 and P2. On the other hand, the existence of an MMN was tested by a one-sample t-test against zero for the amplitude of the difference wave. Additionally, the relationship between initial adaptation, subsequent adaptation effects, and MMN was examined through correlation and backward stepwise linear regression analyses. Specifically, in the regression model, the N1 and P2 initial adaptations and subsequent adaptations were the independent variables (IVs), and the MMN peak amplitude was the dependent variable (DV). The elimination criterion of the backward regression was $p > .10$. This means that the IV with the lowest partial correlation with the DV, which reached the criterion $p > .10$, was removed in each step until all variables that remained in the model were $p < .10$. All statistical tests mentioned above were conducted using IBM SPSS Statistics Version 25 (IBM, Armonk, NY, USA).

3. Results

Figure 2 shows the adaptation patterns depicted by the peak amplitudes of N1 and P2 along the first ten

tones. Details are described below.

3.1 N1 Adaptation

The adaptation curve of the first ten tones from the average N1 peak data was plotted based on the peak amplitudes in the N1 time window. A steep decrease (less negative) in N1 amplitude was found between the 1st and 2nd tones, then they reached a plateau (Figure 2a). Paired-sample t-tests were conducted to compare the average N1 peak amplitude elicited by each successive tone pair. Results showed that the N1 amplitude of the 2nd tones ($M = -0.71 \mu V$, $SD = 0.56 \mu V$) was significantly less negative than that of the 1st tones ($M = -1.51 \mu V$, $SD = 0.77 \mu V$; $t_{36} = -6.68$, $p < .001$, $d = 0.72$). Moreover, there was a rebound effect, as shown by a significant increase (more negative) in the N1 amplitude from the 2nd to the 3rd tones ($M = -0.99 \mu V$, $SD = 0.60 \mu V$; $t_{36} = 3.91$, $p < .001$, $d = 0.43$). No other significant difference was found in other tone pairs (all $p > .007$ based on the Holm-Bonferroni correction). Based on the trend analysis across the 1st to 10th tones, a significant linear trend was found ($F_{1,36} = 17.06$, $p < .001$, $MSE = 4.40$, $\eta_p^2 = 0.32$). However, no significant linear trend was found across the 2nd to 10th tones ($F_{1,36} = 0.08$, $p = .78$, $MSE = 0.02$, $\eta_p^2 = 0.002$), demonstrating that there was no evidence showing that a continued amplitude decrement was followed by the initial decrease from the 1st to 2nd tones (Figure 2a).

3.2 P2 Adaptation

Likewise, the average peak amplitudes of the P2 were first extracted in the first ten positions to generate adaptation curves. The P2 amplitude showed an increasing trend along with the first ten stimuli (Figure 2b). Paired-sample t-tests on amplitude showed no significant differences between individual tone pairs based on the Holm-Bonferroni-adjusted p -value ($p > .006$). However, a significant linear trend was shown in the trend analysis from the 1st to 10th tones ($F_{1,36} = 26.90$, $p < .001$, $MSE = 7.43$, $\eta_p^2 = 0.43$), and also from the 2nd to 10th tones ($F_{1,36} = 33.28$, $p < .001$, $MSE = 7.64$, $\eta_p^2 = 0.48$). These results illustrate that a continuous amplitude increase happened in the P2 time window, which was not only limited to the initial two tones (Figure 2b). The ERPs of the first ten tone positions are shown in Figure 3.

3.3 MMN

A one-sample t-test of the difference wave of deviants (tones in the 1st position) minus final tones in the 4th to 30th positions confirmed that the average peak amplitude was significantly smaller than zero ($M = -1.01 \mu V$, $SD = 0.60 \mu V$; $t_{36} = -10.28$, $p < .001$), showing that the MMN was elicited. The MMN waveform and topography with fronto-central negativity and temporal positivity are shown in Figure 4.

3.4 Adaptation and MMN

The descriptive statistics of the amplitudes of the N1 and P2 initial adaptation and subsequent adaptation effects and the MMN are shown in Table 1.

3.4.1 Correlation Analysis

The results of the Pearson correlation of the variables are shown in Table 2. A significant, positive, and strong correlation between the amplitudes of MMN and N1 initial adaptation was found ($r_{35} = .67$, $p < .001$), which means that participants who exhibited a stronger N1 initial adaptation effect showed a larger MMN (Figure 5a). No other significant correlation related to the MMN amplitude was found (all $p > .008$ based on Holm-Bonferroni correction).

3.4.2 Regression Analysis

To further investigate the relationship between adaptation and MMN, a backward stepwise regression was performed to clarify which and how each adaptation effect contributes to the MMN. First, the four adaptation variables measured by amplitudes were entered into the regression model, while the MMN peak amplitude acted as the DV. Only N1 initial adaptation (β (standardized beta) = 0.72; $p < .001$) and P2 subsequent adaptation amplitudes ($\beta = 0.33$; $p = .009$) survived in the final model ($F_{2,34} = 20.50$; $p < .001$; see Figure 5b for the correlation between the P2 subsequent adaptation effect and MMN). According to the squared

semipartial correlation, which indicates the unique contribution of an independent variable to the dependent variable (Aloe & Becker, 2010), these two variables explained more than 50% of the MMN variance (49.98% and 10.43% respectively). The standardized coefficients of each variable and the adjusted R squares of the initial and final models of the amplitudes of adaptation and MMN are shown in Table 3.

To confirm that the initial and subsequent adaptation effects did not partial each other out, partial correlations were conducted. The partial correlation between the MMN and the N1 adaptation amplitudes when the N1 subsequent adaptation effect was controlled, and the partial correlation between the MMN and the P2 subsequent adaptation amplitudes when the P2 initial adaptation effect was controlled, remained the same as the corresponding correlations reported above. Hence, the initial and subsequent adaptation effects that were relevant to the regression analysis did not partial each other out. The results were reported in Table S2.

3.4.3 Additional Analyses

Although we tried to balance the trial number by including only the final standards but not all standards in our analyses, the trial numbers were still unequal between the deviant, 2nd tone, and final tone conditions. Therefore, the same analyses were conducted with a fixed number of trials in these three conditions based on the trial number of the final tone condition (the condition with the least trial numbers) remained in each participant. The results were similar, with N1 initial adaptation and P2 subsequent adaptation amplitudes predicting the MMN amplitude in the regression model. However, N1 subsequent adaptation was also a significant predictor. Detailed results are reported in Supplementary Information.

3.4.4 Topographic Analysis

To explore whether the topographic distributions of the two adaptation effects were different (and thereby having different underlying neural sources; Michel & Murray, 2012), a Topographic Analysis of Variance (TANOVA) was conducted in RAGU (Koenig et al., 2011) by comparing individual N1 initial adaptation (peak amplitudes of deviants–peak amplitudes of the 2nd tones) and P2 subsequent adaptation (peak amplitudes of the 2nd tones–peak amplitude of final tones in the 4th to 30th positions) with 5000 randomization runs (see Figure 6 for the corresponding scalp topographies and Figure 7 for the scalp topographies for N1 subsequent adaptation and P2 initial adaptation). In order to focus on the topographic distribution, the maps were normalized for strength (GFP = 1). The result revealed that the topographic maps of N1 initial adaptation and P2 subsequent adaptation were significantly different ($p < .05$), indicating that the topographic distributions, and therefore the underlying sources of these two adaptation effects, were disparate. The gradients of the N1 initial adaptation effect were steepest over left superior temporal regions, while the gradients of the P2 subsequent adaptation effect were steepest over bilateral frontal regions. These findings are in agreement with the initial adaptation taking place in auditory cortex regions and the model reestablishment effect in bilateral frontal regions.

4. Discussion

Neural adaptation is a robust phenomenon that reflects one mechanism of how the brain makes use of previous experience with stimuli (e.g., Grill-Spector et al., 2006). In the auditory domain, most studies have utilized stimulus pairs or a series of stimulus repetitions to investigate adaptation, without specifically examining the adaptation patterns across individual tones. In contrast, the present study examined N1 and P2 adaptation patterns, with a comparison between initial and subsequent repetitions. While previous MMN studies used different paradigms and methods to discriminate the adaptation and model adjustment accounts of MMN, and some of them attempted to control the adaptation effect to examine a pure model adjustment component of MMN (e.g., Jacobsen & Schröger, 2001), the present study investigated the relationship between MMN and adaptation patterns in N1 and P2. Importantly, the expectations was maintained by presenting tones with a fixed probability in a long train. The adaptation effects reflected by the amplitudes were found in the N1 during the initial tone repetitions. For the P2 amplitude, a linear increase with repetitions was shown, which might indicate a memory trace or model reestablishment effect. In terms of amplitudes, the MMN was mainly explained by the N1 adaptation effect induced by the initial tones and the continuous P2 adaptation

effect triggered by subsequent tones. Details of the adaptation patterns are discussed below.

4.1 N1 Adaptation at the Initial Stage

The steep amplitude decrease from the 1st tone to the 2nd tone in the N1 adaptation effect matched our hypothesis and most previous findings (e.g., Bourbon et al., 1987; Budd et al., 1998; Lagemann et al., 2012; Recasens et al., 2015; Rosburg, 2004; Rosburg et al., 2006). This means that N1 adaptation occurs quickly with simple tone stimuli that are presented in rapid succession when the expectations are maintained. Nevertheless, these results may not generalize to conditions with longer inter-stimulus intervals (ISI) as previous studies have shown that the steep amplitude decrease only appeared when the ISI was short, but the further decrease was observable when the ISI was longer (e.g., Fruhstorfer et al., 1970; Özesmio et al., 2000; Sambeth et al., 2004; c.f. Bourbon et al., 1987; Budd et al., 1998; Rosburg et al., 2010). In addition, a previous study has found that the major contributor of the N1 was the temporal lobe in the one-second ISI condition, but in longer ISI conditions, sources in brain regions other than the auditory cortex have become more active (Hari et al., 1982). As we used a short ISI (580 ms) in the present study, the steep decrease might be ascribed to the ISI.

Additionally, a rebound was shown between the 2nd tone and the 3rd tone according to the adaptation curve formed by N1 amplitude (Figure 2a). This was not expected by the adaptation account, but it might be related to a similar effect found in a previous study using dynamic causal modeling (DCM) to examine the adaptation effect represented by the intrinsic connections in A1 (Garrido et al., 2009a). They interpreted the initial decrease of intrinsic connectivity from the 1st tone to the 2nd tone as reduced estimated precision of predictions, triggered by the deviants, and the subsequent increase as a gradual recovery due to learning. Thus, the rebound found between the 2nd and 3rd tones in the N1 adaptation effect in the present study may be in accordance with the interpretation from the study by Garrido et al. (2009a) that the adaptation effect happened in the A1 may incorporate the predictive component, and the brain only needs a few repetitions to generate predictions. Importantly, the present finding extended this interpretation to the circumstance where expectations are maintained. In other words, the predictive component in the adaptation effect can be automatically generated.

4.2 P2 Adaptation: A Memory Trace Effect

The P2 amplitude showed a continuously increasing trend along the first ten tones, which did not match our hypothesis and some previous findings where a steep decrease of P2 amplitude was found in the first repetition only and a plateau afterwards (Rosburg & Sörös, 2016; Rosburg et al., 2010). However, this continuous P2 increase can be interpreted as repetition positivity (RP), and it was also found in two studies by Costa-Faidella et al. (2011a, 2011b). In addition, Recasens et al. (2015) found a repetition enhancement in the sustained field time window (230–270 ms after stimulus onset), a time window close to P2. These discrepancies might be caused by the degree of expectations and SOA due to the different paradigms. In the study by Rosburg and Sörös (2016), a fixed train of eight tones was adopted, with the sixth tone as a deviant and the others as standards. Therefore, participants were able to predict the tone pattern. In contrast, in the present study, participants could not expect what the next tone would be as a deviant might happen anytime with a 15% probability. In addition, the studies by Costa-Faidella et al. (2011a, 2011b) and Recasens et al. (2015) also adopted a paradigm with three different numbers of tones in local trains that might lead to less solid expectation. Hence, expectations may modulate the adaptation pattern revealed by P2. Another possible reason for the discrepancies is the different times allowed for recovery from adaptation. A longer ISI (976 ms) between each tone and the insertion of interval (6000–7000 ms) between trains of tones were used in the study by Rosburg and Sörös (2016), whereas a shorter ISI (580 ms) was adopted without any inter-train interval in the present study, and short ISIs were also used by Costa-Faidella et al. (2011a, 2011b) and Recasens et al. (2015). Hence, the continuous increase of P2 may only appear when the time for recovery from adaptation is limited, while a sharp decrease of P2 in the initial two tones may be observed when more time is allowed. The above two factors may also explain the steep decrease in P2 amplitude found in Rosburg et al. (2010), who adopted a similar design as Rosburg and Sörös (2016). Furthermore, the different paradigms used between studies might also contribute to the discrepancies. Besides the present study, the studies by

Costa-Faidella et al. (2011a, 2011b) and Recasens et al. (2015) also adopted a roving paradigm, which might facilitate memory trace strengthening and reestablishment because the tones were unpredictable. In contrast, in paradigms that contain discontinuous stimulus trains or more predictable standard tones, such as the stimulus pair or traditional oddball paradigms, less memory trace strengthening and reestablishment were needed (Cooper et al., 2013). This further substantiated the relationship between the RP and memory trace as sensory memory needs to be updated constantly during the roving paradigm (Cooper et al., 2013). As these postulations are speculative as a direct comparison has yet to be made, factors that modulate the relationship between RP and adaptation deserve more attention in future research. However, the important implication is that the adaptation effect examined in the stimulus pair and traditional oddball paradigms may not be generalized to the roving paradigm and the circumstance when expectations are maintained.

As mentioned above, the increase in P2 can be interpreted as an RP. Although the topography of the P2 subsequent adaptation shows a negative frontal-central component (Figure 6b), this was due to the reverse calculation method of the adaptation effect (2nd tone – final tone instead of final tone – 2nd tone). Nonetheless, the RP found in the present study had a later onset compared with a previous study by Haenschel et al. (2005), in which they compared the RP between two, six, and 36 standard repetitions in healthy adults. They found that the RP, which happened from around 50–250 ms post-stimulus, was larger in conditions with more standard repetitions, and RP contributed to most of the MMN. Therefore, they postulated that RP is an ERP correlate of adaptation, a mechanism that facilitates memory trace formation in the A1. However, it was unknown whether the larger RP and MMN appeared after 36 standard repetitions were due to a longer memory trace or a higher precision of the prediction made by the participants because, after a certain time, participants might easily predict that a deviant would appear after 36 standard repetitions if there had been no deviant at the 2nd and 6th positions. However, in the present study, where participants could not predict whether the next tone would be deviant or not, RP, as shown by a continuous amplitude increase along with stimuli, was still found, but with a later onset in the P2 time window, compared with that (around 50 ms) in the study by Haenschel et al. (2005). While this did not refute the interpretation by Haenschel et al. (2005) that RP signifies adaptation, a mechanism underlying memory trace formation, the present finding suggested that the latency of the RP may be modulated by the precision of the prediction. Specifically, a later onset may be shown in the RP when the precision of the prediction decreases. Conversely, the RP had an earlier onset because of a higher precision of the prediction model in participants in the study by Haenschel et al. (2005) due to a predictable stimulus pattern.

4.3 Adaptation and MMN

According to the regression analysis, amplitudes of N1 initial adaptation and P2 subsequent adaptation both predicted the MMN significantly, and they explained 49.98% and 10.43% of the MMN variance respectively. While the effect of N1 initial adaptation matched the adaptation hypothesis of MMN, the contribution of P2 subsequent adaptation amplitudes to MMN implied that the adaptation hypothesis of MMN may not be sufficient because it proposed that the N1 adaptation alone could explain the MMN. In addition, it is difficult to use a pure adaptation mechanism to account for the N1 rebound effect. Therefore, although the present study emphasizes the contribution of the adaptation effect to MMN, it does not refute the model adjustment or the predictive coding accounts. On the contrary, the main findings of the present study supported a predictive coding account of MMN, which corroborated with most previous findings (e.g., Alain et al., 1999; Herholz et al., 2009; Symonds et al., 2017; Wacongne et al., 2011). Importantly, the findings suggested that MMN is made up of two different processes that correspond to the RP: One is the less negative inclination in N1 during the first repetition that may signify a purer adaptation effect, whereas the other one is the P2 subsequent adaptation with a positive deflection reflecting memory trace formation and model reestablishment. Crucially, the N1 initial adaptation effect may reflect the degree of model adjustment after the appearance of deviants, while the MMN quantifies the degree of error detected from the model. Hence, the positive correlation between N1 initial adaptation and MMN implied that participants who were the most sensitive to the tone change also had the most precise models. In addition, the increasing P2 along with repetitions is consistent with the predictive coding account, which proposes that the prediction error is minimized due to the matching between the top-down predictions and bottom-up inputs along

tone repetitions (Friston, 2005), and this explanation integrates both adaptation and model adjustment accounts (Garrido et al., 2008). Notably, the present study illustrated that the predictive coding account was supported even when the expectations were maintained by random stimulus arrangement based on the adaptation findings and the different topographies of N1 initial adaptation and P2 subsequent adaptation.

Based on our regression findings, it is important to take different components and time windows into consideration when examining the relationship between adaptation and MMN. For the N1, the initial adaptation contributes to the MMN, but for the P2, the subsequent adaptation predicts it. In addition, the present findings suggested that when investigating adaptation or its relationship to MMN, future studies should focus on both N1 and P2. Examining only one component may obstruct the discovery of comprehensive adaptation effects. Importantly, isolating the N1 and P2 processes may illuminate the relationship between adaptation and MMN.

4.4 Implications, Limitations, and Future Studies

This study is theoretically significant because it sheds light on the relationship between stimulus repetition, adaptation, and MMN. While some previous studies examined the adaptation and MMN separately (e.g., Budd et al., 1998; Haenschel et al., 2005), the relationship between adaptation and MMN was elucidated by tracing the adaptation pattern along a sequence of trials. It is also practically significant as understanding the adaptation patterns and the mechanism of MMN may enhance the effectiveness of clinical applications, such as the diagnosis of dyslexia using the adaptation pattern and MMN, as some previous studies revealed weaker adaptation and smaller MMN in dyslexics, compared with healthy controls (e.g., Baldeweg et al., 1999; Jaffe-Dax et al., 2017).

It is important to note that the adaptation effect and MMN can be influenced by many factors, not only including stimulus characteristics such as the frequency difference of the tones (e.g., Butler, 1968), the tone duration (e.g., Lanting et al., 2013), the number of repetitions (e.g., Baldeweg, 2007) and the ISI (e.g., Budd et al., 1998; Herrmann et al., 2016; Lanting et al., 2013; Pereira et al., 2014) but also variables related to the participants such as expectations and attention (e.g., Costa-Faidella et al., 2011a; Hari et al., 1979; Herholz et al., 2009; Todorovic et al., 2011). While it may be a limitation that the present study did not manipulate some of these variables, almost all of these factors remained constant throughout the experiment so they should not bias the results. However, future studies can examine how they may modulate the MMN and adaptation findings.

For limitations, since we only focused on the frequency differences in the present study, it is unknown whether the adaptation patterns and the relationship between adaptation effects and MMN can be generalized to deviants with other features (e.g., intensity, duration, and abstract pattern, etc.), although based on previous findings, we would expect adaptation plays a less important role in MMN when the repetition rule is not involved (Carbajal & Malmierca, 2018). In addition, future studies should consider adding a control condition, in which the same tones as the standards of the experimental condition are presented but they are embedded in different tones to avoid adaptation, to distinguish the adaptation and prediction error components (Carbajal & Malmierca, 2018). Overall, more studies are needed to examine how the variables mentioned above interact with adaptation and MMN when expectations are maintained.

5. Conclusion

To conclude, the present study utilized a roving paradigm that maintained expectations and showed that the adaptation patterns were diverse in the N1 and P2 time windows. Additionally, the N1 initial adaptation and the P2 subsequent adaptation, or the RP, contributed to MMN significantly. Hence, while the N1 initial adaptation does play a role in MMN, it cannot explain the entire MMN as proposed by the adaptation hypothesis, without taking the RP into account. Theoretically, the present study showed that under a paradigm that maintains expectations, the precision of prediction is still pertinent to the adaptation effects reflected by the N1 amplitude and RP. Practically, the diverse adaptation patterns in the N1 and P2 components and their discrete relationships to MMN imply the importance of isolating the two MMN processes signified by N1 and P2 when investigating adaptation and MMN in future studies.

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Tables

Table 1

Descriptive Statistics of the Peak Amplitudes of MMN and Adaptation in N1 and P2 (N = 37)

Variable	Mean	SD
MMN amplitude	-1.01	0.60
N1 initial adaptation amplitude	-0.79	0.72
N1 subsequent adaptation amplitude	0.06	0.44
P2 initial adaptation amplitude	0.08	0.79
P2 subsequent adaptation amplitude	-0.20	0.41

Table 2

Pearson Correlations between the Peak Amplitudes of MMN and adaptations in N1 and P2 ($N = 37$)

	1	2	3	4	5
1. MMN amplitude	-	.67*	-.07	.23	.22
2. N1 initial adaptation amplitude	-	-	-.47*	.51*	-.16
3. N1 subsequent adaptation amplitude	-	-	-	.24	.46*
4. P2 initial adaptation amplitude	-	-	-	-	-.32
5. P2 subsequent adaptation amplitude	-	-	-	-	-

Note. *Significant p -values with Holm-Bonferroni corrections.

Table 3

Standardized Coefficients and Adjusted R^2 in the Regression Analysis of the Amplitudes of Adaptation Effects and MMN ($N = 37$)

Variable	Model	Model
	Initial	Final
N1 initial adaptation amplitude	0.83*	0.72*
N1 subsequent adaptation amplitude	0.20	-
P2 initial adaptation amplitude	-0.06	-
P2 subsequent adaptation amplitude	0.23	0.33*
Adjusted R^2	.52	.52

Note. * $p < .01$

Figure Captions

Figure 1. Roving paradigm used in the present study, with the calculation methods of the amplitudes of initial adaptation, subsequent adaptation, and MMN.

Figure 2. The adaptation curves based on the N1 (a) and P2 (b) peak amplitudes in each position of the first ten tones (error bars indicate standard deviations; $N = 37$). *significant p -values based on paired-sample t-tests of each consecutive tone pair with Holm-Bonferroni corrections.

Figure 3. The ERPs of the first ten tones indicated by different colors ($N = 37$). Data were pooled from 25 fronto-central electrodes (black dots at the top-left corner).

Figure 4. (a) Waveform of MMN, deviants and last standards in 4th to 30th tones in each sequence ($N = 37$). The average MMN waveform (black) calculated by subtracting the amplitudes in the final position of each train of stimuli (4th position or after) from that in the deviants. Waveforms of deviants and the final tones are shown in red and blue respectively. The highlighted part indicates the MMN time window (76–196 ms). (b) Topography of MMN. From left to right, the topographic maps of deviants, final tones in 4th to 30th positions, and the corresponding MMN.

Figure 5. Scatter plots of significant correlations or regressions between MMN and the variables related to the adaptation effects, including (a) N1 initial adaptation amplitude and (b) P2 subsequent adaptation amplitude. Each dot indicates a datum from each participant ($N = 37$).

Figure 6. Scalp topographies based on the average individual peak amplitude ($N = 37$). (a) From left to right, the topographic maps of deviants, 2nd tones, and the ensuing initial adaptation in the N1. (b)

From left to right, the topographic maps of 2nd tones, final tones (4th to 30th positions), and the ensuing subsequent adaptation in the P2.

Figure 7. Scalp topographies based on the average individual peak amplitude ($N = 37$). (a) From left to right, the topographic maps of 2nd tones, final tones (4th to 30th positions), and the ensuing subsequent adaptation in the N1. (b) From left to right, the topographic maps of deviants, 2nd tones, and the ensuing initial adaptation in the P2. Please note the different scales used in different topographies for clarity.

Figures

Figure 1

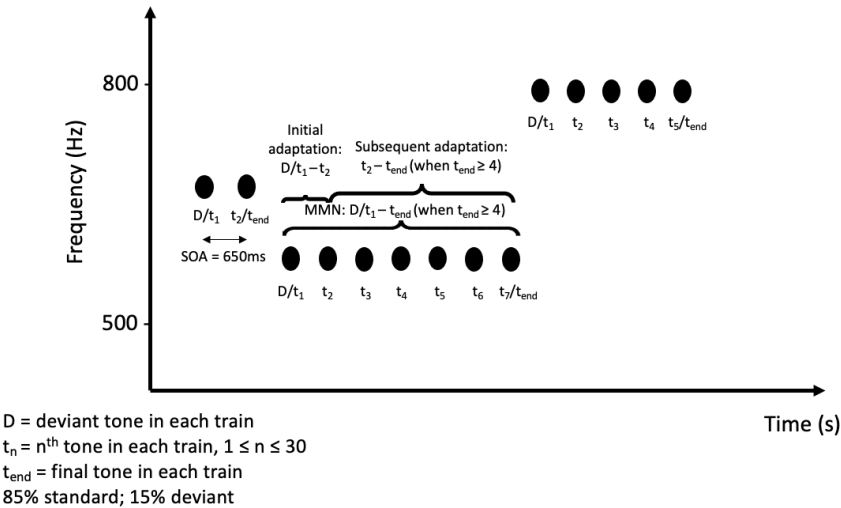


Figure 2

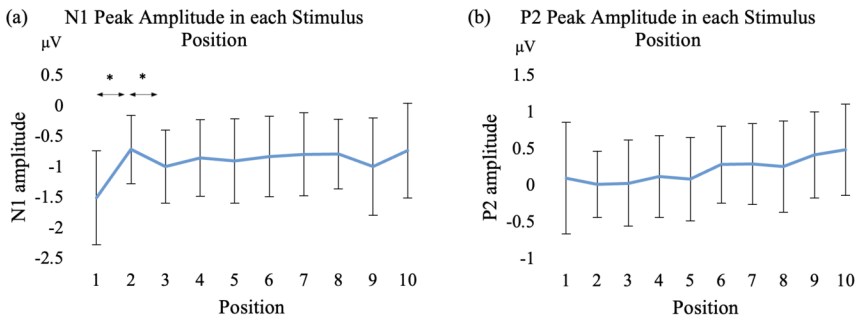


Figure 3

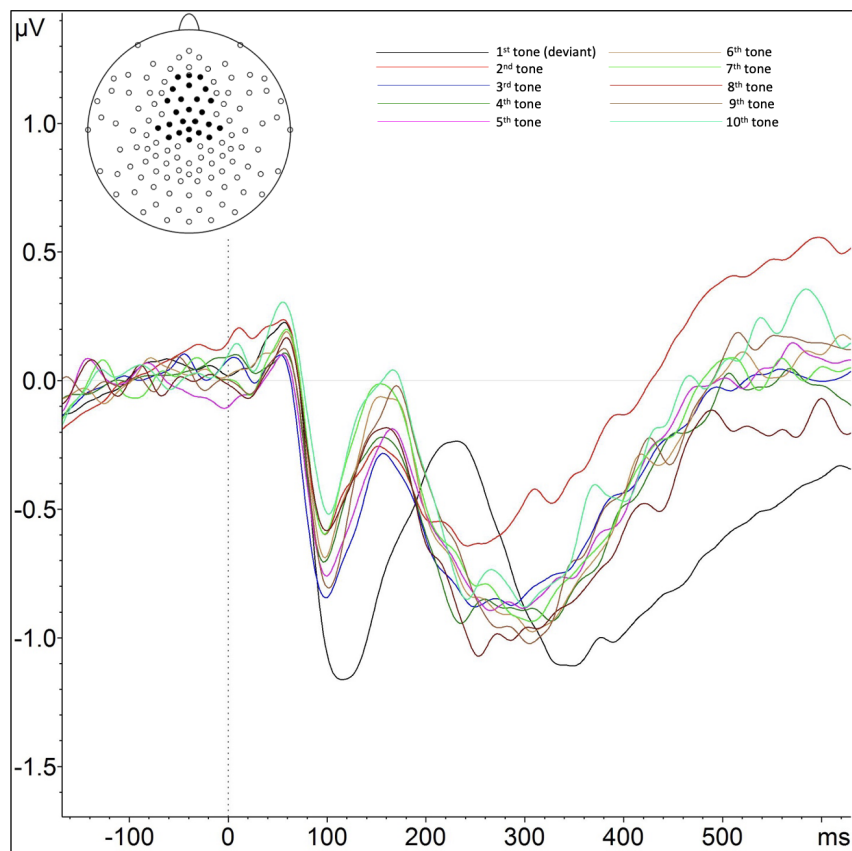


Figure 4

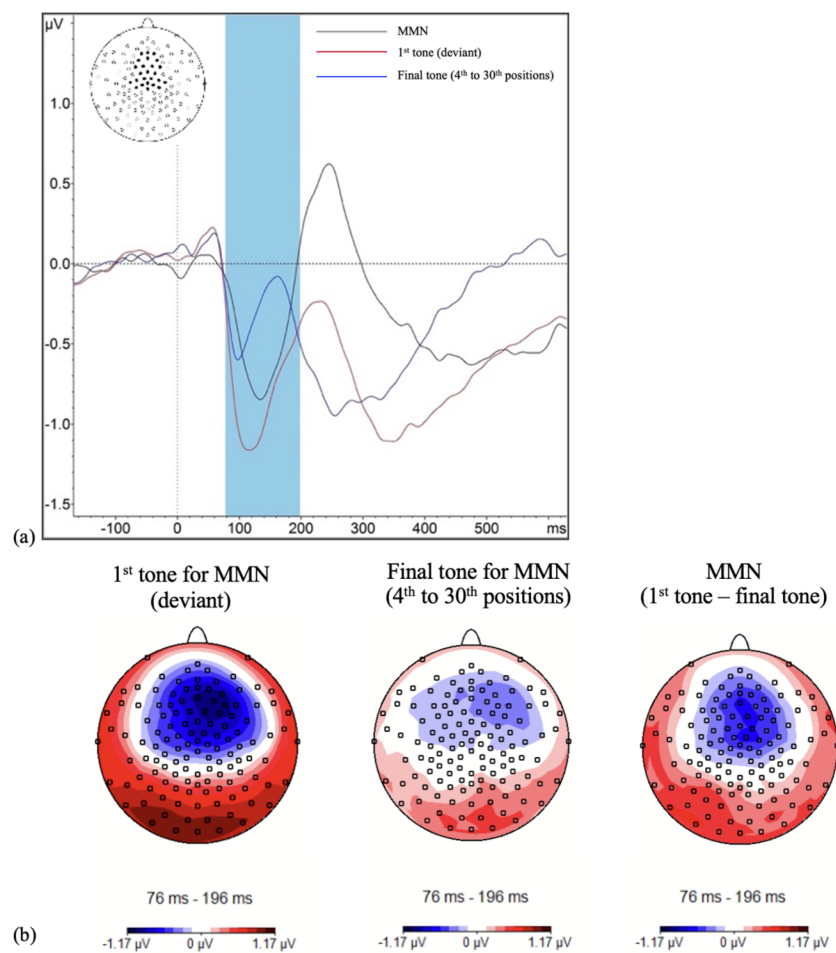


Figure 5

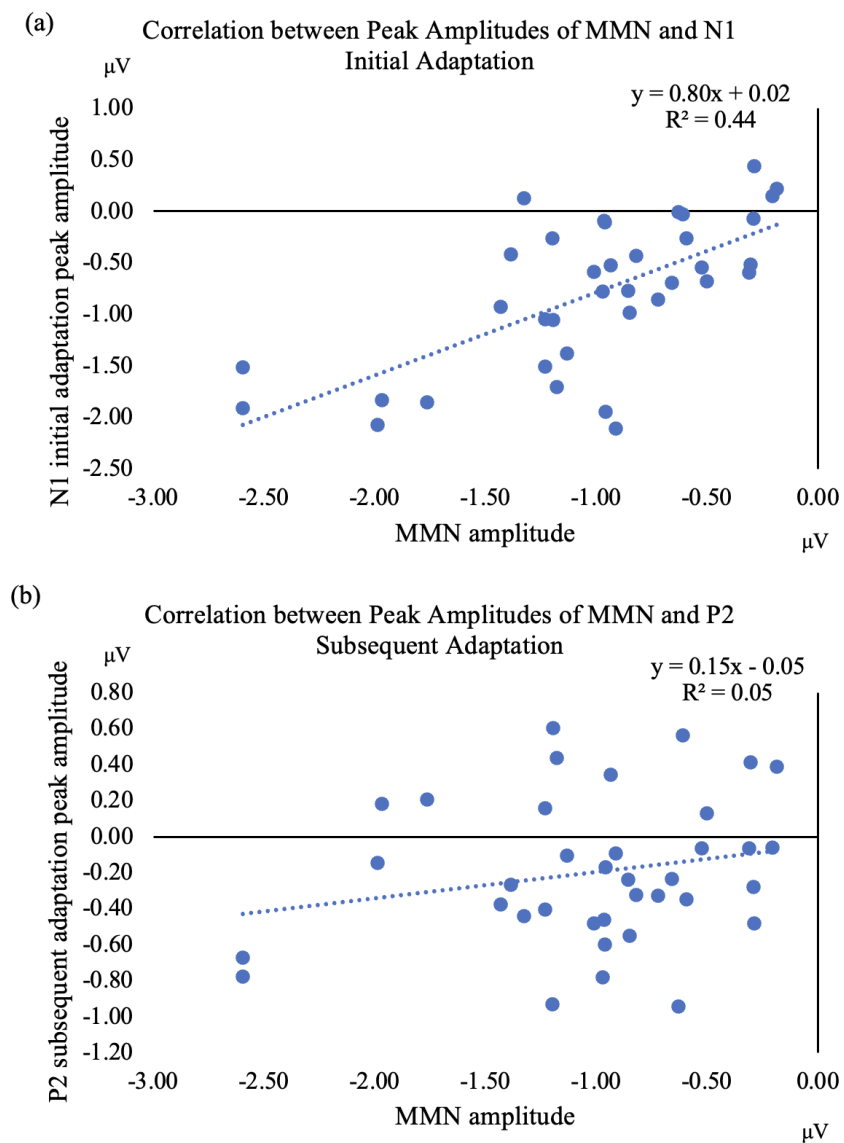


Figure 6

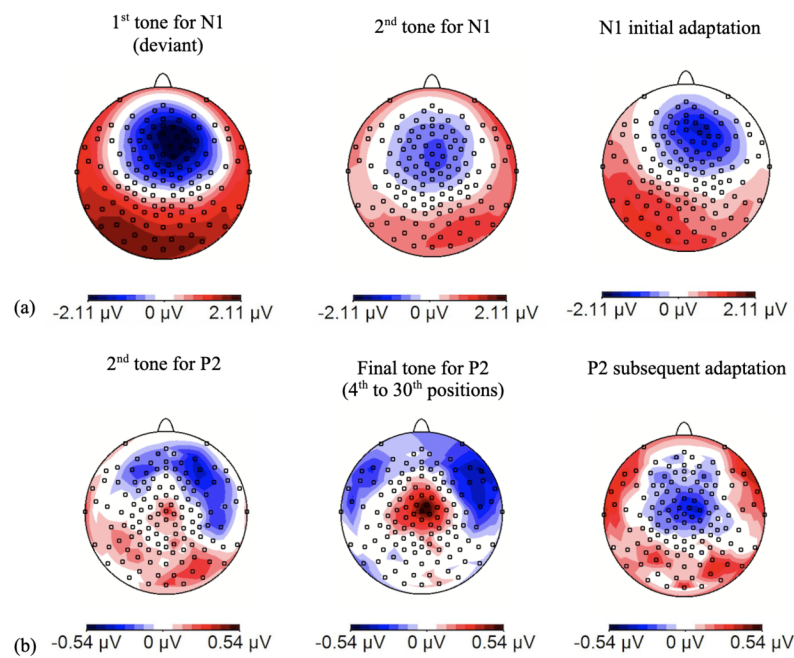


Figure 7

