Research Report

The neural generators of the mismatch responses to Mandarin lexical tones: An MEG study

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ABSTRACT

The present magnetoencephalography study used the cortically constrained minimum-norm estimates of human brain activity to elucidate functional roles of neural generators for detecting different magnitudes of lexical tones changes. A multiple-deviant oddball paradigm was used in which the syllable "yi" with a low-dipping tone (T3) was the common standard sound and the same syllable with a high-level tone (T1) or a high-rising tone (T2) were the large and small deviant sounds, respectively. The data revealed a larger magnetic mismatch field (MMNm) for large deviant in the left hemisphere. The source analysis also confirmed that the MMNm to lexical tone changes was generated in bilateral superior temporal gyri and only the large deviant revealed left lateralization. A set of frontal generators was activated at a later time and revealed differential sensitivities to the degree of deviance. The left anterior insula, the right anterior cingulate cortex, and the right ventral orbital frontal cortex were activated when detecting a large deviant, whereas the right frontal-opercular region was sensitive to the small deviant. These frontal generators were thought to be associated with various top-down mechanisms for attentional modulation. The time frequency (TF) analysis showed that large deviants yielded large theta band (5–7 Hz) activity over the left anterior scalp and the left central scalp, while small deviants yielded large alpha band activity (9–11 Hz) over the posterior scalp. The results of TF analyses implied that mechanisms of working memory and functional inhibition involved in the processes of acoustic change detection.

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1.   Introduction

The ability to detect changes in the environment is crucial for humans. In the literature, mismatch negativity (MMN) is an event-related brain potential (ERPs) and has been used to index the automatic and pre-attentive change detection. The magnetic mismatch negativity (MMNm) is its magnetocephalographic (MEG) counterpart, also known as a MMF (Alho et al., 1998; Phillips et al., 2000; Pulvermüller et al., 2003). The MMN has been observed in the auditory system in response to changes in frequency, duration, or intensity (Näätänen et al., 1992, 1997; Shestakova et al., 2002, 2003), though some evidence suggests similar ERP activity in the visual (Czigler, 2013; Takacs et al., 2013; Tales et al., 1999) and somatosensory systems (Kekoni et al., 1997; Restuccia et al., 2007).

The auditory MMN is elicited with an auditory oddball paradigm in which rare sounds (deviant stimuli) occasionally occur in a sequence of repetitive sound (standard stimuli), and it is operationally measured by subtracting the ERPs that are elicited in response to the standard stimulus from that elicited in response to the deviant stimulus. In adults, the MMN typically peaks between 100 and 200 ms after the onset of deviation in frontal–central electrodes. MMN can be elicited even when the participant does not attend to the stimuli, such as while they are reading a book or watching a silent movie. As discriminability between the standard and the deviant stimuli increases, MMN amplitudes increase, whereas peak latencies decrease. The memory-mismatch hypothesis, which is a widely accepted interpretation of MMN, suggests that MMN is elicited when an acoustic event deviates from a memory record describing the immediate history of the sound sequence (Näätänen et al., 1978). However, MMN has also been observed when the regularity of a sound pattern is violated; thus, as an extension of the memory-mismatch hypothesis, the regularity-violation hypothesis proposes that MMN occurs when a previously encoded acoustic regularity is violated (Winkler, 2007).

Giard et al. (1990) transformed scalp-potential maps to current source density maps and showed that two sets of neural generators, one from the temporal lobes and one from the right frontal lobe, may contribute to the MMN response. These findings have been supported by studies that demonstrated reduced MMN amplitudes in patients with lesions in the frontal and temporal lobes (Alain et al., 1998; Alho et al., 1994). Since then, a number of studies have used functional magnetic resonance imaging (fMRI), MEG, and high-density electroencephalography (EEG) to uncover the cerebral origin of the MMN. Findings of a generator in the auditory cortex in the superior temporal gyrus (STG) have been repeatedly replicated. However, considerable variation has been reported in the foci of the activation in the frontal regions, including the left or right ventrolateral prefrontal cortex, parts of the medial frontal (or cingulate cortex), and the right precentral cortex(Deouell, 2007; Doeller et al., 2003; Giard et al., 1990; Opitz et al., 2002; Rinne et al., 2005; Schönwiesner et al., 2007). Neither the precise frontal brain structures subserving change detection nor their functional significance in MMN processes are fully understood.

The traditional view suggests that the STG is associated with establishing memory traces and monitoring the attributes of an incoming stimulus, while the frontal generator is associated with the involuntary triggering of attention that is invoked by the deviant stimuli (Giard et al., 1990; Näätänen and Michie, 1979). More recent studies have manipulated the size of deviance in order to further elucidate the functional roles of the STG and the frontal generators in deviancy processing. It was expected that the more salient a deviant was, the more likely it was to trigger an attention switch and to show stronger activation in the frontal generator. Schönwiesner et al. (2007) used event-related fMRI and high-density EEG to show that the frontal generator activation peaks around 50 ms after the STG generator. Moreover, activity in the inferior frontal gyrus (IFG) was, in fact, insensitive to the magnitude of changes, while the activity in the STG did show such modulation. Their data suggested that the automatic change processing consists of at least three stages: initial detection in the primary auditory cortex, detailed analysis in the posterior STG and planum temporale, and the judgment of sufficient novelty for the allocation of attentional resources in the mid-ventrolateral prefrontal cortex (Schönwiesner et al., 2007).

Other studies have suggested that the frontal MMN generator is not directly connected to the switching of attention, as previously suggested, but that it might be related to an involuntary amplification or contrast enhancement mechanism that tunes the auditory change detection system (Deouell, 2007; Doeller et al., 2003; Opitz et al., 2002). An fMRI study conducted by Opitz et al. (2002) demonstrated that superior temporal activity is directly correlated with the size of the pitch deviation (30% and 100%) and that the activity in the right fronto-opercular cortex is *inversely* related to the deviation magnitude. Furthermore, the strength of the temporal activation correlated with the amplitude of the change-related ERP around 110 ms after stimulus onset, while the frontal activation correlated with the change-related ERP around 150 ms. Opitz et al. (2002) have suggested that the right fronto-opercular cortex may be more involved when the deviance is less salient, and it indexes a contrast-enhancing mechanism for sharpening the processing of the incoming stimulus. This hypothesis was supported by a follow-up fMRI study by Doeller et al. (2003) that used three levels of pitch changes (667 Hz, 833 Hz, and 1000 Hz) and a standard pitch of 500 Hz. Their results have also shown that activation in the right STG increases with the magnitude of the frequency change, while activation in the right IFG to the small changes is stronger than those to the large changes.

To sum up, the cumulative lines of evidence have suggested that, in addition to the STG, other generators in the left and/or right IFG and in the medial part of the frontal cortex may also contribute to the elicitation of MMN. However, the exact location of the frontal region for auditory change detection and how the saliency of the deviance modulates the activation of these generators needs further investigation. One of the possible reasons for the inconsistent findings may be the methodological limitation of using fMRI and ERP to investigate the cortical origin of MMN. It is known that ERP has excellent temporal resolution when examining various stages of cognitive processes in different time windows. However, due to volume conduction, each electrode on the scalp reflects a summation of activity from a variety of cortical regions that could be remote from the actual location of the source. As for fMRI, although it has the potential to localize brain activity with a millimeter resolution, the slow

hemodynamic responses provide low temporal resolution and pose a particular difficulty for fMRI in separating generators of the different ERP components (such as N1, MMN, and P3a) from each other over time. In contrast, MEG provides excellent temporal and spatial resolutions and thus might be able to resolve the various stages of processing and to estimate the corresponding cortical generators of the ERP/MEG components at a millisecond resolution. Therefore, the present study aimed to take advantage of MEG to delineate the spatial-temporal dynamics of MMNm generators in response to different magnitude of changes in Mandarin lexical tones.

Mandarin Chinese is a tonal language that exploits variations in pitch at the syllable level in order to determine lexical meaning. For example, by applying one of four tones, the syllable *yi* has distinct meaning (e.g. *yi1* 'clothes'; *yi2* 'aunt'; *yi3* 'chair'; *yi4* 'easy'). The four lexical tones are categorized phonologically as a high-level tone (T1), a high-rising tone (T2), a low-dipping tone (T3), and a high-falling tone (T4). A number of studies have suggested that the pitch contour and pitch height are crucial for characterizing Mandarin tones (Gandour and Harshman, 1978; Gandour, 1983; Jokisch and Jensen, 2007; Klimesch et al., 2006; Lin et al., 2007). In terms of pitch contour and direction, T2 and T3 are more acoustically similar than T1 and T3. Tonal discrimination and identification studies have confirmed that T2 and T3 are more often confused with one another compared to other tonal pairs (Gandour and Harshman, 1978; Gandour, 1983).

Previous ERP studies have used the MMN paradigm to investigate the brain responses to lexical tone changes. Luo et al. (2006) first examined MMN responses in native Mandarin speakers, investigating changes in initial consonants (*bai1, sai1, dai1, tai1*) and lexical tone changes (*bai1, bai2, bai3, bai4*). An opposite pattern of hemisphere lateralization for the MMN response to the lexical tone and to the consonant contrasts was found. Regardless of deviance magnitude, tonal changes elicited greater MMN magnitude and stronger dipole strength in the right hemisphere, whereas consonant changes elicited greater responses in the left hemisphere. However, in another passive oddball paradigm, Gu et al. (2013) presented pitch contrasts to native Cantonese speakers using both lexical stimuli (including three level tones, /ji55/, /ji33/, and /ji11/) and acoustic stimuli (i.e. harmonic tones matched with speech stimuli for duration, amplitude envelope, and F0). The results revealed left lateralized MMN responses in native Cantonese speakers for both lexical and acoustic pitch processing, while the MMN elicited by duration and intensity was right lateralized.

Xi et al., (2010) investigated MMN responses in native Mandarin responses to speech and nonspeech stimuli. T2 and T4 syllables were digitally manipulated and used as endpoint stimuli to create a 10-interval tonal continuum. Based on behavioral task data, an across-category stimulus pair and within-category stimulus pair were determined, and nonspeech stimuli were created from harmonic tones matched for pitch, amplitude and duration. Regardless of deviant or stimulus type, MMN responses were marginally larger in the right scalp than in the left scalp. More importantly, the MMN responses for across-category contrast were larger than those for within-category contrast in the left hemisphere for both lexical tones and for harmonic tones. In a follow-up fMRI study, Zhang et al.

(2011) used the same set of speech stimuli to demonstrate that both within- and across-category deviant conditions elicited greater activation in the right superior temporal gyrus (STG) than the standard condition did. Interestingly, they found that relative to the within-category condition, the across-category condition elicited more activation in the left middle temporal gyrus, suggesting its role in processing high-level phonological representations (Zhang et al., 2011).

ERP studies have also indicated that the deviance magnitude in lexical tone changes affects the latency and amplitude of MMNs (Chandrasekaran et al., 2007; Cheng et al., 2013; Lee et al., 2012; Tsang et al., 2011). For example, acoustically distinct T3/T1 contrast yielded a larger MMN with an earlier peak latency than the acoustically similar T3/T2 contrast did (Chandrasekaran et al., 2007; Cheng et al., 2013). However, the acoustical similarity effect on MMN was only found in native Chinese speakers, but not in native English speakers (Chandrasekaran et al., 2007). Regarding Cantonese lexical tones, Tsang et al. (2011) demonstrated that the amplitude and latency of MMN were sensitive to the size of the pitch level change, while the latency of P3a captured the presence of pitch contour.

Contrasts of lexical tones have also been examined in terms of maturation. Cheng et al. (2013) investigated the development of mismatch responses to Mandarin lexical tones in newborns and infants at 6-month-olds. The T3/T1 contrast elicited a positive mismatch response (P-MMR) at birth but an adult-like MMN at 6 months of age. For the T3/T2 contrast, no significant MMR was seen in newborns, whereas a P-MMR was found in 6-month-old infants (Cheng et al., 2013). A similar pattern was also found in preschoolers ages 4–6 (Lee et al., 2012).

This MEG study aimed to elucidate the functional roles of MMNm generators in detecting different magnitudes of changes in Mandarin lexical tones. The size-of-deviance effect on mismatch responses was examined with a multi-deviant oddball paradigm (Näätänen et al., 2004) with T3 as the common standard, T1 as a large deviant, and T2 as a small deviant. According to the contrast enhancement hypothesis (Doeller et al., 2003; Opitz et al., 2002), the STG was expected to exhibit stronger activation for the acoustically distinct T3/T1 contrast than for the acoustically similar T3/T2 contrast, while the frontal generator was expected to reveal a reverse pattern. To fully explore the brain dynamics of the MMNm activity, the wavelet-based trial-by-trial analysis was used to measure the amplitude of neural oscillations. Although the size of deviance has shown a robust effect in measurements of averaged waveforms in the MMN/MMNm literature, it remains unclear whether the time-frequency behavior of MMN/MMNm responses would show the size-of-deviance effect. EEG/MEG studies have demonstrated that deviant stimuli elicit stronger theta and alpha bands activities than standard stimuli do (Bishop et al., 2010; Fuentemilla et al., 2008; Hsiao et al., 2009; Lin et al., 2007). Furthermore, studies have indicated that theta synchronization is associated with working memory and attention, such as encoding new information from sensory inputs (Benchenane et al., 2011). On the other hand, the alpha inhibition hypothesis proposes that alpha activity is associated with the top-down control of posterior brain areas (Jokisch and Jensen, 2007;

Klimesch et al., 2006). Based on the assumptions that different cognitive functions are related to activity in different frequency bands, this study elucidated the MMNm related activity in theta and alpha bands in response to small and large deviants. It is expected that both large and small deviants might trigger different processes of auditory change detection, and the size of deviance might affect the strength of theta and alpha oscillations.

2. Results

2.1. MMNm responses in cluster-based random permutation analysis

The cluster-based random permutation analysis of MEG waveforms indicated that the T3/T1 contrast yielded four
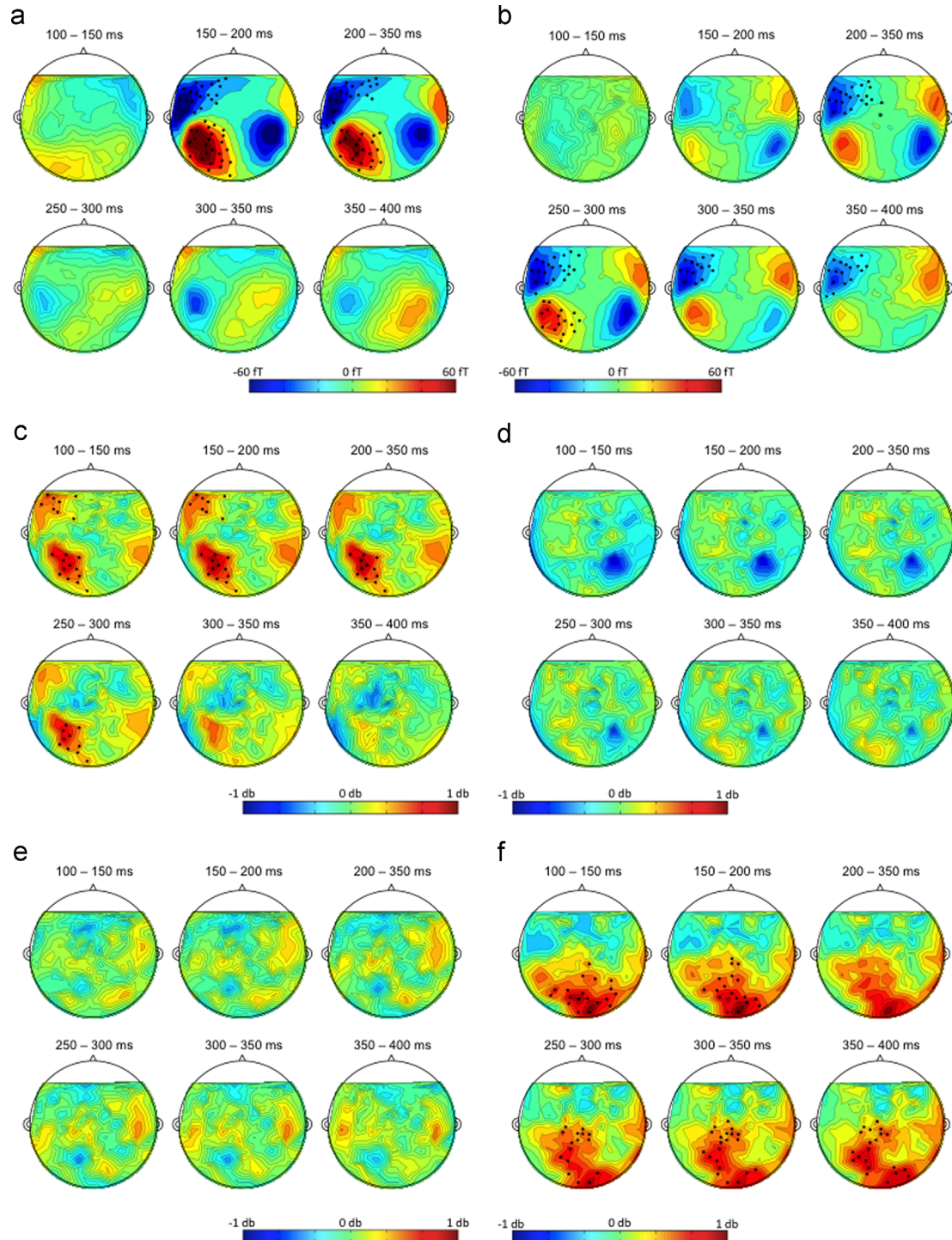

Fig. 1 – Topographical plots of the differential activities of event-related fields (a and b), theta band activity (c and d), and alpha band activity (e and f) in six time windows. Black dots indicate clusters of sensors with significant differences between T1 and T3, and between T2 and T3. (a) MMNm, T1 vs. T3, (b) MMnm, T2 vs. T3, (c) theta band (5-7 Hz), T1 vs. T3, (d) theta band (5-7 Hz), T2 vs. T3, (e) alpha band (9-11 Hz), T1 vs. T3 and (f) alpha band (9-11 Hz), T2 vs. T3.

significant clusters over the left scalp from 150 to 200 ms and from 200 to 250 ms. Fig. 1a shows the topography and the significant results for T3/T1 contrast. The negative clusters (meaning a large negative magnetic field in response to the deviant) were in the left-anterior scalp, and the positive clusters (meaning a large positive magnetic field in response to the deviant) were in the left-central scalp. On the other hand, the T3/T2 contrast also elicited significant clusters over the left scalp. In Fig. 1b, the negative clusters in the left-anterior scalp were significant from 200 to 400 ms, and the positive clusters in the left-central scalp were significant from 250 to 300 ms. Although there seemed to be another pair of clusters over the right scalp, there was no significant effect in the right hemisphere.

2.2. Conventional analyses for MMNm responses

Figs. 2d and e show the averaged MMNm amplitudes and latencies for the T1/T3 and T2/T3 contrasts in each hemisphere. The analysis of the MMNm latencies showed significant main effects of contrasts ($F(1, 11)=5.23$, $p<.05$) and hemisphere ($F(1, 11)=12.96$, $p<.01$). The T3/T1 contrast revealed an earlier MMNm than the T3/T2 contrast did (mean$\pm$SD: 178 ± 8 ms and 210 ± 9 ms for the T3/T1 and T3/T2 contrasts, respectively). The peak latency of the MMNm in the left hemisphere was earlier than that of the right hemisphere (mean$\pm$SD: 184 ± 5 ms and 206 ± 7 ms for the left and right MMNm, respectively). The interaction was not significant ($F(1, 11)=.05$, $p>.8$).
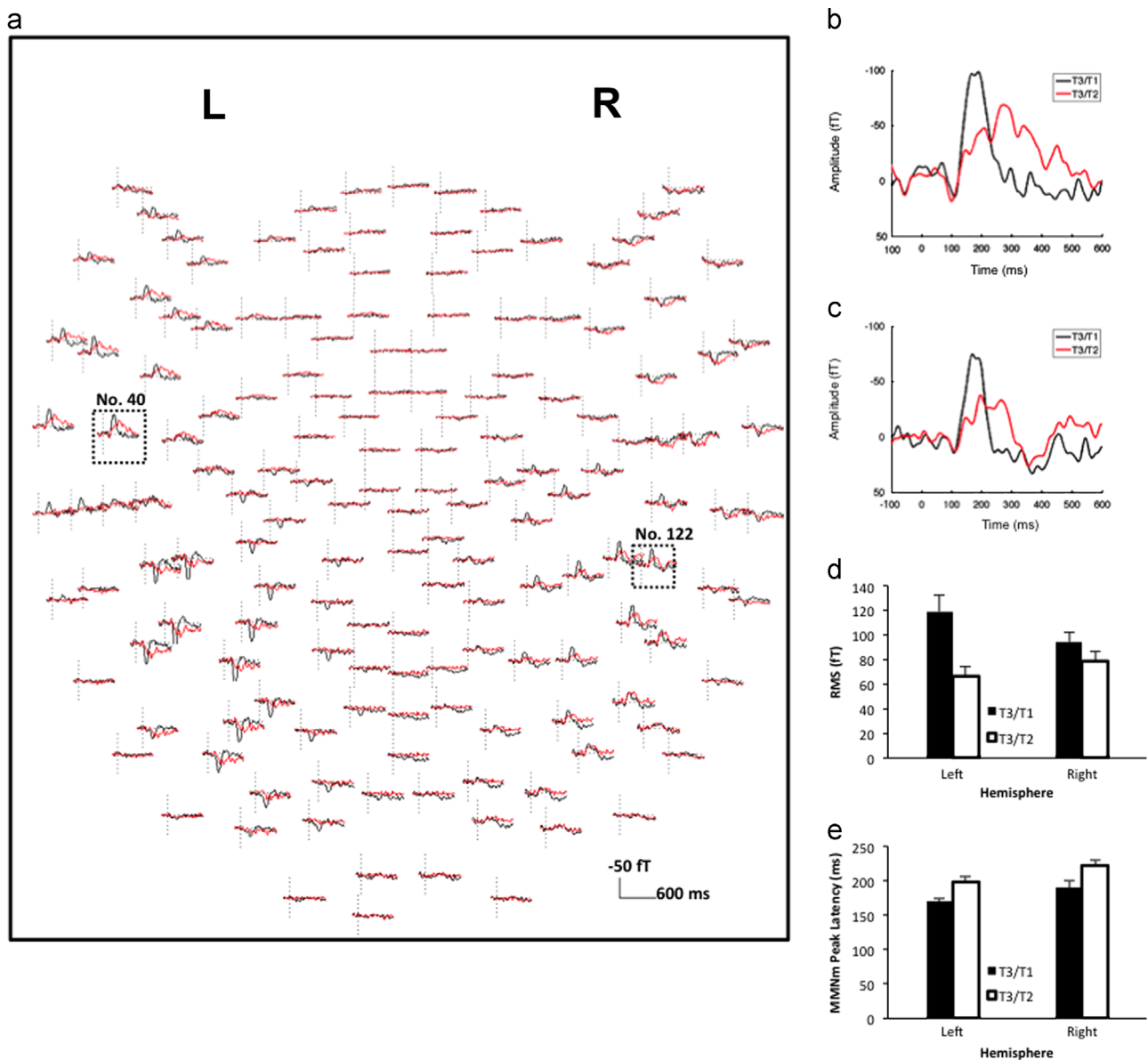

Fig. 2 – (a) Grand-averaged MMNm responses for each lexical tone contrast that was recorded with 157 gradiometers. The sensor array is viewed from above with the nose pointing upwards. The MMNm waveforms for the T3/T1 and T3/T2 contrasts are plotted in black and red, respectively. The MMNm waveforms in sensor No. 40 and No. 122 are displayed in (b) and (c). (d) The MMNm amplitudes averaged across participants. (e) The MMNm peak latencies averaged across participants.
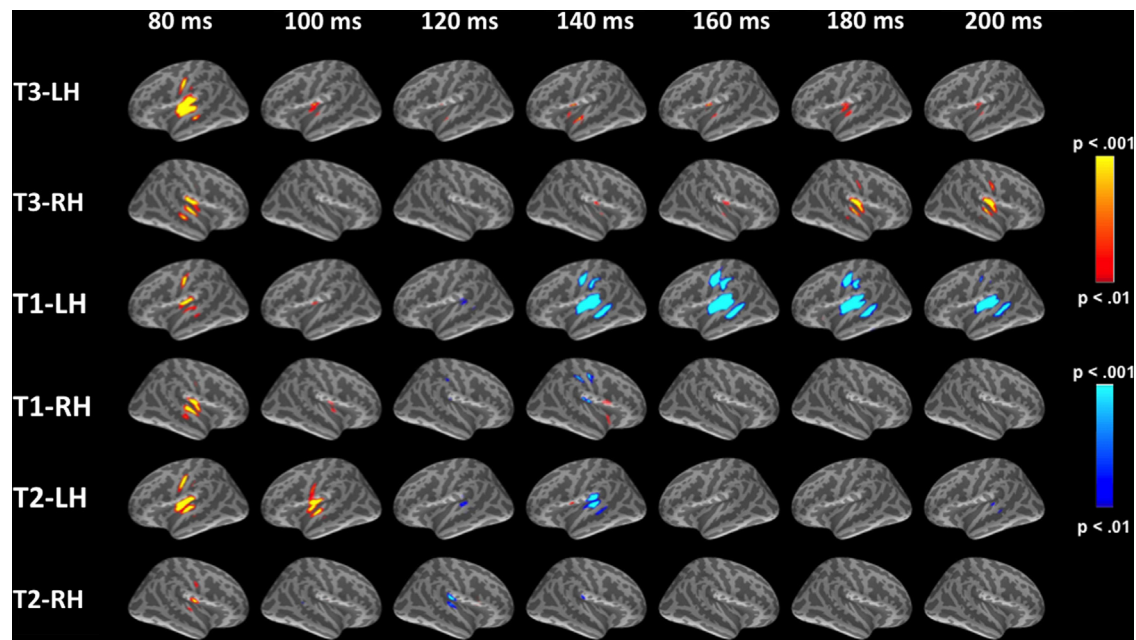
Fig. 3 – Grand-averaged dSPM maps for each type of stimuli in both hemispheres shown at 20-ms intervals. Positive (red) values indicate current flowing outward from the cortical surface, whereas negative (blue) values indicate current flowing inward. Significance levels relative to baseline noise estimates are indicated with color bars.

2.3. Results of TF responses

The cluster-based random permutation analysis of the theta frequency range (5–7 Hz) showed that the T3/T1 contrast yielded significant clusters ($p<.001$) from 100 to 300 ms, and the theta band response to the standard was not significantly different from that to small deviants. Fig. 1c shows that large deviants elicited larger theta power than the standard did, and the effects were over the left-anterior scalp and the left-central scalp.

For the alpha frequency range (9–11 Hz), interestingly, it was the T3/T2 contrast that yielded significant clusters ($p<.001$) from 100 to 200 ms and from 250 to 400 ms, and the alpha band response to the standard was not significantly different from that to the large deviants. Fig. 1f shows that small deviants elicited larger alpha power than the standard did, and the effects were referring to the posterior-central scalp.

2.4. The dynamic statistical parametric maps for the MMNm responses

The averaged dynamic statistical parametric maps (dSPMs) for each type of stimuli are shown in Fig. 3, and they exhibited a clear pattern of early activity in response to all three types of stimuli at ~80 ms in Heschl's gyrus in both hemispheres. The standard (T3) then showed significant activity in the insula in both hemispheres at about 140 ms, and it lasted to 200 ms. The estimated activities for both the large and small deviants were mainly in the temporal and frontal regions. For the large deviant (T1), the activity started from the STG in both hemispheres (from 100 ms to 200 ms), and it spread to the left MTG (from 130 ms to 200 ms), the left insula (from 140 ms to 180 ms), the right ventral-orbital frontal cortex (~140 ms), and the anterior cingulate cortex (~190 ms). As for the small deviant (T2), the activities were mainly found in the STG in both hemispheres (from 100 ms to 140 ms), and the left anterior insula (from 100 ms to 140 ms).

Fig. 4 presents the dSPMs for the T3/T1 and T3/T2 contrasts. In the T3/T1 contrast, significant activity was first seen in the STG in both hemispheres at about 140 ms, and it lasted to 200 ms with a strong left lateralization. The T3/T1 contrast also demonstrated significant activity in the left MTG (from 140 ms to 200 ms), the left anterior insula (from 155 ms to 185 ms), the right anterior cingulate cortex (from 180 ms to 200 ms), the right ventral-orbital frontal cortex (from 185 ms to 195 ms), and the right MTG (190 ms to 200 ms). For the T3/T2 contrast, the activity started in the STG in both hemispheres (from 180 ms to 200 ms), and it spread to the MTG of both hemisphere (~190 ms), and the right fronto-opercular cortex (from 195 ms to 200 ms). Fig. 5 shows the estimated strength of the activities that were elicited in response to each contrast in the four regions of interest, including the left
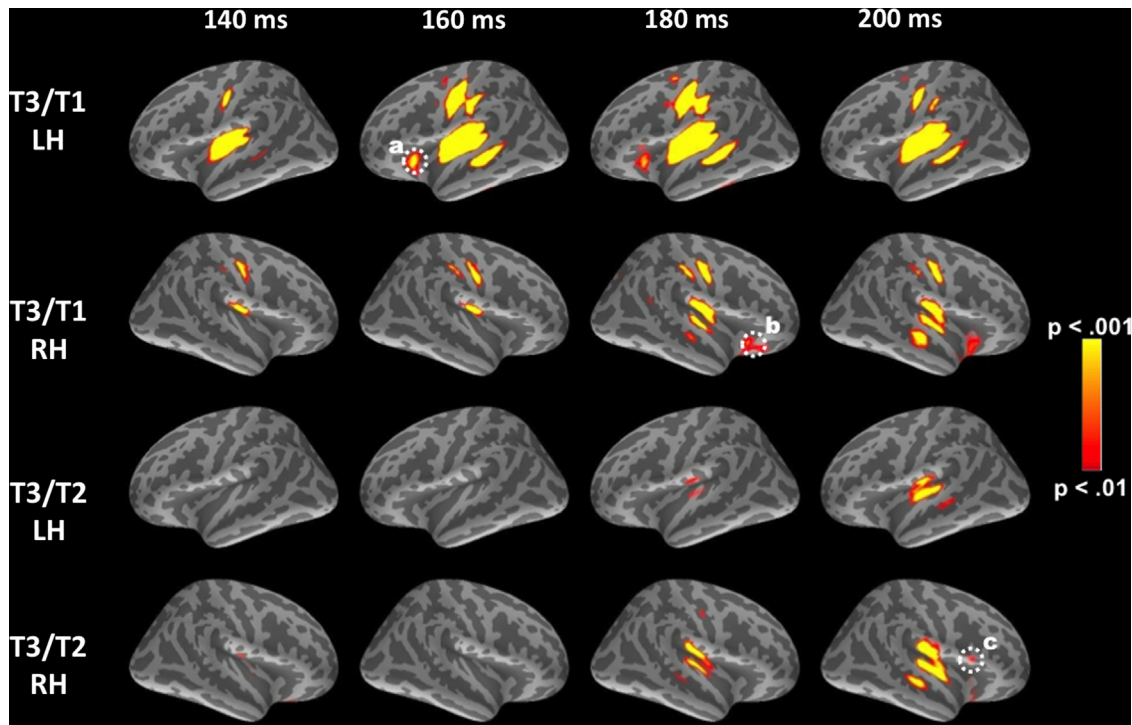
Fig. 4 – Grand-averaged dSPM maps for each lexical tone contrast. The significance levels relative to baseline noise estimates are indicated with color bars. The results show that the left anterior insula and right ventral orbital frontal cortex (the white dashed circle next to "a" and "b", respectively) contributed to the MMNm activity for T3/T1 contrast and that the right frontal-opercular regions (the white dashed circle next to "c") contributed to the MMNm activity for the T3/T2 contrast.
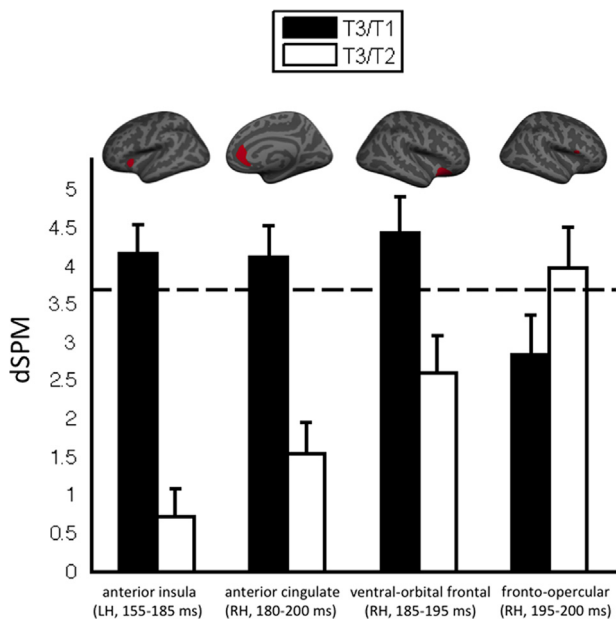

Fig. 5 – Bar plots for the differential dSPMs in four regions in the frontal lobe. The dashed line indicates the significance threshold ($p < .01$) relative to the baseline noise estimates.

anterior insula (Talairach co-ordinates: $x = -28$, $y = 21$, and $z = 1$), the right anterior cingulate ($x = 8$, $y = 40$, $z = 1$), the right ventral-orbital frontal cortex ($x = 30$, $y = 23$, $z = -12$), and the right fronto-opercular cortex ($x = 52$, $y = 15$, $z = 9$).

3. Discussion

The present MEG study aimed to investigate the neural generators underlying the MMNm elicited in response to lexical tone changes and their functional roles in detecting the changes. In order to achieve this goal, infrequent deviants, T1 and T2, were paired with a frequent standard, T3, to induce large and small lexical tone changes. The source analysis for brain response to auditory input revealed that activation in the left Heschl's gyrus at 80 ms was stronger than that in the right hemisphere counterpart, regardless of stimulus type (Fig. 3). Furthermore, the sensor-based analysis showed that both large and small deviants yielded significantly more activity than the standard stimuli did in the left scalp, but not in the right scalp (Figs. 1a and 1b). Consistent with previous studies (Gu et al., 2013), these results indicate a left hemisphere dominance for processing Mandarin lexical tones. The same inference has been drawn from some studies using dichotic listening tasks. That is, native speakers of tonal languages, such as Thai (Van Lancker and Fromkin, 1973), Norwegian (Moen, 1993), and Mandarin Chinese (Wang et al., 2001, 2004), show a right-ear advantage (i.e., a left hemisphere dominance) in the tonal processing of their own languages.

By analyzing difference waves, the MMNm responses show sensitivity to the size of lexical tone changes. Similar to findings of previous ERP studies (Chandrasekaran et al., 2007; Cheng et al., 2013; Lee et al., 2012), the acoustically

distinct T1/T3 contrast elicited an earlier and larger MMNm than the acoustically similar T2/T3 contrast did. This confirmed that the T1/T3 contrast was easier to discriminate and therefore revealed a much more pronounced MMNm response than the T2/T3 contrast did. However, such an effect of the size of deviance was found in the left hemisphere but not in the right hemisphere, which suggests a left hemispheric dominance of MMNm to Mandarin lexical tone changes.

The left lateralization of the lexical tone MMNm was further supported by the distributed source analysis of the MMNm generator, especially for the large deviant contrast. The source analysis showed that the T1/T3 MMNm was initially generated in the STG in both hemispheres at 140 ms with a stronger activation in the left hemisphere than that in the right hemisphere. The averaged dSPMs also displayed a network of later activation from 160 ms to 200 ms, located in the left insula, the right anterior cingulate, and the right mid-ventrolateral prefrontal cortex. This is consistent with the hypothesis that the left hemisphere is dominant in detecting phonetic changes and is potentially linked to the language-specific structures that are located in the left hemisphere (Phillips et al., 2000; Pulvermüller et al., 2003; Pulvermüller and Shtyrov, 2006). Although the T2/T3 MMNm was also generated in the STG in both hemispheres at 180 ms, no strong left lateralization was found. However, a slightly later activation was found in the right ventral-orbital frontal cortex around 200 ms. These data confirm that a major part of the MMNm activities is generated in the auditory cortex and that there is slightly delayed activation of the generators in the frontal cortex (Alho, 1995; Lin et al., 2007; Opitz et al., 2002; Rinne et al., 2000).

Most critically, these findings demonstrate that the size of the deviance affects laterality and the time course of activation in the temporal and frontal cortexes. This might explain the inconsistent findings regarding hemispheric dominance for detecting lexical tone changes that have been reported in previous studies (Chandrasekaran et al., 2007; Luo et al., 2006; Xi et al., 2010). For example, Luo et al. (2006) observed that lexical tone contrasts result in larger MMN amplitudes in the right scalp than those in the left scalp. This suggested right-hemisphere dominance in the early auditory processing of lexical tones. Since their study was aimed to examine the MMN responses to tonal and segmental changes, all of the possible combinations of the four lexical tones were used, so there was no need to analyze the MMN for each contrast separately. The right-hemisphere dominance of MMN responses in their study might be due to their analyses of lexical tones contrasts – both similar and dissimilar contrasts were averaged in their analysis.

The data presented here shows that small deviant contrasts involve less left-lateralized activation in the auditory cortex and greater activation in the right frontal cortex at a later time window. This finding supports the assumption that the degree to which the left and right hemispheres contribute to sound encoding can be modified by small acoustic changes (Kasai et al., 2001; Tervaniemi and Hugdahl, 2003). The effects of deviant size shown here are also comparable to previous studies that have shown that cross-category contrasts reveal larger MMN responses than within-category contrasts in the

left scalp, but not in the right scalp (Xi et al., 2010; Zhang et al., 2011). The discrepancies across studies with respect to the laterality of lexical tone discrimination may have been due to confounds in the study design and the data analysis. Our data has suggested that combining different lexical tone contrasts all together may not results in the ability to address this issue adequately.

The present study also demonstrated the existence of MMNm generators in frontal regions, including the left insula, the right mid-ventrolateral prefrontal cortex, the right anterior cingulate, and the right ventral-orbital frontal cortex, outside of the main superior temporal ones. These findings confirmed the framework of the spatiotemporal dynamics underpinning the detection of acoustic changes (Doeller et al., 2003; Opitz et al., 2002; Schönwiesner et al., 2007). In addition, the present results demonstrated a time lag of ∼20 ms between the initial MMNm response in the STG and that in the frontal cortex. Regarding the T3/T1 contrast, the MMNm activity in the left anterior insula, the right ventral-orbital frontal cortex, and the right anterior cingulate cortex lagged by 10 ms, 20 ms, and 40 ms, respectively, compared to the MMNm activity in the STG regions. As for the T3/T2 contrast, the MMNm activity in the right frontal-opercular lagged by 30 ms compared to that in the STG regions, and the MMNm activity in the right ventral-orbital frontal cortex preceded that in the STG regions by 20 ms. These finding were congruent with those of previous ERP/MEG studies that have shown that the frontal activities generally lag the STG activity by 3–60 ms (see Deouell, 2007 for a review). De Sanctis et al. (2009) used small changes in pitch (15%) to elicit the MMN response, and they also demonstrated that frontal activity precedes the temporal activity (Yago et al., 2001). A time lag between the temporal and frontal generators underlying MMN elicitation suggests that the frontal generators may provide top-down modulation for the deviance detection system in the temporal cortex.

Early work by Näätänen et al. (1992) has suggested that the MMN results from a comparison of present auditory input and the memory traces of previous sounds. The temporal generator may be associated with the pre-attentive sensory memory mechanism for deviance detection. However, the mechanisms that underlie frontal generators remain unclear. The current data found that differential sensitivities to large and small deviances were seen in a set of frontal generators, including the left anterior insula and the right anterior cingulate cortex for the T1/T3 contrast, the right frontal-opercular for the T2/T3 contrast, and the right ventral-orbital frontal cortex for both contrasts. This implies that the frontal generators conduct various kinds of higher-level cognitive processing, such as involuntary attention switching, salience detection or top-down modulation, that support the deviance detection system in the temporal cortex.

Both the large and small contrasts revealed a later activation in the right ventral-orbital frontal cortex. According to the regularity-violation hypothesis, MMN generation is based on predictive models in the brain that encode auditory sensory and abstract information within the same structure and that produce predictions about what sounds are likely to be encountered in the near future (Winkler, 2007). The evaluating process would be triggered after the presentation of a deviant stimulus, regardless of the magnitude of

changes. The right ventral-orbital frontal cortex may associate with such a process and support its role in the evaluation of working memory representations (Schnyer et al., 2005).

Other studies have suggested that the frontal generators may be involved in various mechanisms for attention modulation that are triggered by deviant stimuli. One is the switching of attention to the deviants (Näätänen and Michie, 1979; Näätänen, 1990), which predicts that a large change in acoustic features would associate with large frontal activity. Accordingly, the manipulation of the deviance magnitude would reveal a positive correlation between the deviance magnitude and the magnitude of the MMNm activity (Opitz et al., 2002). Our findings indicate that activities in the left anterior insula and the right anterior cingulate cortex were only involved in the MMNm responses to T3/T1 contrast but not in those to T3/T2 contrast. This suggests that these two regions might be responsible for the involuntary switching of attention. FMRI studies have demonstrated that the anterior insula responds strongly to deviant stimuli that are embedded in a stream of continuous stimuli and that it thus plays a more prominent role in the detection of salient stimuli, while other studies have suggested that the anterior cingulate may play a prominent role in action selection (Crottaz-Herbette and Menon, 2006; Downar et al., 2001; Linden et al., 1999).

In addition to the findings of frontal sources, the present time-frequency analysis indicates that the large deviant elicited large theta band power over the left anterior scalp. These findings also support the assumption that theta power might be associated with retaining relevant information in the prefrontal cortex (Benchenane et al., 2011; Jensen and Tesche, 2002; Klimesch, 1999). Taken together, our findings suggested that the anterior insula and the anterior cingulate cortex may form a salience network that functions to segregate the most relevant stimuli among the internal and extra personal stimuli in order to guide behavior (Menon and Uddin, 2010; Sridharan et al., 2008).

The source analysis reveals significant right frontal-opercular activation for the T2/T3 contrast but not for the T1/T3 contrast. The data are consistent with the findings of previous studies that have observed a reversed pattern in the right frontal cortex, which shows stronger dipole strength or blood oxygen level-dependent responses with low differentiability of the pitch deviants and standards (Doeller et al., 2003; Opitz et al., 2002; Rinne et al., 2005). The prefrontal mechanism is probably associated with a top-down modulation of the deviance detection system in the STG (Doeller et al., 2003). Accordingly, the right frontal-opercular might be associated with a contrast enhancement mechanism.

The time-frequency analysis of the alpha band activity also provides evidence for the top-down modulation of detecting deviances in response to small deviants. EEG studies have argued that posterior alpha band activity is associated with the inhibition mechanism for prioritizing sensory and motor information (Jensen et al., 2012). For example, large activity in alpha band would accompany the voluntary top-down inhibition of prepotent motor responses (Hummel et al., 2002), and competing working-memory input (Jokisch and Jensen, 2007; Klimesch, 1999). Therefore, the large alpha activity in T3/T2 contrast seems to indicate that the inhibitory mechanism is involved in the processing of

distinguishing between the standard and the small deviant sounds (Giard et al., 1990; Shalgi and Deouell, 2007).

3.1. Conclusion

Our MEG data revealed that native Mandarin speaker's MMNm response to lexical tone changes was initially generated in the STG in both hemispheres. A greater left-lateralization in STG and MTG was found in hearing large deviance (T1/T3 contrast), which indicated a left-hemisphere dominance for detecting large lexical tone changes. We also observed that the laterality may decrease as the differences between the standard and deviant sounds become less discriminable. In addition, the lexical tone MMNm was involved in the activities in several frontal regions, which may reflect various top-down modulation effects. The right ventral-orbital frontal cortex may index the evaluation processing of memory representations in the predictive coding framework (Winkler, 2007). The left anterior insula and right anterior cingulate cortex might involve switching of attention to the salient changes, while the right frontal-opercular was associated with involuntary amplification or functional inhibition mechanisms and revealed greater responses to smaller acoustic changes. Finally, by exploring the time-frequency patterns, this study also indicated that the theta and alpha oscillations might be associated with retaining relevant information and the inhibitory mechanism, respectively, in the processes of acoustic change detection.

4. Experimental procedures

4.1. Participants

Twelve Mandarin-speaking adults aged 18–30 years participated in this study (3 males). All participants were right-handed, and they did not have a history of neurological or psychological disorders. The current study was approved by the Human Subject Research Ethics Committee/Institutional Review Board of Academia Sinica, Taiwan. Written consent forms were obtained from all participants.

4.2. Stimuli

All of the stimuli were meaningful syllables in Mandarin Chinese, consisting of three Mandarin syllables, including yi1 (T1, "cloth"), yi2 (T2, "aunt"), and yi3 (T3, "chair"), which shared the same vowel /i/ but had different tonal contours. T3 was assigned as the standard, and T1 and T2 as were assigned as the deviants. The same set of stimuli has been used in previous MMN studied (e.g. Lee et al., 2012). According to the similarity in the tonal contours between the standard and each deviant, the T3/T1 pair represented the larger deviant contrast and the T3/T2 pair represented the smaller deviant contrasts.. All of the stimuli were produced by a female native Mandarin speaker and recorded with a 44.1 kHz sampling rate. The intensities and durations of the digitized stimuli were normalized to 70 dB and 250 ms, respectively with Sony Sound Forge 9.0.

4.3. Task

The participants reclined in a magnetically shielded room, and they were instructed to watch a silent movie while passively listening to the auditory stimuli during the experiments. Auditory stimuli were delivered binaurally to the participants' ears with sound tubing. In the multiple-deviant paradigm (Näätänen et al., 2004), the experiment started with 20 trials of standard sounds, which were followed by 1000 trials with 20% deviant (10% large deviant sounds and 10% small deviant sounds) and 80% standard sounds. The order of the stimuli was pseudorandomized, with at least two successive standard sounds between the deviant sounds. Across all participants, the average number of standard preceding large and small deviants were 4.05 (s.d.: .09) and 3.95 (s.d.: .07), respectively, and there was no significant difference ($t(11)=2.02$, $p>.05$). In each trial, the stimuli lasted 250 ms with an inter trial interval of 500 ms.

4.4. Procedures for data acquisition

MEG data were recorded continuously with a 157-channel axial gradiometer whole-head MEG system (Yokogawa Electric Corporation, Tokyo, Japan). A band-pass filter (DC to 100 Hz) was applied during the recording with a sampling frequency of 1 kHz. Prior to the MEG acquisition, five small electromagnetic coils were affixed to the participant's forehead. A Polhemus FASTRAK 3-D digitizer was used to digitize each subject's head shape and the locations of these coils with reference to three cranial landmarks in order to establish a head coordinate system for each participant. After digitization, the participant was positioned in the MEG recording system, which was situated in the magnetically shielded room. The position of these coils was localized with respect to the MEG sensors. This information was used for the co-registration between the MEG coordinate system to each participant's structural magnetic resonance images (MRIs).

4.5. Data analyses

In off-line processes, the MEG data were first noise reduced with a time-shift principal component analysis algorithm (de Cheveigné and Simon, 2007). The continuous MEG data were then epoched into 100-ms pre-stimulus intervals and 600-ms post-stimulus intervals, and baseline-corrected with the pre-stimulus data. Trials with amplitude variations that were larger than 3 pT were excluded from the subsequent analyses. Then, the trials of each type of stimuli were averaged and low-pass filtered at 40 Hz.

4.5.1. Analyzing MMNm activity in MEG waves
To evaluate the spatial-temporal differences between standard and each deviant, a cluster-based random permutation analysis (Maris and Oostenveld, 2007) was conducted in mean amplitudes of six successive epochs of 50 ms each, from 100 ms to 400 ms. This procedure allowed for identification of the temporal courses at which the mismatch effect appeared and could affectively handle the multiple-comparisons problem. First, a simple dependent-samples t-test was performed at each sensor. All sensors that exceeded a significance level ($\alpha=.05$) were

identified and formed clusters. For each cluster, a cluster-level test statistic was calculated by taking the sum of all the individual t-statistics within that cluster. Next, a null distribution was created by computing 1000 randomized cluster-level test statistics. Finally, the actually observed cluster-level test statistics were compared against the null distribution, and clusters falling in the highest or lowest 2.5th percentile were considered significant.

A conventional approach for analyzing MMN/MMNm responses is to estimate difference waves by subtracting the activities to the standard from those to the deviant. Therefore, based on the cluster-level statistics, we selected 10 sensors in the left and right hemispheres to do the following analysis. The mismatch waveforms were obtained by subtracting the magnetic field to the standard T3 from those to the large deviant T1 and to the small deviant T2 respectively. Figs. 6a–d show overlays of the mismatched waveforms for the T3/T1 and T3/T2 contrasts in 10 selected sensors (color filled sensors) in the left and right hemispheres of a participant. The sensors were selected based on the findings in the present cluster-level analysis and that in Phillips et al. (2000) that the MMNm response had a magnetic pattern of the polarity inversion across the lateral sensors during the time window from 150 to 300 ms. Accordingly, different sets of sensors were selected over the two hemispheres for each contrast and each participant. The red lines indicate the root mean square (RMS) field strengths that were calculated from the selected sensors. The MMNm latency was defined as the time point that the RMS waveform reached the highest peak amplitude in the 150- to 300-ms interval. The MMNm amplitude was measured by averaging the RMS across a 20-ms time window that centered at the MMNm peak latency. The MMNm amplitudes and latencies were subjected to repeated-measures analyses of variance (ANOVAs) with the contrasts (T3/T1 and T3/T2 contrasts) and hemispheres (left and right) as within-subject factors.

4.5.2. Time-frequency analyses
Time-frequency (TF) analyses were performed with the Field-trip software package, a Matlab-based toolbox dedicated to the analysis of electromagnetic and electrophysiological data (http://www.ru.nl/fcdonders/fieldtrip/). TF representations of the single trial data were then obtained by computing the squared norm of the result of the convolution of complex Morlet wavelets with the MEG data. We used wavelets with a 7-cycle width, with frequencies ranging from 1 to 30 Hz, in 1 Hz steps. TF representations were then averaged over trials for each stimulus for each participant. The average power values thus obtained were expressed as a percentage change relative to the power in a baseline interval from 300 to 100 ms prior to word onset. Based on previous studies of MMN and MMNm, we focused on the TF responses in theta band (averaged across frequency bins from 5 to 7 Hz) and alpha band (from 9 to 11 Hz). Activities within these frequency bands were averaged before performing the cluster-based permutation test. The same cluster-based random permutation analysis described in Section 4.5.1. was conducted for analyzing the TF responses by using the mean power of six successive epochs of 50 ms each, from 100 to 400 ms.
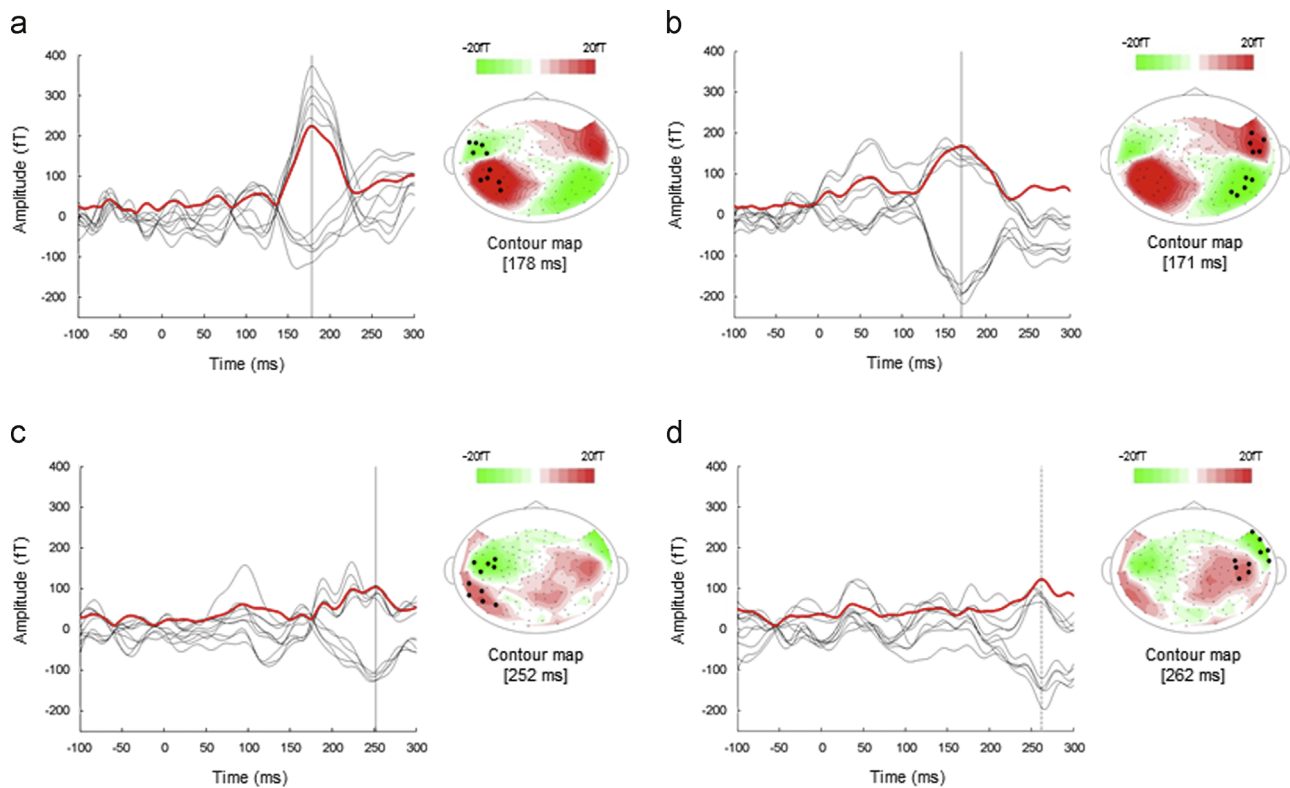
Fig. 6 – Magnetic mismatch field (MMNm) responses from a representative participant for each contrast (T3/T1 or T3/T2) in each hemisphere (LH or RH). The MMNm waveforms (black lines) were measured by subtracting the magnetic fields for the standard sounds from that to those for the deviant sounds. The red lines are the Root Mean Square waveforms that were measured from 10 sensors that showed the field patterns of MMNm (see Section 4.5.1). The contour maps show the differential magnetic field distributions for the two contrasts at the time of the MMNm peaks in the left hemisphere (a and c) and those in the right hemisphere (b and d).

4.6. Source analysis

The participants' structural MRIs were processed with Free-Surfer (CorTechs Labs, La Jolla, CA, USA and MGH/HMS/MIT Athinoula A. Martinos Center for Biomedical Imaging, Charleston, MA, USA) in order to create a cortical reconstruction of each participant's brain. The MNE toolbox (MGH/HMS/MIT Athinoula A. Martinos Center for Biomedical Imaging) was then used to calculate a cortically constrained L2 minimum-norm solution for each participant's MEG data (Dale and Sereno, 1993; Hämäläinen and Ilmoniemi, 1994). A source space of 5124 activity points was created on each reconstructed surface. The boundary-element model method was used on the activity at each source in order to calculate the forward solution (the magnetic field estimated at each MEG sensor). This forward solution was then employed to create the inverse solution, which identified the spatio-temporal distribution of the activity over sources that best accounted for each participant's grand-averaged MEG data. The resulting minimum-norm estimates were converted into a dSPM, which measured the noise-normalized activation at each source in order to avoid some of the inaccuracies of the standard minimum-norm calculations (Dale et al., 2000; Dhond et al., 2001). Then, the estimated source activity for each type of stimuli and each contrast was averaged across all participants with cortical surface alignment of the corresponding anatomical features (Fischl et al., 1999).

Anatomical locations of the activating regions were based on the Desikan–Killiany gyral atlas provided by FreeSurfer (Desikan et al., 2006). Fig. 3 shows the average dSPMs for each type of stimuli across all participants at selected time points of interest. The positive (red) dSPM values indicate current flowing outward from the cortical surface, whereas the negative (blue) values indicate current flowing inward. Fig. 4 shows the average dSPMs for the T3/T1 and T3/T2 contrasts in both hemispheres. The significance of the modulation at each site was calculated with a F test (Dale et al., 2000; Dhond et al., 2001). All activity in the figures was significant at $p < .01$. The full red responses indicate a significance of $p < .01$ and bright yellow indicates a significance of $p < .001$.

Authors' contributions

CYL and CHH participated in designing this study and writing the paper. SKL and CHH analyzed data. YYH and CHH performed research.

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REFERENCES

Alain, C., Woods, D.L., Knight, R.T., 1998. A distributed cortical network for auditory sensory memory in humans. Brain Res. 812, 23–37.

Alho, K., Woods, D.L., Algazi, A., Knight, R.T., Naatanen, R., 1994. Lesions of frontal cortex diminish the auditory mismatch negativity. Electroencephalogr. Clin. Neurophysiol. 91, 353–362.

Alho, K., 1995. Cerebral generators of mismatch negativity (MMN) and its magnetic counterpart (MMNm) elicited by sound changes. Ear Hear. 16, 38–51.

Alho, K., Winkler, I., Escera, C., Huotilainen, M., Virtanen, J., Jaaskelainen, I.P., Pekkonen, E., Ilmoniemi, R.J., 1998. Processing of novel sounds and frequency changes in the human auditory cortex: magnetoencephalographic recordings. Psychophysiology 35, 211–224.

Benchenane, K., Tiesinga, P.H., Battaglia., F.P., 2011. Oscillations in the prefrontal cortex: a gateway to memory and attention. Curr. Opin. Neurobiol. 21, 475–485.

Bishop, D.V., Hardiman, M.J., Barry, J.G., 2010. Is auditory discrimination mature by middle childhood? A study using time-frequency analysis of mismatch responses from 7 years to adulthood. Dev. Sci. 14, 402–416.

Chandrasekaran, B., Krishnan, A., Gandour, J.T., 2007. Mismatch negativity to pitch contours is influenced by language experience. Brain Res. 1128, 148–156.

Cheng, Y.-Y., Wu, H.-C., Tzeng, Y.-L., Yang, M.-T., Zhao, L.-L., Lee, C.-Y., 2013. The development of mismatch responses to mandarin lexical tones in early infancy. Dev. Neuropsychol. 38, 281–300.

Crottaz-Herbette, S., Menon, V., 2006. Where and when the anterior cingulate cortex modulates attentional response: combined fMRI and ERP evidence. J. Cogn. Neurosci. 18, 766–780.

Czigler, I., 2013. Visual mismatch negativity and categorization. Brain Topogr..

Dale, A.M., Sereno, M.I., 1993. Improved localization of cortical activity by combining Eeg and Meg with Mri cortical surface reconstruction – a linear-approach. J. Cogn. Neurosci. 5, 162–176.

Dale, A.M., Liu, A.K., Fischl, B.R., Buckner, R.L., Belliveau, J.W., Lewine, J.D., Halgren, E., 2000. Dynamic statistical parametric mapping: combining fMRI and MEG for high-resolution imaging of cortical activity. Neuron 26, 55–67.

de Cheveigné, A., Simon, J.Z., 2007. Denoising based on time-shift PCA. J. Neurosci. Methods 165, 297–305.

Deouell, L.Y., 2007. The frontal generator of the mismatch negativity revisited. J. Psychophysiol. 21, 188–203.

De Sanctis, P., Molholm, S., Shpaner, M., Ritter, W., Foxe, J.J., 2009. Right hemispheric contributions to fine auditory temporal discriminations: high-density electrical mapping of the duration mismatch negativity (MMN). Front. Integr. Neurosci. 3.

Desikan, R.S., Segonne, F., Fischl, B., Quinn, B.T., Dickerson, B.C., Blacker, D., Buckner, R.L., Dale, A.M., Maguire, R.P., Hyman, B.T., Albert, M.S., Killiany, R.J., 2006. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. Neuroimage 31, 968–980.

Dhond, R.P., Buckner, R.L., Dale, A.M., Marinkovic, K., Halgren, E., 2001. Spatiotemporal maps of brain activity underlying word generation and their modification during repetition priming. J. Neurosci. 21, 3564–3571.

Doeller, C.F., Opitz, B., Mecklinger, A., Krick, C., Reith, W., Schroger, E., 2003. Prefrontal cortex involvement in preattentive auditory deviance detection: neuroimaging and electrophysiological evidence. Neuroimage 20, 1270–1282.

Downar, J., Crawley, A.P., Mikulis, D.J., Davis, K.D., 2001. The effect of task relevance on the cortical response to changes in visual and auditory stimuli: an event-related fMRI study. Neuroimage 14, 1256–1267.

Fischl, B., Sereno, M.I., Dale, A.M., 1999. Cortical surface-based analysis. II: inflation, flattening, and a surface-based coordinate system. Neuroimage 9, 195–207.

Fuentemilla, L., Marco-Pallares, J., Munte, T.F., Grau, C., 2008. Theta EEG oscillatory activity and auditory change detection. Brain Res. 1220, 93–101.

Gandour, J.T., Harshman, R.A., 1978. Crosslanguage differences in tone perception: a multidimensional scaling investigation. Lang. Speech 21, 1–33.

Gandour, J.T., 1983. Tone perception in far Eastern-languages. J. Phon. 11, 149–175.

Giard, M.H., Perrin, F., Pernier, J., Bouchet, P., 1990. Brain generators implicated in the processing of auditory stimulus deviance: a topographic event-related potential study. Psychophysiology 27, 627–640.

Gu, F., Zhang, C., Hu, A., Zhao, G., 2013. Left hemisphere lateralization for lexical and acoustic pitch processing in Cantonese speakers as revealed by mismatch negativity. Neuroimage 83, 637–645.

Hämäläinen, M.S., Ilmoniemi, R.J., 1994. Interpreting magnetic fields of the brain: minimum norm estimates. Med. Biol. Eng. Comput. 32, 35–42.

Hsiao, F.J., Wu, Z.A., Ho, L.T., Lin, Y.Y., 2009. Theta oscillation during auditory change detection: an MEG study. Biol. Psychol. 81, 58–66.

Hummel, F., Andres, F., Altenmüller, E., Dichgans, J., Gerloff, C., 2002. Inhibitory control of acquired motor programmes in the human brain. Brain 125, 404–420.

Jensen, O., Tesche, C.D., 2002. Frontal theta activity in humans increases with memory load in a working memory task. Eur. J. Neurosci. 15, 1395–1399.

Jensen, O., Bonnefond, M., VanRullen, R., 2012. An oscillatory mechanism for prioritizing salient unattended stimuli. Trends Cogn. Sci. 16, 200–206.

Jokisch, D., Jensen, O., 2007. Modulation of gamma and alpha activity during a working memory task engaging the dorsal or ventral stream. J. Neurosci. 27, 3244–3251.

Kasai, K., Yamada, H., Kamio, S., Nakagome, K., Iwanami, A., Fukuda, M., Itoh, K., Koshida, I., Yumoto, M., Iramina, K., Kato, N., Ueno, S., 2001. Brain lateralization for mismatch response to across- and within-category change of vowels. Neuroreport 12, 2467–2471.

Kekoni, J., Hamalainen, H., Saarinen, M., Grohn, J., Reinikainen, K., Lehtokoski, A., Naatanen, R., 1997. Rate effect and mismatch responses in the somatosensory system: ERP-recordings in humans. Biol. Psychol. 46, 125–142.

Klimesch, W., 1999. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. Brain Res. Brain Res. Rev. 29, 169–195.

Klimesch, W., Sauseng, P., Hanslmayr, S., 2006. EEG alpha oscillations: the inhibition-timing hypothesis. Brain Res. Brain Res. Rev. 53, 63–88.

Lee, C.-Y., Yen, H.-L., Yeh, P.-W., Lin, W.-H., Cheng, Y.-Y., Tzeng, Y.-L., Wu, H.-C., 2012. Mismatch responses to lexical tone, initial consonant, and vowel in Mandarin-speaking preschoolers. Neuropsychologia 50, 3228–3239.

Lin, Y.Y., Hsiao, F.J., Shih, Y.H., Yiu, C.H., Yen, D.J., Kwan, S.Y., Wong, T.T., Wu, Z.A., Ho, L.T., 2007. Plastic phase-locking and magnetic mismatch response to auditory deviants in temporal lobe epilepsy. Cereb. Cortex 17, 2516–2525.

Linden, D.E., Prvulovic, D., Formisano, E., Vollinger, M., Zanella, F.E., Goebel, R., Dierks, T., 1999. The functional neuroanatomy of target detection: an fMRI study of visual and auditory oddball tasks. Cereb. Cortex 9, 815–823.

Luo, H., Ni, J.T., Li, Z.H., Li, X.O., Zhang, D.R., Zeng, F.G., Chen, L., 2006. Opposite patterns of hemisphere dominance for early auditory processing of lexical tones and consonants. Proc. Natl. Acad. Sci. USA 103, 19558–19563.

Maris, E., Oostenveld, R., 2007. Nonparametric statistical testing of EEG- and MEG-data. J. Neurosci. Methods 164, 177–190.

Menon, V., Uddin, L.Q., 2010. Saliency, switching, attention and control: a network model of insula function. Brain Struct, Funct. 214, 655–667.

Moen, I., 1993. Functional lateralization of the perception of Norwegian word tones—evidence from a dichotic listening experiment. Brain Lang. 44, 400–413.

Näätänen, R., Gaillard, A.W., Mantysalo, S., 1978. Early selective-attention effect on evoked potential reinterpreted. Acta Psychol. 42, 313–329.

Näätänen, R., Michie, P.T., 1979. Early selective-attention effects on the evoked potential: a critical review and reinterpretation. Biol. Psychol. 8, 81–136.

Näätänen, R., 1990. The role of attention in auditory information-processing as revealed by event-related potentials and other brain measures of cognitive function. Behav. Brain Sci. 13, 201–232.

Näätänen, R., Teder, W., Alho, K., Lavikainen, J., 1992. Auditory attention and selective input modulation: a topographical ERP study. Neuroreport 3, 493–496.

Näätänen, R., Lehtokoski, A., Lennes, M., Cheour, M., Huotilainen, M., Iivonen, A., Vainio, M., Alku, P., Ilmoniemi, R.J., Luuk, A., Allik, J., Sinkkonen, J., Alho, K., 1997. Language-specific phoneme representations revealed by electric and magnetic brain responses. Nature 385, 432–434.

Näätänen, R., Pakarinen, S., Rinne, T., Takegata, R., 2004. The mismatch negativity (MMN): towards the optimal paradigm. Clin. Neurophysiol. 115, 140–144.

Opitz, B., Rinne, T., Mecklinger, A., von Cramon, D.Y., Schroger, E., 2002. Differential contribution of frontal and temporal cortices to auditory change detection: fMRI and ERP results. Neuroimage 15, 167–174.

Phillips, C., Pellathy, T., Marantz, A., Yellin, E., Wexler, K., Poeppel, D., McGinnis, M., Roberts, T., 2000. Auditory cortex accesses phonological categories: an MEG mismatch study. J. Cogn. Neurosci. 12, 1038–1055.

Pulvermüller, F., Shtyrov, Y., Ilmoniemi, R., 2003. Spatiotemporal dynamics of neural language processing: an MEG study using minimum-norm current estimates. Neuroimage 20, 1020–1025.

Pulvermüller, F., Shtyrov, Y., 2006. Language outside the focus of attention: the mismatch negativity as a tool for studying higher cognitive processes. Prog. Neurobiol. 79, 49–71.

Restuccia, D., Della Marca, G., Valeriani, M., Leggio, M.G., Molinari, M., 2007. Cerebellar damage impairs detection of somatosensory input changes. A somatosensory mismatch-negativity study. Brain: A J. Neurol. 130, 276–287.

Rinne, T., Alho, K., Ilmoniemi, R.J., Virtanen, J., Naatanen, R., 2000. Separate time behaviors of the temporal and frontal mismatch negativity sources. Neuroimage 12, 14–19.

Rinne, T., Degerman, A., Alho, K., 2005. Superior temporal and inferior frontal cortices are activated by infrequent sound duration decrements: an fMRI study. Neuroimage 26, 66–72.

Schnyer, D.M., Nicholls, L., Verfaellie, M., 2005. The role of VMPC in metamemorial judgments of content retrievability. J. Cogn. Neurosci. 17, 832–846.

Schönwiesner, M., Novitski, N., Pakarinen, S., Carlson, S., Tervaniemi, M., Näätänen, R., 2007. Heschl's gyrus, posterior superior temporal gyrus, and mid-ventrolateral prefrontal cortex have different roles in the detection of acoustic changes. J. Neurophysiol. 97, 2075–2082.

Shalgi, S., Deouell, L.Y., 2007. Direct evidence for differential roles of temporal and frontal components of auditory change detection. Neuropsychologia 45, 1878–1888.

Shestakova, A., Ceponiene, R., Huotilainen, M., Yaguchi, K., 2002. Involuntary attention in children as a function of sound source location: evidence from event-related potentials. Clin. Neurophysiol. 113, 162–168.

Shestakova, A., Huotilainen, M., Ceponiene, R., Cheour, M., 2003. Event-related potentials associated with second language learning in children. Clin. Neurophysiol. 114, 1507–1512.

Sridharan, D., Levitin, D.J., Menon, V., 2008. A critical role for the right fronto-insular cortex in switching between central-executive and default-mode networks. Proc. Natl. Acad. Sci. USA 105, 12569–12574.

Takacs, E., Sulykos, I., Czigler, I., Barkaszi, I., Balazs, L., 2013. Oblique effect in visual mismatch negativity. Front. Hum. Neurosci. 7, 591.

Tales, A., Newton, P., Troscianko, T., Butler, S., 1999. Mismatch negativity in the visual modality. Neuroreport 10, 3363–3367.

Tervaniemi, M., Hugdahl, K., 2003. Lateralization of auditory-cortex functions. Brain Res. Brain Res. Rev. 43, 231–246.

Tsang, Y.K., Jia, S., Huang, J., Chen, H.C., 2011. ERP correlates of pre-attentive processing of Cantonese lexical tones: the effects of pitch contour and pitch height. Neurosci. Lett. 487, 268–272.

Van Lancker, D., Fromkin, V.A., 1973. Hemispheric specialization for pitch and "tone": evidence from Thai. J. Phon. 1, 101–109.

Wang, Y., Jongman, A., Sereno, J.A., 2001. Dichotic perception of Mandarin tones by Chinese and American listeners. Brain Lang. 78, 332–348.

Wang, Y., Behne, D.M., Jongman, A., Sereno, J.A., 2004. The role of linguistic experience in the hemispheric processing of lexical tone. Appl. Psycholinguist. 25, 449–466.

Winkler, I., 2007. Interpreting the mismatch negativity. J. Psychophysiol. 21, 147–163.

Xi, J., Zhang, L., Shu, H., Zhang, Y., Li, P., 2010. Categorical perception of lexical tones in Chinese revealed by mismatch negativity. Neuroscience 170, 223–231.

Yago, E., Escera, C., Alho, K., Giard, M.H., 2001. Cerebral mechanisms underlying orienting of attention towards auditory frequency changes. Neuroreport 12, 2583–2587.

Zhang, L., Xi, J., Xu, G., Shu, H., Wang, X., Li, P., 2011. Cortical dynamics of acoustic and phonological processing in speech perception. PloS One 6, e20963.