# Differentiating the neural generators of ERANm and MMNm: An MEG study

Seung-Goo KIM[1,3], Bong-Soo KIM[2,3], Chun Kee CHUNG[2,3]

[1]MEG Center, Seoul National University Hospital, 110-744 Seoul, Korea, [2]Department of Neurosurgery, Seoul National University College of Medicine, 110-744 Seoul, Korea, [3]Interdisciplinary Program in Cognitive Science, Seoul National University, 151-742 Seoul, Korea

Biomag 2010
17th International Conference on Biomagnetism
March 28 - April 1, 2010
Dubrovnik, Croatia

## INTRODUCTION

Incongruent event in sequential musical context could induce two related but distinct electromagnetic physiological responses. Music-syntactically incongruous chord function progression, such as Neapolitan sixth instead of Tonic after Dominant at the cadence, could elicit the early right anterior negativity (ERAN) [1] whereas acoustically incongruent sound might evoke the mismatch negativity (MMN) [2].

Though ERAN can be assumed as a specific kind of abstract MMN [3], the difference from other types of abstract MMN is that ERAN responses reply on the stored musical syntax in a long-term memory format[4].

The present study aimed to measure ERANm and MMNm (the magnetic counterparts of ERAN and MMN) in the same musical context, and to differentiate the neural substrates of ERANm and MMNm using Magnetoencephalography (MEG).

## MATERIALS AND METHODS

*Musical contexts*

Musical contexts were composed of to contain 5 sequential chords in the previous studies [1], [4]. 50 % of sequences had a harmonically congruent progression at the cadence (**Figure 1.A**). 25% of sequences had a harmonically incongruent progression, Neapolitan sixth at the 3th position, and the other 25% of sequences had the Neapolitan sixth at the 5rd position (**Figure 1.B**). The Neapolitan sixth chords at the 5th position is the most incongruent chord function in the presented stimuli, thus it was assumed that they would evoke ERANm response.

Some of harmonically congruent chords were acoustically incongruent. That is, the most of chords were played in the Piano, but 10% of congruent chords were played in deviant instruments such as the Organ or the Synthesizer. Due to the rare occurrences and the acoustic saliency, these chords were expected to raise MMNm responses.

All chords were played using *Cubase* 5, *VST collection volume 1* and *The Grand 3* (Steinberg, Hamburg, Germany). The duration of the all chords was 0.75 seconds, and the last 5th chord was followed by 0.75 seconds pause, resulting in 4.5 seconds for a sequence. The sequences were transposed to all 12 Major keys to control the effect of different pitch. Then the stimuli were presented for 40 times in a block, and 240 sequences throughout 6 blocks, resulting in 126 congruent sequences, 90 harmonically incongruent sequences and 54 acoustically deviant sequences played.

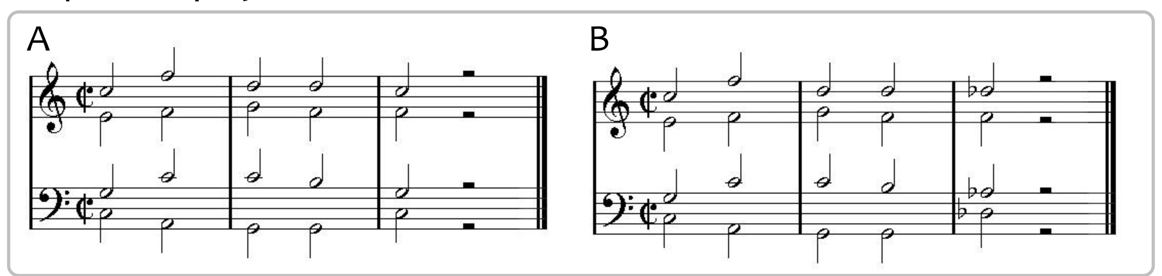


**Figure 1.** Examples of harmonically congruent sequence (A) and incongruent sequence (B)

*MEG recording*

Using a whole-head 306 channel *Elekta Neuromag Vectorview system* (Elekta Neuromag Oy, Helsinki, Finland), in which two gradiometers and one magnetometer are combined as a single sensor unit, we have recorded MEG data with electrooculography (EOG) and elctrocardiography (ECG) to reject the epoch with those artifacts in 600.615 Hz sampling rate. 4 coils were attached to the participants scalp and digitized to obtain the head position information.

4 non-musicians participated in the present experiment (3 females, mean age=30.25 yr). One participants were excluded for exceed artifacts in MEG data. The participants were asked to press a button when they heard a chord in a different timbre. This task is used in the previous studies [1], [4] to control and monitor the arousal level of participants during the repetitive chords were presented. The auditory stimuli were presented approximately at 65 DB SPL using *STIM 2* (Neuroscan, NC, US) to the participants in the magnetically shield room via air tubes.

*Preprocessing and equivalent current dipole analysis*

The environmental noise were eliminated using signal space separation method (*Maxfilter* [5]) built in *Neuromag* software (Elekta Neuromag Oy, Helsinki, Finland). The MEG data were transformed to the head position in the first block within each participant. The artifacts from eye-movements were visually inspected and rejected. The trials between 200 msec pre-onset and 600 msec post-onset of the target chord were averaged across blocks using custom *MATLAB* (The MathWorks, MA, US) codes.

The target chords were the harmonically congruent chord in the 5th position, the harmonically incongruent chord in the 5th position, both played with the Piano to analyze ERANm responses. For MMNm responses, all congruent chords played with the Piano and all chords played with the deviant instruments were averaged to increase signal-to-noise ratio.

Neural generators were localized using the difference magnetic field between conditions obtained by subtracting the averaged MEG data of the harmonically or acoustically congruent condition from the data of the incongruent condition. A band pass filter 2~20 Hz was applied. Using the subsets of gradiometers covering the right or left temporal and frontal regions, in where the responses were maximal, the gradient of magnetic fields were used to located the neuronal sources. Single Equivalent Current Dipoles (ECDs) were estimated using *Xfit* built in Neuromag for the maximal peaks for ERANm and MMNm. From the subgroup of gradiometers, only ECDs with the goodness of fit (GOF) more than 80% were selected. The computed dipoles were superimposed on the available MRIs for one subject (Subject 1). The co-registration of MEG and MRI data was manually done by identifying the three cardinal landmarks (naison and the two auricular points) on MRI slices. The locations of dipoles of other subjects (Subject 2 and Subject 3) without MRIs were also compared as well. Due to the small number of participants in the present study, any statistical evaluation across subjects were not applied.

*Minimum norm estimation analysis*

Additionally, using MRI data of Subject 1, Minimum norm estimation (MNE) approach was employed. First, using *FreeSurfer* (Athinoula A. Martinos Center for Biomedical Imaging, MA, US) the T1-weighted MRI data was tessellated and reconstructed as a triangular mesh for each hemisphere [6], [7]. After that, using *MNE suite* (Athinoula A. Martinos Center for Biomedical Imaging, MA, US), a realistic boundary element method (BEM) mesh of inner skull was constructed using water shed algorithm assuming a homogeneous element, which is sufficient for MEG data. 7,844 source locations were constructed spacing 7 mm on the constructed cortical surface. Then the coordinate systems of MRI and MEG were co-registrated using digitized spatial information of cardinal points, HPI coils and points on the scalp via a semi-automated way to compute the forward model. The inverse operator has been computed with loose constraint [8] and depth weighting [9].

## RESULTS

Acoustically incongruent chords evoked the peak on the root mean square (RMS) curve of the subgroup covering the right temporal and frontal lobes with a mean latency of 202.4 msec post-onset. Harmonically incongruent chords evoked the peak on the RMS curve with a mean latency of 194.3 msec post-onset. On the left hemispheres, no ECDs were estimated with more than 80% GOF between 150 and 250 msec post-onset.

In Subject 1, the ECD for ERANm at 201.6 ms post-onset (**Figure 2. A**) was located on the inferior frontal gyrus (Head coordinate= (46.0, 25.2, 71.2); **Figure 2.B**) while the ECD for MMNm at 177.0 ms post-onset (**Figure 2. C**) is located on the right superior temporal sulcus (Head coordinate (mm)= (59.1, 16.16, 55.7); **Figure 2.D**). The ECD for ERANm was 9 mm anterior than the ECD for MMNm. The pattern of estimated distributed current shows the differences between acoustic incongruent and syntactic incongruence (**Figure 3**).

For Subject 2, the location of ECD for ERANm was 21 mm posterior than the ECD for MMNm. And for subject 3, the location of ECD for ERANm was 9 mm anterior than the ECD for MMNm as Subject 1. Refer to **Table 1** for details of fitted dipoles.

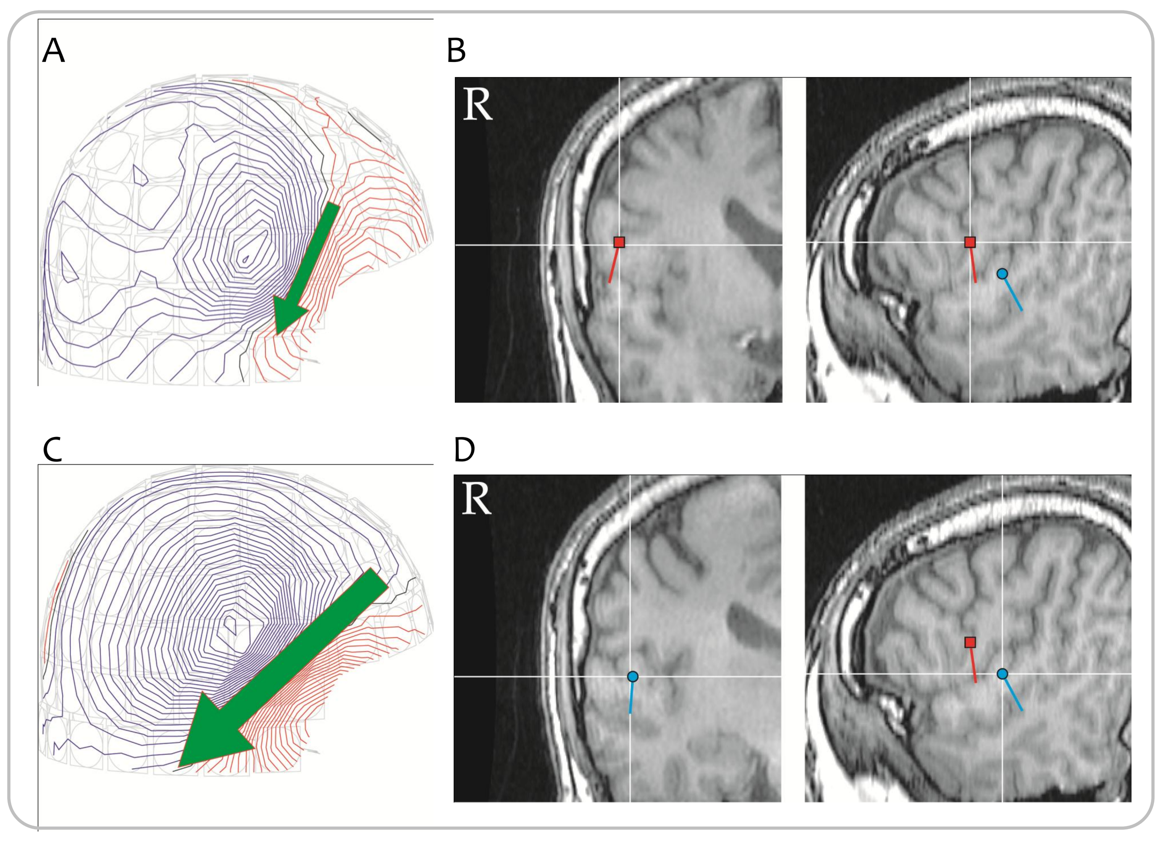


**Figure 2.** ECD and magnetic field map for ERANm (A) and superimposed on MRI (B; red squares) and for MMNm (C), (D; blue circles).

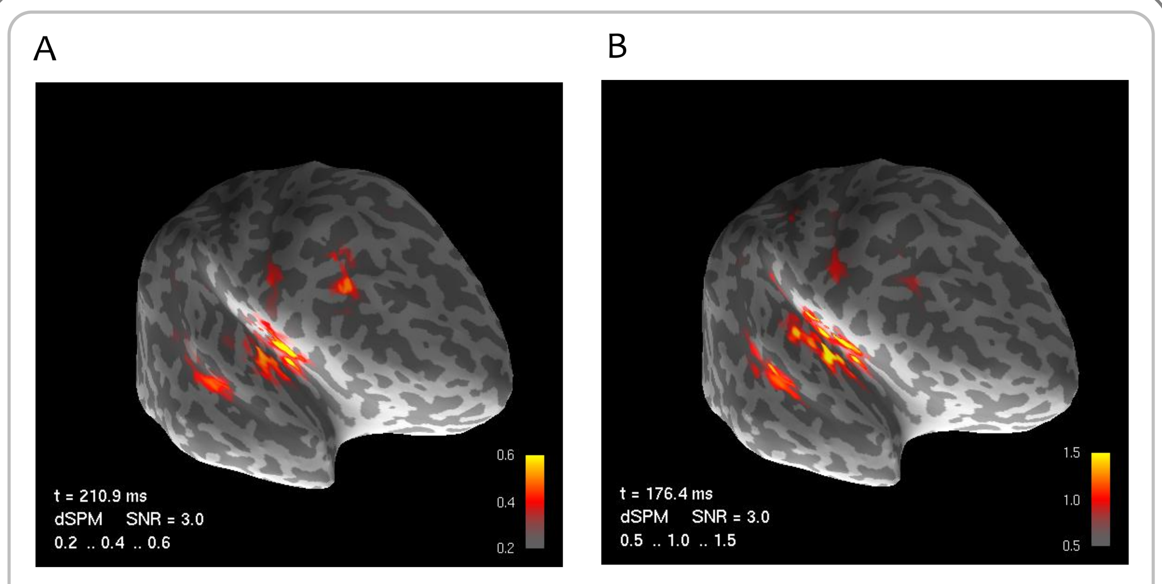


**Figure 3.** Distributed current estimation for ERANm (A) and for MMNm (B). Note that the scale s are different for each panel.

| Subject | Dipole | Latency (ms) | Head coordinate (x, y, z; mm) | | | GOF (%) |
|---|---|---|---|---|---|---|
| Subject 1 | ERANm | 201.6 | 46.0 | 25.2 | 71.2 | 85.5 |
| | MMNm | 177.0 | 59.1 | 16.2 | 55.7 | 96.5 |
| Subject 2 | ERANm | 179.2 | 40.6 | 9.0 | 57.9 | 94.0 |
| | MMNm | 175.9 | 42.1 | 28.9 | 84.4 | 81.6 |
| Subject 3 | ERANm | 204.5 | 61.3 | 8.1 | 43.4 | 82.1 |
| | MMNm | 254.3 | 46.6 | -1.1 | 63.1 | 91.5 |

**Table 1.** the dipoles extracted from difference between acoustic or syntactic deviances and standards.

## DISCUSSION

The present study has investigated the locations of neural generators involving in processing the acoustic deviances and syntactic violation in the same musical contexts using MEG. As suggested in an EEG study with source location analysis [10], the different spatial distribution of neural activities is demonstrated in the our data. The difference between the responses to the different musical instruments was dominant in the auditory cortex whereas the difference subject to musical syntax was both auditory cortex and frontal cortex.

Many studies indicated that the neural source of MMN is predominantly on the auditory cortex [11] with interaction of other regions in the brain such as frontal cortex. There has been a approach to understand the MMN response as an amplitude- and latency-modulated N100 response [12]. This view suggests that the neural generators of MMN is not necessarily distinct to those of N100 response. Following this point of view, the early activities elicited from an novel auditory stimulus are mainly on the auditory cortex.

The ERAN response is suggested as to share the many parts of neural mechanism underlying MMN response [3]. What is different in ERAN from MMN is believed to be involvement of musical syntactic rules which are processed in frontal regions. Thus ERAN may reflect more cognitive processing than MMN relays on the auditory memory.

Our result also suggests that neural substrates processing musical syntax and acoustic rarity could be differentiated.

## ACKNOWLEDGEMNETS

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MEST) (No. KRF2007-313-H00006 and 2009-0081342).

## REFERENCES

1. Koelsch, S., et al., *Brain indices of music processing: "Non-musicians" are musical.* Journal of Cognitive Neuroscience, 2000. 12(3): p. 520-541.
2. Naatanen, R., A.W.K. Gaillard, and S. Mantysalo, *EARLY SELECTIVE-ATTENTION EFFECT ON EVOKED-POTENTIAL REINTERPRETED.* Acta Psychologica, 1978. 42(4): p. 313-329.
3. Koelsch, S., *Music-syntactic processing and auditory memory: Similarities and differences between ERAN and MMN.* Psychophysiology, 2009. 46(1): p. 179-190.
4. Koelsch, S., et al., *Differentiating ERAN and MMN: An ERP study.* Neuroreport, 2001. 12(7): p. 1385-1389.
5. Taulu, S., J. Simola, and M. Kajola, *Applications of the signal space separation method.* Ieee Transactions on Signal Processing, 2005. 53(9): p. 3359-3372.
6. Dale, A.M., B. Fischl, and M.I. Sereno, *Cortical Surface-Based Analysis: I. Segmentation and Surface Reconstruction.* NeuroImage, 1999. 9(2): p. 179-194.
7. Fischl, B., et al., *High-resolution intersubject averaging and a coordinate system for the cortical surface.* Human Brain Mapping, 1999. 8(4): p. 272-284.
8. Lin, F.-H., et al., *Distributed current estimates using cortical orientation constraints.* Human Brain Mapping, 2006. 27(1): p. 1-13.
9. Lin, F.-H., et al., *Assessing and improving the spatial accuracy in MEG source localization by depth-weighted minimum-norm estimates.* NeuroImage, 2006. 31(1): p. 160-171.
10. Villarreal, E.A.G., et al. Harmony Wants to Sit in the Front: Different Brain Responses to Violations in Chord Progressions. in European Society for the Cognitive Sciences of Music. 2009. Jyvaskyla, Finland.
11. Alho, K., Cerebral Generators of Mismatch Negativity (MMN) and Its Magnetic Counterpart (MMNm) Elicited by Sound Changes. Ear and Hearing, 1995. 16(1): p. 38-51.
12. May, P.J. and H. Tiitinen, The MMN is a derivative of the auditory N100 response. Neurol Clin Neurophysiol, 2004. 2004: p. 20.

Seoul National University
[University] Main Campus : Seoul National University, Gwanak 599 Gwanak-ro, Gwanak-gu, Seoul 151-742, Korea
Medical Campus: Yongon 103 Daehangno, Jongno-gu, Seoul 110-799, Korea
[ Hospital ] Yongon 101 Daehangro, Jongno-gu, Seoul 110-744, Korea
MEG CENTER SEOUL NATIONAL UNIVERSITY HOSPITAL