

Manuscript Number: HEARES-D-14-00093R3

Title: Neural correlates of perceptual grouping effects in the processing of sound omission by musicians and nonmusicians

Article Type: Research paper

Keywords: Perceptual grouping; Omission; Predictive coding theory; Magnetoencephalography; Musical experience.

Corresponding Author: Dr. Kentaro Ono,

Corresponding Author's Institution: Kyoto University

First Author: Kentaro Ono

Order of Authors: Kentaro Ono; Christian F Altmann; Masao Matsuhashi; Tatsuya Mima; Hidenao Fukuyama

Abstract: Perceptual grouping is the process of organizing sounds into perceptually meaningful elements. Psychological studies have found that tones presented as a regular frequency or temporal pattern are grouped according to gestalt principles, such as similarity, proximity, and good continuity. Predictive coding theory suggests that this process helps create an internal model for the prediction of sounds in a tone sequence and that an omission-related brain response reflects the violation of this prediction. However, it remains unclear which brain areas are related to this process, especially in paying attention to the stimuli. To clarify this uncertainty, the present study investigated the neural correlates of perceptual grouping effects. Using magnetoencephalography (MEG), we recorded the evoked response fields (ERFs) of amateur musicians and nonmusicians to sound omissions in tone sequences with a regular or random pattern of three different frequencies during an omission detection task. Omissions in the regular sequences were detected faster and evoked greater activity in the left Heschl's gyrus (HG), right postcentral gyrus, and bilateral superior temporal gyrus (STG) than did omissions in the irregular sequences. Additionally, an interaction between musical experience and regularity was found in the left HG/STG. Tone-evoked responses did not show this difference, indicating that the expertise effect did not reflect the superior tone processing acquired by amateur musicians due to musical training. These results suggest that perceptual grouping based on repetition of a pattern of frequencies affects the processing of omissions in tone sequences and induces more activation of the bilateral auditory cortex by violating internal models. The interaction in the left HG/STG may suggest different styles of processing for musicians and nonmusicians, although this difference was not reflected at the behavioral level.

Highlights:

- Sound omission in a tone sequence elicits the omission-related response (OR).
- We studied the effect of perceptual grouping on ORs.
- ORs were measured in musicians and nonmusicians using magnetoencephalography.
- ORs were increased by perceptual grouping and localized in the auditory cortex.
- The grouping effect was left-side dominant in musicians but not in nonmusicians.

1 Proposed journal section: Research Papers

2

3

4

5 Neural correlates of perceptual grouping effects in
6 the processing of sound omission by musicians and
7 nonmusicians

8

9

10 Kentaro Ono, Christian F. Altmann, Masao Matsushashi, Tatsuya Mima, and
11 Hidenao Fukuyama

12

13

14 Human Brain Research Center, Graduate School of Medicine,

15 Kyoto University, Kyoto, 606-8507, Japan

16

17

18

19

20 **Address correspondence to:**

21 Kentaro Ono, PhD

22 Human Brain Research Center, Graduate School of Medicine

23 Kyoto University, Kyoto, 606-8507, Japan

24 Phone: ++81-75-751-3695

25 Fax: ++81-75-751-3202

26 E mail: onoken@kuhp.kyoto-u.ac.jp

27

28

29 **Keywords:**

30 Perceptual grouping, Omission, Predictive coding theory, Magnetoencephalography,

31 Musical experience

32

33 **Abbreviations:**

34 OR, omission-related response; MEG, magnetoencephalography; HG, Heschl's gyrus;

35 STG, superior temporal gyrus; MMN, mismatch negativity; ISI, inter-stimulus interval;

36 AC, auditory cortex; MRI, magnetic resonance imaging; RMS, root mean square;

37 ANOVA, analysis of variance; RT, reaction time; SD, standard deviation.

38

39

40

41

Abstract

42 Perceptual grouping is the process of organizing sounds into perceptually meaningful
43 elements. Psychological studies have found that tones presented as a regular frequency
44 or temporal pattern are grouped according to gestalt principles, such as similarity,
45 proximity, and good continuity. Predictive coding theory suggests that this process helps
46 create an internal model for the prediction of sounds in a tone sequence and that an
47 omission-related brain response reflects the violation of this prediction. However, it
48 remains unclear which brain areas are related to this process, especially in paying
49 attention to the stimuli. To clarify this uncertainty, the present study investigated the
50 neural correlates of perceptual grouping effects. Using magnetoencephalography (MEG),
51 we recorded the evoked response fields (ERFs) of amateur musicians and nonmusicians
52 to sound omissions in tone sequences with a regular or random pattern of three different
53 frequencies during an omission detection task. Omissions in the regular sequences were
54 detected faster and evoked greater activity in the left Heschl's gyrus (HG), right
55 postcentral gyrus, and bilateral superior temporal gyrus (STG) than did omissions in the
56 irregular sequences. Additionally, an interaction between musical experience and
57 regularity was found in the left HG/STG. Tone-evoked responses did not show this
58 difference, indicating that the expertise effect did not reflect the superior tone

59 processing acquired by amateur musicians due to musical training. These results suggest
60 that perceptual grouping based on repetition of a pattern of frequencies affects the
61 processing of omissions in tone sequences and induces more activation of the bilateral
62 auditory cortex by violating internal models. The interaction in the left HG/STG may
63 suggest different styles of processing for musicians and nonmusicians, although this
64 difference was not reflected at the behavioral level.

65

66

67

68

69

70

71

72

73

74

75

76

77

1. Introduction

78 In an orchestral performance, a musical piece is produced by multiple sequences of
79 tones played in parallel. The auditory system can extract the structural components of
80 the piece, such as its melody and rhythm, from this mixture of tones using processes
81 that integrate acoustic information over time. Together, these processes are called
82 perceptual grouping, and psychological studies have identified the rules for grouping
83 sound features, such as similarity, proximity or good continuity (Bregman, 1990;
84 Deutsch, 2012; Koffka, 1935). Bregman (1990) suggested that two types of perceptual
85 grouping exist: one is stimulus-driven and works preattentively in a short time window,
86 while the other requires higher cognitive functions such as attention and/or
87 experience-based knowledge, and has a longer time window.

88 A wording to predictive coding theory, cortical circuits create internal models
89 to generate predictions about incoming stimuli (Friston and Kiebel, 2009a, 2009b;
90 Friston, 2005). An evoked response may occur reflecting the transient expression of a
91 prediction error, which results from comparison between the bottom-up inputs from
92 lower cortical/subcortical areas and top-down predictions from higher cortical areas.
93 Several studies have applied this theory to explain the early stages of auditory
94 processing (Bendixen et al., 2012; Winkler and Czigler, 2012; Winkler, 2007; Winkler et

95 al., 2009). Key to this explanation is that an internal model is created by spectral or
96 temporal regularity, which is extracted from a tone sequence. Mismatch negativity
97 (MMN) and the omission-related response (OR), both of which are elicited by deviation
98 (a deviant tone or the omission of a tone) from a sequence of repetitive tone stimuli, can
99 be interpreted as resulting from the violation of the prediction. In particular, the OR is
100 suitable for investigating prediction-related brain activity because it does not overlap
101 with the response elicited by the stimulus. Previous studies have shown that an OR can
102 be elicited by a tone omission in an unattended tone sequence at an inter-stimulus
103 interval (ISI) of less than 200 ms (Alain et al., 1989; Hughes et al., 2001; Raij et al.,
104 1997; Snyder and Large, 2005; Tarkka and Stokic, 1998; Todorovic et al., 2011;
105 Wacongne et al., 2011; Yabe et al., 2001, 1997). Together with Bregman's idea and the
106 predictive coding theory, these results can be interpreted as resulting from a violation of
107 a prediction based on pre-attentive perceptual grouping based on temporal regularity.
108 The OR in the absence of attention is localized in the auditory cortex (AC) (Raij et al.,
109 1997; Todorovic et al., 2011), which may be involved in prediction and pre-attentive
110 perceptual grouping.

111 Several neurophysiological studies have elicited ORs at an ISI longer than
112 200 ms when the participants paid attention to the stimuli (Alain et al., 1989;

113 Joutsiniemi and Hari, 1989; Penney, 2004). These results suggest that an OR to tone
114 sequences with long ISI can occur as a result of a violation of a prediction based on
115 attentive perceptual grouping. However, the neural correlates of this phenomenon
116 remain unclear. Thus, we aimed to find the neural correlates of prediction based on
117 attentive perceptual grouping in a tone sequence with a regular frequency pattern. We
118 hypothesized that, when participants paid attention to the stimuli, a repetitive frequency
119 pattern would cause perceptual grouping and help create stronger predictions about
120 incoming stimuli, compared to a tone sequence with a random pitch pattern. Thus, a
121 violation of this prediction by an omission in a tone sequence with a pitch pattern would
122 evoke a stronger OR than would an omission in a random tone sequence. To clarify this
123 issue, we compared the brain magnetic responses evoked by omissions in regular and
124 random tone sequences using magnetoencephalography (MEG).

125 In addition, we evaluated the impact of musical experience on the grouping
126 effect. Musical training normally includes the structural analysis of musical pieces,
127 which should improve the ability to extract regular patterns from a tone sequence
128 because the structural components of a piece (e.g., melody, chord progression, meter,
129 etc.) are established by pitch and/or rhythm patterns. Although psychological studies
130 have demonstrated that perceptual grouping depends on experience (Bhatara et al.,

131 2013; Dewar et al., 1977; Gobet and Simon, 1996; Idson and Massaro, 1976; Iversen et
132 al., 2008; Saariluoma, 1989; Simon and Chase, 1973), no study has investigated the
133 neural correlates of this phenomenon. Thus, we tested the hypothesis that musical
134 training influences the brain mechanisms involved in the perceptual grouping of
135 frequency patterns, leading to more pronounced patterns of cortical activation in
136 musicians than in nonmusicians.

137

138

139

2. Methods

140 *2.1 Participants*

141 The participants consisted of 13 amateur musicians (7 males and 6 females) who
142 regularly played musical instruments, such as piano, guitar, violin, and cello, with an
143 average experience of 13 ± 5 years (mean \pm standard deviation [SD]), and 14
144 nonmusicians (11 males and 3 females) who had no instrumental experience, except for
145 lessons in school. All participants were right-handed with an average age of 22 ± 2 years
146 and provided written informed consent to participate in the experiment. Although we
147 did not measure the participants' hearing thresholds, none of them reported difficulty in
148 discriminating the stimuli. The participants also did not report any neurological or

149 hearing problems. The experiment was performed in accordance with the ethical
150 standards of the Declaration of Helsinki and the guidelines approved by the local ethics
151 committee of the Graduate School of Medicine and Faculty of Medicine, Kyoto
152 University.

153

154 *2.2 Stimuli*

155 Pure tones (50-ms duration, 5-ms onset/offset ramps, 65 dB SPL) with three different
156 frequencies (C5: 523 Hz, E5: 659 Hz, and G5: 784 Hz) were created as wave files using
157 the Audacity software program (ver. 2.0.3; <http://audacity.sourceforge.net/>). A silent
158 period with a length of 500 ms was created as the omission stimulus. Each tone
159 sequence was constructed of these tones, presented either in a regular pattern of “CEG”
160 (regular sequence) or pseudo-randomly (irregular sequence), with an ISI of 450 ms (Fig.
161 1A). In the irregular sequence, randomization was controlled so as not to present the
162 same frequency more than three times consecutively, and at least three tones were
163 presented between omissions.

164

165 *2.3 Procedure*

166 Participants were seated in a chair in a magnetically shielded room. The tone sequences

167 were presented through earphones, which was coupled to the ear by a silicon tube and
168 the ear insert (E-A-R-tone 3A, Aearo Corporation, Indianapolis, USA). The earphone
169 was connected to an amplifier (Roland SRQ-2031, Roland Corporation, Hamamatsu,
170 Japan) outside of the shielded room. Participants were instructed to press a button with
171 their right index finger as quickly as possible upon noticing any omission in the
172 sequence. Because perceptual grouping facilitates the processing of deviant stimuli in a
173 tone sequence (Idson and Massaro, 1976; Jones et al., 1982; Mondor and Terrio, 1998;
174 Royer and Garner, 1970), the response time was used to characterize the effect of
175 perceptual grouping.

176 Each sequence was presented in three separate blocks. Six blocks were
177 conducted in total, and the order of the blocks was randomized between participants. In
178 each block, approximately 7% of the tones were replaced with a silent period. In total,
179 2520 tones and 180 omissions (60 omissions for each tone) were presented in regular
180 and irregular sequences. An additional restriction for the regular sequence was that, after
181 each omission, the sequence started again from the C tone (e.g., CEGCEGCE_CEG...)
182 to maintain the repetition of the CEG pattern.

183 At the end of the experiment, we asked the participants whether they had
184 recognized the regular sequence as a CEG pattern, and all participants reported that they

185 had.

186

187 *2.4 MEG acquisition*

188 Event-related fields (ERFs) were recorded with a 306-channel whole-head
189 magnetoencephalography (MEG) system (Vectorview, Elekta Neuromag Oy, Finland).

190 The head position was determined using four indicator coils attached to the scalp. In
191 addition, three head landmarks (the nasion and bilateral preauricular points) and head
192 shape were recorded for each participant using a spatial digitizer (Polhemus Inc.,

193 Colchester, VT, USA) before the experiment. These data were used for co-registration
194 with the T1 anatomical image of each participant obtained using a 0.2 T magnetic

195 resonance imaging (MRI) machine (Signa Profile, GE Health Care, Waukesha, WS,
196 USA). The ERFs were recorded with a band-pass filter (0.1 to 200.0 Hz) and a sampling

197 rate of 600 Hz. To reduce external noise, we used spatiotemporal signal space separation
198 (tSSS) methods (MaxFilter, Elekta Neuromag Oy, Helsinki, Finland) with a correlation

199 window of 900 s, which covered the entire length of each block, and a correlation limit
200 of 0.980. The acquired data were low-pass filtered using a fifth-order Butterworth

201 zero-phase filter with a cut-off frequency of 40 Hz. The time window of each epoch
202 lasted between 50 ms prestimulus and 450 ms poststimulus, and the prestimulus period

203 was used for baseline correction. Peak-to-peak differences of more than 3.0 pT/cm were
204 used as rejection criteria.

205

206 *2.5 MEG sensor level analysis*

207 To analyze the temporal waveform of the brain response evoked by omission at the
208 sensor level, we calculated the root mean square (RMS) values of 20 planar
209 gradiometers that separately covered the temporal lobe in the right and left hemispheres.
210 The same array of sensors was employed in all participants. Because the observed
211 waveforms of the brain response evoked by omission exhibited a gradual increase with
212 no specific peak, the mean value from 100 to 400 ms after omission onset was analyzed
213 using four-way analysis of variance (ANOVA) with the factors musical experience,
214 regularity, position of omission (C, E, or G tone), and laterality (left or right
215 hemisphere) using R software (ver. 2.15.2; R Foundation for Statistical Computing,
216 Vienna, Austria; <http://www.R-project.org>). Post-hoc analyses were conducted using
217 lower-level ANOVAs and paired *t*-tests with multiple comparison using Shaffer's
218 modified Bonferroni correction (Shaffer, 1986).

219

220 *2.6 MEG source level analysis*

221 To localize the possible source of the OR and compare the activation of the source
222 between conditions, we used an empirical Bayesian approach, as implemented in SPM8
223 (Wellcome Trust Centre for Neuroimaging, University College London, UK).
224 Participants' T1 images were normalized to the Montreal Neurological Institute (MNI)
225 brain template, and the inverses of the parameters were used to wrap a cortical template
226 mesh to each individual MR space. Co-registration between the MEG sensor positions
227 and T1 images was achieved by manually detecting three fiducial points in both the MR
228 image and the head-shape measurement taken using the spatial digitizer. To generate the
229 forward model, the lead-field for each sensor was calculated for the dipoles at each
230 point in the cortical mesh using a single shell model. The model was then inverted using
231 the multiple sparse priors (MSP) algorithm (Friston et al., 2008; Mattout et al., 2006).
232 To evaluate the cortical distribution evoked by omission in detail, reconstructed maps
233 were created for each 100-ms time window from 100 to 400 ms after omission onset.
234 These maps were exported as three-dimensional images into the MNI space and
235 smoothed using a Gaussian filter with a 12-mm full-width at half maximum (FWHM).

236 For group analysis, general-linear-model-based statistical analysis with random
237 field theory was conducted using SPM8. To visualize the averaged distribution of brain
238 activation evoked by omission, the reconstructed maps for the omission of C, E, and G

239 tones between 100 and 400 ms after omission onset were pooled separately for the
240 regular and irregular sequences and analyzed by one-sample *t*-tests, comparing the
241 activation with zero, at an uncorrected threshold of $p < 0.005$. To investigate the effects
242 of the experimental variables, we conducted a three-way ANOVA with the factors
243 musical experience, regularity, and position of omission at an uncorrected threshold of p
244 < 0.001 for each 100 ms window from 100 to 400 ms after omission onset. All maps
245 were projected to the MNI template. The MNI coordinates of these voxels were then
246 converted to Talairach space using GingerALE (Laird et al., 2010), and Talairach Client
247 was used for anatomical labeling (Lancaster et al., 2007). To further investigate the time
248 course of the contribution of activated areas, we conducted region of interest (ROI)
249 analysis. The amplitude of each dipole in a 10-mm diameter circle centered upon the
250 selected ROI in the cortical mesh was averaged for each time point for each participant.
251 The mean of these values at each 100-ms time window from 100 to 400 ms was then
252 calculated. The ROI activity was then analyzed using ANOVAs.

253 To test the possibility that the effect of musical experience on the OR simply
254 reflected the larger brain response elicited by tones in musicians, as shown in previous
255 studies (Pantev et al., 2003, 1998), we conducted a source level analysis for
256 tone-evoked ERFs. Reconstructed maps were created in the same way as for the OR and

257 analyzed using a three-way ANOVA with the factors musical experience, regularity, and
258 position of omission.

259

260 *2.7 Behavioral data analysis*

261 The time difference between the onset of omission (the time at which the missing tone
262 had been expected) and the button press was calculated as reaction time (RT). The mean
263 and SD of the RT were analyzed using a three-way ANOVA with the factors musical
264 experience, regularity, and position of omission. Post-hoc analyses were conducted
265 using lower-level ANOVAs and paired *t*-tests with multiple comparisons using Shaffer's
266 modified Bonferroni correction (Shaffer, 1986).

267

268

269

3. Results

270 *3.1 Behavioral data*

271 The group mean RT is presented in Fig. 1B. A three-way ANOVA with the factors
272 musical experience, regularity, and position of omission showed main effects of
273 regularity ($F [1, 25] = 5.24, p = 0.031$) and position of omission ($F [2, 50] = 6.68, p =$
274 0.002), although neither a main effect nor an interaction related to musical experience

275 were observed. Multiple comparisons revealed that the omission of the C tone was
276 detected faster than omissions of the other tones. The three-way ANOVA of the SD also
277 showed main effects of regularity ($F [1, 25] = 7.71, p = 0.010$) and position of omission
278 ($F [2, 50] = 6.54, p = 0.003$). Multiple comparisons revealed that the SD for the
279 omission of the C tone was larger than omissions of the other tones. The rate of correct
280 detection for the omissions was over 95%, and did not vary significantly across
281 conditions.

282

283 *(Fig. 1 around here)*

284

285 *3.2 Analysis of magnetic fields evoked by omissions*

286 An example of the ERF waveform for one musician (Fig. 1C) is typical in not showing
287 a clear peak; instead, the amplitude increased gradually after 100 ms of omission onset.
288 The group means of the RMS values of the responses evoked by the omissions are
289 plotted in Fig. 2. A four-way ANOVA with the factors musical experience, regularity,
290 position of omission, and laterality showed main effects of regularity ($F [1, 25] = 30.04,$
291 $p < 0.001$) and laterality ($F [1, 25] = 6.27, p = 0.019$), although no main effect or
292 interaction related to musical experience were observed. These results indicate that

293 omission evoked a larger brain response for regular than for irregular sequences,
294 irrespective of musical experience (Fig. 3).

295

296 *(Fig. 2 and Fig. 3 around here)*

297

298 Fig. 4A depicts the average cortical activation between 100 and 400 ms after
299 omission onset. Despite the lack of stimulus input, activation was observed in the
300 bilateral temporal and frontal lobes. Three-way ANOVAs with the factors musical
301 experience, regularity, and position of omission for each 100 ms time window from 100
302 to 400 ms after omission onset showed similar results. From 100 to 200 ms, the analysis
303 showed a main effect of regularity in the left Heschl's gyrus (HG) and right postcentral
304 gyrus, as well as an interaction between musical experience and regularity in the left
305 HG. From 200 to 300 ms, the ANOVA showed a main effect of regularity in the bilateral
306 superior temporal gyrus (STG) and an interaction between musical experience and
307 regularity in the left STG. These areas showed stronger activation in response to
308 omission in regular than in irregular sequences (Fig. 4B). From 100 to 200 ms and 200
309 to 300 ms, an interaction between musical experience and regularity was found in the
310 left STG (Fig. 4C). No main effects or interactions were detected from 300 to 400 ms.

311 The peak coordinates of the activated areas are listed in Table 1.

312

313 *(Fig. 4 and Table 1 around here)*

314

315 To further analyze the interaction between musical experience and regularity in
316 the left STG from 100 to 300 ms, we conducted a ROI analysis for this area. The mean
317 ROI activity was analyzed using separate two-way ANOVAs with the factors musical
318 experience and time (100 to 200 ms, 200 to 300 ms) for the regular and irregular
319 sequences. For the regular sequences, the ANOVA showed main effects of musical
320 experience ($F [1, 25] = 5.91, p = 0.023$) and time ($F [1, 25] = 19.05, p < 0.001$),
321 indicating stronger activation in musicians than in nonmusicians (Fig. 5). The ANOVA
322 for the irregular sequences showed no significant differences.

323

324 *(Fig. 5 around here)*

325

326 To test the possibility that the differences in the activated areas observed
327 between musicians and nonmusicians were based on differences in the brain activation
328 evoked by tones, the cortical distribution of the activation was analyzed using a

329 three-way ANOVA with the factors musical experience, regularity, and position of
330 omission. No significant difference in activation was observed for each 100 ms time
331 window from 100 to 400 ms after tone onset, indicating that musical training did not
332 yield greater cortical activation by the pure tones employed in the present experiment.

333

334

335

4. Discussion

336 Both behavioral and neurophysiological differences were observed in the processing of
337 omissions between regular and irregular sequences. Better detection performance and
338 larger ERFs were associated with omissions in regular sequences than in irregular
339 sequences. Source-level analysis showed that omissions in the regular sequences
340 elicited stronger activation in the bilateral HG/STG than did those in the irregular
341 sequences. Based on predictive coding theory, these results can be interpreted to
342 indicate that activity in the auditory cortex is related to the matching between an internal
343 predictive model and an actual stimulus input.

344

345 *4.1 Influence of perceptual grouping on the processing of sound omission*

346 We expected that the repetition of C, E, and G tones in a fixed order (CEGCEG...)

347 would elicit perceptual grouping of the pitch pattern (CEG). The participants' faster
348 detection performance for the regular sequence agrees with the results of previous
349 studies, which have shown that perceptual grouping improves the detection and
350 recognition of target stimuli (Idson and Massaro, 1976; Jones et al., 1982; Mondor and
351 Terrio, 1998; Royer and Garner, 1970). In addition, the participants reported
352 recognizing the regular sequence as a repetition of a CEG pattern. Therefore, we believe
353 that the fixed order presentation of the C, E, and G tones in the regular sequence elicited
354 perceptual grouping of the CEG pattern.

355 From a predictive coding perspective, our results can be interpreted as follows:
356 the perceptual grouping of the CEG pattern strengthened top-down modulation from
357 higher-level brain areas and allowed stronger predictions to be created about incoming
358 tones than for the irregular sequences. Disagreement between this prediction and the
359 input caused a larger prediction error in the regular sequence, resulting in a larger OR.
360 This was reflected by the significant activation difference around the bilateral HG/STG
361 between the regular and irregular sequences, suggesting that these regions were engaged
362 in comparing the prediction with the stimulus input. The meaning of the activation in
363 the right postcentral gyrus is, however, unclear. To the best of our knowledge, no
364 previous study has examined the involvement of this region in perceptual grouping.

365 Future research may clarify the importance of the region for this process.

366 Predictive coding theory based interpretation of the OR has previously been
367 applied to results of experiments in which the participants were instructed to ignore the
368 stimuli (Bendixen et al., 2012, 2009; Winkler and Czigler, 2012; Winkler, 2007; Winkler
369 et al., 2009). For example, Bendixen et al. (2009) used repetition of a pair of tones with
370 150-ms ISI and found that the amplitude of the OR depended on the predictability of the
371 tones. This predictability-dependent difference was observed within 100 ms after
372 omission onset, suggesting the occurrence of stimulus-driven prediction. Our findings
373 can also be interpreted in light of this theory: in the present case, the prediction was
374 created by modulation from a higher cortical level, such as attentional modulation. The
375 latency difference of the OR between Bendixen et al (2009) and the present study may
376 reflect this difference in type of prediction. This explanation would be in line with that
377 of Bregman (1990), who suggested two mechanisms for perceptual grouping, a rapid
378 stimulus-driven mechanism and a slower mechanism based on higher cognitive
379 functions such as voluntary attention and/or experience-based knowledge. In light of the
380 predictive coding theory and Bregman's theory, the results of Bendixen et al (2009) may
381 reflect stimulus-driven prediction and pre-attentive perceptual grouping, while our
382 findings may reflect top-down prediction and attentive perceptual grouping.

383

384 *4.2 Impact of musical experience on perceptual grouping*

385 For omission in the regular sequence, musicians showed stronger activation in the left
386 STG than did nonmusicians, suggesting a stronger contribution of the left auditory
387 cortex in perceptual grouping. This result is in line with those of previous studies, which
388 have shown that the left hemisphere contributes to musical processing in musicians
389 during behavioral tasks (Bever and Chiarello, 1974; Burton et al., 1989; Messerli et al.,
390 1995) and neuroimaging studies (Boh et al., 2011; Evers et al., 1999; Hirshkowitz et al.,
391 1978; Matsui et al., 2013; Ono et al., 2011; Vuust et al., 2005). Left-hemisphere
392 dominance in analytical listening and right-hemisphere dominance in holistic listening
393 have been proposed, as has the idea that musicians' left hemisphere contribution to
394 auditory processing reflects an analytical listening strategy that differs from the holistic
395 listening strategy of nonmusicians (Bever and Chiarello, 1974; Burton et al., 1989;
396 Johnson, 1977; Messerli et al., 1995; Morais et al., 1982; Peretz and Morais, 1983).
397 Musical training generally includes the structural analysis of musical phrases as well as
398 practice with musical instruments. This training may induce analytical listening of tone
399 sequences, which may be reflected by the stronger activation in the left STG in
400 musicians than in nonmusicians.

401 While brain activity showed expertise effects, behavioral performance did not
402 show such effects. Although the reason for this incongruity is unclear, task demand may
403 be involved. Because the rate of correct detection was over 95 %, the task may have
404 been too easy for both musicians and nonmusicians, resulting in a ceiling effect. In this
405 case, it would have been difficult to find significant differences between the groups. A
406 more complicated task requiring more cognitive resources may have led to a significant
407 difference between musicians and nonmusicians at the behavioral level. Additionally,
408 the difference of listening strategy between musicians and nonmusicians may not have
409 led to differing performance in the detection task. Finally, the fact that all musicians
410 were amateurs may have contributed to the incongruity of the behavioral and MEG data.
411 Although we did not question the participants regarding the length of their musical
412 training per day or week, they were not trained as intensively as professional musicians.
413 This degree of musical training may have been insufficient to result in a behavioral
414 difference.

415 Another measure for which we did not find an effect of musical experience was
416 the tone-evoked response. This result is not surprising as the effects of musical
417 experience appear in a use-dependent manner (Lütkenhöner et al., 2006; Pantev et al.,
418 2001, 1998). For example, Pantev et al. (1998) found an increase in the N1 response to

419 piano tones in musicians that did not occur for pure tones. While piano tones are often
420 encountered in musical training, pure tones are rarely experienced. Thus, after long-term
421 musical training, more neurons may be involved in processing musical stimuli, while no
422 change may occur for the brain processing of pure tones.

423

424

425 *5. Conclusions*

426 In summary, the perceptual grouping of pitch pattern in a tone sequence affected the
427 processing of omissions in the sequence, both behaviorally and neurophysiologically.
428 Our findings are in general agreement with those of earlier work suggesting the
429 predictive nature of the auditory system. In addition, our results suggest that perceptual
430 grouping elicited higher predictability for tones in a regular sequence, allowing for the
431 faster detection of omissions, and also engaged the bilateral HG/STG in comparing the
432 prediction and stimulus. Musical experience also influenced the neural processing of
433 omissions, possibly reflecting a difference in listening strategy acquired through
434 long-term musical training.

435

436

437

Acknowledgements

438 The authors thank Ms. Yu Fukuda for her assistance with the programming of the
439 experiment and MEG measurement. This work was supported by the Japan Society for
440 the Promotion of Science (JSPS) KAKENHI Grant-in-Aid for Young Scientists (B)
441 (24730618) to K.O. The authors have no conflicts of interest to declare.

442

443

444

445

446

447

448

449

450

451

452

453

454

455

References

- 456 Alain, C., Richer, F., Achim, A., Saint Hilaire, J.M., 1989. Human intracerebral
457 potentials associated with target, novel, and omitted auditory stimuli. *Brain Topogr.*
458 1, 237–245.
- 459 Bendixen, A., SanMiguel, I., Schröger, E., 2012. Early electrophysiological indicators
460 for predictive processing in audition: a review. *Int. J. Psychophysiol.* 83, 120–131.
- 461 Bendixen, A., Schröger, E., Winkler, I., 2009. I heard that coming: event-related
462 potential evidence for stimulus-driven prediction in the auditory system. *J.*
463 *Neurosci.* 29, 8447–51.
- 464 Bever, T.G., Chiarello, R.J., 1974. Cerebral dominance in musicians and nonmusicians.
465 *Science* 21, 94–97.
- 466 Bhatara, A., Boll-Avetisyan, N., Unger, A., Nazzi, T., Höhle, B., 2013. Native language
467 affects rhythmic grouping of speech. *J. Acoust. Soc. Am.* 134, 3828–3843.
- 468 Boh, B., Herholz, S., Lappe, C., Pantev, C., 2011. Processing of complex auditory
469 patterns in musicians and nonmusicians. *PLoS One* 6, e21458.
- 470 Bregman, A., 1990. *Auditory scene analysis. The perceptual organization of sound.*
471 MIT Press, Cambridge MA.
- 472 Burton, A., Morton, N., Abbess, S., 1989. Mode of processing and hemisphere
473 differences in the judgement of musical stimuli. *Br. J. Psychol.* 80, 169–180.
- 474 Deutsch, D., 2012. *The psychology of music*, 3rd ed. Academic Press.
- 475 Dewar, K.M., Cuddy, L.L., Mewhort, D.J., 1977. Recognition memory for single tones
476 with and without context. *J. Exp. Psychol. Hum. Learn.* 3, 60–67.
- 477 Evers, S., Dannert, J., Rödding, D., Rötter, G., Ringelstein, E.B., 1999. The cerebral
478 haemodynamics of music perception. A transcranial Doppler sonography study.
479 *Brain* 122, 75–85.

- 480 Friston, K., 2005. A theory of cortical responses. *Philos. Trans. R. Soc. Lond. B. Biol.*
481 *Sci.* 360, 815–836.
- 482 Friston, K., Harrison, L., Daunizeau, J., Kiebel, S., Phillips, C., Trujillo-Barreto, N.,
483 Henson, R., Flandin, G., Mattout, J., 2008. Multiple sparse priors for the M/EEG
484 inverse problem. *Neuroimage* 39, 1104–20.
- 485 Friston, K., Kiebel, S., 2009a. Cortical circuits for perceptual inference. *Neural*
486 *Networks* 22, 1093–1104.
- 487 Friston, K., Kiebel, S., 2009b. Predictive coding under the free-energy principle. *Philos.*
488 *Trans. R. Soc. Lond. B. Biol. Sci.* 364, 1211–21.
- 489 Gobet, F., Simon, H.A., 1996. Recall of rapidly presented random chess positions is a
490 function of skill. *Psychon. Bull. Rev.* 3, 159–163.
- 491 Hirshkowitz, M., Earle, J., Paley, B., 1978. EEG alpha asymmetry in musicians and
492 non-musicians: A study of hemispheric specialization. *Neuropsychologia* 16,
493 125–128.
- 494 Hughes, H.C., Darcey, T.M., Barkan, H.I., Williamson, P.D., Roberts, D.W., Aslin,
495 C.H., 2001. Responses of human auditory association cortex to the omission of an
496 expected acoustic event. *Neuroimage* 13, 1073–1089.
- 497 Idson, W.L., Massaro, D.W., 1976. Cross-octave masking of single tones and musical
498 sequences: The effects of structure on auditory recognition. *Percept. Psychophys.*
499 19, 155–175.
- 500 Iversen, J.R., Patel, A.D., Ohgushi, K., 2008. Perception of rhythmic grouping depends
501 on auditory experience. *J. Acoust. Soc. Am.* 124, 2263–2271.
- 502 Johnson, P.R., 1977. Dichotically-stimulated ear differences in musicians and
503 nonmusicians. *Cortex* 13, 385–389.
- 504 Jones, M.R., Boltz, M., Kidd, G., 1982. Controlled attending as a function of melodic
505 and temporal context. *Percept. Psychophys.* 32, 211–218.
- 506 Joutsiniemi, S.-L., Hari, R., 1989. Omissions of auditory stimuli may activate frontal
507 cortex. *Eur. J. Neurosci.* 1, 524–528.

- 508 Koffka, K., 1935. Principles of Gestalt psychology. Hartcourt Brace, New York, NY.
- 509 Laird, A.R., Robinson, J.L., McMillan, K.M., Tordesillas-Gutiérrez, D., Moran, S.T.,
510 Gonzales, S.M., Ray, K.L., Franklin, C., Glahn, D.C., Fox, P.T., Lancaster, J.L.,
511 2010. Comparison of the disparity between Talairach and MNI coordinates in
512 functional neuroimaging data: validation of the Lancaster transform. *Neuroimage*
513 51, 677–683.
- 514 Lancaster, J.L., Tordesillas-Gutiérrez, D., Martinez, M., Salinas, F., Evans, A., Zilles,
515 K., Mazziotta, J.C., Fox, P.T., 2007. Bias between MNI and Talairach coordinates
516 analyzed using the ICBM-152 brain template. *Hum. Brain Mapp.* 28, 1194–1205.
- 517 Lütkenhöner, B., Seither-Preisler, A., Seither, S., 2006. Piano tones evoke stronger
518 magnetic fields than pure tones or noise, both in musicians and non-musicians.
519 *Neuroimage* 30, 927–937.
- 520 Matsui, T., Tanaka, S., Kazai, K., Tsuzaki, M., Katayose, H., 2013. Activation of the
521 left superior temporal gyrus of musicians by music-derived sounds. *Neuroreport* 24,
522 41–45.
- 523 Mattout, J., Phillips, C., Penny, W.D., Rugg, M.D., Friston, K.J., 2006. MEG source
524 localization under multiple constraints: an extended Bayesian framework.
525 *Neuroimage* 30, 753–767.
- 526 Messerli, P., Pegna, A., Sordet, N., 1995. Hemispheric dominance for melody
527 recognition in musicians and non-musicians. *Neuropsychologia* 33, 395–405.
- 528 Mondor, T.A., Terrio, N.A., 1998. Mechanisms of perceptual organization and auditory
529 selective attention: The role of pattern structure. *J. Exp. Psychol. Hum. Percept.*
530 *Perform.* 24, 1628–1641.
- 531 Morais, J., Peretz, I., Gudanski, M., 1982. Ear asymmetry for chord recognition in
532 musicians and nonmusicians. *Neuropsychologia* 20, 351–354.
- 533 Ono, K., Nakamura, A., Yoshiyama, K., Kinkori, T., Bundo, M., Kato, T., Ito, K., 2011.
534 The effect of musical experience on hemispheric lateralization in musical feature
535 processing. *Neurosci. Lett.* 496, 141–145.

- 536 Pantev, C., Oostenveld, R., Engelien, A., Ross, B., Roberts, L.E., Hoke, M., 1998.
537 Increased auditory cortical representation in musicians. *Nature* 392, 811–814.
- 538 Pantev, C., Roberts, L.E., Schulz, M., Engelien, A., Ross, B., 2001. Timbre-specific
539 enhancement of auditory cortical representations in musicians. *Neuroreport* 12,
540 169–174.
- 541 Pantev, C., Ross, B., Fujioka, T., Trainor, L.J., Schult, M., Schulz, M., 2003. Music and
542 learning-induced cortical plasticity. *Ann. N. Y. Acad. Sci.* 999, 438–450.
- 543 Penney, T.B., 2004. Electrophysiological correlates of interval timing in the
544 Stop-Reaction-Time task. *Brain Res. Cogn. Brain Res.* 21, 234–249.
- 545 Peretz, I., Morais, J., 1983. Task determinants of ear differences in melody processing.
546 *Brain Cogn.* 2, 313–330.
- 547 Raij, T., McEvoy, L., Mäkelä, J.P., Hari, R., 1997. Human auditory cortex is activated
548 by omissions of auditory stimuli. *Brain Res.* 745, 134–143.
- 549 Royer, F., Garner, W., 1970. Perceptual organization of nine-element auditory temporal
550 patterns. *Percept. Psychophys.* 7, 115–120.
- 551 Saariluoma, P., 1989. Chess player's recall of auditorily presented chess positions. *Eur.*
552 *Journal Cogn. Psychol.* 1, 309–320.
- 553 Shaffer, J., 1986. Modified sequentially rejective multiple test procedures. *J. Am. Stat.*
554 *Assoc.* 81, 826–831.
- 555 Simon, H.A., Chase, W.G., 1973. Skill in Chess. *Am. Sci.* 61, 394–403.
- 556 Snyder, J.S., Large, E.W., 2005. Gamma-band activity reflects the metric structure of
557 rhythmic tone sequences. *Brain Res. Cogn. Brain Res.* 24, 117–126.
- 558 Tarkka, I.M., Stokic, D.S., 1998. Source localization of P300 from oddball, single
559 stimulus, and omitted-stimulus paradigms. *Brain Topogr.* 11, 141–151.
- 560 Todorovic, A., van Ede, F., Maris, E., de Lange, F.P., 2011. Prior expectation mediates
561 neural adaptation to repeated sounds in the auditory cortex: an MEG study. *J.*
562 *Neurosci.* 31, 9118–9123.

- 563 Vuust, P., Pallesen, K.J., Bailey, C., van Zuijen, T.L., Gjedde, A., Roepstorff, A.,
564 Østergaard, L., 2005. To musicians, the message is in the meter pre-attentive
565 neuronal responses to incongruent rhythm are left-lateralized in musicians.
566 *Neuroimage* 24, 560–564.
- 567 Wacongne, C., Labyt, E., van Wassenhove, V., Bekinschtein, T., Naccache, L., Dehaene,
568 S., 2011. Evidence for a hierarchy of predictions and prediction errors in human
569 cortex. *Proc. Natl. Acad. Sci. U. S. A.* 108, 20754–20759.
- 570 Winkler, I., 2007. Interpreting the Mismatch Negativity. *J. Psychophysiol.* 21, 147–163.
- 571 Winkler, I., Czigler, I., 2012. Evidence from auditory and visual event-related potential
572 (ERP) studies of deviance detection (MMN and vMMN) linking predictive coding
573 theories and perceptual object representations. *Int. J. Psychophysiol.* 83, 132–143.
- 574 Winkler, I., Denham, S.L., Nelken, I., 2009. Modeling the auditory scene: predictive
575 regularity representations and perceptual objects. *Trends Cogn. Sci.* 13, 532–540.
- 576 Yabe, H., Tervaniemi, M., Reinikainen, K., Näätänen, R., 1997. Temporal window of
577 integration revealed by MMN to sound omission. *Neuroreport* 8, 1971–1974.
- 578 Yabe, H., Winkler, I., Czigler, I., Koyama, S., Kakigi, R., Sutoh, T., Hiruma, T.,
579 Kaneko, S., 2001. Organizing sound sequences in the human brain: the interplay of
580 auditory streaming and temporal integration. *Brain Res.* 897, 222–227.
- 581
- 582
- 583
- 584
- 585
- 586
- 587

588

Legends

589 *Fig. 1*

590 Sequence of stimuli and behavioral performance in the detection task. **A.** Sequence of
591 stimuli used in the experiment. In the regular sequence, C, E, and G tones were
592 presented as a repetition of a CEG pattern, whereas in the irregular sequence the tones
593 were presented pseudo-randomly. **B.** Reaction time in the detection task. Error bars
594 display the standard error of the mean (SEM). M = musicians; NM = nonmusicians. **C.**
595 Examples of the magnetoencephalography (MEG) waveform evoked by the omission of
596 the C tone in the irregular sequence for one musician. Waveforms from 20 gradiometers
597 that covered the temporal lobe in each hemisphere were superimposed.

598

599 *Fig. 2*

600 Time course of the root mean square (RMS) amplitude of the omission-related response
601 (OR). **A.** RMS amplitude of the OR in musicians. **B.** RMS amplitude of the
602 omission-related response in nonmusicians.

603

604 *Fig. 3*

605 RMS amplitude of the brain response evoked by the omission between 100 and 400 ms

606 after omission onset. The asterisks represent $p < 0.001$.

607

608 *Fig. 4*

609 Reconstructed maps showing significantly activated brain areas and the results of the
610 three-way analysis of variance (ANOVA) with the factors musical experience, regularity,
611 and position of omission. **A.** Visualization of the brain areas significantly activated
612 between 100 and 400 ms after sound omission in the regular and irregular sequences, as
613 determined by one-sample t tests (uncorrected $p < 0.005$). **B.** Brain areas showing a
614 main effect of regularity in the three-way ANOVA for the time windows from 100 to
615 200 ms and from 200 to 300 ms (uncorrected $p < 0.001$). **C.** Brain areas showing an
616 interaction between musical experience and regularity in the three-way ANOVA for the
617 time windows from 100 to 200 ms and from 200 to 300 ms (uncorrected $p < 0.001$). L =
618 left; R = right.

619

620 *Fig. 5*

621 Mean amplitude of the region of interest (ROI) activity. The ROI was located in the left
622 superior temporal gyrus (STG), which was defined by the brain area showing the
623 interaction between musical experience and regularity in the three-way ANOVA for the

624 time windows from 100 to 200 ms and from 200 to 300 ms (Fig. 4C). M = musicians;

625 NM = nonmusicians. A.U. = arbitrary unit.

Figure01

[Click here to download high resolution image](#)

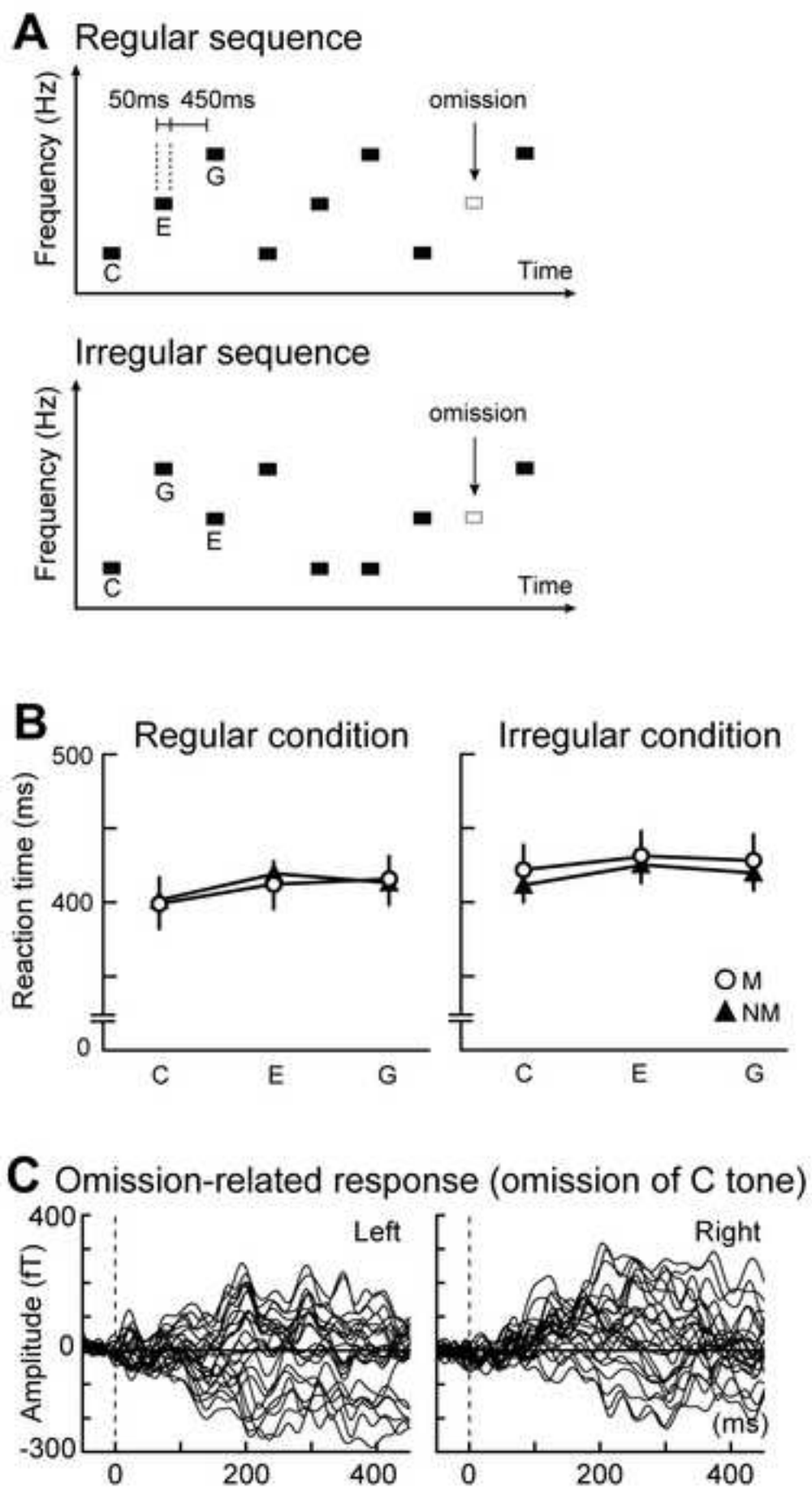


Figure02

[Click here to download high resolution image](#)

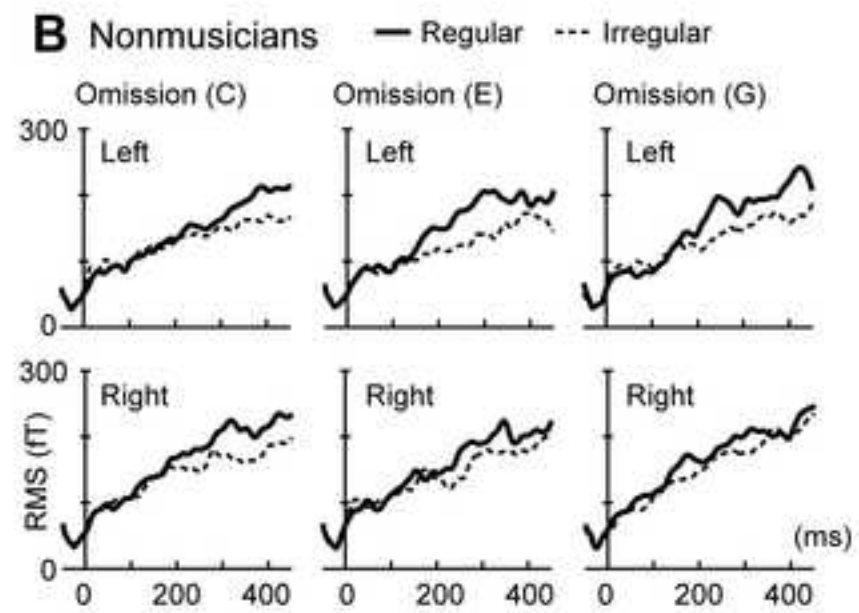
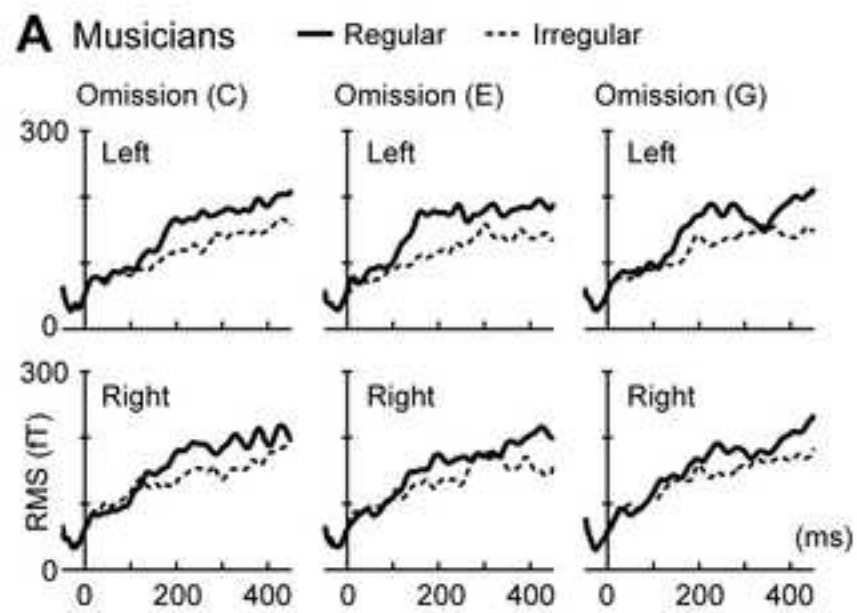
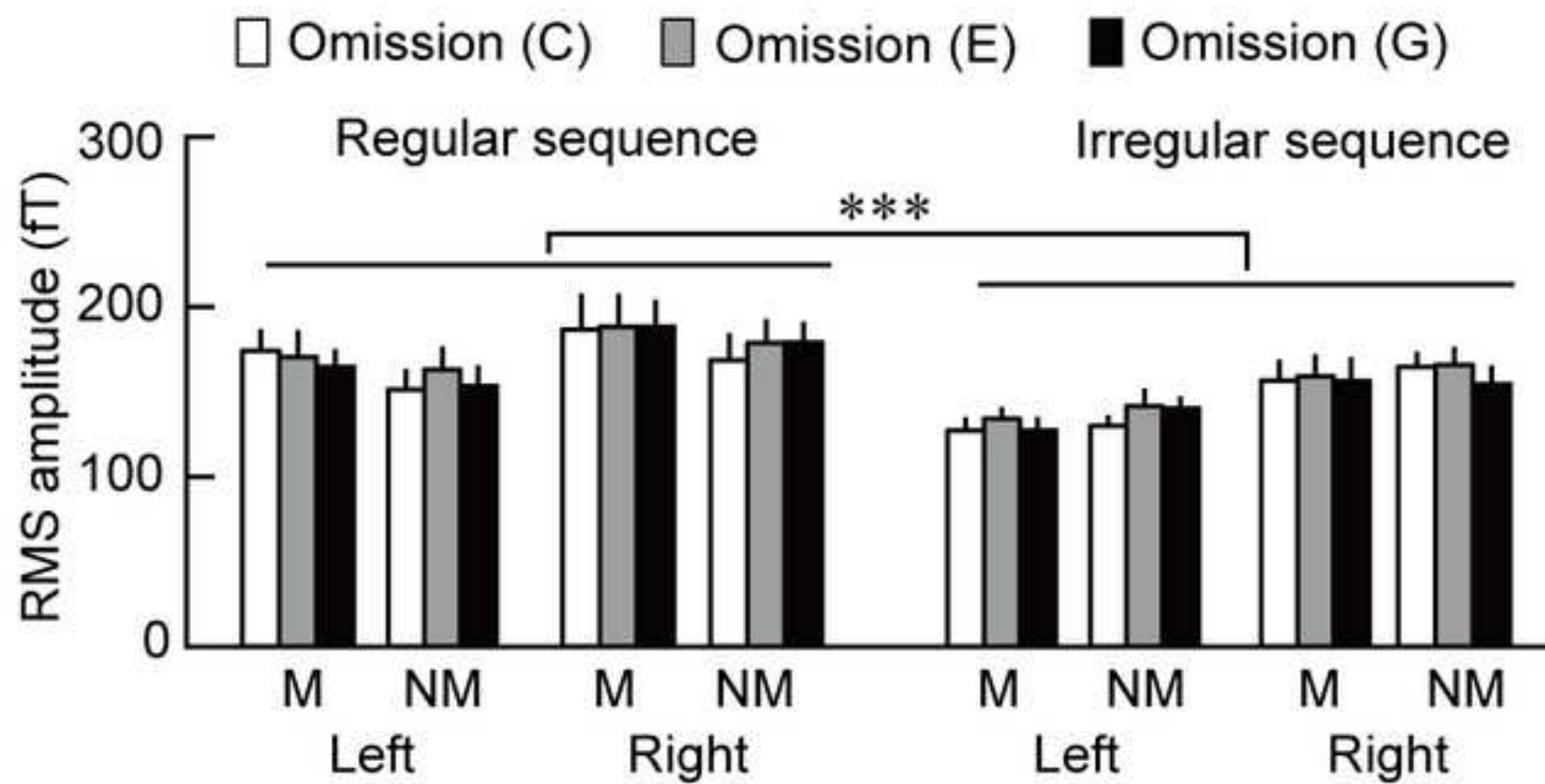
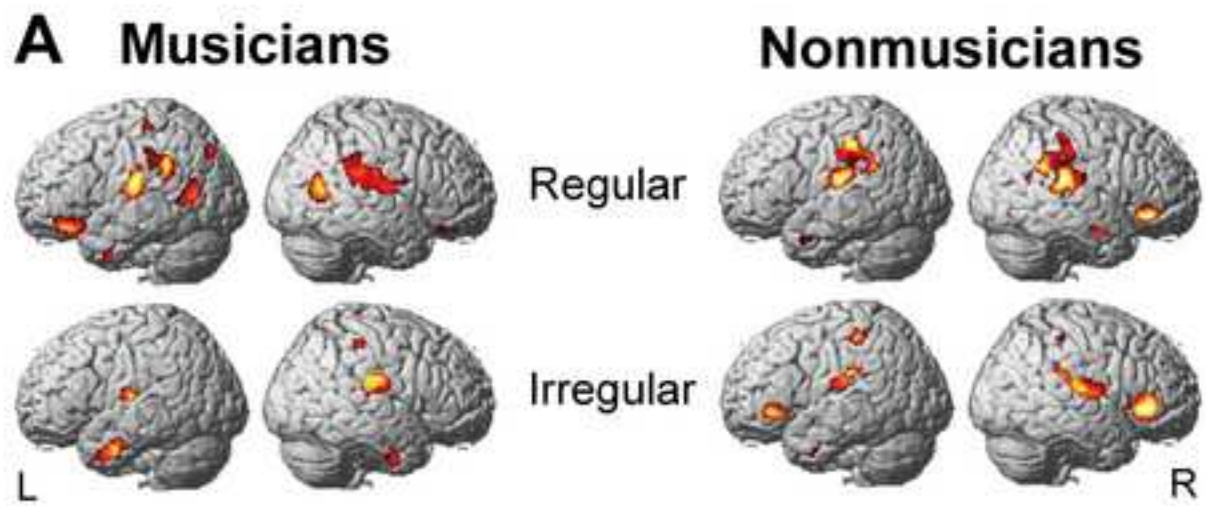


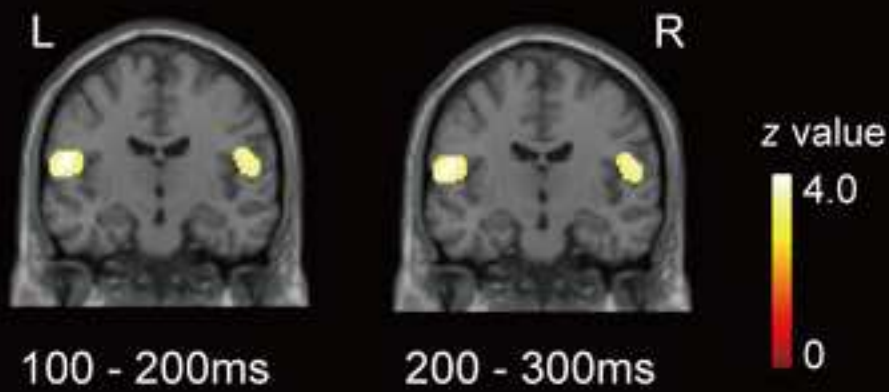
Figure03

[Click here to download high resolution image](#)





B Main effect of regularity (Regular > Irregular)



C Interaction between experience and regularity

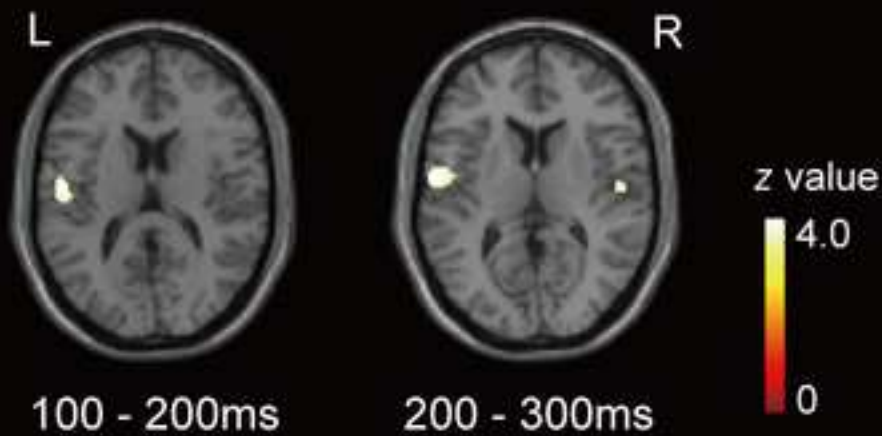


Figure05

[Click here to download high resolution image](#)

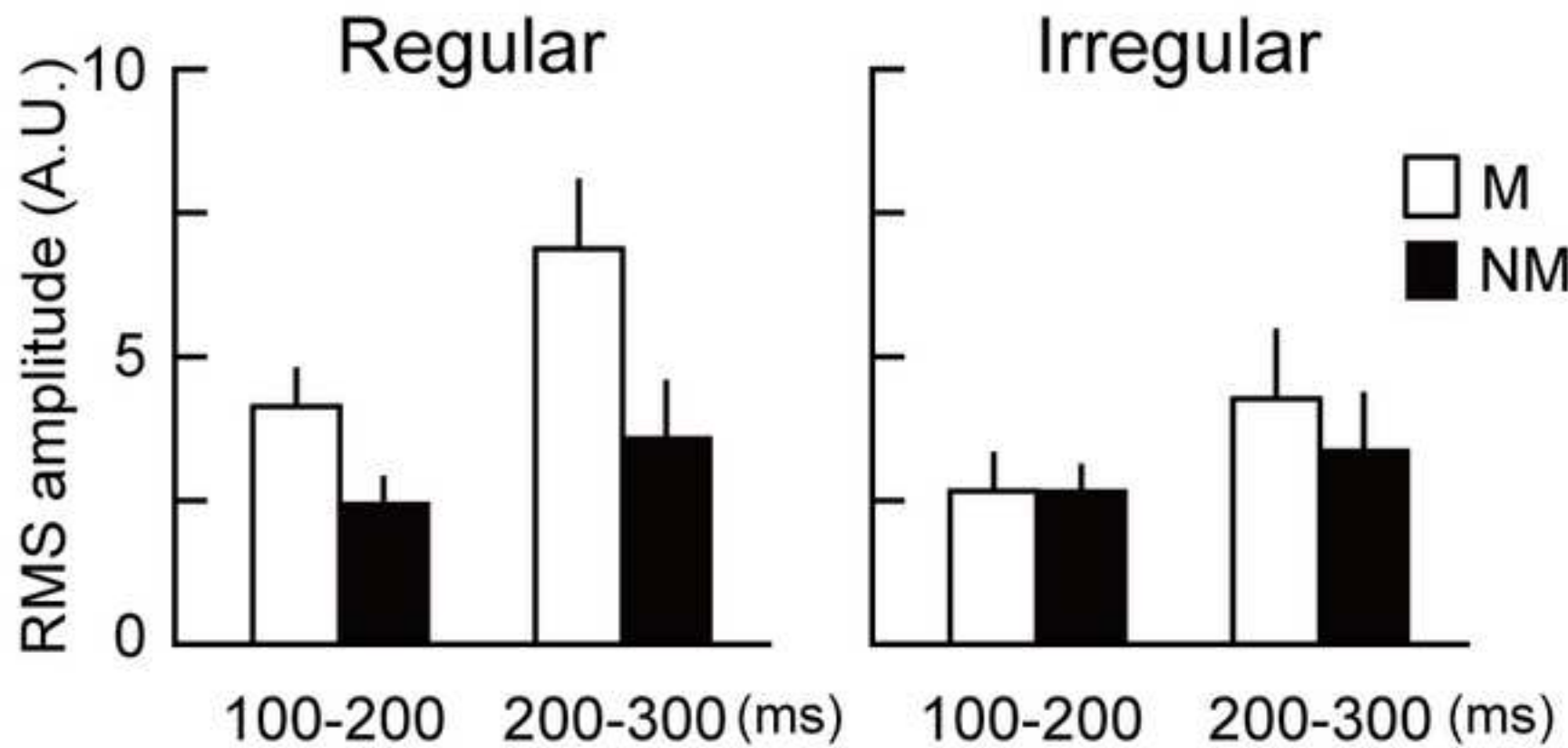


Table 1

Peak coordinates of significantly activated areas for each 100-ms time window in the three-way ANOVA with factors musical experience, regularity, and position of the omission (uncorrected $p < 0.001$).

Brain area (Brodmann's Area [BA])	Peak coordinates (x, y, z)			Number of voxels	z value
100-200 ms					
<i>Main effect of regularity (Regular > Irregular)</i>					
Left Heschl's gyrus [BA41]	-51	-16	13	426	3.87
Right postcentral gyrus [BA43]	48	-12	18	57	3.30
<i>Interaction of musical experience and regularity</i>					
<i>([Regular – Irregular] in musicians > [Regular - Irregular] in nonmusicians)</i>					
Left Heschl's gyrus [BA41]	-51	-16	13	142	3.51
200-300 ms					
<i>Main effect of regularity (Regular > Irregular)</i>					
left superior temporal gyrus [BA22]	-53	-11	8	561	4.06
right superior temporal gyrus [BA22]	50	-12	9	328	3.66
<i>Interaction of musical experience and regularity</i>					

([Regular – Irregular] in musicians > [Regular - Irregular] in nonmusicians)

left superior temporal gyrus [BA22]	-55	-7	6	209	3.43
-------------------------------------	-----	----	---	-----	------
