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Double dissociation between rules and memory in music: An event-related potential study

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Abstract

Language and music share a number of characteristics. Crucially, both domains depend on both rules and memorized representations. Double dissociations between the neurocognition of rule-governed and memory-based knowledge have been found in language but not music. Here, the neural bases of both of these aspects of music were examined with an event-related potential (ERP) study of note violations in melodies. Rule-only violations consisted of out-of-key deviant notes that violated tonal harmony rules in novel (unfamiliar) melodies. Memory-only violations consisted of in-key deviant notes in familiar well-known melodies; these notes followed musical rules but deviated from the actual melodies. Finally, out-of-key notes in familiar well-known melodies constituted violations of both rules and memory. All three conditions were presented, within-subjects, to healthy young adults, half musicians and half non-musicians. The results revealed a double dissociation, independent of musical training, between rules and memory: both rule violation conditions, but *not* the memory-only violations, elicited an early, somewhat right-lateralized anterior-central negativity (ERAN), consistent with previous studies of rule violations in music, and analogous to the early left-lateralized anterior negativities elicited by rule violations in language. In contrast, both memory violation conditions, but *not* the rule-only violation, elicited a posterior negativity that might be characterized as an N400, an ERP component that depends, at least in part, on the processing of representations stored in long-term memory, both in language and in other domains. The results suggest that the neurocognitive rule/memory dissociation extends from language to music, further strengthening the similarities between the two domains.

Language and music share a range of characteristics (Besson and Schön, 2001, Maess et al., 2001, Patel, 2003, Koelsch, 2005). Of particular interest here, both domains crucially rely on both rules and memorized representations. In both language and music, higher-order structures (e.g., sentences and melodies) are made up of basic units (e.g., words and notes) that are arranged in a rule-governed hierarchical configuration. Language and music also both depend on long-term memorized representations that are at least partly idiosyncratic, that is, not entirely derivable from rules. For example, in language one must memorize various types of lexical knowledge, such as the sequence of phonemes /c/, /a/, and /t/ and that this refers to a furry, four-legged animal, as well as the fact that the combination of words “let the cat out of

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the bag" means "disclose a secret." Likewise in music, a familiar tune must be memorized as a particular sequence of notes and rhythms.

The neurocognition of this rule/memory distinction has been well-studied in language but not in music. In language, evidence suggests that the two capacities rely on at least partially distinct neural bases. Double dissociations between rules and memory have been found using a variety of empirical approaches, including lesion studies of patients (Damasio, 1992, Goodglass, 1993, Ullman et al., 1997), neuroimaging (Newman et al., 2001, Friederici et al., 2003b), and event-related potentials (ERPs) (De Vincenzi et al., 2003, Sanders and Neville, 2003, Friederici et al., 2004).

ERPs have been particularly revealing. Violations of grammatical rules, e.g., in syntactic phrase structure or morpho-syntax, often elicit a "biphasic" pattern of ERPs. Initial negativities, generally found around 150–200 or 300–500 ms, and commonly referred to as (early) left anterior negativities – (E)LANs – due to their typical scalp distribution, are followed by later positivities (500–1000 ms), often called P600s due to their positivity and typical onset latency (Neville et al., 1991, Friederici et al., 1996, Coulson et al., 1998). LANs seem to be automatic, have been linked to aspects of grammatical structure building, and appear to depend at least in part on left frontal lobe structures (Hahne and Friederici, 1997, Friederici et al., 1998, Friederici et al., 1999b, Hagoort and Brown, 2000, Newman et al., 2007). The late positivities, by contrast, have a central-posterior distribution, seem to be controlled rather than automatic, have been implicated (at least in part) in aspects of syntactic integration, and appear to involve left temporal/temporo-parietal structures and the basal ganglia (Osterhout and Holcomb, 1992, Hahne and Friederici, 1997, Friederici et al., 1998, Kaan et al., 2000, Friederici, 2002, Friederici et al., 2003a).

Lexical-conceptual processing generally elicits bilateral central-to-posterior negativities known as N400s, which typically occur from about 250 to 500 ms post-stimulus (Kutas and Hillyard, 1980, Friederici et al., 1999a, Kutas and Federmeier, 2000, Hinojosa et al., 2001, Laurent et al., 2006). N400s seem to reflect one or more possibly related processes, including access to representations in long-term memory (thus the component is modulated by the frequency of the stimulus) and contextual integration, that is, the integration of the given stimulus with the current context held in working memory and with established long-term knowledge (Kutas and Federmeier, 2000). For example, reading or hearing a word that does not match the preceding context and long-term knowledge (e.g., "*He shaved off his moustache and city*.") elicits an N400, as would seeing a picture of a city or hearing a sound of a car horn honking following the same sentence fragment (Van Petten and Rheinfelder, 1995, McPherson and Holcomb, 1999, Kutas and Federmeier, 2000, Federmeier and Kutas, 2001). Based on findings from patient, neuroimaging, and intracranial recording studies, N400s seem to reflect activity in multiple brain areas, including temporal neocortex, ventrolateral prefrontal areas, and medial temporal lobe structures, including the hippocampus (Kutas and Federmeier, 2000).

ERP studies of rule violations in music have yielded results intriguingly similar to those found in language. In a series of musical chords, harmonically inappropriate or dissonant chords generally elicit anterior negativities in a similar time window (about 150 to 280 ms) as some of the earlier LANs (i.e., ELANs) found in language studies (Verleger, 1990, Paller et al., 1992, Patel et al., 1998, Koelsch et al., 2000, Koelsch et al., 2002b, Koelsch et al., 2002c, Loui et al., 2005, Leino et al., 2007). However, whereas the negativities elicited by rule violations in language are generally left lateralized, those elicited by rule violations in music are usually right lateralized, or sometimes bilateral – hence the term early (right) anterior negativity, or E(R)AN – and have been linked to frontal lobe structures in both hemispheres (Maess et al., 2001, Koelsch et al., 2002a).

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Later bilateral or right-lateralized anterior negativities (N5s/Late Negativities – 450–1500 ms) have also been elicited by the same types of rule violations in music (Koelsch et al., 2000, Koelsch et al., 2002b, Koelsch et al., 2002c, Loui et al., 2005). Although it has been suggested that these negativities may be similar to the N400s found in language studies, reflecting musical "meaning" conveyed by the violations (Koelsch, 2005), the fact that they have an anterior scalp distribution and are elicited by rule-based violations suggests that they might also or instead be related to rule processing. Finally, musical rule violations also typically elicit late central to posterior positivities, in both melodies (Verleger, 1990, Paller et al., 1992, Besson and Faïta, 1995) and chord sequences (Patel et al., 1998, Koelsch et al., 2000, Regnault et al., 2001, Koelsch et al., 2002c). Interestingly, the later anterior negativities seem to be observed only (though not always; Steinbeis et al., 2006) when subjects do not attend to the violations (Koelsch et al., 2000, Koelsch et al., 2002b, Koelsch et al., 2002c, Loui et al., 2005), resulting in the reduction of the temporally overlapping late positivities that may mask the negativities due to additivity effects (Paller et al., 1992, Besson and Faïta, 1995, Koelsch et al., 2002c).

In contrast, the processing of idiosyncratic, non-rule-based, aspects of long-term memorized representations has not been well studied in music. In particular, we are aware of no ERP studies examining this issue. Moreover, to our knowledge, N400s have not been directly elicited by music in any studies. Note that although one study investigated in-key note ("diatonic") violations in melodies, these notes actually appeared to violate musical rules, for example, non-tonic notes following leading notes (Besson and Faïta, 1995, Besson and Schön, 2001). Indeed, in a separate group of subjects, these violations in *unfamiliar* melodies were detected 46% of the time by musicians and 31% of the time by non-musicians, suggesting that at least some of these notes violated non-memory-based aspects of the melodies. Interestingly, the "diatonic" violations, as well as out-of-key note ("non-diatonic") violations, appeared to elicit negativities between 200–400 ms in *familiar* melodies but not in unfamiliar melodies. However, these negativities were only shown in the figures and not reported in the text, and were immediately followed by large positivities that may have masked the negativites in later time windows due to additivity effects. It is thus unclear whether or not these negativities were related to N400s.

Despite the fact that N400s have not clearly been elicited by note violations in familiar melodies, neuroimaging studies have revealed that a similar network of brain areas is involved in processing memorized aspects of both music and language. For instance, semantic judgments of single words (Friederici et al., 2000, Booth et al., 2002, Pilgrim et al., 2002, Chou et al., 2006) and of idioms or metaphors (Rapp et al., 2004, Eviatar and Just, 2006, Zempleni et al., 2007) have been linked to activation of left or bilateral temporal/temporo-parietal regions, including Brodmann's areas (BA) 20 and 21, as well as left or bilateral anterior ventro-lateral prefrontal cortex (BA 45/47). The processing of semantic anomalies has additionally been linked to activation of medial temporal lobe structures, namely the hippocampus and parahippocampal gyrus (Newman et al., 2001). Each of these brain regions has also been activated during familiarity judgments of music, or while processing familiar as compared to unfamiliar melodies (Platel et al., 1997, Platel et al., 2003, Satoh et al., 2006, Plailly et al., 2007), suggesting at least partly overlapping neural substrates involved in processing memorized aspects of both music and language.

In the present ERP study we examine the rule/memory contrast in music within subjects. Two types of note violations were examined in the same set of well-known melodies, as well as in matched novel melodies. "In-key" deviant notes in well-known melodies were appropriate with respect to musical rules but differed from the actual melody, thus serving as memory-based violations in well-known but not novel melodies. "Out-of-key" deviant notes violated rules of musical tonality. In novel melodies, out-of-key notes served solely as rule violations, whereas in well-known melodies, the notes violated both rules *and* memory. To ensure that each subject was actually familiar with each well-known melody, only those well-known melodies that that

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particular subject rated as familiar and novel melodies rated as unfamiliar in a separate test session were included for analysis. To reduce the attention-related late positivity, subjects were not informed of the in-key and out-of-key violations, but instead made responses about the timbre of the last note in each melody. We predicted a double dissociation between rule and memory violations: ERANs for rule violations but not for purely memory violations, and N400s for memory violations but not for purely rule violations. Finally, to probe whether these effects vary according to musical training, we included musical training as a factor in the experimental design: half the subjects were musicians and half were non-musicians.

Methods

Participants

We tested 64 adult (32 male, 32 female) monolingual native speakers of American English. Because knowledge of the well-known melodies in this study is largely culturally dependent, none of the subjects had lived outside the United States for more than six months before the age of 18. None of the subjects had any known developmental, neurological, or psychiatric disorders, and all had normal or corrected hearing and vision. Half the subjects (16 male, 16 female) were musicians, having at least 5 years of musical training, and half (16 male, 16 female) were non-musicians, with one year or less of musical training. Musical training was defined as private instrument or voice lesions, or participation in a musical ensemble such as band, orchestra, or chorus. Due to ERP data loss from extensive noise, one female non-musician was excluded, and a new female non-musician was tested in her place. All subjects were right-handed (Oldfield, 1971). Familial sinistrality, defined as one or more left-handed or ambidextrous individuals among biological parents or full siblings, was matched across musicians (4 males, 5 females) and non-musicians (4 males, 5 females). The musicians and non-musicians did not differ in age (musicians: mean=22.8 years, SE=0.7; non-musicians: mean=22.5, SE=0.6; $t(62)=0.39$, $p=0.699$) or education (musicians: mean=15.9 years, SE=0.5; non-musicians: mean=15.6, SE=0.4; $t(62)=0.50$, $p=0.617$). As expected, the musicians had significantly more years of musical training than the non-musicians (musicians: range 5–24 years, mean=10.6, SE=0.8; non-musicians: range 0–1 years, mean=0.3, SE=0.1; $t(31)=13.73$, $p<0.001$). Research methods were approved by the Institutional Review Board at Georgetown University. All subjects gave written informed consent and received monetary compensation for their participation.

Stimuli

The stimuli consisted of 240 melodies, which ranged from 5.0 to 18.0 seconds in length (mean = 9.8 seconds), and contained between 10 and 36 notes (mean = 17.8 notes). The melodies were created in MIDI format, using Finale Version 3.5.1 (Coda Music), and were then converted to WAV files with a “grand piano” Sound Font, using MidiSyn Version 1.9 (Future Algorithms). All melodies were in the key of C-major or A-minor, whose natural minor scale contains the same notes as the C-major scale. Half of the melodies (120) were segments from well-known tunes, including traditional, folk, children’s, patriotic, holiday, classical, and “pop” music, as well as themes from movies, television, and Broadway musicals (for a full list of the well-known melodies, see Appendix). The other half (120) were novel melodies composed by one of the authors (Miranda). Each novel melody was exactly matched to one of the 120 well-known melodies with respect to tempo, length, and implied harmony. To minimize the potential of subjects falsely recognizing the novel melodies as their matched well-known melodies, distinctive rhythms in some of the novel melodies were slightly altered.

Three versions of each well-known and novel melody were created: *control*, *in-key violation*, and *out-of-key violation* (Fig. 1). The control melodies (the original versions) contained no violations. Each melody with an in-key violation contained one note that differed

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from its corresponding control melody. The in-key violation notes never violated rules of musical tonality/harmony, and did not constitute abnormal pitch intervals with the preceding or following note. For listeners familiar with a given well-known melody, however, the in-key deviant note violated the memorized sequence of notes. In contrast, the in-key "deviant" notes in novel melodies did not constitute such violations, since the note sequences in these melodies had presumably not been previously encountered, and thus should not have been memorized. Each out-of-key violation melody contained a harmonically deviant note, that is, a note that violated the implicit harmony at that point in the melody. Therefore, out-of-key deviant notes constituted violations of musical rules in both well-known and novel melodies, as well as violations of the memorized note sequences in familiar well-known melodies.

Thus the stimuli consisted of 120 pairs of well-known/novel melodies, with control, in-key violation and out-of-key violation conditions for each. Within each set of six matched conditions (well-known/novel melody pairs in control, in-key, and out-of-key versions), the target notes – i.e., the deviant notes or corresponding control notes – occurred at the same time relative to the onset of the melodies. Moreover, the note(s) within an interval of 600 ms immediately preceding and following the target notes were the same in all six conditions. All target notes were 600 ms in length and had the same pitch across each well-known/novel pair of control, in-key and out-of-key conditions. In a majority of the melodies (103 out of the 120 sets), the target note was equivalent to a quarter note in a 4/4 or 3/4 time signature. These 103 melodies were presented at a tempo of 100 beats per minute. In the 17 remaining sets of melodies, the target note was equivalent to a quarter note in 6/8 time (9 melodies) or a dotted quarter note in 4/4 or 3/4 time (8 melodies), and were presented at a tempo of either 66.7 or 150 beats per minute, respectively. To increase the likelihood that subjects would be familiar with each well-known melody before the onset of the target note, each target note began after the mean recognition time for the melody in which it occurred, based on response times for familiar-rated melodies from a previous behavioral study (Wood and Ullman, 2005, Miranda and Ullman, Under Review).

In 25% of the melodies the final note was a timbre deviant. For these melodies, the timbre of the last note was altered using the "Wahwah Effect" in Audacity Version 1.2.0, resulting in a muffled piano sound. For each melody containing a timbre deviant, the corresponding melodies in each of the remaining five conditions also contained the same timbre deviant. To prevent overlap between ERP responses to the timbre deviants and the target notes of interest, the onset of each timbre deviant occurred at least 1200 ms after the onset of the preceding in-key, out-of-key, or control target note.

Counterbalancing and presentation order

In the previous behavioral study we found that novel melodies were rated as more familiar when they were heard after, as compared to before, their well-known counterparts (Wood and Ullman, 2005). In contrast, no such priming effects were found for well-known melodies that followed their matched novel melodies. To avoid any such well-known-to-novel priming effects in the present study, novel melodies were always presented before their well-known counterparts. To counterbalance the stimuli appropriately, and to satisfy various constraints, including that novel melodies had to occur before their well-known counterparts, the items were presented in the following manner. Each subject completed three experimental runs, with each run containing 60 different melodies that were presented in equal proportions (10 each) across each of the six conditions (well-known and novel melodies, in control, in-key, out-of-key conditions). Thus, each subject heard a total of 180 melodies – 30 melodies in each of the six conditions. To avoid the previously observed priming effects, the 30 well-known melodies in the first run were not followed by their corresponding novel melodies in the subsequent runs. Likewise, the 30 novel melodies in the third run were not preceded by their corresponding

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well-known melodies. For the 60 novel melodies in the first and second runs that were followed by their 60 corresponding well-known melodies in the second and third runs, respectively, the matched well-known and novel melodies were presented in different control/violation conditions. With this design, all six conditions of the 120 well-known/novel melody pairs (that is, 720 melody versions) were presented once across every four subjects (within musicians or non-musicians, balanced across males and females), with the presentation order counterbalanced across the four subjects. The melodies in each run were presented in a different pseudo-random order for each subject, with restrictions on the number of each melody type (well-known vs. novel), violations, and timbre deviants that could occur in a row.

Procedure

Subjects were seated 70 cm from a 16 inch CRT monitor in a dark quiet testing room. The melodies were presented via ER-4 insert earphones (Etymotic Research) at approximately 70 dB. Five hundred milliseconds prior to each melody, a fixation cross appeared in the center of the screen. The cross remained until the end of the melody, when it was replaced by the words “Same” and “Different”, which remained until the subject responded by pressing either the left or right mouse button, respectively. Prior to the experimental session, subjects were instructed to listen to each melody and determine whether the “sound quality” (i.e., timbre) of the final note was the same or different as that of the preceding notes. Subjects were not informed about the in-key and out-of-key violations. Each subject was given a practice session containing 12 different melodies, which were presented in equal proportions (2 each) across the six experimental conditions. Three of the practice melodies (25%) contained timbre deviants. Visual feedback (“Correct” or “Incorrect”) was given in the practice session, but not in the subsequent experimental session.

Follow-up Behavioral Assessments

To test each subject’s familiarity with the melodies s/he had been presented with, all subjects returned (after 1 to 7 days) for a follow-up behavioral test session. Each subject was presented with the control versions (with no timbre deviants) of the 180 well-known and novel melodies that had been presented to that particular subject in the ERP experiment. To ensure that the behavioral measures reflected the subject’s familiarity of each melody prior to the target note in the ERP study, melodies were presented only up to and not including the target note. The runs were presented to each subject in the same order as in the ERP study, although the melodies within each run were presented in a new pseudo-randomized order, with the same ordering restrictions as described above. After listening to each melody, subjects were prompted to rate their familiarity with the melody on a scale from 1 to 5, with a rating of “1” indicating “very unfamiliar,” and a rating of “5” indicating “very familiar.” Prior to presentation of the melodies, subjects were instructed to base their familiarity ratings on how familiar they were with each melody before participating in the ERP session. These ratings were then used to identify “familiar” melodies (well-known melodies rated 4 or 5) and “unfamiliar” melodies (novel melodies rated 1 or 2) for each subject, for inclusion in the ERP analyses (see below). Differences in behavioral results between musicians and non-musicians were analyzed using two-tailed t-tests (SPSS 15.0).

EEG Recordings, Pre-Processing, and Analysis

Scalp EEG was continuously recorded in DC mode at a sampling rate of 500 Hz from 64 electrodes mounted in an elastic cap (Electro-Cap International) and referenced to the left mastoid. Impedance at each scalp electrode was reduced to 5kΩ or below. The EEG was amplified by Neuroscan SynAmps^2 amplifiers, and filtered on-line with a band-pass filter (DC to 100 Hz, 24-dB/octave attenuation). Electrodes were also placed above and below the right eye and on the outer canthi of both eyes to measure vertical and horizontal eye movements and

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eye-blinks. Off-line, the EEG was re-referenced to the average of the left and right mastoids, and filtered with a band-pass filter (0.1 to 40 Hz, 24-dB/octave attenuation). Eye-blinks (determined by reference to vertical EOG) were removed from the raw EEG using an ocular artifact reduction algorithm in SCAN 4.3.3 (Compumedics Neuroscan). Trials (the EEG from 200 ms before to 1000 ms after the onset of the target note) containing additional artifacts exceeding 100 Hz at any given scalp electrode were excluded from analysis.

ERPs time-locked to the onset of each target note were averaged by condition type for each subject at each electrode site, using a 200-ms pre-stimulus baseline. For each violation and control condition, the computation of ERP averages for each subject was restricted to either well-known melodies that the given subject rated in the follow-up behavioral session as “familiar” (given a familiarity rating of 4 or 5) or novel melodies that were rated as “unfamiliar” (given a familiarity rating of 1 or 2). These correctly rated melodies will henceforth be referred to as “familiar” and “unfamiliar” melodies.

ERPs were statistically evaluated over nine regions of interest (ROIs; Fig. 2): left anterior (F1, F3, F5, F7, FF1, FF3, FP3), right anterior (F2, F4, F6, F8, FF2, FF4, FP4), midline anterior (FZ), left central (C1, C3, C5, T3), right central (C2, C4, C6, T4), midline central (CZ), left posterior (P1, P3, P5, T5, PO3, TO1, O1), right posterior (P2, P4, P6, T6, PO4, TO2, O2), and midline posterior (POZ).

Mean amplitudes for each condition were computed for appropriate time windows for each ERP component of interest. The time windows were selected on the basis of previous research and visual inspection of the grand averages across all conditions that showed the component in question. Visual inspection of the waveforms suggested that the time windows for each component were similar across all conditions showing the component.

Repeated measures ANOVAs were performed on each time window (SAS 9.1). In all cases the Huynh-Feldt correction was applied to account for the violation of sphericity assumption. The threshold for significance used in all analyses was $p \leq 0.05$ (two-tailed). Separate ANOVAs were performed for lateral and midline ROIs. For the sake of simplicity, and because results were always similar for lateral and midline ROIs, only analyses on lateral ROIs are reported here, unless the ERP component under investigation was clearly larger over the midline than lateral sites, in which case only midline analyses are reported.

For each of the four violation/control contrasts (unfamiliar in-key, unfamiliar out-of-key, familiar in-key, and familiar out-of-key), each time window for which visual inspection suggested a component of interest was analyzed with three levels of analysis. These analyses allowed us to identify the ROIs in which the component was most prominent, and to reveal any musician/non-musician differences.

In the first-level analyses, the ANOVAs on the lateral ROIs included four factors: Violation (2 levels: violation vs. control), Hemisphere (2 levels: left vs. right), Anterior/Posterior (3 levels: anterior, central, and posterior), and Musical Training (2 levels: musicians vs. non-musicians). ANOVAs on the midline ROIs included three of these factors (Violation, Anterior/Posterior, and Musical Training). Only interactions between Violation and one or both scalp-distribution factors (Hemisphere, Anterior/Posterior) were included in these models. The mean ERP amplitude for each condition in the time window constituted the dependent measure.

Any significant interactions were followed up with the second-level analyses, which included only those factors in the interaction, and allowed us to identify the set of ROIs in which the effect was most prominent (the “area of activation”).

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This area of activation was examined with third-level analyses that included Musical Training as well as relevant scalp-distribution factors, allowing us to examine possible effects of these factors on the component of interest, while avoiding interference from temporally-overlapping components with other areas of activation.

Finally, after all components had been analyzed in each contrast, we further examined each component of interest by directly comparing the different violation/control contrasts in which the component had been found. The difference waves (the difference of the mean amplitudes of the two contrasted conditions) of the relevant violation/control contrasts constituted the dependent measure in these ANOVAs, which included the factors Hemisphere, Musical Training and Violation Condition (up to three levels: unfamiliar out-of-key, familiar in-key, familiar out-of-key), or just Musical Training and Violation Condition for midline analyses. All main effects and interactions (not just those including Violation Condition) were included, allowing us to examine effects of Hemisphere and Musical Training across violation conditions.

Results

Behavioral Results

In the ERP experiment, subjects accurately judged the presence (mean=97.4%, SE=1.2%) and absence (mean=98.1%, SE=0.60%) of timbre violations, with no significant differences between musicians and non-musicians (*P*s>0.09). In the follow-up behavioral session, the familiarity ratings of the well-known melodies (mean=4.23, SE=0.06) differed between musicians (mean=4.44, SE=0.06) and non-musicians (mean=4.02, SE=0.09; $t(52)=3.76$, $p<0.001$), whereas the ratings of novel melodies (mean = 1.49, SE = 0.04) did not (musicians: mean=1.47, SE=0.05; non-musicians: mean=1.51, SE=0.05; $t(62)=0.58$, $p=0.562$). The subjects rated 78.9% (SE=1.7%) of the well-known melodies as familiar and 88.2% (SE=1.0%) of the novel melodies as unfamiliar. More well-known melodies were rated as familiar by musicians (mean=84.4%, SE=1.7%) than non-musicians (mean=73.5%, SE=2.6%; $t(62)=3.54$, $p=0.001$), whereas no such difference was observed for the novel melodies (musicians: mean=88.3%, SE=1.5%; non-musicians: mean=88.2%, SE=1.4%; $t(62)=0.08$, $p=0.940$).

ERP Results

Visual inspection of the waveforms indicated a characteristic auditory P1-N1-P2 complex for all conditions (i.e., in both violation and control conditions), in addition to five ERP components elicited by the violation conditions as compared to the control conditions (Fig. 3). Time windows for each of these five components were selected on the basis of previous research and visual inspection of the waveforms: 150–270 ms for an early anterior-central negativity elicited by out-of-key violations in both familiar and unfamiliar melodies; 220–380 ms for a posterior negativity elicited by both in-key and out-of-key violations in familiar melodies; 270–350 ms for an anterior-central positivity also elicited by both types of violations in familiar melodies; 500–700 ms for a later anterior negativity elicited by all three violation conditions; and 500–700 ms for a late posterior positivity also elicited by all three violation conditions.

Violation/Control Contrasts

In-key violations in unfamiliar melodies: These “violations” did not constitute actual violations of either musical rules or known musical melodies, and thus were not predicted to elicit any ERP components, as compared to control target notes in unfamiliar melodies. Indeed, visual inspection suggested no clear ERP effects in this contrast (Fig. 3b), so the initial set of three-level analyses was not performed (see below for further analyses on this condition).

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Out-of-key violations in unfamiliar melodies: Analyses were performed on the time windows of the three components suggested by visual inspection (Fig. 3b): 150–270 ms for the early anterior-central negativity, 500–700 ms for the later anterior negativity, and 500–700 ms for the late posterior positivity. Analysis of the 150–270 ms window with the first-level ANOVA (that is, with factors Violation, Hemisphere, Anterior/Posterior and Musical Training on lateral ROIs; see Methods) elicited a significant Violation by Anterior/Posterior interaction ($F(4,312)=12.07$, $p<0.0001$), with no other significant interactions that included both Violation and either of the scalp-distribution factors (Hemisphere, Anterior/Posterior). The second-level analyses revealed that although the negativity extended across all lateral ROIs, it was clearly greatest at anterior and central ROIs (anterior: $F(1,63)=33.31$, $p<0.0001$, central: $F(1,63)=30.72$, $p<0.0001$, posterior: $F(1,63)=9.33$, $p=0.003$). Therefore the anterior and central lateral ROIs were selected as the "area of activation" for further targeted analyses. The third-level analyses on this anterior-central area of activation (factors Violation, Hemisphere and Musical Training, collapsing across anterior and central levels of the factor Anterior/Posterior) elicited the expected main effect of Violation ($F(1,61)=63.13$, $p<0.0001$), confirming the anterior-central negativity. No interactions with Violation were obtained, indicating that the negativity did not vary across the hemispheres or between musicians and non-musicians.

In the 500–700 ms time window, the first level ANOVA again elicited only a Violation by Anterior/Posterior interaction ($F(4,312)=12.47$, $p<0.0001$), with no other significant interactions that included both Violation and either scalp-distribution factor. The second-level analyses revealed that the anterior ROIs showed a significant negativity ($F(1,63)= 14.59$, $p=0.0003$), with no significant effect for the central ROIs ($F(1,63)=1.18$, $p=0.282$), and a significant positivity for the posterior ROIs ($F(1,63)=30.35$, $p<0.0001$). To investigate the anterior area of activation, a third-level ANOVA was performed on the anterior lateral ROIs. This revealed a main effect of Violation ($F(1,61)=14.45$, $p=0.0003$), confirming the anterior negativity, and no significant interactions of Hemisphere or Musical Training with Violation.

To further examine the posterior positivity in the 500–700 ms time window, a third level analyses was performed over the posterior area of activation (posterior lateral ROIs). This analysis revealed only a main effect of Violation ($F(1,61)=30.07$, $p<0.0001$), verifying the positivity, with no significant interactions between Violation and either of the other two factors (Hemisphere and Musical Training).

In-key violations in familiar melodies: Analyses were performed on three time windows: 220–380 ms for the posterior negativity, 270–350 ms for the anterior-central positivity, and 500–700 ms for both the later anterior negativity and the late posterior positivity (Fig. 3a). In the 220–380 ms window, the first-level ANOVA revealed only a significant Violation by Anterior/Posterior interaction ($F(4,312)=16.30$, $p<0.0001$). The second-level analyses confirmed that the negativity was restricted to the posterior ROIs ($F(1,63)=2.19$, $p=0.0009$), with significant positivities at anterior ($F(1,63)=4.85$, $p=0.031$) and central ($F(1,63)=5.63$, $p=0.021$) ROIs. The third-level analyses on the posterior lateral ROIs revealed only a main effect of Violation ($F(1,61)=11.93$, $p=0.001$).

In the 270–350 ms time window, visual inspection of the waveforms suggested that the anterior-central positivity was much larger at midline than lateral ROIs (Fig. 3a), so we report ANOVAs only on midline ROIs (see Methods). The first-level ANOVA revealed only a Violation by Anterior/Posterior interaction ($F(5,309)=13.52$, $p<0.0001$). Second-level analyses confirmed the anterior-central area of activation, with significant positivities at anterior ($F(1,63)=20.16$, $p<0.0001$) and central ($F(1,63)=9.46$, $p=0.007$) ROIs, and a marginally significant negativity at the posterior ROI ($F(1,63)=3.54$, $p=0.064$). The third-level ANOVA on the anterior and central midline ROIs revealed a main effect of Violation ($F(1,61)=37.83$, $p<0.0001$), reflecting the positivity over this area of activation. Additionally, this ANOVA yielded a significant

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interaction between Violation and Musical Training ($F(2,61)=3.71$, $p=0.030$), reflecting a greater positivity for musicians than non-musicians (Fig. 4), although the positivity was significant in both groups (musicians: $F(1,31)=31.09$, $p<0.0001$; non-musicians: $F(1,31)=8.55$, $p=0.006$).

In the 500–700 ms time window, the first-level ANOVA again showed only a Violation by Anterior/Posterior interaction ($F(4,312)=12.86$, $p<0.0001$). Second-level analyses revealed that the negativity was indeed restricted to the anterior ROIs ($F(1,63)=10.62$, $p=0.002$), with significant positivities at central ($F(1,63)=6.96$, $p=0.011$) and posterior ($F(1,63)=27.76$, $p<0.0001$) ROIs. The third-level analysis on anterior lateral ROIs revealed only the expected main effect of Violation ($F(1,61)=10.79$, $p=0.002$), verifying the anterior negativity.

The second level analyses revealed that the positivity in the 500–700 ms time window was significantly greater over posterior than central ROIs ($F(2,126)=4.27$, $p=0.016$). The third-level analysis on posterior lateral ROIs revealed a main effect of Violation ($F(1,61)=28.44$, $p<0.0001$), as well as an interaction between Violation and Musical Training ($F(2,61)=4.16$, $p=0.020$), with musicians showing a larger positivity than non-musicians. Follow-up analyses showed that the positivity was significant only for musicians ($F(1,31)=46.84$, $p<0.0001$; non-musicians: non-significant positivity, $F(1,31)=2.61$, $p=0.116$).

Out-of-key violations in familiar melodies: Analyses were performed on the time windows of the five components suggested by visual inspection (Fig. 3a): 150–270 ms for the early anterior-central negativity, 220–380 ms for the posterior negativity, 270–350 ms for the anterior-central positivity, and 500–700 ms for the later anterior negativity and the late posterior positivity.

In the 150–270 ms time window, the first-level ANOVA elicited only a Violation by Anterior/Posterior interaction ($F(4,312)=4.64$, $p=0.001$). The second-level analyses revealed the same pattern as that observed in this time window for out-of-key violations in unfamiliar melodies: whereas the negativity extended across all lateral ROIs, it was greatest at anterior and central ROIs (anterior: $F(1,63)=36.75$, $p<0.0001$; central: $F(1,63)=34.95$, $p<0.0001$; posterior: $F(1,63)=21.28$, $p<0.0001$). Moreover, it was significantly smaller in posterior than in central ($F(2,126)=6.73$, $p=0.002$) and anterior ($F(2,126)=7.23$, $p=0.001$) ROIs, but did not differ between anterior and central ROIs ($F(2,126)=0.96$, $p=0.385$), confirming that the negativity was most prominent across anterior and central ROIs. The third-level analysis, on anterior and central lateral ROIs, revealed only the expected main effect of Violation ($F(1,61)=72.07$, $p<0.0001$).

The first-level ANOVA in the 220–380 ms time window showed only a Violation by Anterior/Posterior interaction ($F(4,312)=10.15$, $p<0.0001$). The posterior distribution of the negativity was confirmed by second-level analyses (posterior: $F(1,63)=19.41$, $p<0.0001$; central: $F(1,63)=0.16$, $p=0.687$; anterior: $F(1,63)=0.01$, $p=0.937$). The third-level analysis, on posterior lateral ROIs, revealed only the predicted main effect of Violation ($F(1,61)=19.24$, $p<0.0001$).

The anterior-central positivity in the 270–350 ms time window again appeared to be largest over midline ROIs (as was observed for in-key violations in familiar melodies), and thus only analyses on the midline ROIs are reported. The first-level ANOVA revealed a Violation by Anterior/Posterior interaction ($F(5,309)=14.25$, $p<0.0001$), as well as a three-way interaction between Violation, Anterior/Posterior, and Musical Training ($F(6,309)=4.61$, $p=0.0002$). Second-level analyses confirmed the anterior-central distribution of the positivity, with a significant positivity at anterior ($F(1,63)=13.08$, $p=0.0006$) and central ($F(1,63)=10.58$, $p=0.002$) ROIs, and a significant negativity at the posterior ROI ($F(1,63)=4.58$, $p=0.036$). Second-level analyses following up on the three-way interaction revealed that only musicians

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showed the anterior-central positivity (musicians: anterior: $F(1,31)=15.72$, $p=0.0004$; central: $F(1,31)=11.17$, $p=0.002$; posterior: $F(1,31)=1.24$, $p=0.273$; non-musicians: anterior: $F(1,31)=0.92$, $p=0.344$; central: $F(1,31)=0.89$, $p=0.352$; posterior: negativity, $F(1,31)=5.20$, $p=0.030$). The third-level ANOVA, on the anterior-central midline area of activation, yielded the expected main effect of Violation ($F(1,61)=36.37$, $p<0.0001$), and an interaction between Violation and Musical Training ($F(2,61)=11.02$, $p<0.0001$), with musicians showing a greater positivity than non-musicians. Follow-up analyses revealed that only musicians showed a significant positivity (musicians: $F(1,31)=38.82$, $p<0.0001$; non-musicians: $F(1,31)=2.41$, $p=0.131$).

The first level ANOVA in the 500–700 ms window showed only a Violation by Anterior/Posterior interaction ($F(4,312)=78.79$, $p<0.0001$). Second-level analyses confirmed the anterior distribution of the negativity (anterior ROIs: $F(1,63)=36.99$, $p<0.0001$), with significant positivities at central ($F(1,63)=25.98$, $p<0.0001$) and posterior ($F(1,63)=169.08$, $p<0.0001$) ROIs. The third-level analysis on anterior lateral ROIs revealed only the expected main effect of Violation ($F(1,61)=36.99$, $p<0.0001$), verifying the anterior negativity.

The second level analyses showed that the positivity in the 500–700 ms time window was significantly greater at posterior than at central ROIs ($F(2,126)=33.88$, $p<0.0001$). The third-level analysis examining the positivity over posterior lateral ROIs revealed the predicted main effect of Violation ($F(1,61)=172.99$, $p<0.0001$), as well as a significant interaction between Violation and Musical Training ($F(2,61)=3.56$, $p=0.034$). Although the positivity was larger for musicians than for non-musicians, the effect was significant for both groups (musicians: $F(1,31)=152.90$, $p<0.0001$; non-musicians: $F(1,31)=47.31$, $p<0.0001$).

Comparisons of Contrasts for each ERP Component of Interest—Before directly comparing the violation/control contrasts found above for each component, we statistically examined whether the components were indeed absent in those contrasts *not* analyzed above, due to their apparent absence on the basis of visual inspection. For all such contrasts, ANOVAs with the single factor Violation were performed in the appropriate time windows and areas of activation. These revealed no significant effects, confirming visual inspection.

Early Anterior-Central Negativity (150–270 ms): This component was found for out-of-key violations in both unfamiliar and familiar melodies (Fig. 3 and 5a). In both cases the effect was most prominent across anterior and central lateral ROIs. It might be argued that visual inspection of the waveforms suggests a very slight negativity within this time window for in-key violations in familiar melodies (Fig. 3 and 5a). However, an ANOVA on the anterior and central lateral ROIs confirmed that this negativity did not reach significance in the 150–270 ms time window ($F(1,63)=2.59$, $P=0.113$). Moreover, direct comparisons of the difference waves (violation minus control) in this time window and anterior-central area of activation revealed that both types of out-of-key violations elicited significantly greater negativity than in-key violations in familiar melodies (out-of-key familiar vs. in-key familiar: $F(1,63)=39.32$, $P<0.0001$; out-of-key unfamiliar vs. in-key familiar: $F(1,63)=18.95$, $P<0.0001$).

To follow up on the significant early anterior-central negativities in the two out-of-key violation conditions, we performed an ANOVA on the difference waves for these conditions in the anterior-central area of activation, with factors Hemisphere, Musical Training and Violation Condition (2 levels, for the difference waves for out-of-key violations in unfamiliar and familiar melodies). All main effects and interactions were included in the model (see Methods). The analysis revealed no main effect of Violation Condition ($F(1,62)=1.31$, $p=0.257$), indicating that the amplitude of the early anterior-central negativity did not significantly differ between out-of-key violations in unfamiliar and familiar melodies. The only significant result was a main effect of Hemisphere ($F(1,62)=4.44$, $p=0.039$), indicating a greater negativity in the right

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hemisphere across both violation conditions (that is, it was right-lateralized), although follow-up analyses revealed that the negativity was significant in both hemispheres (left: $t(62)=4.33$, $p<0.0001$; right: $t(62)=6.92$, $p<0.0001$).

Posterior Negativity (220–380 ms): This effect was found for both in-key and out-of-key violations in familiar melodies (Fig. 3a and 5b), and was restricted to posterior lateral ROIs in both cases. The ANOVA on the difference waves of these two contrasts in this posterior area of activation revealed no significant main effects or interactions, indicating that the amplitude of the posterior negativity did not significantly differ between the two violation conditions, between musicians and non-musicians, or between the two hemispheres (that is, it was bilaterally distributed).

Anterior-Central Positivity (270–350 ms): This component was found for in-key and out-of-key violations in familiar melodies (Fig. 3a), with the effect found in anterior and central (midline) ROIs in both cases. The ANOVA on the difference waves of these contrasts in these ROIs revealed first, a main effect of Musical Training ($F(1,62)=5.69$, $p=0.020$), reflecting a larger positivity across both violation conditions for musicians than for non-musicians (Fig. 4), and second, a significant interaction between Violation Condition and Musical Training ($F(1,62)=8.51$, $p=0.005$). Follow-up analyses showed that the positivity was significant for musicians ($t(62)=5.09$, $p<0.0001$), but only marginally significant for non-musicians ($t(62)=1.72$, $p=0.091$). Moreover, musicians showed a significantly greater positivity for out-of-key than in-key violations ($F(1,31)=7.75$, $p=0.009$), whereas no significant difference between these contrasts was observed for non-musicians ($F(1,31)=1.69$, $p=0.204$).

Anterior Negativity (500–700 ms): This effect was found for all three violation conditions: out-of-key violations in both unfamiliar and familiar melodies, and in-key violations in familiar melodies (Fig. 3). In all cases the negativity was restricted to anterior ROIs. The ANOVA on the three difference waves in anterior lateral ROIs revealed three significant effects. First, a main effect of Violation Condition ($F(2,124)=3.57$, $p=0.031$) was found. This indicated a greater negativity for out-of-key violations in familiar melodies as compared to in-key violations in familiar melodies ($F(1,63)=5.62$, $p=0.021$) and out-of-key violations in unfamiliar melodies ($F(1,63)=5.07$, $p=0.028$), with no significant difference between the latter two ($F(1,63)>0.01$, $p=0.950$). Second, a main effect of Hemisphere ($F(1,62)=7.39$, $p=0.009$) reflected an overall greater negativity over the right than left hemisphere, though the effect was significant in both hemispheres (left: $t(62)=2.92$, $p=0.005$; right: $t(62)=6.08$, $p<0.0001$). Third, a Hemisphere by Musical Training interaction ($F(1,62)=6.71$, $p=0.012$) reflected the finding that musicians showed no significant effect of Hemisphere ($F(1,31)=0.01$, $p=0.926$; Fig. 4a), whereas the negativity was right-lateralized in non-musicians ($F(1,31)=12.96$, $p=0.001$), who showed a significant negativity on the right ($t(31)=5.59$, $p<0.0001$) but not the left ($t(31)=0.81$, $p=0.424$; Fig. 4b).

Late Posterior Positivity (500–700 ms): The late positivity was also found for all three violation conditions (Fig. 3). In all cases the positivity was largest over posterior ROIs. The ANOVA on the difference waves of the three contrasts in lateral posterior ROIs revealed two effects: a main effect of Violation Condition ($F(2,124)=39.56$, $p<0.0001$), and a significant interaction between Violation Condition and Musical Training ($F(2,124)=4.89$, $p=0.009$). Follow-up ANOVAs were run to compare each of the three pairs of difference waves, with the factors Violation Condition, Musical Training, and their interaction in each ANOVA. These analyses revealed that out-of-key violations in familiar melodies elicited a significantly larger positivity than either in-key violations in familiar melodies ($F(1,62)=74.05$, $p<0.0001$) or out-of-key violations in unfamiliar melodies ($F(1,62)=75.84$, $p<0.0001$), which themselves did not differ from each other ($F(1,62)=0.67$, $p=0.415$). In addition, these follow-up analyses revealed interactions between Violation Condition and Musical Training in the comparisons between

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out-of-key violations in unfamiliar melodies and both in-key ($F(1,62)=6.93$, $p=0.011$) and out-of-key ($F(1,62)=8.36$, $p=0.005$) violations in familiar melodies (Fig. 4). This reflected, first of all, the finding that musicians showed a significantly greater positivity for in-key violations in familiar melodies than out-of-key violations in unfamiliar melodies ($F(1,31)=7.36$, $p=0.011$), whereas non-musicians showed, if anything, a trend for the opposite effect ($F(1,31)=1.38$, $p=0.249$). Moreover, the difference in the effect between out-of-key violations in familiar and unfamiliar melodies was greater for musicians than for non-musicians, although the former showed a significantly greater positivity than the latter both in musicians ($F(1,31)=93.63$, $p<0.0001$) and non-musicians ($F(1,31)=13.20$, $p=0.001$).

Summary and Discussion

In this study, a double dissociation was observed between rule and memory violations in music. Early anterior-central negativities were elicited by out-of-key violations in both unfamiliar and familiar melodies, whereas posterior negativities were elicited by both in-key and out-of-key violations in familiar melodies. The amplitude of the early anterior-central negativity did not differ between the two out-of-key (rule) violation conditions, while the amplitude of the posterior negativity did not differ between the two memory-based violations, (i.e., the two types of violations in familiar melodies). These results suggest that the early anterior-central negativity is driven by violations of musical rules, independent of familiarity, that is, independent of whether the melody is memorized or not, whereas the posterior negativity is driven by violations of memorized (familiar) representations, regardless of whether or not the deviant note violates musical rules. Thus the two components appear to be independent of one another.

The early anterior-central negativity is similar in scalp distribution and latency to the early (right) anterior negativity, or E(R)AN, found in previous studies of harmonic rule violations in melodies (Verleger, 1990, Paller et al., 1992) and chord sequences (Patel et al., 1998, Koelsch et al., 2000, Koelsch et al., 2002b, Koelsch et al., 2002c, Koelsch et al., 2005, Loui et al., 2005, Leino et al., 2007). In these previous studies the negativities were either right-lateralized (Patel et al., 1998, Koelsch et al., 2000, Koelsch et al., 2002b, Koelsch et al., 2002c, Koelsch et al., 2005) or bilateral (Paller et al., 1992, Loui et al., 2005, Leino et al., 2007). In the present study, the early anterior-central negativity was significantly right-lateralized, but only when analyzed across both out-of-key violation conditions (i.e., in both familiar and unfamiliar melodies). In one study of musical rule violations, musicians showed a larger ERAN than non-musicians (Koelsch et al., 2002b). This difference was not statistically observed here, although visual inspection of the waveforms suggests a trend in this direction (Fig. 4).

Posterior negativities have not previously been reported in ERP studies of music, even by studies that examined violations in familiar melodies. In one study of out-of-key violations in well-known melodies (Verleger, 1990), in which subjects were informed about the violations, a posterior positivity began around 200 ms and thus may have masked any posterior negativity. Additionally, since behavioral results were not reported, it is not clear whether the subjects were actually familiar with the melodies. Paller *et al.* 1992 also examined ERP responses to out-of-key violations in well-known melodies. In this case 99% were judged as familiar. No posterior negativities were apparent for these deviants, even when the positivities were somewhat diminished by reducing attention to the violations. However, it is possible that the positivities still masked a posterior negativity. In addition, the absence of such a negativity could be explained by the 800-ms delay prior to the final (target) note in all melodies. This delay itself violated the melody, and may have disrupted the memory-based context necessary to elicit the posterior negativity. Finally, Besson *et al.* 1995 also examined melody-final pitch violations in both familiar and unfamiliar melodies. Both out-of-key violations and in-key violations were examined, though the latter appear to have violated other musical rules (see

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discussion in Introduction above). In familiar but not unfamiliar melodies, both out-of-key and in-key violations appeared to elicit a central-posterior negativity between about 200–400 ms, immediately preceding the late positivity. However, the negativity only appeared in the waveform figures and was not mentioned in the text. The present study differed from each of these studies: subjects were not informed about the violations and were instructed to attend to other aspects of the stimuli; ERPs were only analyzed for melodies that were familiar; note violations occurred in the appropriate temporal context within each melody; and the study included violations of memorized representations that did not violate any musical rules.

We suggest that the posterior negativity can be characterized as an N400. Both the scalp distribution and latency seem consistent with N400s, which vary from posterior to central distributions, and in latency from about 250 to 500 ms (Kutas and Hillyard, 1980, Friederici et al., 1999a, Kutas and Federmeier, 2000, Hinojosa et al., 2001). Note that although the negativity was posteriorly distributed compared to typical N400s, it is possible that its distribution extended more centrally, but was hidden by additivity effects from the temporally overlapping anterior-central positivity (Fig. 3). Additionally, some evidence suggests that the posterior negativity appears to have extended beyond the 220–380 ms time window, but was largely masked by additivity effects from the subsequent posterior positivity. First, in-key deviants in familiar melodies, which elicited significantly smaller late posterior positivities than out-of-key deviants in familiar melodies, also elicited longer posterior negativity latencies (based on visual inspection; Fig. 3). Second, non-musicians, who showed significantly smaller posterior positivities than musicians to both in-key and out-of-key violations in familiar melodies, also showed longer posterior negativities than musicians (Fig. 4). Perhaps most importantly, in the one case in which the posterior positivity was non-significant (i.e., in-key violations in familiar melodies, in non-musicians; see Fig. 6), the posterior negativity continued to about 500 ms, further strengthening the view that the negativity can indeed be characterized as an N400.

While the N400 is most commonly known for being elicited by semantic violations in language, similar negativities have also been found for line drawings (Holcomb and McPherson, 1994, Federmeier and Kutas, 2001), photos of objects (McPherson and Holcomb, 1999), faces (Bobes et al., 1994), and environmental sounds (Van Petten and Rheinfelder, 1995). Most notable with respect to the present findings is an ERP study by Bobes *et al.* 1994, in which subjects viewed photos of faces, some of which contained altered features that were detectable only if the faces were familiar. Similar to the in-key deviants in familiar melodies examined in the present study, the altered faces elicited a posteriorly distributed N400 *only* in subjects who were previously familiar with the faces. Thus, N400s appear to be elicited by violations of familiar (i.e., memorized) stimuli across perceptual/cognitive domains. Note also that because the in-key violations in the present study do not seem to be related to any violation or anomaly of meaning, the apparent N400 observed here suggests that this component may not be restricted to semantics, but rather may extend to the processing of non-semantic information in long-term memory (Ullman, 2004).

Additional studies are clearly necessary to further clarify the nature of the posterior negativity. In particular, the true time window of the negativity could be revealed by additional reductions of potentially additive effects from any subsequent posterior positivity. For instance, having subjects read a book or play a video game during presentation of the melodies may further reduce attention to the note violations, thus diminishing the attention-related positivities. However, it is not yet clear whether such shallow processing of the stimuli would be sufficient to elicit the posterior negativities. Alternatively, future studies could examine whether the posterior negativity may be more strongly elicited by other tasks, such as those with greater involvement of the memorized representations (e.g., making a familiarity judgment after each melody). In addition, one would ideally investigate N400s using in-key violations in familiar

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melodies in non-musician subjects, since this condition did not elicit a significant posterior positivity in non-musicians in the present study. Future studies will also be necessary to reveal whether or not the neural generators of the musical posterior negativity overlap, partially or wholly, with those of N400s elicited by lexical-semantic violations in language and other domains (e.g., see Koelsch et al. (2005) for one approach that investigated the relationship between the anterior negativities in language and music).

It is also possible that the posterior negativity is not related to the N400. For instance, the time window of the posterior negativity overlaps partially with that of the anterior-central positivity (P3a, see below for discussion), which was also elicited only by familiar melody violations. Thus, it might be argued that the posterior negativity simply reflects the negative end of the P3a dipole. In such a case the posterior negativity and P3a would be expected to correlate in amplitude across the different subject groups and conditions. However, the P3a was significantly larger for musicians than for non-musicians, while there were no differences in the posterior negativity between musicians and non-musicians. Additionally, the P3a was larger for out-of-key than in-key violations for musicians but not for non-musicians, whereas no such interactions were observed for the posterior negativity. Thus it is unlikely that these two ERP components reflect opposite ends of a single dipole.

It is also possible that the posterior negativity may be related to N400s, but was not elicited by violations of the melodies themselves. For example, a majority of the melodies used in the present study (103 out of 120, based on responses from a pilot study with different subjects) are linked to lyrics. Since melodies and their lyrics are strongly associated with one another in memory (Hebert and Peretz, 2001), a familiar melody note violation could potentially be interpreted as a prosodic violation of the lyrics associated with that melody. Thus the posterior negativity could in principle be related to N400 or N400-like components that have been elicited by prosodic violations in speech (Bostanov and Kotchoubey, 2004, Mietz et al., 2007) – although it should be pointed out that in the current study it is not clear how many subjects knew how many of the lyrics.

Finally, it is clear that evidence from converging methodologies will be important for elucidating the neural generators of the posterior negativity. For instance, neuroimaging studies could reveal whether the brain areas activated in response to in-key violations in familiar melodies are similar to those activated by (lexical-)semantic anomalies in language and other domains (see above), while lesion studies may reveal whether damage to these brain regions results in deficits in detecting these musical violations.

In addition to the early right anterior-central negativity (ERAN) and posterior negativity (apparent N400), three other ERP components were observed. First, an anterior-central positivity was elicited by both types of violations in familiar melodies. The scalp distribution and time window (270–350 ms) of this component is consistent with that of a P3a, which is thought to reflect the automatic orientation of attention to a novel/deviant stimulus (Münte et al., 1998, Koelsch et al., 2000, Tervaniemi et al., 2005). The fact that the positivity was found for familiar but not unfamiliar melodies may be due to increased attentional shift to violations of the highly specific expectancies generated by familiar note sequences. This may also help explain the finding that the positivity was larger in musicians than in non-musicians, and within musicians, was larger for out-of-key than in-key violations. Additionally, previous studies using auditory “oddball” tasks have shown reduced P3a components in non-musicians (Tervaniemi et al., 2005), and in patients with musical processing deficits (Münte et al., 1998).

Second, a later anterior negativity (500–700 ms) was generated by all three violation conditions. This component is consistent with the bilateral or right-lateralized N5/Late

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Negativity components elicited in musical chord sequences by harmonically incongruous chords (Koelsch et al., 2000, Koelsch et al., 2002b, Koelsch et al., 2002c, Loui et al., 2005), tone clusters (Koelsch et al., 2000), and timbre deviants (Koelsch et al., 2000). In the present study the negativity was bilateral in musicians and right-lateralized in non-musicians, consistent with behavioral and neuroimaging studies that have found greater right hemisphere dominance for processing music in non-musicians, as compared to musicians (Bever and Chiarello, 1974, Johnson et al., 1977, Messerli et al., 1995, Evers et al., 1999, Ohnishi et al., 2001). The different patterns of activation across violation conditions between the early anterior-central negativity and the later anterior negativity suggest that these are indeed different components. Whereas the early anterior-central negativity was observed only for out-of-key violations (and did not differ between familiar and unfamiliar melodies), the later anterior negativity was largest for the out-of-key violations in familiar melodies (which constituted both rule *and* memory violations), and smaller but equivalent to one another for in-key violations in familiar melodies and out-of-key violations in *un*familiar melodies. Thus, the N5/Late Negativity does not appear to reflect solely rule-based or solely memory-based processes, but rather seems to be influenced by additive expectancies generated by both.

Third, a late posterior positivity (500–700 ms) was observed, again for all three violation conditions. Late positivities have also been found in many other studies of musical violations, in both familiar and unfamiliar melodies, as well as in chord sequences (Verleger, 1990, Paller et al., 1992, Besson and Faïta, 1995, Patel et al., 1998, Koelsch et al., 2000, Koelsch et al., 2002c). Although the present study was designed to diminish the late positivity by reducing attention to in-key and out-of-key violations, all but one subject (a non-musician) reported noticing these violations. Importantly however, the late posterior positivity was not large enough to mask the N5/anterior negativity that occurred in a similar time window. In fact, the late positivity and anterior negativity showed the same pattern of activation across the violation conditions. This suggests that the differences among the violation conditions were not due to additivity effects between these two components, and that the late posterior positivity also seems to reflect additive rule- and memory-based expectancies. Finally, musicians showed significantly larger late posterior positivities than non-musicians for in-key and out-of-key violations in familiar melodies, but not for out-of-key violations in unfamiliar melodies. These effects may reflect differences between musicians and non-musicians in the amount of attention allocated to violations in the familiar melodies.

Together, the results from the present study suggest that different neural mechanisms are involved in rule-governed and memory-based processing in melodies, and that these mechanisms are independent from one another. The study demonstrates a double dissociation analogous to that observed for grammatical and lexical-conceptual processing in language, and thus suggests and extension of the rule/memory dissociation in language to the domain of music. While the anterior negativities in music and language have previously been linked to both overlapping and partially distinct structures in frontal cortex, future studies should reveal whether N400s generated by the two domains also reflect activity from the same and/or overlapping neural substrates.

Acknowledgements

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Appendix

Well-known Melody Stimuli

Addam's Family Theme

Amazing Grace

America

America (from *West Side Story*)

America the Beautiful

Anchors Aweigh

Andy Griffith Theme

Angels We Have Heard on High

Auld Lang Syne

Baby Bumble Bee

Back to the Future Theme

Battle Hymn of the Republic

B-I-N-G-O

California Girls

Chariots of Fire Theme

Clementine

Coca Cola Theme

Colonel Bogey March

Deck the Halls

Ding Dong! The Witch is Dead

Dixie

Do Your Ears Hang Low

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Edelweiss

Eine Kleine Nachtmusik

For He's a Jolly Good Fellow

Frere Jacques

Frosty the Snowman

Go Tell It on the Mountain

God Bless America

Good King Wenceslas

Habanera (from *Carmen*)

Hail to the Chief

Happy Birthday

Hark! the Herald Angels Sing

Heart and Soul

Here Comes Santa Claus

Holly Jolly Christmas

How Much is that Doggie in the Window

Hush Little Baby

I Feel Pretty (from *West Side Story*)

I'm a Little Teapot

Imperial March (from *Star Wars*)

Inspector Gadget Theme

It's a Small World

It's Beginning to Look a Lot Like Christmas

Itsy Bitsy Spider

I've Been Working on the Railroad

Jesus Loves Me

Jingle Bells

John Jacob Jingleheimer Schmidt

Jolly Old Saint Nicholas

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Joyful Joyful We Adore Thee

Jurassic Park Theme (End Credits)

Killing Me Softly

Korobochka (Theme from *Tetris* Nintendo Game)

Let it Snow

London Bridge is Falling Down

Long Long Ago

Mary Had a Little Lamb

Meet the Flintstones (from *The Flintstones*)

Minuet in G (from Anna Magdalena's Notebook)

Ninety-nine Bottles of Beer

O Christmas Tree (O Tannenbaum)

O Come, All Ye Faithful

O Holy Night

Oh Little Town of Bethlehem

Oh Susanna

Old MacDonald

Oscar Meyer Theme

Over the River and Through the Woods

Pomp and Circumstance

Pop Goes the Weasel

Puff the Magic Dragon

Raiders March (from *Indiana Jones: Raiders of the Lost Ark*)

Rock-a-Bye Baby

Rockin' Around the Christmas Tree

Row Row Row Your Boat

Rudolph the Red Nosed Reindeer

Seventy-Six Trombones

Silent Night

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Silver Bells

Simple Gifts

Skip to my Lou

Someone's in the Kitchen with Dinah (section of "I've Been Working on the Railroad")

Spoonful of Sugar (from *Mary Poppins*)

Star Spangled Banner

Ta-ra-ra Boom-der-e

The Ballad of Gilligan's Isle (from *Gilligan's Island*)

The Entertainer

The Farmer in the Dell

The First Noel

The Godfather Theme

The Lion Sleeps Tonight

The More We Get Together

The Muffin Man

The Rose

The Song That Never Ends

The Wheels on the Bus

This Land is Your Land

This Old Man

Three Blind Mice

Top Gun Theme

Toreador March (*from Carmen*)

Turkey in the Straw

Twelve Days of Christmas

Twinkle Twinkle Little Star

United States Army Anthem (The Caissons Go Rolling Along)

United States Marine Hymn

Up on the Housetop

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We Wish You a Merry Christmas

Wedding March (from *A Midsummer Night's Dream*)

What Child is This

When the Saints Go Marching In

When You Wish Upon a Star

Wiegenlied (Cradle Song)

Winnie the Pooh Theme

Yankee Doodle

You Are My Sunshine

You're a Grand Old Flag

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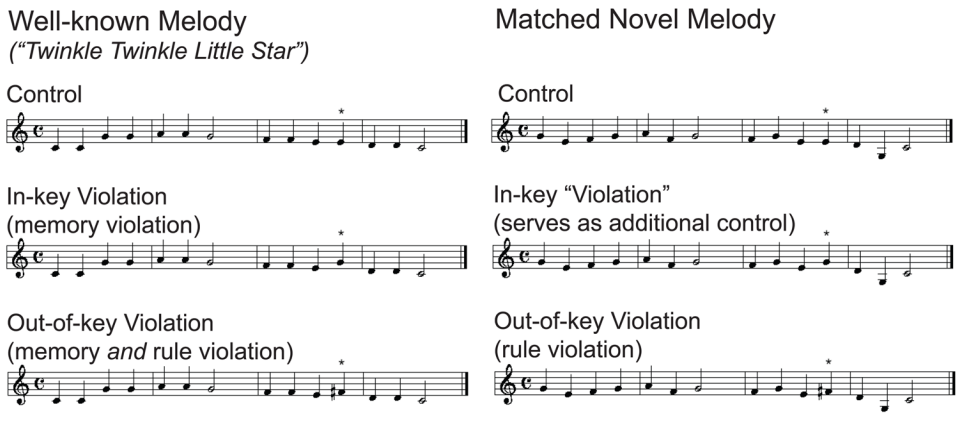

Fig. 1.
Examples of the stimuli used in the experiment. Asterisks indicate target control or violation notes.

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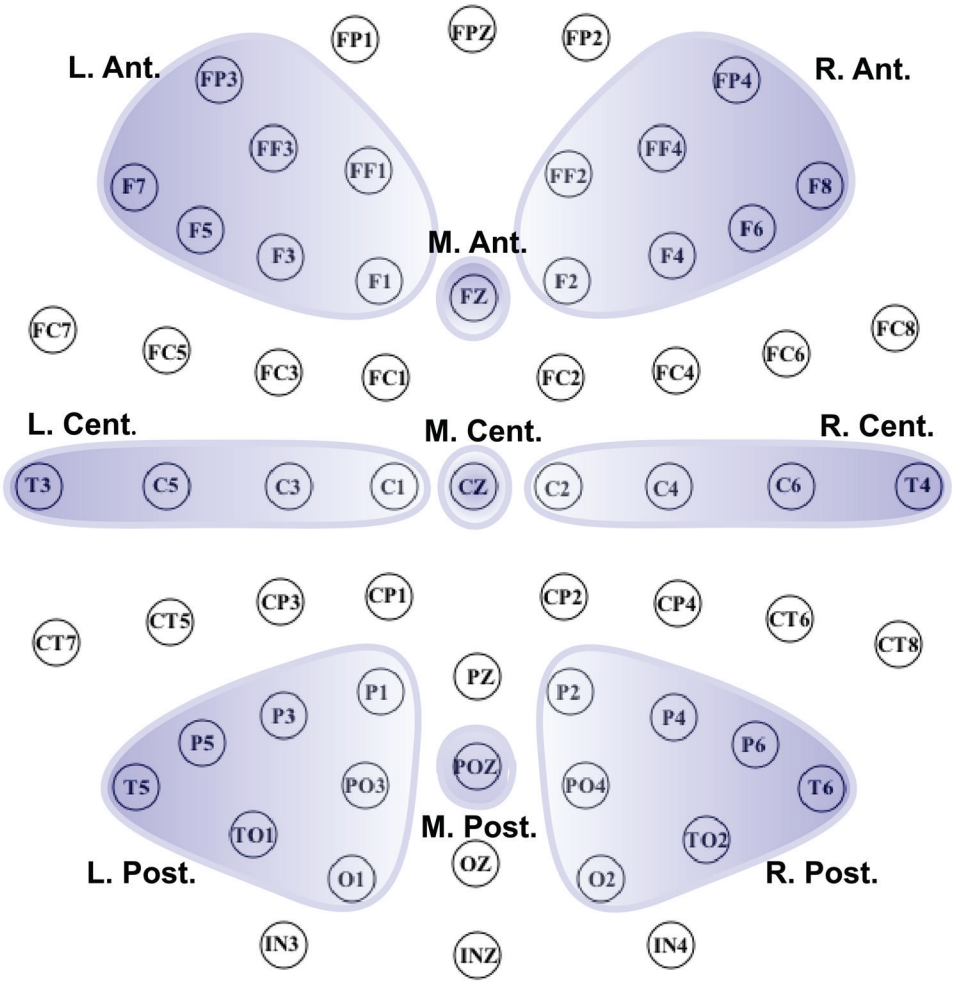

Fig. 2.

Regions of interest (ROIs) used for statistical analyses of ERP data: Left Anterior (L. Ant): average of F1, F3, F5, F7, FF1, FF3, and FP3; Right Anterior (R. Ant.): average of F2, F4, F6, F8, FF2, FF4, and FP4; Midline Anterior (M. Ant): includes only FZ; Left Central (L. Cent.): average of C1, C3, C5, and T3; Right Central (R. Cent.): average of C2, C4, C6, and T4; Midline Central (M. Cent.): includes only CZ; Left Posterior (L. Post.): average of P1, P3, P5, T5, PO3, TO1, and O1; Right Posterior (R. Post.): average of P2, P4, P6, T6, PO4, TO2, and O2; and Midline Posterior (M. Post.): includes only POZ.

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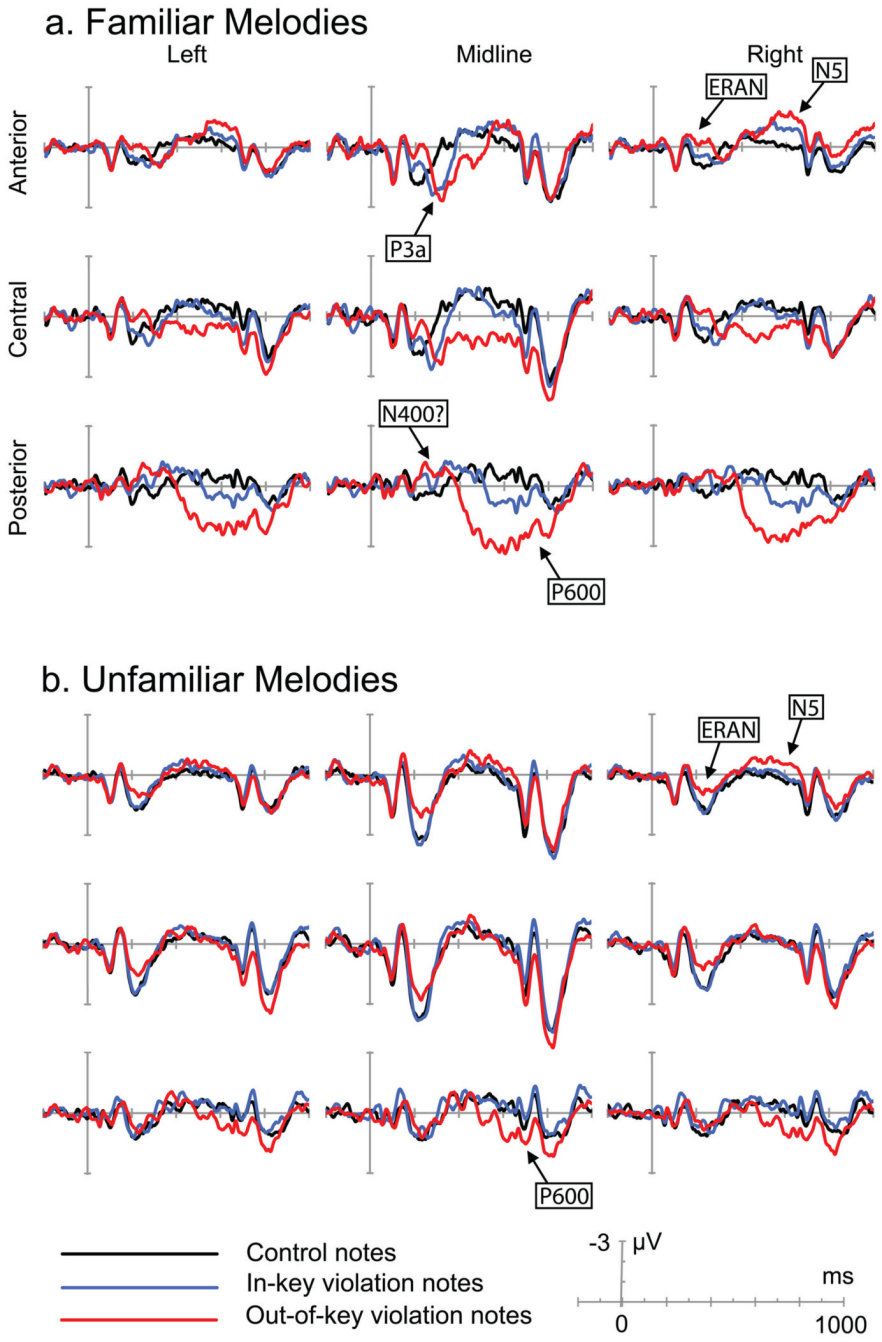

Fig. 3.

Grand average ERPs for control notes (black line), in-key violations (blue line), and out-of-key violations (red line) in (a) familiar melodies and (b) unfamiliar melodies. Timing is displayed in milliseconds. Negative voltage is plotted upward. The ordinate indicates the onset of the target note (onset of the subsequent note occurred 600 ms later). Individual plots represent average waveforms from all electrodes within each of the nine regions of interest. Arrows indicate the five ERP components of interest: the early anterior-central negativity (ERAN), the posterior negativity (N400), the anterior-central positivity (P3a), the later anterior negativity (N5), and the late posterior positivity (P600).

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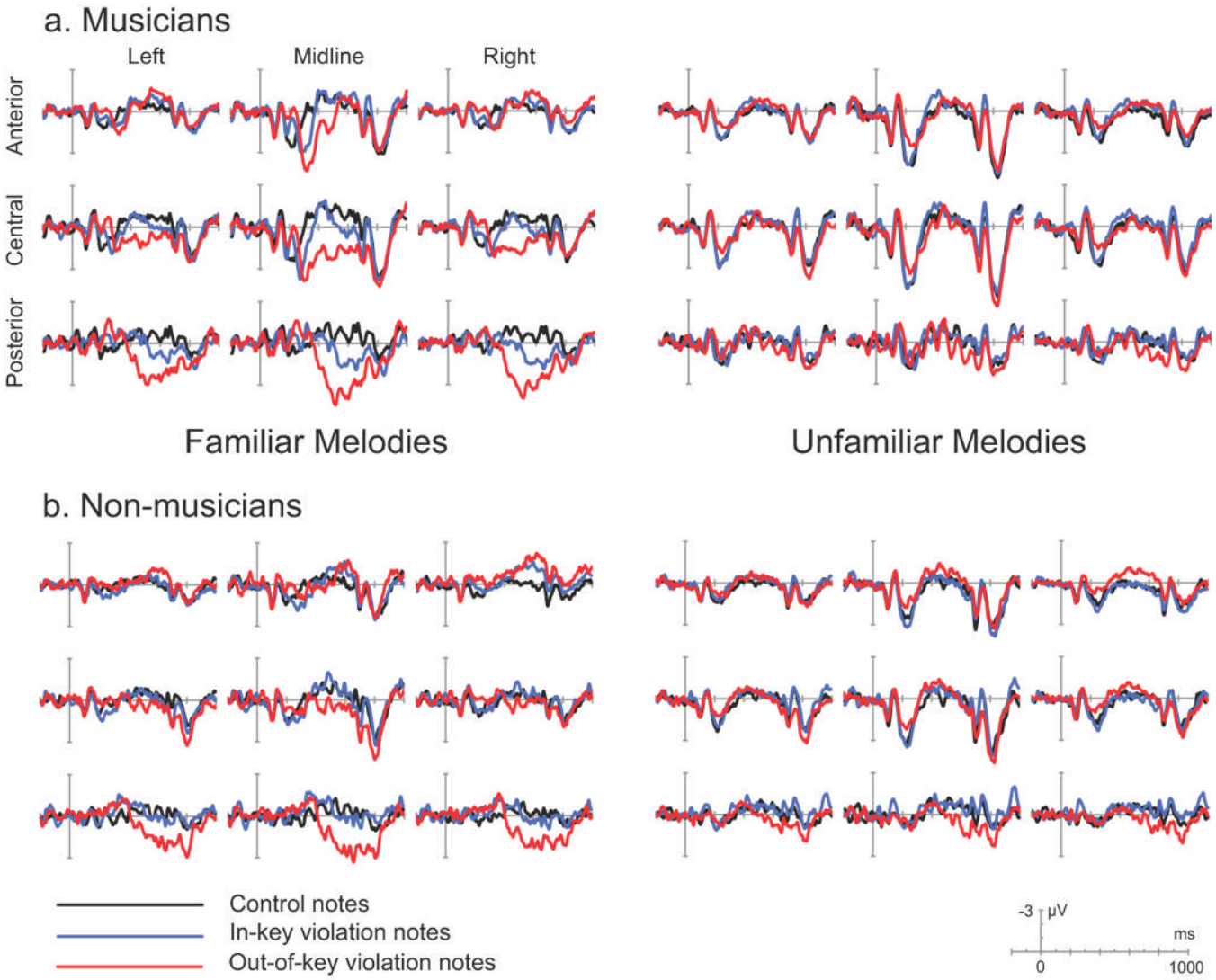

Fig. 4.

Average ERPs for (a) musicians and (b) non-musicians: for familiar melodies (left column) and unfamiliar melodies (right column). Individual plots represent average waveforms from all electrodes within each of the nine regions of interest.

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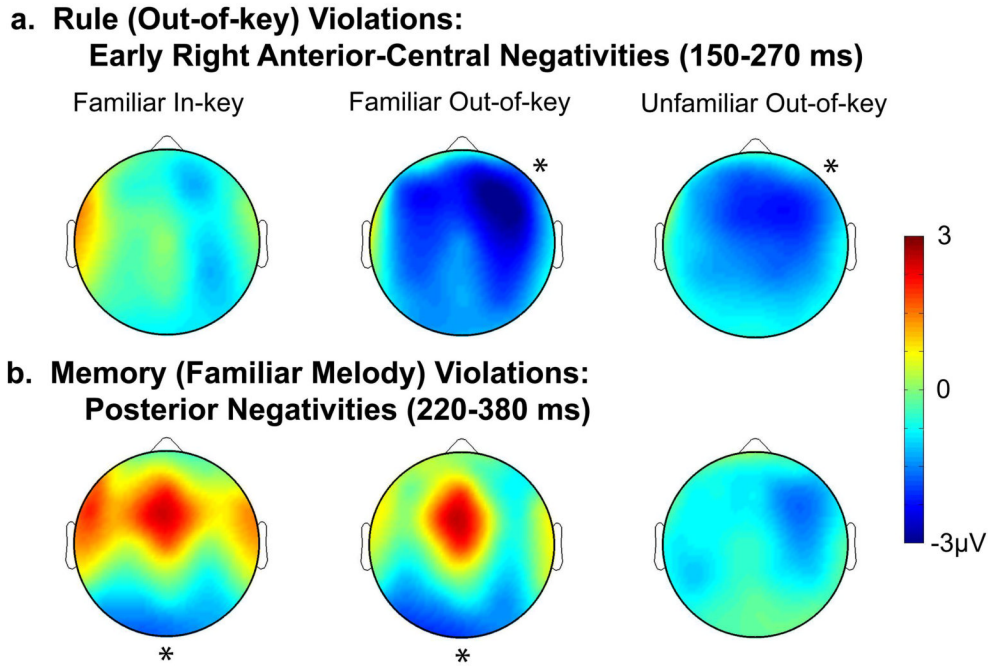

Fig. 5.

Scalp topographic maps showing the distribution of the two ERP components of primary interest, averaged across all 64 subjects. The maps represent difference waves across the specified time windows for each violation/control contrast (i.e., in-key violations in familiar melodies minus control notes in familiar melodies, out-of-key violations in familiar melodies minus control notes in familiar melodies, and out-of-key violations in unfamiliar melodies minus control notes in unfamiliar melodies). Where significant, these components are indicated by an asterisk. Early anterior-central negativities (a) were elicited by rule violations (out-of-key violations in both familiar and unfamiliar melodies) but not by notes that violated only memorized representations (in-key violations in familiar melodies). Posterior negativities (b) were elicited by violations of memorized representations (both types of violations in familiar melodies) but not by violations only of rules (out-of-key violations in unfamiliar melodies). Note that the time window for the anterior-central positivity (270–350 ms) – also elicited by familiar melody violations – falls within the time window for the posterior negativity (220–380 ms), and thus the anterior-central positivity is evident in the scalp topographic maps shown here for familiar melody violations.

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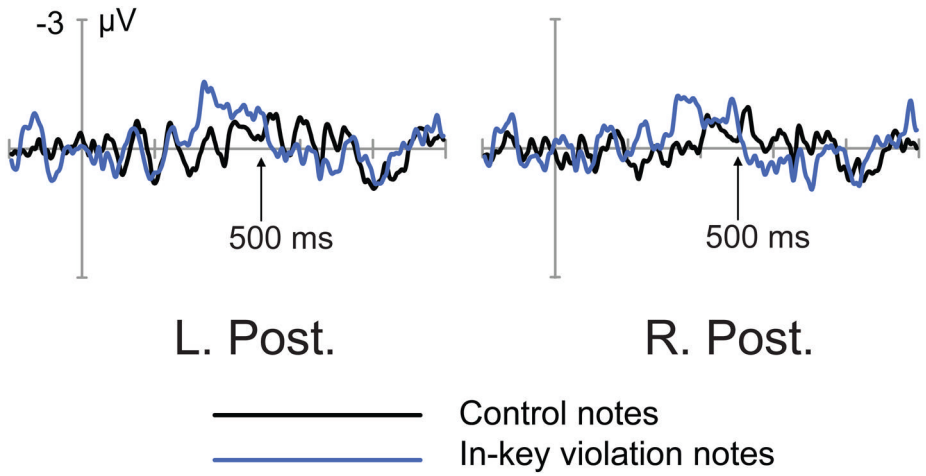

Fig. 6.

Average ERP waveforms for the non-musician group, shown for control notes in familiar melodies (black line), and in-key violations in familiar melodies (blue line). Individual plots represent average waveforms from all electrodes within the left and right posterior regions of interest. In this condition and subject group there was no significant late posterior positivity, and the posterior negativity extended to approximately 500 ms, supporting the view that this component can be characterized as an N400.