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Musical experience, plasticity, and maturation: issues in measuring developmental change using EEG and MEG

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The neuroscientific study of musical behavior has become a significant field of research during the last decade, and reports of this research in the popular press have caught the imagination of the public. This enterprise has also made it evident that studying the development of musical behavior can make a significant contribution to important questions in the field, such as the evolutionary origins of music, cross-cultural similarity and diversity, the effects of experience on musical processing, and relations between music and other domains. Studying musical development brings a unique set of methodological issues. We discuss a select set of these related to measurement of the electroencephalogram (EEG) and magnetoencephalogram (MEG). We use specific examples from our laboratory to illustrate the types of questions that can be answered with different data analysis techniques.

Keywords: music development; EEG; MEG; artifact; oscillatory responses; beta band; gamma band

Origins of electroencephalogram and magnetoencephalogram activity

Electroencephalography (EEG) measured at the surface of the head is largely blind to action potentials and mainly reflects the summation of postsynaptic field potentials.[1–4] When a neurotransmitter acts on a single cell, it creates an electric dipole around that cell. For example, an excitatory neurotransmitter can cause current to flow into the apical dentrites of a cell, creating a net negativity outside this area of the cell. At the same time, current will flow out of the cell in the region of the cell body and basal dentrites creating a positivity outside the cell at this point. Together, these two actions create a small dipole. When many (hundreds of thousands) neurons are aligned and depolarize at the same time, the small dipoles they create will sum into a field that is large enough to measure at the surface of the head.[5–9] Because pyramidal cells tend to be aligned and perpendicular to the cortical surface, it is likely that EEG largely reflects their activity. It is important to note that to the extent that neurons are differentially excitatory and inhibitory and to the extent that they are oriented in different directions, as can happen with the folding of the cortex, their postsynaptic activity can cancel. Thus, much of the neural activity in the brain is opaque to EEG recordings.[10]

A further complication in interpreting EEG activity measured at the surface of the head is that cortical tissue is conductive and thus electrical fields will to some extent spread in all directions, blurring spatial specificity at the surface of the head. In addition, different components of the head, such as the skull and eye holes, have different effects on volume conductance, and thus dipoles originating in different brain regions will be differentially distorted. From a developmental perspective, the skull is thinner and the fontanels do not close until some months after birth, leading to age-specific differences in the distortion of the fields.[11] These factors complicate determination of the source location of EEG activity at different ages.

An electrical dipole has an associated magnetic field perpendicular to the electrical dipole, oriented according to the right-hand rule. Such magnetic fields can be measured with magnetoencephalography (MEG), which uses an array of superconducting quantum interference devices (SQIDS).[12–14] Near the surface of the head, the magnetic fields

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generated by the brain are on the order of a few femtotesla, which is several orders of magnitude smaller than magnetic fields in the ambient environment, so a magnetically shielded room and active noise cancellation are necessary. Magnetic fields are not smeared by brain tissue, so determination of the brain source location of measured activity can be more precise with MEG than EEG, but also because of this, sources oriented radially to the surface of the head cannot be seen with MEG.

EEG and MEG have certain advantages over functional magnetic resonance imaging (fMRI). They have excellent temporal resolution of less than a millisecond (compared with several seconds for fMRI), so long as appropriate sampling rates are used. Unlike fMRI, both EEG and MEG are silent, which is particularly advantageous for auditory work. EEG also has the ethical advantage over fMRI of being noninvasive and virtually risk free. EEG has some advantages over MEG for developmental research. In particular, it is difficult to get infants and young children to stay still, and EEG is more tolerant of movement artifacts. Although segments of the EEG on which movement occurred might need to be eliminated (because the EEG sensors sit on the head), once movement has stopped, clean recordings can resume. With MEG, however, the child sits or lies down with his or her head in the rigid structure of the dewar containing the SQIDS, so if the head moves significantly with respect to the dewar, the MEG recordings cannot be continued. EEG is also much cheaper to purchase and operate, and portable EEG machines are becoming common, allowing easier access to special populations. On the other hand, because MEG is transparent to head tissues, it has better spatial resolution of the measured signals.

Animal studies using electrodes inserted into cortical tissue indicate that extracellular electrical field potential patterns show complex patterns of electrical sources and sinks across the six cortical layers.[7,8] In general, however, it appears that depolarizations in deeper layers with passive returns above will appear on the surface as positivities, whereas depolarizations in more superficial layers with passive returns below will appear on the surface as negativities.[5,6,8] This is important for interpreting EEG in infants and young children as the cortex matures in a layer-specific fashion. For example, although cell bodies in auditory areas are essentially all in place by birth, maturation of neurofilament expression that enables fast axon potentials and meaningful communication between neurons occurs in certain layers before others.[15] Neurofilament is expressed only in layer I at birth. Its expression in deeper cortical layers (lower III, IV, V, and VI) can be seen by 4 months and reaches adult levels by 3 to 5 years of age. Neurofilament is not expressed in upper layers (I, II, and upper III) until 5 years of age, and does not reach adult levels until about 12 years of age. Thus it would be expected that event-related potentials (ERPs) derived from EEG recordings would look very different early in development and, in particular, contain more positive components early on.[9] Indeed this is what is generally found.[16–24]

Issues in recording EEG early in development

There are two main issues specific to measuring EEG in infants and young children. First, attention spans are limited and young participants tire quickly, so experiments must be short. The number of trials needed depends on a number of factors including the size of the component of interest, the efficiency of the signal processes techniques used for analysis, and the amount of noise or artifact in the recordings. The faster the electrodes can be placed on the head and impedances checked, the more time will be left for the EEG recording. In this regard, high impedance systems involving nets of electrodes imbedded in sponges that are dipped into a conducting saline solution can be applied much more quickly than electrodes in low impedance systems requiring electrogel and abrasion of the skin. However, the former may be more subject to noise and may not be ideal for measuring small fast components such as those originating from the brain stem. Second, it can be difficult to keep young participants from moving excessively. Because muscle movements generate electrical field potentials an order of magnitude larger than potentials originating in the brain when measured at the surface of the head, the more the participant moves, the noisier will be the EEG recordings. Interestingly, young infants tend to move less than older infants, with the most challenging ages in this regard being between about 1 and 3 years. During electrode application and EEG recording, it is helpful to have one researcher whose job is to distract infants with toys, videos appropriate for infants, soap bubbles, and so on. If the infant is sitting on the parent's lap, the parent can also help by gently holding the infant's hands away from the electrodes. Figure 1 shows how to happily and efficiently place an electrode net on an infant.

Data preprocessing: dealing with artifact in developmental recordings

In addition to brain activity related to the processes of interest, measured EEG signals also contain "noise," largely in the forms of movement artifact and brain activity irrelevant to the processes of interest.[1,10] In order to see the activity of interest, typically many trials are presented and the resulting activity averaged across trials. Assuming that the timing of the noise is unrelated to that of the signal, the more the trials are averaged together, the better the signal-to-noise ratio. However, given that the amplitude of movement artifact can be an order of magnitude larger than that of the signal, additional methods are typically necessary to get a good signal-to-noise ratio within a reasonable number of trials. In the most common approach, here called conventional trial rejection (CTR), entire trials containing large amplitude artifact at any electrode are eliminated from the average. This approach works well for most adult data for which there are few trials contaminated with movement artifact. However, for data from infants or young children, CTR can result in the elimination of most of the data. A second approach in common usage is specific to the elimination of eye movements and involves modeling the dipolar sources of eye movements.[25] In addition to the recordings of experimental interest, EEG can be recorded for each subject in response to eye blinks and eye movements, and EEG sources related to eye movements can be modeled. These sources can then be eliminated subject by subject in the EEG data from the experiment of interest. Unfortunately this method does not work well with infants and young children whose eye blinks and eye movements are variable and not temporally confined.[26] There is also the problem of eliciting eye movements, and spending time recording eye movements takes time away from the recordings of experimental interest. A third approach is to perform independent component analysis (ICA) on the EEG data.[27,28] In adult data, the first few (largest) components of the analysis will be noise and these can be eliminated to reveal the signals of interest. Unfortunately, infant artifact often behaves differently. Rather than consisting of predominantly eye movements, infants can make sudden whole head movements, jaw movements, and scrunch the backs of their necks. Furthermore, such movements can cause an electrode to temporarily make a bad connection with the scalp. Fujioka *et al.* have illustrated that ICA does not typically work well with infant data.[29]

He *et al.*[16] introduced a method of independent channel rejection (ICR) whereby, if a particular electrode shows a high amplitude artifact on a particular trial, the data from that electrode are eliminated on that trial, but data from "clean" electrodes are kept. Thus, ICR assumes that electrodes can be differentially contaminated with artifact on the same trial. With this method, much less data are eliminated than with CTR, in which data from all electrodes are eliminated when there is a contaminated electrode. Mourad *et al.*[30] generalized the idea of ICR and developed the artifact blocking (AB) algorithm in which all trials are retained, but artifact is "blocked" or reduced as follows. This algorithm assumes that amplitudes greater than a certain threshold reflect artifact and attempts to reduce them toward zero by estimating a smoothing matrix that, when multiplied by the original EEG data matrix (electrode by time), creates a "clean" version of the EEG data matrix. In some regards, AB is similar to interpolation, in which an eliminated electrode is estimated from the surrounding electrodes, but it has the advantage of being completely atheoretical (does not require any knowledge of EEG conduction or brain and skull properties) and is computationally much less demanding.

Fujioka *et al.* [29] extensively compared ICR, CTR, and AB methods. They recorded real infant EEG activity in the absence of a stimulus and then repeatedly imbedded an artificially generated, and therefore known, EEG signal. They then analyzed the data using each of the three artifact rejection methods and compared the ability of each at extracting the known EEG signal. They found that ICR and AB were much better than CTR at extracting the EEG signal. Correlations between the embedded and extracted signals were much higher and residual variance much lower for ICR and AB than for CTR. Furthermore, CTR showed greater spatial distortion across the scalp than the other methods and AB showed the least spatial distortion, which

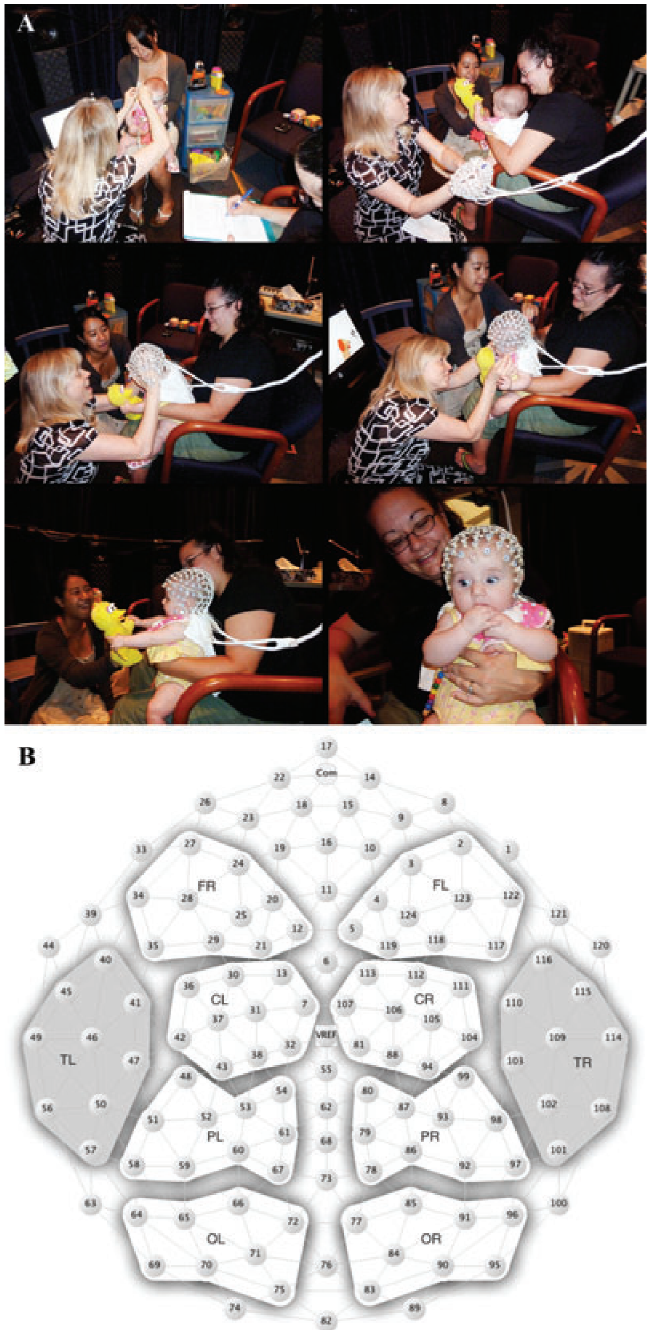


Figure 1. (A) Series of photographs illustrating placing an electrode net on an infant. The circumference of the infant's head is measured to determine net size while the mother fills out a questionnaire. Then one experimenter distracts the infant with toys while the second experimenter places the net on the infant's head and adjusts the placement of the electrodes. Once the net is on, it is quite comfortable and most infants are content. Photos by Nicole Folland. (B) For data analysis, the channels across the head can be averaged within each area to increase signal-to-noise ratio. From work by He *et al.*[16] Reprinted with permission of MIT Press Journals.

is particularly important when attempting to locate the sources of activity in the brain. To a large extent, the differences across methods appeared to be related to the amount of data that remained for analysis after artifact rejection. Thus, for adult data, AB might be less useful, but for data from infants and young children, it can offer a marked improvement over traditional methods.

Using EEG and MEG to understand musical development: examples using different data analysis techniques

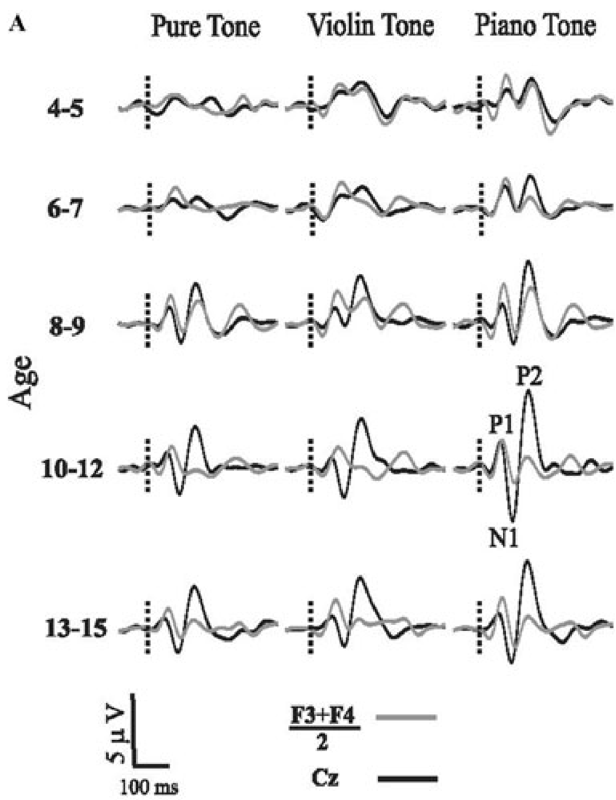
Time waveforms

EEG activity reflecting the processing of a sound event is termed an event-related potential (ERP). In the time domain, ERPs consist of a series of positive or negative deflections (components) across time from the onset of the sound that reflect activity from the nuclei of the brainstem (first 15 ms after sound onset), primary auditory cortex (middle latency responses; up to 50 ms), and areas beyond (late potentials; 50 ms and later). From a developmental perspective, differences across age can be measured in all components. From a musical perspective, effects of musical training can be seen in brainstem encoding,[31] middle latency responses,[32] as well as in various components of the late potentials.[33–37] A few examples from our lab will be described to illustrate the types of questions that can be addressed by examining time waveforms.

Perhaps one of the most interesting findings in the development of auditory ERPs is that components originating in secondary auditory cortex, N1 and P2, show a very protracted developmental trajectory. Note that because N1 and P2 are processed in auditory areas around the Sylvian fissure, the fields that they produce at the surface of the head are oriented such that for N1, a negativity is seen at frontal sites in conjunction with a positivity at posterior sites, and vice versa for P2. Although obligatory responses to sound in adults, these components are so small as to be difficult to measure in children 4 to 5 years of age. With increasing age, they increase in amplitude and decrease in latency, reach a maximum amplitude around 10 to 12 years of age, and subsequently decrease in amplitude, reaching stable adult levels in the late teenage years (see Fig. 2A).[36,38,39] The development of these components appears to be affected by musical experience in that they are larger in adult musicians than nonmusicians. Furthermore, they are larger in 4- to 5-year-old children taking music lessons compared to children not taking music lessons (see Fig. 2B).[36] In sum, examining the developmental trajectories and effects of musical experience on various components in the time domain can yield valuable information about when processing develops for different musical features, and differential effects of musical experience at different ages.

Difference waves and mismatch responses

As discussed in the previous section, some EEG components that are obligatory responses to sound in adults, such as N1, are very small or nonexistent during infancy.[36,38,40,41] Interestingly, although N1 originates in superficial layers of auditory cortex, it likely reflects feedback from other cortical areas[6,8,42] and is sensitive to attentional manipulations.[43,44] On the other hand, automatic (preattentive) responses to occasional changes in an ongoing stream of sounds elicit mismatch responses that are likely processed largely within auditory cortex. In adults, such changes elicit a frontal negativity at the surface of the head between 130 ms and 250 ms accompanied by a reversal at occipital sites.[45,46] A mismatch response can also be elicited in young infants in response to occasional changes in pitch,[16,17,21,47–50] duration,[51,52] and tonal patterns.[18,53] However, in young infants, only a slow frontally positive mismatch response is typically evident.[9] The age at which the negative response emerges appears to depend to some extent on the feature that is changed. For occasional changes in pitch, at 2 months the slow positive response dominates, but the negative response can be seen at 3 months and is quite robust at 4 months (Fig. 3), whereas for temporal gap detection and changes in melodic patterns, the negative response does not emerge until later.[51,53] Interestingly, at intermediate ages, both the positive and negative mismatch responses can be seen at the same time, in the same infants, suggesting that they have different cortical origins.[16] With respect to musical training, mismatch negativity is larger in musicians than in nonmusicians for changes in melodies in transposition without accompaniment[54] and in polyphonic contexts.[55] There are few studies involving musical experience in young infants. However, one study exposed infants for 20 min a day for a week to melodies in either guitar or marimba timbre.[50] Subsequently, mismatch



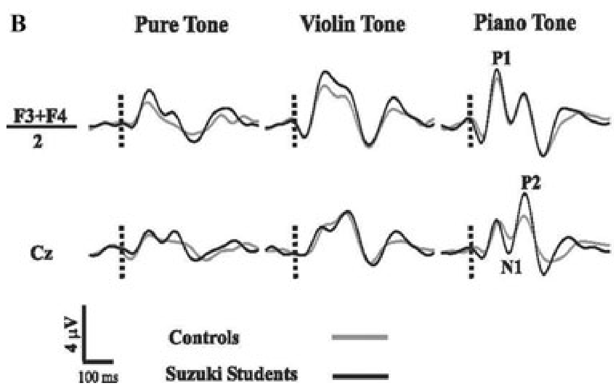


Figure 2. Development of ERPs elicited by pure, violin, and piano tones. (A) P1 reaches a maximum at 8 to 9 years of age at frontal (F2, F4) sites and diminishes thereafter. N1 reaches a maximum at 10 to 12 years of age at the vertex (Cz) and diminishes thereafter. (B) P1 and N1 are enhanced for piano tones in Suzuki piano students. The dotted vertical line represents the onset of the stimulus. From work by Shahin *et al.*[35] Adapted with permission of Wolters Kluwer/Kippincott, Williams & Wilkins.

responses were measured to quartertone changes in the pitch of a repeating tone, in one block with tones in guitar timbre and in another block with tones in marimba timbre. Differential responses were found favoring the timbre to which infants had been familiarized.

In sum, mismatch responses provide a rich context in which to measure the development of many

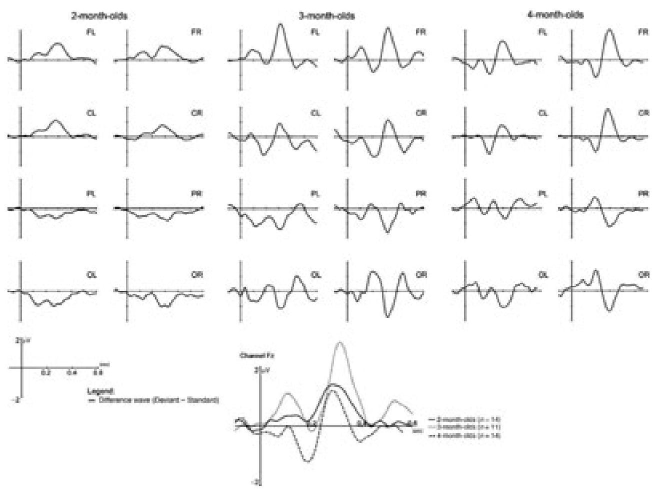


Figure 3. Development of mismatch responses to pitch change in 2-, 3-, and 4-month-old infants. Grand average difference waves are shown for each age group (filtered between 0.5 and 20 Hz), illustrating the slow positive difference wave at 2 months of age and the emergence of the mismatch negativity with increasing age. Difference waves at electrode Fz are overlaid for the three age groups at the bottom. The vertical axis represents the onset of the sound. From work by He *et al.*[16] Reprinted with permission of MIT Press Journals.

aspects of musical perception and the effects of musical experience at different ages.

Oscillatory responses

Even in the absence of specific stimulation, EEG and MEG recordings reveal ongoing oscillatory brain activity thought to reflect communication between networks of neurons. Indeed, one view is that the evoked potentials described in the last two sections reflect phase alignment of ongoing oscillatory activity that becomes entrained for analyzing a particular input.[56] Thus, changes in oscillatory rhythms in response to an auditory stimulus can reveal important aspects of stimulus processing. Oscillatory responses have been classified into five main frequency ranges, delta (0–4 Hz), theta (4–8), alpha (8–12), beta (12–30), and gamma (30–100), roughly according to proposed associated brain functions. A full discussion is beyond the scope of this paper, but can be found in recent reviews.[57,58] However, oscillatory responses change greatly over development, can be affected by attention, and can also reflect-specific effects of experience and training.[59–63] Thus we predict that they will be used increasingly in the study of musical development. Here, we briefly give examples in the alpha, beta, and gamma frequency ranges.

In the resting state, alpha is a dominant rhythm in the adult brain, and it decreases in amplitude in selective regions with stimulus presentation in different modalities.[64–65] Similar desynchronization can be seen in infancy, such that alpha-band oscillations originating from auditory cortex (termed tau) decrease in amplitude with auditory stimulus presentation.[66] However, the dominant tau frequency suppressed by sound changes with development: at 4 months of age it is 4 Hz, and by 12 months of age it is 6 Hz. Effects of experience on this development remain unknown, but further studies of the tau rhythm have the potential to increase our understanding of the development of musical sound processing.

Beta band activity has long been of interest as it is a dominant frequency in the motor system and its amplitude modulates with motor movement.[67] Recent studies indicate that the amplitude of beta activity originating in auditory cortex is modulated by the presentation of a steady beat.[68] In particular, beta amplitude decreases after each beat and rebounds before the onset of the next beat (Fig. 4). This rebound occurs across different beat tempi, indicating that the brain is predicting the timing of the next beat.[69] Applying such analyses to developmental data has the potential to further our understanding of developmental and experiential aspects of musical rhythm processing.

Gamma band activity is of interest in the auditory system as it is thought to reflect attention,

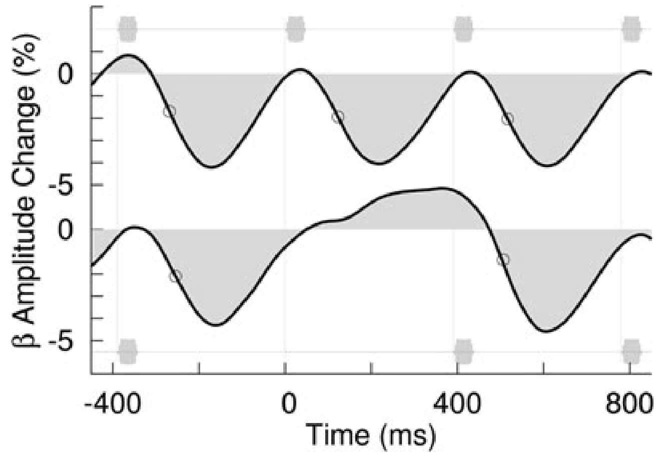


Figure 4. Beta modulation by sound presentation. The time series for event-related changes in beta (15–20 Hz) activity is shown in response to a regular stimulus sequence (top) and in response to the omission of an expected stimulus (bottom). The sound stimulus is shown above for the regular sequence and below for the omission sequence. Beta activity decreases in amplitude following stimulus onset and rebounds prior to onset of the next stimulus. From work by Fujioka *et al.*[68] Reprinted with permission from John Wiley & Sons.

anticipation, and expectation[70–72] and the binding of auditory features into a unitary percept.[73] Gamma band activity (indeed, any oscillatory activity) can be analyzed in two different categories, evoked and induced. Evoked activity is phase locked to the onset of a stimulus, and can therefore be seen by averaging the EEG or MEG signal over many trials. Induced activity, on the other hand, is also modulated by the presentation of a stimulus, but in this case it is not phase locked to the onset of the stimulus such that averaging across trials leads to canceling of the signal.[74] Thus, this type of activity must be analyzed on a trial-by-trial basis. However, because it is thought to reflect the entrainment of ongoing intrinsic brain activity with an external stimulus, it is of great interest for understanding attention and the interaction of top–down and bottom–up processes. Shahin *et al.* examined the effects of musical experience on induced gamma band activity.[61] They found that the presentation of a musical tone produced waves of increases in gamma band activity that lasted for at least half a second after stimulus onset. Furthermore, induced gamma band activity was greater in adult musicians compared to nonmusicians. Perhaps of most interest, two groups of 4-year-old children, one beginning music lessons and the other engaged in an equal amount of other extracurricular activity such as playing sports, were measured at the onset of lessons and one year later. Neither group showed any significant gamma band activity at first measurement. At the second measurement, only the group undergoing musical training showed significant gamma band activity, such that the groups did not differ at first measurement, but did differ at the second measurement (Fig. 5).

In sum, to date oscillatory activity has not been used extensively in studies of musical development. However, it holds much promise as a technique that can reveal how the brain processes music and the effects of development and experience.

Machine-learning approaches

The predominant approach to EEG and MEG data analysis is to identify features and components, study how they are affected by various manipulations, and relate them to processes of interest. Machine-learning approaches differ in that they are atheoretical and examine a vast array of data features simultaneously to determine those that best classify according to an outcome variable. They have been used with EEG data, for example, to detect seizure in infants[75] and epileptic adults,[76] and to predict responses of schizophrenic patients to different medications.[77] In terms of development, machine learning was recently applied to EEG data measured in response to musical sounds in order to predict the

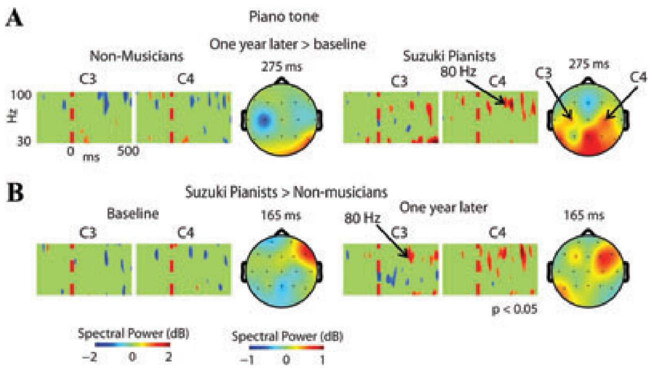


Figure 5. Development of induced gamma band activity in 4- to 5-year-old children. Spectral power of gamma band activity at central channels (C3/C4) and topographies (middle) at the peak amplitude. (A) Initial measurements contrasted with measurements one year later in nonmusician children (left) and Suzuki pianists (right) in response to piano tones. Only the Suzuki group shows evidence of gamma-band activity (periodic red signals) after one year of music lessons. (B) Contrasts between the two groups show that at the initial measurement, the groups do not differ in gamma-band activity (left) but that they do differ after one year of music lessons (right). The dotted line shows onset of the piano tones. From work by Shahin *et al.*[61] Reprinted with permission from Elsevier.

age of infants.[78] Such techniques show potential for the study of effects of musical training on brain development.

Voxel-based source waveform analysis of MEG data

As discussed previously, EEG and MEG have the advantage over fMRI of very fine temporal resolution that allows the study of oscillatory brain responses. fMRI remains superior for determining the locations of activity in the brain, but much research has been invested to develop better techniques for determining the source locations of EEG and MEG activity measured at the surface of the head. As an example, Fujioka *et al.* have used a procedure for estimating the time waveforms of MEG data in every 5 × 5 × 5 mm voxel across the brain.[79] Briefly, it involves using synthetic aperture magnetometry, a spatial beamforming technique,[80] in conjunction with a common head model derived from MRI data, and applying this to time domain-averaged MEG waveforms.[81] Such techniques have successfully localized activity in auditory and motor cortices[69,82] as well as in deeper sources, including the hippocampus[69,83] and amygdala.[84]

As an example, the beta band data described previously, in which the presentation of a steady auditory beat-evoked amplitude modulations in beta-band activity in auditory areas was subject to a whole-head analysis.[69] Interestingly, even though the stimulus was auditory and there was no movement or suggestion to move, correlated modulation of activity in the beta band was seen across a wide range of motor-related areas including sensorimotor cortex, inferior frontal gyrus, supplementary motor area, and cerebellum.

At present, such techniques have not yet been applied to questions in musical development, nor have they yet been developed successfully for EEG data where activity from different sources is smeared to a greater extent at the surface of the head. But it is clear that these techniques are promising for studies of musical development and the effects of experience.

Conclusions

Collecting or analyzing developmental EEG and MEG data is not easy. However, as illustrated by the few examples from our laboratory in this paper, EEG and MEG data can contribute substantially to our understanding of musical development and the effects of musical training on brain development. Furthermore, new data analysis techniques examining oscillatory behavior, classification according to machine-learning approaches, and voxel-based source waveform extraction across the whole head offer great promise for future studies of musical development.

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Conflicts of interest

The author declares no conflicts of interest.

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