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A gene-maturation-environment model for understanding sensitive period effects in musical training

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Adult ability in complex cognitive domains, including music performance, is commonly thought of as the product of gene-environment interactions, where genetic predispositions influence and are modulated by experience resulting in the final phenotypic expression. Recently, however, the important contribution of maturation to gene-environment interactions has become better understood. Thus the timing of exposure to specific experience, such as music training, has been shown to produce long-term impacts on adult behavior, as well as on brain structure and function. The goal of this paper is to formulate a model of gene-maturation-environment interactions in the context of musical skill, and to illustrate how this framework can provide an important window into understanding how predispositions, brain development and experience interact.

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Introduction

As with most complex abilities, adult musical skill is the product of genetic and environmental contributions that interact with each other in multiple ways. Genes encode individual differences in specific abilities and they also interact with the environment to passively and actively influence the development of skills [1••,2••]. Genes also control neural and physical maturation, such that different brain networks and abilities have developmental peaks at different ages [3,4••]. Across all major neural systems it has been shown that relevant experience has greater effects during periods of peak maturational change, which have been termed sensitive or critical periods [3,4••,5•,6•]. The goal of this paper is to present current evidence for sensitive period effects for musical training and to present a gene-environment-maturation model for the development of musical skill.

Evidence for sensitive periods in music training

A sensitive period is a window in development when specific experience has long-term effects on behaviour and the brain [5•; and See Box 1]. Examples include better grammar and accent when a second language is acquired early [7,8] and improved restoration of hearing function with earlier cochlear implantation [9]. This is in contrast to a critical period where specific experience is *required* for appropriate behavior and brain function to develop [3]. Most complex cognitive functions are characterized by sensitive rather than critical periods: there are better and worse times to learn a second language, pick up a musical instrument or start playing chess, but these skills can be acquired to some degree at any time of life. This is because complex abilities require the contribution of interacting brain networks whose structure and function are more and less plastic at different stages of maturation. Brain maturation across development can be thought of as a cascade of sensitive and critical periods that are more or less responsive to particular experience [4••,10•]. Further, it is critical to keep in mind brain regions and their associated functions do not develop in isolation, but within connected networks where both earlier and later maturing regions can influence development. Further, maturation can be influenced from the bottom up by incoming sensory information, or by top-down influences from higher level cognitive areas [11••,12•]. Reciprocal communication between networks is likely an important ongoing contributor to brain and behavioural maturation, which has been termed *interactive specialization*, which posits that maturation affects not just individual regions, but functionally connected networks and their organization [11••; and See Box 2].

Anecdotal evidence from the lives of famous musicians suggests that early age of start (AoS) of training can promote the development of extraordinary skill in adulthood [13]. (Mozart, who mastered the piano at age 4–5 and performed professionally throughout his childhood is probably the most famous example.) Early empirical

Box 1 Sensitive and critical periods

A sensitive period is a window in development when specific experience has particularly potent effects on brain plasticity, and thus long-term effects on structure and function [5•]. This differs from a critical period where exposure to specific experience is *required* for appropriate behaviour and neural development to occur. The classic example of a critical period is 'lazy eye' syndrome in which early visual deprivation in one eye results in irremediable loss of acuity and responsiveness in visual cortex [3]. Whereas the effects of early deprivation in lazy eye cannot be changed later in life, this is typically not the case for more complex behaviours, such as musical achievement or second language learning.

Work in rodents has shown that the critical period for frequency tuning in auditory cortex occurs between 11 and 14 days postnatally, whereas tuning for frequency modulation occurs later [10•]. The fact that the same auditory experience before or after the critical period does not produce the same effects suggests that immature neural systems do not have a uniform potential for plasticity across maturation and are simply awaiting stimulation. It is thought that both sensitive and critical windows are opened by a combination of maturational readiness – programmed peaks of plasticity controlled by genes – and exposure to the appropriate quantity and quality of experience [3,4••,10•]. Biological mechanisms underlying the opening of sensitive periods initially depend on adequate maturation of GABA-ergic inhibitory networks that regulate changes in cellular and synaptic architecture in the presence of appropriate sensory stimulation. Closing of these windows depends largely on final maturation of inhibitory networks, which regulate a constellation of cellular and molecular mechanisms that brake plasticity, including myelination and development of perineuronal nets [3,4••,10•]. Limiting plasticity, and thus fixing behavioural repertoires and neural representations, stabilizes function, forming a basis for on-going learning and development. On-going developmental plasticity is regulated by the balance of excitatory and inhibitory mechanisms, and is influenced by the specifics of experience.

On the basis of this understanding of the underlying biological mechanisms, it is better to think of the distinction between sensitive and critical periods as a continuum: one in which genetics, the mechanisms underlying opening and closing, and experience may contribute more or less strongly depending on the functional system and the maturational time-point. Further, there is growing evidence of sensitive or critical period effects in multiple regions of cortex, each of which has a specific temporal window (for example, see Bedny in this issue). The timing of sensitive periods will thus depend on the maturational time-line of relevant regions and the time-line of the behaviours that they control. So throughout the entire developmental process we can imagine a cascade of sensitive periods that open and close at different times and which are sensitive to different types of experience [3,4••,10•]. Further, because brain maturation occurs within connected networks, plasticity induced during one sensitive period may contribute to learning and plasticity in more or less mature regions [11••,12•]. This is consistent with the greater temporal variability of sensitive period effects for more complex functions. Basic sensory and motor functions that are represented in a single cortical or subcortical region may have earlier, more clearly defined and less malleable windows for plasticity. More complex abilities, such as language or music, which are represented across multiple functional regions – some of which develop into adulthood – may have broader, more variable windows for change, and multiple functional routes for plasticity.

Together, this suggests that plasticity during a sensitive period may generate meta-plastic effects where change during the open window may serve as a scaffold on which later experience can build [20]. The concept of meta-plasticity originates from studies of hippocampal learning mechanisms, and denotes the idea that experience can change the potential for plasticity of a synapse [63•, For review see Ref.: 79]. Evidence for behavioural meta-plasticity comes from animal and human studies showing that early stress shapes learning later in life [80]. Evidence for metaplastic effects resulting from music training comes from studies showing that musicians have enhanced learning of sensory and motor skills [41–43], and greater increases in M1 activity during learning [81].

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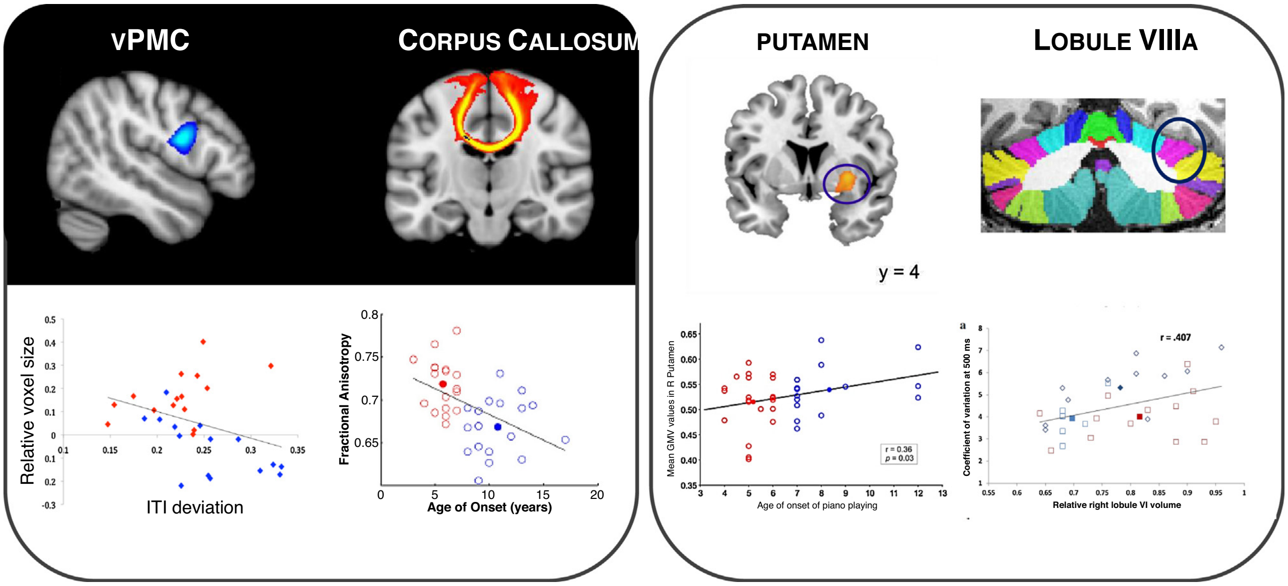
evidence for the impact of AoS came from studies of 'perfect' or 'absolute' pitch – the ability to name the pitch height of isolated tones. A large-scale study found that 78% of musicians with absolute pitch began their training before age 6 [14]. Initial evidence for the effect of AoS on the brain came from work showing that the surface area of the anterior corpus callosum was larger in those who began training before age 7 [15]. However, there was no control for years of experience, thus the observed differences could be related to the fact that early starters had more years of experience than late starters of the same age. Further, there were no measures of musical skill, and thus brain structural differences could not be linked to relevant behavior. Therefore, to systematically examine the effect of AoS, we conducted a series of studies comparing musical abilities and brain structure in adult musicians who began training before and after age7 [Early trained $\leq$ age 7 (ET); Late-trained $\geq$ age 7 (LT)]. Importantly, groups were matched for years of music experience, years of formal training, and hours of current practice [16–22]. We also assessed global cognitive function and working memory. Data from these studies are summarized in Figure 1.

Across all studies, we found that ET musicians out-perform LT musicians on measures of rhythm synchronization and melody discrimination. Further, ET musicians showed enlargement of ventral premotor cortex (vPMC) that was related to performance on the rhythm task [19]. We also found that ET musicians had enhanced white matter (WM) integrity in the posterior mid-body of the corpus callosum (CC), the location of fibres connecting primary motor (M1) and the premotor cortex (PMC) in the two hemispheres [20]. Intriguingly, in the same sample, we showed that ET musicians had *smaller* volumes of cerebellar lobules IV, V and VI, and that smaller volumes were related to reduced variability on an auditory-motor timing task [21]. We have recently replicated this finding, and shown that the cerebellar and cortical volumes are inversely correlated [23]. This suggests that plasticity in the two regions is interdependent, and is consistent with evidence that connected regions change together across development [11••,24••]. It is also consistent with data showing that ET pianists had smaller grey matter (GM) volume in the right putamen, and lower timing variability when playing musical scales [22].

Figure 1



Current Opinion in Behavioral Sciences

Effects of early musical training on brain structure.

Figure 1 (left to right): The first panel shows expansion of right vPMC in ET versus LT musicians and the relationship between vPMC volume and performance on a rhythm synchronization task (ET = red; LT = blue) [18]. The second panel shows greater fractional anisotropy (FA; blue) in the posterior mid-body of the corpus callosum and its connections to motor and premotor cortex (yellow–red). The graph below shows the relationship between FA in this region and AoS [19]. The third panel shows enhanced volume of the right putamen in ET musicians and the relationship with AoS [21]. The fourth panel shows the region of decreased cerebellar volume in lobule VI and its relationship to tapping variability (ET = light blue; LT = red; non-musicians = dark blue [20].

We have interpreted these findings based on data about the function of these regions, the timing of their normative maturation, and the relative contribution of genes and environment to their variability (See Box 2 and Figure 2). Developmental data show that GM volume of anterior motor regions, including M1 and PMC have a peak rate of change between the ages of 6 and 8 [25]. The PMC is known to be involved in auditory-motor integration [26] and is thought to play a key role in motor timing [27]. The size of the posterior mid-body of the CC also has a maturational peak in middle childhood [28], and adult variability in this region has a strong unique environmental contribution [29]. This part of the CC connects M1 and PMC, and is related to bimanual coordination in children and adolescents [30]. In contrast, peak maturation in the cerebellum occurs later, between the ages of 12 and 18 [31]. The cerebellum is structurally homogeneous, with subregions connected through feedforward and feedback loops to the rest of the brain [32]. In motor control, these circuits are known to play a role in error-correction, optimization and instantiation of forward models. Because they are uniform and connect to all regions of the cortex, it is hypothesized that they may also perform the same role in optimizing a wide variety of sensory and cognitive functions [33]. The cerebellar regions we found to be smaller in ET musicians are connected to frontal motor and association regions, including M1 and PMC [32]. Because these regions are functionally connected, plasticity effects of early training on cortical regions may be partially mediated by cerebellar optimization mechanisms that result in greater efficiency and thus reduced volume. On the basis of these data, we hypothesize that early experience during periods of peak maturation promotes brain plasticity, and that regional differences in genetic permeability mean that some brain regions are more susceptible to the impact of training than others. Our findings emphasize that the impact of early experience occurs at a network level, with changes in one region influencing changes in connected regions.

Differential effects of AoS and type of training were revealed by a recent study in which we compared the effect bilingualism and music training on the structure of the arcuate fasciculus (AF) [34]. The AF is a white matter pathway that connects posterior auditory cortex and frontal motor regions, and whose structure has been linked to language in the left hemisphere [35] and to music in the right hemisphere [36]. All participants in our study exhibited a left-greater-than-right asymmetry in the volume of the long segment of the AF, consistent with previous findings [37]. This portion of the AF has been linked to left-hemisphere dominance for language, and it is hypothesized that its structure may be largely under genetic control [38]. In an interesting dissociation, simultaneous bilinguals, who acquired their L2 in the first year of life showed an increased volume of the left long segment and a greater leftward asymmetry, while ET musicians showed an increased volume of the right long-segment and reduced leftward asymmetry. These findings suggest that very early, intensive bilingual experience can modify a white matter pathway that is typically under strong genetic control, whereas music training at a later period in childhood affects the right hemisphere, which may be more open to on-going experience. These results support the idea that brain plasticity depends on region-specific differences in malleability by experience, the age at which experience begins as well as the type of experience.

If the observed differences in behaviour and brain structure between adult ET and LT musicians are hypothesized to result from the interaction between AoS and experience, an important question is how soon after training in childhood do they appear? To address this we tested whether AoS affected musical skills in childhood after four years of lessons. To do so, we compared melody discrimination and rhythm synchronization in groups of ET and LT children using age-normed scores [39]. Groups were matched for years of music lessons and hours of weekly practice, as well as working memory, global cognitive function and socio-economic status [40]. We found that ET children performed better than their LT counterparts on a simple melody discrimination task, and that across groups, AoS and global cognitive function independently predicted discrimination scores. There were no group differences or effects of AoS for the rhythm synchronization or a transposed melody discrimination task, but working memory ability predicted these scores. In addition, weekly practice predicted transposed melody discrimination. These results illustrate the combined effects of maturation, training and cognitive abilities on the development of musical skills. Further, they suggest that basic pitch abilities mature earlier than more complex auditory and motor functions, and/or that children who begin early have advantages in pitch processing. Finally, in this study and in a previous sample of adults, we were able to validate that the age range where early training has its strongest effect is between the ages of 7 and 9 [17].

Box 2 Brain maturation

Maturational changes in brain structure are continuous throughout the lifespan. Maturation is controlled by genes and modulated by environmental stimulation generally proceeding from primary sensory and motor regions to frontal and parietal association areas [24••]. Brain regions do not develop in isolation, but rather in structurally and functionally connected networks [82] that may also share timelines of modulatory gene expression [24••].

Following birth, across the brain the number of synapses, and therefore the volume of grey matter (GM), continues to increase for between 3 and 15 months [83]. Afterward, synapses are reduced through pruning, a process thought to underlie early experience-dependant specialization, including perceptual narrowing for native language speech sounds [4••]. Studies of brain development based on structural magnetic resonance imaging (MRI) show that GM volume and cortical thickness (CT) peak in childhood (6–10) and then decrease across adolescence and into adulthood. During the same period, white matter (WM) volume increases and then remains relatively stable into older adulthood [84,85]. Patterns of cortical thinning and WM growth proceed from primary sensorimotor to frontal, parietal and temporal association areas. GM thinning and WM expansion are largely the result of increased axonal myelination and proliferation of glial cells within the cortical ribbon, which shift the GM/WM boundary measured by MRI [85]. While the surface area or extent of cortical regions is thought to be largely under genetic control, individual variation in CT is thought to reflect a combination of accumulated genetic and environmental effects [86••].

Along with frontal-parietal and temporal networks, some subcortical regions also have relatively late peaks of structural change. Cerebellar volume peaks in adolescence [31], at a time that coincides with changes in its functional interaction with connected cortical regions [87]. The cerebellum forms loop connections with many regions of the cortex, and is thought to be important for optimization of sensory, motor and cognition function [33]. Later maturation of the cerebellum may thus be linked to parallel peaks in the fronto-parietal cortical networks to which it is connected. Finally, the striatum, a region important for the processing of reward (including musical reward) also appears to peak in adolescence [13–17,77] at a time that coincides with changes in dopamine modulation of incentive reward [78].

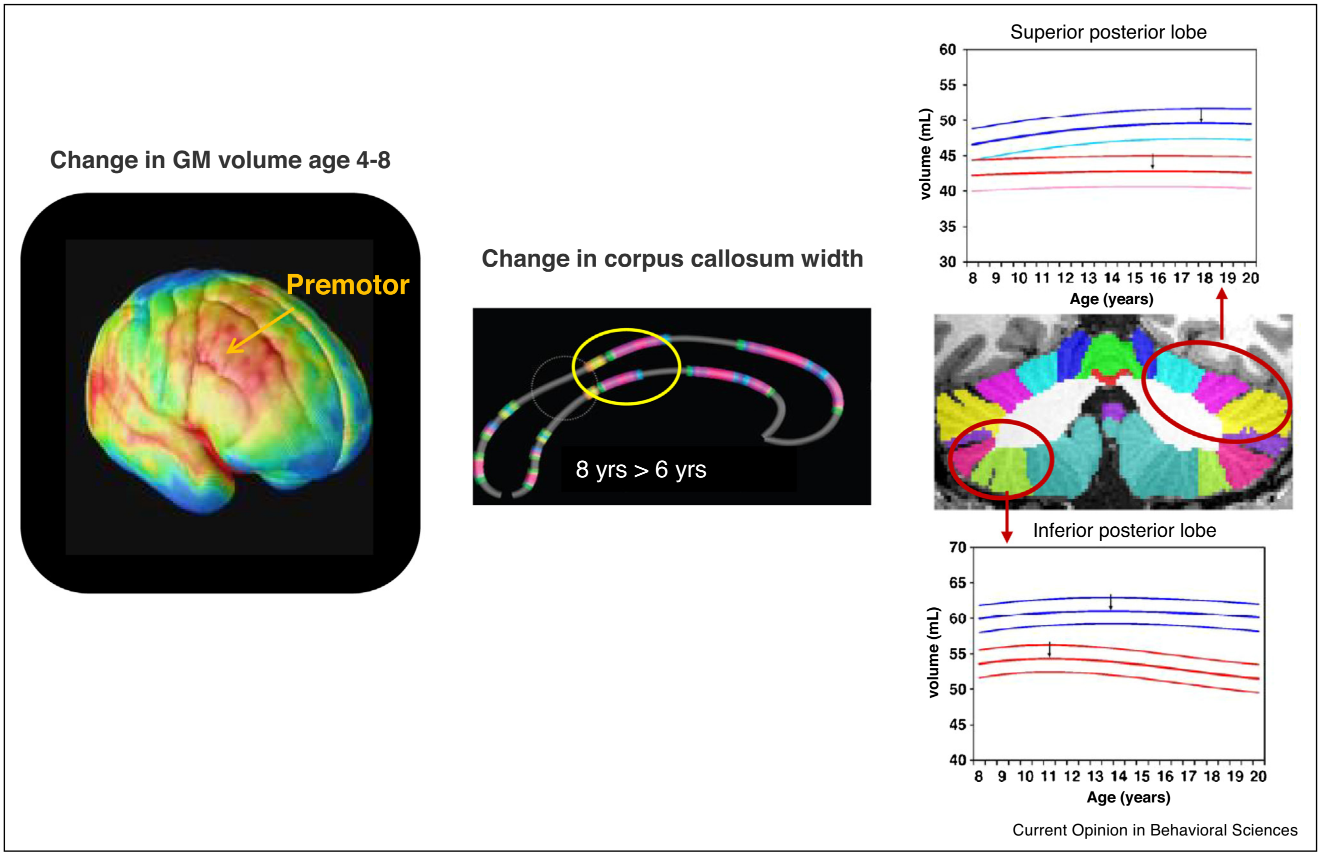
Together, current data show a pattern of rapid growth in the first 1–2 years of life that is largely genetically controlled, and which underpins maturation of basic sensory and cognitive functions. Across childhood and adolescence, maturational changes occur largely in WM density and connectivity within and between cortical networks that underlie complex sensorimotor and cognitive processes. These changes are thought to be more strongly modulated by experience. Putting together information about brain maturation with known changes in behaviour across development presents an intriguing contradiction. Peak cortical maturation of sensorimotor networks occurs in middle childhood, but basic perceptual and motor abilities develop much earlier. Additionally, sensorimotor abilities and their associated neurophysiological markers continue to develop after their childhood peak through adolescence and into early adulthood [12•,88,89]. We can make sense of this contradiction by hypothesizing that development may rely on interactions between more mature, low-level sensory and motor processes and less mature, higher-level processes [11••,12•]. These interactions can thus bootstrap processing in less mature regions. This may first occur in infancy between early developing brainstem regions and later-developing cortex, and in childhood between primary cortical areas and later developing frontal-parietal areas. Interactions between earlier and later developing networks is likely an ongoing feature of development and has been termed *interactive specialization* [11••]. These findings lead to a more complex picture of brain maturation where regional maturation depends on both local changes and network-level properties.

Integrating these results with those of adult ET musicians, we hypothesize that early training has an immediate impact on skills such as simple melody discrimination that rely on earlier-maturing regions including auditory cortex. Better simple melody discrimination skills may then promote acquisition of more complex skills, such as transposition or even rhythm synchronization. More crucially, we propose that early practice exerts a meta-plastic effect in which experience promotes the long-term potential for learning and plasticity when exposed to additional training [See Box 1 for a more detailed description of the concept and neurophysiological bases of meta-plasticity]. Thus, we hypothesize that abilities, such as transposition and rhythm synchronization, which do not show immediate gains in early trained children, would be more readily acquired because early experience has primed the underlying neural systems to learn. This is consistent with evidence that adult musicians show better learning of new sensory and motor skills [41–43]. These more complex skills might also require further cognitive and physical maturation as well as additional training.

Training-related plasticity in childhood

The hypothesis that the observed effects of early AoS are partly the result of training-dependent plasticity is consistent with longitudinal studies of music training in childhood showing structural and functional changes in auditory and motor cortex, as well as the corpus callosum after 1–2 years of practice [44–48]. In these studies, no behavioural or neurophysiological differences were observed before the start of training, even though the groups self-selected to take music lessons, and thus might represent children with pre-existing skills or predilections. The fact that these changes occur in similar regions of the auditory-motor network that have been shown to differ after long-term training in adults supports the inference that these differences can be attributed in part to training. It is also consistent with a recent study comparing brain structure in monozygotic twins who were discordant for music practice. It found that the twins who played an instrument had greater cortical thickness in auditory and motor regions as well as WM enhancements in the corpus callosum compared to those who did not [49••]. Because these twins start life with an identical genetic makeup and

Figure 2



Maturational changes in brain structure in regions associated with early musical training.

Figure 2 (left to right): The first panel shows changes in whole brain GM volume between ages 4–8 (hot colours are regions of greater change) [23]. The second panel shows changes in the width of the mid-sagittal corpus callosum between the ages of 6–8 [26]. Yellow circle indicates the region of the posterior mid-body where differences were found between ET and LT musicians [19]. The third panel shows the developmental trajectories of GM volume in cerebellar regions [29], including those that showed decreased volume in ET compared to LT musicians [20].

can be supposed to have a very similar family environment, this study provides the strongest evidence thus far that observed differences in brain structure between musicians and non-musicians can be attributed to the effects of training.

Individual differences: possible genetic contributions

Although direct evidence for specific genetic contributions to musical skill is currently limited [50], there is indirect evidence for possible structural or functional predispositions that are related to better performance and learning of musical tasks. A study of 8–10 year-old children taking music lessons found that the volume of auditory cortex was larger in those who practiced more, and was associated with measures of music aptitude, as well as behavioural and physiological measures of auditory processing [51•]. Further, aptitude accounted for a greater proportion of the variance in auditory cortex volume than practice time. The authors interpreted their findings as suggesting that auditory cortex volume might be a pre-existing anatomical feature that contributes to long-term development of musical skills. However, it is also possible that training-related plastic changes had already occurred in the period preceding the study, as most children had already been playing for 1–2 years.

Genome-wide association studies have linked musical abilities to genes involved in development of the cochlea and auditory brainstem [50]. But as with other complex abilities such as language and IQ, the likelihood that single genes account for the broad range of individual differences in a complex function is small. Twin studies in a sample with a range of musical experience have shown that genes appear to account for a moderate portion of the variance in music abilities [52]. They also show that the propensity to practice appears to be heritable [53], and that personality variables such as 'openness to experience' are associated with lifetime practice [54]. These findings are supported by correlational evidence that musical ability is linked to cognitive and personality variables in addition to practice [55]. Finally, an enriched musical environment in childhood is associated with greater musical achievement later in life, and also increases the relative contribution of genetic variability to achievement [56]. The evidence for genetic contributions to musical ability closely parallels that for global cognitive function (IQ), which has been found to be highly heritable, but which is also modulated by family and social environment, as well as personality [For review see Ref.: 1••]. Comparison with other complex cognitive functions reminds us that the simple idea that either genes or environment alone contribute to variability in musical skill should give way to a more sophisticated appreciation of the range of gene-environment interactions and their impact on ability.

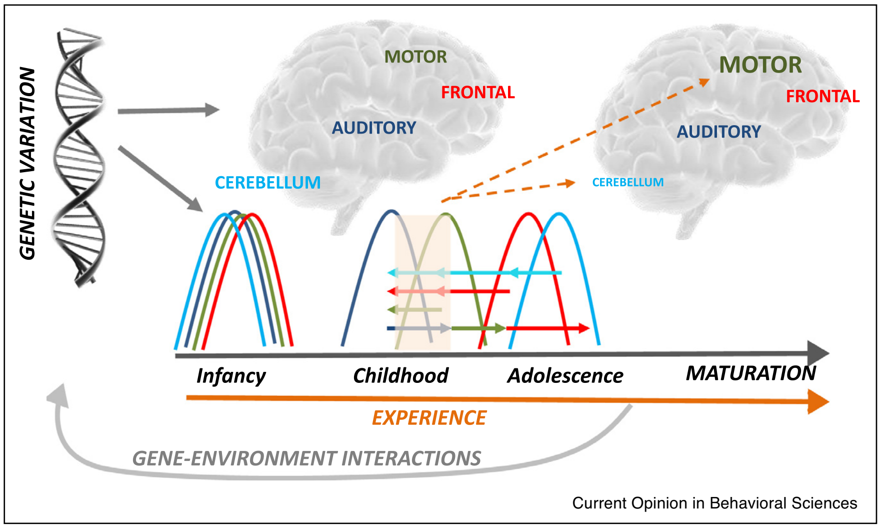
Individual differences: predisposing factors

Even in untrained adults, individual differences, particularly in the auditory-motor network, are linked to musical abilities and the capacity to learn. For example, in a sample selected to have a range of musical experience, GM concentration and cortical thickness in auditory and parietal regions was found to be related to the ability to discriminate melodies which had been transposed [57]. Further, WM integrity in the left arcuate fasciculus and the temporal segment of the CC were found to predict individual differences in auditory-motor synchronization [58]. The ability to learn musical skills has also been linked to individual variation in auditory and motor regions of the brain. In a longitudinal where non-musicians learned to play short piano melodies, greater activity in auditory cortex when listening to the melodies before training began predicted how fast people learned [59]. Similarly, greater responsivity to pitch differences in auditory cortex before training was related to later rate of micro-melody learning [60]. In a study of cello learning, greater activity in the supplementary motor area, as well as its degree of connectivity with auditory cortex during passive listening before training was positively correlated with learning success [61]. Finally, WM connectivity between auditory and motor regions was also related to melody learning success [62].

Why is music such an effective driver of sensitive-period plasticity?

We have argued that musical training that begins during a sensitive period promotes long-term changes in brain and behaviour. But what features of music training produce these effects? One obvious answer is practice – lots of practice. When children begin lessons they typically play only a few hours per week [39,51•], but the average total duration of training for musicians in the studies reviewed here was 15–20 years. This is the equivalent of thousands of hours of practice across a large portion of a person's life. While the idea that simply practicing long enough will result in expertise has been debunked [For review, see Ref. [53]], length of training is typically strongly related to both brain differences and performance [63•]. Thus, long-term practice and related plasticity can build upon effects of early AoS based on both behavioural scaffolding and metaplastic effects that promote later learning. The nature of music training may also be particularly effective in promoting plasticity. As a musician practices, he or she engages in a repeated cycle of prediction, feedback and error-correction [64,65]. Feedback and error-correction are key components of motor learning, and studies of both motor and sensory learning show that functional and structural changes in the brain are driven by decreases in error and improved precision [66]. Thus, error-driven learning, particularly during periods of high developmental plasticity may be an important contributor to structural brain changes. Music training may also be particularly potent because it is inherently multi-sensory sensory

Figure 3



Current Opinion in Behavioral Sciences

Gene-maturation-environment interaction model.

Figure 3 illustrates the gene-maturation-environment model, with genetic variation codes for individual differences in brain structure as well as maturational changes. Maturation is shown to have two distinct bursts, one during infancy (the first two years of life) and another during childhood and adolescence. Different regions, such as auditory, motor, frontal and cerebellum have peaks of maturational change at different times. Experience during a sensitive period in childhood (orange bar) can have differential effects on structure in different regions. Plasticity in early and later maturing regions can have feedforward and feedback effects on connected regions. Experience can also modify plasticity through gene-environment interactions.

(combining hearing, sight and touch), and co-activation of circuits deriving from multiple senses may drive plasticity more strongly than input from a single sense [67].

A final feature that is likely crucial in promoting plasticity is the rewarding nature of music and the pleasure of accurate performance. The intrinsic pleasure derived from music appears to be common to most people [68], and is hypothesized to be based on the same dopamine-modulated, predictive systems that regulate reward in other domains [69,70]. Learning to produce a rewarding stimulus, such as music, is thus likely to be rewarding to the player. We also know that the reward value of what is learned strongly influences learning and plasticity. Animal studies show that brain plasticity associated with auditory learning is greater when the information to be learned is rewarded, or behaviourally relevant [71]. Importantly, dopamine has been shown to modulate motor learning in both humans and animals [72–74], possibly through the reinforcement and habit-formation circuitry of the striatum [75,76]. The interaction of music training and reward may be at its peak during late childhood and adolescence when brain structures and mechanisms associated with motivation are developing rapidly [77,78].

Model

On the basis of these findings and existing models [2••,4••], we propose a multidimensional gene-maturation-environment framework for the development of musical skill (See Figure 3). Under this framework, genetic variation produces individual differences in musically relevant abilities such as auditory perception and motor control, as well as in non-specific cognitive and personality factors including general cognitive ability and openness to experience, that contribute to the potential for training. These individual differences interact with experience in passive and active ways to push or pull for development of skill. Genes also control maturation, and the timing of structural and functional changes differs across brain regions and networks, producing a cascade of maturational effects [4••]. Early and late maturing regions interact, and experience can drive change through both bottom-up sensorimotor processes and through top-down cognitive influences, consistent with the concept of interactive specialization [11••,12•]. We propose that the timing of music experience interacts with both predispositions and maturation to influence long-term behavioural and brain plasticity. Early music training may initially affect earlier maturing, lower-level sensory processes such as pitch discrimination, but this training and its related plasticity may also have a metaplastic effect, laying the foundation for augmented development of later maturing sensorimotor integration abilities. Further, interactions within connected brain networks may produce different kinds of plastic effects: for example, structural enlargement in PMC, but structural reductions in connected regions of the cerebellum. Taken together, we propose that early training has a metaplastic effect where early training promotes brain plasticity that makes a region or network more receptive to future experience. Thus early training can be seen as a scaffold on which later experience can build [20].

In this way, musical skill appears to be similar to other complex abilities, in which there is strong evidence for heritability, but also good evidence that individual variability can be moderated by experience [1••]. One important source of this variability may be the age at which training begins.

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Conflict of interest statement

Nothing declared.

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References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. Sauce B, Matzel LD: **The paradox of intelligence: heritability**
•• **and malleability coexist in hidden gene-environment interplay**. *Psychol Bull* 2018, **144**:26-47.

This paper presents a comprehensive review of the genetics of intelligence and the importance of gene-environment interactions. Particular emphasis is given to the impact of typical models of gene-environment variation and their impact on the resulting assessment of their relative contributions.

2. Ullen F, Hambrick DZ, Mosing MA: **Rethinking expertise: a**
•• **multifactorial gene-environment interaction model of expert performance**. *Psychol Bull* 2016, **142**:427-446.

Presents the first model for interactions between genes and environment and their contributions to musical ability.

3. Hensch TK, Quinlan EM: **Critical periods in amblyopia**. *Vis Neurosci* 2018, **35**:E014.

4. Werker JF, Hensch TK: **Critical periods in speech perception:**
•• **new directions**. *Annu Rev Psychol* 2015, **66**:173-196.

A comprehensive review of cellular mechanisms underlying plasticity during critical periods derived from animal models and their relationship to sensitive periods in language development.

5. Knudsen E: **Sensitive periods in the development of the brain**
• **and behavior**. *J Cognit Neurosci* 2004, **16**:1412-1425.

A foundational paper that gives complete and thoughtful presentation of animal models of sensitive and critical periods.

6. Penhune V: **Musical expertise and brain structure: the causes**
• **and consequences of training**. In *The Oxford Handbook of Music and the Brain.* Edited by Thaut MH, Hodges DA. Oxford University Press; 2018.

A review of recent work on structural brain plasticity in the context of musical training with an emphasis on studies of sensitive period effects.

7. Hartshorne JK, Tenenbaum JB, Pinker S: **A critical period for second language acquisition: evidence from 2/3 million english speakers**. *Cognition* 2018, **177**:263-277.

8. Flege JE, Yeni-Komshian G, Liu S: **Age constraints on second-language acquisition**. *J Memory Lang* 1999, **41**:78-104.

9. Kral A, Sharma A: **Developmental neuroplasticity after cochlear implantation**. *Trends Neurosci* 2012, **35**:111-122.

10. Voss P *et al.*: **Dynamic brains and the changing rules of**
• **neuroplasticity: implications for learning and recovery**. *Front Psychol* 2017, **8**:1657.

An up-to-date review of sensitive period effects in the auditory system based on animal models.

11. Johnson MH: **Interactive specialization: a domain-general**
•• **framework for human functional brain development?** *Dev Cogn Neurosci* 2011, **1**:7-21.

An insightful and theoretically rigourous presentation models of brain maturation and their relationship to development. Explains the evidence and logic behind the Interactive Specialization model.

12. Eggermont JJ, Moore JK: **Morphological and functional**
• **development of the auditory nervous system**. In *Springer Handbook of Human Auditory Development.* Edited by Werner L, Fay RR, Popper AN. Springer; 2012:61-105.

An excellent synthetic review of developmental plasticity in the auditory system drawing on animal and human work in the context of auditory deprivation and cochlear implants. Particular emphasis is placedon the role of top-down and bottom-up influences on structural and functional maturation.

13. Jorgensen H: **Instrumental learning: is an early start a key to success?** *Br J Music Educ* 2011, **18**:227-239.

14. Baharloo S *et al.*: **Absolute pitch: an approach for identification of genetic and nongenetic components**. *Am J Hum Genet* 1998, **62**:224-231.

15. Schlaug G *et al.*: **Increased corpus callosum size in musicians**. *Neuropsychologia* 1995, **33**:1047-1055.

16. Bailey J, Penhune VB: **A sensitive period for musical training: contributions of age of onset and cognitive abilities**. *Ann N Y Acad Sci* 2012, **1252**:163-170.

17. Bailey JA, Penhune VB: **The relationship between the age of onset of musical training and rhythm synchronization performance: validation of sensitive period effects**. *Front Neurosci* 2013, **7**:227.

18. Bailey JA, Penhune VB: **Rhythm synchronization performance and auditory working memory in early- and late-trained musicians**. *Exp Brain Res* 2010, **204**:91-101.

19. Bailey JA, Zatorre RJ, Penhune VB: **Early musical training is linked to gray matter structure in the ventral premotor cortex and auditory-motor rhythm synchronization performance**. *J Cogn Neurosci* 2014, **26**:755-767.

20. Steele CJ *et al.*: **Early musical training and white-matter plasticity in the corpus callosum: evidence for a sensitive period**. *J Neurosci* 2013, **33**:1282-1290.

21. Baer L *et al.*: **Regional cerebellar volumes are related to early musical training and finger tapping performance**. *Neuroimage* 2015, **109**:130-139.

22. Vaquero L *et al.*: **Structural neuroplasticity in expert pianists depends on the age of musical training onset**. *Neuroimage* 2016, **126**:106-119.

23. Shenker J, Zatorre RJ, Penhune VB: *The Relationship Between Cerebellar Volume and Cortical Sensorimotor Areas in Early-trained Musicians*. Rome, Italy: Organization for Human Brain Mapping; 2019.

24. Fjell AM *et al.*: **Continuity and discontinuity in human cortical**
•• **development and change from embryonic stages to old age**. *Cereb Cortex* 2019, **29**:3879-3890.

A data-driven approach examining pre-natal and post-natal brain development that shows that clusters of regions change together across development and that these clusters are also related to patterns of gene expression.

25. Giedd J *et al.*: **Brain development during childhood and adolescence: a longitudinal MRI study**. *Nat Neurosci* 1999, **2**:861-863.

26. Zatorre R, Chen J, Penhune V: **When the brain plays music: sensory-motor interactions in music perception and production**. *Nat Rev Neurosci* 2007, **8**:547-558.

27. Merchant H, Harrington DL, Meck WH: **Neural basis of the perception and estimation of time**. *Annu Rev Neurosci* 2013, **36**:313-336.

28. Westerhausen R *et al.*: **Structural and functional reorganization of the corpus callosum between the age of 6 and 8 years**. *Cereb Cortex* 2011, **21**:1012-1017.

29. Chiang MC *et al.*: **Genetics of brain fiber architecture and intellectual performance**. *J Neurosci* 2009, **29**:2212-2224.

30. Kurth F *et al.*: **The right inhibition? Callosal correlates of hand performance in healthy children and adolescents callosal correlates of hand performance**. *Hum Brain Mapp* 2013, **34**:2259-2265.

31. Tiemeier H *et al.*: **Cerebellum development during childhood and adolescence: a longitudinal morphometric MRI study**. *Neuroimage* 2010, **49**:63-70.

32. Kelly R, Strick P: **Cerebellar loops with motor cortex and prefrontal cortex of a non-human primate**. *J Neurosci* 2003, **23**:8432-8444.

33. Sokolov AA, Miall RC, Ivry RB: **The cerebellum: adaptive prediction for movement and cognition**. *Trends Cogn Sci* 2017, **21**:313-332.

34. Vaquero L *et al.*: **What you learn & when you learn it: impact of early bilingual & music experience on the structural characteristics of auditory-motor pathways**. *Neuroimage* 2020, **213**:116689.

35. Hamalainen S *et al.*: **Bilingualism modulates the white matter structure of language-related pathways**. *Neuroimage* 2017, **152**:249-257.

36. Halwani GF *et al.*: **Effects of practice and experience on the arcuate fasciculus: comparing singers, instrumentalists, and non-musicians**. *Front Psychol* 2011, **2**:156.

37. Powell HW *et al.*: **Hemispheric asymmetries in language-related pathways: a combined functional MRI and tractography study**. *Neuroimage* 2006, **32**:388-399.

38. Budisavljevic S *et al.*: **Age-related differences and heritability of the Perisylvian language networks**. *J Neurosci* 2015, **35**:12625-12634.

39. Ireland K *et al.*: **Rhythm and melody tasks for school-aged children with and without musical training: age-equivalent scores and reliability**. *Front Auditory Cognit Neurosci* 2018, **9**.

40. Ireland K, Iyer TA, Penhune VB: **Contributions of age of start, cognitive abilities and practice to musical task performance in childhood**. *PLoS One* 2019, **14**:e0216119.

41. Herholz S, Boh B, Pantev C: **Musical training modulates encoding of higher-order regularities in the auditory cortex**. *Eur J Neurosci* 2011, **34**:524-529.

42. Ragert P *et al.*: **Superior tactile performance and learning in professional pianists: evidence for meta-plasticity in musicians**. *Eur J Neurosci* 2004, **19**:473-478.

43. Rosenkranz K, Williamon A, Rothwell JC: **Motorcortical excitability and synaptic plasticity is enhanced in professional musicians**. *J Neurosci* 2007, **27**:5200-5206.

44. Habibi A *et al.*: **Childhood music training induces change in micro and macroscopic brain structure: results from a longitudinal study**. *Cereb Cortex* 2017:1-12.

45. Hyde KL *et al.*: **Musical training shapes structural brain development**. *J Neurosci* 2009, **29**:3019-3025.

46. Putkinen V *et al.*: **Enhanced development of auditory change detection in musically trained school-aged children: a longitudinal event-related potential study**. *Dev Sci* 2014, **17**:282-297.

47. Shahin A *et al.*: **Modulation of P2 auditory-evoked responses by the spectral complexity of musical sounds**. *Neuroreport* 2005, **16**:1781-1785.

48. Fujioka T *et al.*: **One year of musical training affects development of auditory cortical-evoked fields in young children**. *Brain* 2006, **129**:2593-2608.

49. •• de Manzano O, Ullen F: **Same genes, different brains: neuroanatomical differences between monozygotic twins discordant for musical training**. *Cereb Cortex* 2018, **28**:387-394.
Uses twin methodology to present some of the strongest evidence thus far for the effect of musical training on brain structure.

50. Oikkonen J *et al.*: **Creative activities in music—a genome-wide linkage analysis**. *PLoS One* 2016, **11**:e0148679.

51. • Seither-Preisler A, Parncutt R, Schneider P: **Size and synchronization of auditory cortex promotes musical, literacy, and attentional skills in children**. *J Neurosci* 2014, **34**:10937-10949.
A large-scale study of children taking music lessons that shows that individual differences in the structure and function of auditory cortex are related to musical abilities.

52. Ullen F *et al.*: **Psychometric properties and heritability of a new online test for musicality, the Swedish musical discrimination test**. *Pers Individ Differ* 2014, **63**:87-93.

53. Mosing MA *et al.*: **Practice does not make perfect: no causal effect of music practice on music ability**. *Psychol Sci* 2014, **25**:1795-1803.

54. Butkovic A, Ullen F, Mosing MA: **Personality-related traits as predictors of music practice: underlying environmental and genetic influences**. *Pers Individ Differ* 2015, **74**:133-138.

55. Swaminathan S, Schellenberg EG: **Musical competence is predicted by music training, cognitive abilities, and personality**. *Sci Rep* 2018, **8**:9223.

56. Wesseldijk LW, Mosing MA, Ullen F: **Gene–environment interaction in expertise: the importance of childhood environment for musical achievement**. *Dev Psychol* 2019, **55**:1473-1479.

57. Foster NE, Zatorre RJ: **Cortical structure predicts success in performing musical transformation judgments**. *Neuroimage* 2010, **53**:26-36.

58. Blecher T, Tal I, Ben-Shachar M: **White matter microstructural properties correlate with sensorimotor synchronization abilities**. *Neuroimage* 2016, **138**:1-12.

59. Herholz SC *et al.*: **Dissociation of neural networks for predisposition and for training-related plasticity in auditory-motor learning**. *Cereb Cortex* 2016, **26**:3125-3134.

60. Zatorre RJ, Delhommeau K, Zarate JM: **Modulation of auditory cortex response to pitch variation following training with microtonal melodies**. *Front Psychol* 2012, **3**:544.

61. Wollman I *et al.*: **Neural network retuning and neural predictors of learning success associated with cello training**. *Proc Natl Acad Sci U S A* 2018, **115**:E6056-E6064.

62. Engel A *et al.*: **Inter-individual differences in audio-motor learning of piano melodies and white matter fiber tract architecture**. *Hum Brain Mapp* 2014, **35**:2483-2497.

63. • Herholz S, Zatorre R: **Musical training as a framework for brain plasticity: behavior, function, and structure**. *Neuron* 2012, **76**:486-502.
A comprehensive review of the structural and functional brain plasticity related to short-term and long-term musical training.

64. Patel AD: **Why would musical training benefit the neural encoding of speech? The OPERA hypothesis**. *Front Psychol* 2011, **2**:142.

65. Novembre G, Keller PE: **A conceptual review on action-perception coupling in the musicians' brain: what is it good for?** *Front Hum Neurosci* 2014, **8**:603.

66. Wolpert DM, Diedrichsen J, Flanagan JR: **Principles of sensorimotor learning**. *Nat Rev Neurosci* 2011, **12**:739-751.

67. Lee H, Noppeney U: **Long-term music training tunes how the brain temporally binds signals from multiple senses**. *Proc Natl Acad Sci U S A* 2011, **108**:E1441-E1450.

68. Mas-Herrero E *et al.*: **Individual differences in music reward experiences**. *Music Percept* 2011, **31**:118-138.

69. Salimpoor VN *et al.*: **Predictions and the brain: how musical sounds become rewarding**. *Trends Cogn Sci* 2015, **19**:86-91.

70. Ferreri L *et al.*: **Dopamine modulates the reward experiences elicited by music**. *Proc Natl Acad Sci U S A* 2019, **116**:3793-3798.

71. David SV, Fritz JB, Shamma SA: **Task reward structure shapes rapid receptive field plasticity in auditory cortex**. *Proc Natl Acad Sci U S A* 2012, **109**:2144-2149.

72. Floel A *et al.*: **Dopaminergic influences on formation of a motor memory**. *Ann Neurol* 2005, **58**:121-130.

73. Tremblay PL *et al.*: **Motor sequence learning in primate: role of the D2 receptor in movement chunking during consolidation**. *Behav Brain Res* 2009, **198**:231-239.

74. Tremblay PL *et al.*: **Movement chunking during sequence learning is a dopamine-dependant process: a study conducted in Parkinson's disease**. *Exp Brain Res* 2010, **205**:375-385.

75. Haith AM, Krakauer JW: **Model-based and model-free mechanisms of human motor learning**. *Adv Exp Med Biol* 2013, **782**:1-21.

76. Graybiel AM, Grafton ST: **The striatum: where skills and habits meet**. *Cold Spring Harb Perspect Biol* 2015, **7**:a021691.

77. Urosevic S *et al.*: **Longitudinal changes in behavioral approach system sensitivity and brain structures involved in reward processing during adolescence**. *Dev Psychol* 2012, **48**:1488-1500.

78. Luciana M *et al.*: **Dopaminergic modulation of incentive motivation in adolescence: age-related changes in signaling, individual differences, and implications for the development of self-regulation**. *Dev Psychol* 2012, **48**:844-861.

79. Altenmuller E, Furuya S: **Brain plasticity and the concept of metaplasticity in skilled musicians**. *Adv Exp Med Biol* 2016, **957**:197-208.

80. Schmidt MV *et al.*: **Stress-induced metaplasticity: from synapses to behavior**. *Neuroscience* 2013, **250**:112-120.

81. Hund-Georgiadis M, von Cramon D: **Motor-learning-related changes in piano players and non-musicians revealed by functional magnetic-resonance signals**. *Exp Brain Res* 1999, **125**:417-425.

82. Ball G, Beare R, Seal ML: **Charting shared developmental trajectories of cortical thickness and structural connectivity in childhood and adolescence**. *Hum Brain Mapp* 2019, **40**:4630-4644.

83. Huttenlocher P, Dabholkar A: **Regional differences in synaptogenesis in human cerebral cortex**. *J Comp Neurol* 1997, **387**:167-178.

84. Mills KL *et al.*: **Structural brain development between childhood and adulthood: convergence across four longitudinal samples**. *Neuroimage* 2016, **141**:273-281.

85. Brown TT, Jernigan TL: **Brain development during the preschool years**. *Neuropsychol Rev* 2012, **22**:313-333.

86. •• Amlien IK *et al.*: **Organizing principles of human cortical development—thickness and area from 4 to 30 years: insights from comparative primate neuroanatomy**. *Cereb Cortex* 2016, **26**:257-267.

An impressive and theoretically rich paper comparing developmental trajectories in humans with evolutionary trajectories in non-human primates. An 'evo-devo' take on human brain maturation.

87. Amemiya K *et al.*: **Local-to-distant development of the cerebrocerebellar sensorimotor network in the typically developing human brain: a functional and diffusion MRI study**. *Brain Struct Funct* 2019, **224**:1359-1375.

88. Trainor LJ: **Musical experience, plasticity, and maturation: issues in measuring developmental change using EEG and MEG**. *Ann N Y Acad Sci* 2012, **1252**:25-36.

89. Ferronato PA, Domellof E, Ronnqvist L: **Early influence of auditory stimuli on upper-limb movements in young human infants: an overview**. *Front Psychol* 2014, **5**:1043.