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Apollos Gift and Curse: Making Music as a model for Adaptive and Maladaptive Plasticity

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Abstract: Musicians with extensive training and playing experience provide an excellent model for studying plasticity of the human brain. The demands placed on the nervous system by music performance are very high and provide a uniquely rich multisensory and motor experience to the player. As confirmed by neuroimaging studies, playing music depends on a strong coupling of perception and action mediated by sensory, motor, and multimodal integration regions distributed throughout the brain. A pianist, for example, must draw on a whole set of complex skills, including translating visual analysis of musical notation into motor movements, coordinating multisensory information with bimanual motor activity, developing fine motor skills in both hands coupled with metric precision, and monitoring auditory feedback to fine-tune a performance as it progresses. This article summarizes research on the effects of musical training on brain function, brain connectivity and brain structure. First we address factors inducing and continuously driving brain plasticity in dedicated musicians, arguing that prolonged goal-directed practice, multi-sensory-motor integration, high arousal, and emotional and social rewards contribute to these plasticity-induced brain adaptations. Subsequently, we briefly review the neuroanatomy and neurophysiology underpinning musical activities. Here we focus on the perception of sound, integration of sound and movement, and the physiology of motor planning and motor control. We then review the literature on functional changes in brain activation and brain connectivity along with the acquisition of musical skills, be they auditory or sensory-motor. In the following section we focus on structural adaptions in the gray matter of the brain and in fiber-tract density associated with music learning. Here we critically discuss the findings that structural changes are mostly seen when starting musical training after age seven, whereas functional optimization is more effective before this age. We then address the phenomenon of de-expertise, reviewing studies which provide evidence that intensive music-making can induce dysfunctional changes which are accompanied by a degradation of skilled motor behavior, also termed "musician's dystonia". This condition, which is frequently highly disabling, mainly affects male classical musicians with a history of compulsive working behavior, anxiety disorder or chronic pain. Functional and structural brain changes in these musicians are suggestive of deficient inhibition and excess excitation in the central nervous system, which leads to co-activation of antagonistic pairs of muscles during performance, reducing movement speed and quality. We conclude with a concise summary of the role of brain plasticity, metaplasticity and maladaptive plasticity in the acquisition and loss of musicians' expertise.

Keywords: MUSIC; Brain activation; Brain structure; Metaplasticity; Musician's dystonia

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Introduction: Performing music as a driver of brain plasticity

There can be no doubt that performing music at a professional level is one of the most demanding and fascinating human experiences. It involves the precise execution of very fast and, in many instances, extremely complex movements that must be structured and coordinated with continuous auditory, somatosensory and visual feedback. Furthermore, it requires retrieval of musical, motor, and multi-sensory information from both short-term and long-term memory and relies on continuous planning of an on-going performance in working memory. The consequences of motor actions have to be anticipated, monitored and adjusted almost in real-time (Brown et al., 2015). At the same time, music should be expressive, requiring the performance to be enriched with a complex set of innate and acculturated emotional gestures.

Practice is required to develop all of these skills and to execute these complex tasks. In 1993, Ericsson and his colleagues undertook one of the most influential studies on practice, with students at the Berlin Academy of Music (Ericsson et al. 1993). They considered not only **time invested in practice** but also **quality of practice,** and proposed the concept of "deliberate practice" as a prerequisite for attaining excellence. Deliberate practice combines goal-oriented, structured and effortful practicing with motivation, resources and focused attention. Ericsson and colleagues argued that a major distinction between professional and amateur musicians, and generally between more successful versus less successful learners, is the amount of deliberate practice undertaken during the many years required to develop instrumental skills to a high level (Ericsson and Lehmann, 1996). Extraordinarily skilled musicians therefore exert a great deal more effort and concentration during their practice than less skilled musicians, and are more likely to plan, imagine, monitor and control their playing by focusing their attention on what they are practicing and how it can be improved. Furthermore, they can be eager to build up a network of supportive peers, frequently involving family and friends.

The concept of deliberate practice has been refined since it became clear that not only the **amount** of deliberate practice, but also the **point in life** at which intense goal-directed practice begins are important variables. In the auditory domain for example, sensitive periods – "windows of opportunity" – exist for the acquisition of so-called "absolute" or "perfect" pitch. Absolute pitch denotes the ability to name pitches without a reference pitch. It can be considered as a special case of auditory long term memory and is strongly linked to intense early musical experience, usually before age seven (Baharloo et al., 1998, Miyazaki, 1988; Sergeant, 1968). However, genetic predisposition may play a role since absolute pitch is more common in certain East Asian populations and may run in families (Baharloo et al., 2000; Gregersen et al., 2001). In the sensory-motor domain, early practice before age 7 leads to optimized and more stable motor programs (Furuya et al., 2014a) and to smaller yet more efficient neuronal networks (Vaquero et al.; 2016), compared to practice commencing later in life. This means that for specific sensory-motor skills, such as fast and independent finger movements, sensitive periods exist during development and maturation of the central nervous system, comparable to those for auditory and somatosensory skills (Ragert et al.; 2003).

The issue of **nature vs. nurture**, or genetic predisposition vs. environmental influences and training in musical skills is complex, since the success of training is itself subject to genetic variability. General observation suggests that outcomes will not be identical for all individuals receiving the same amount of training. Evidence supporting the contribution of pre-existing individual differences comes from a large Swedish twin study showing that the propensity to practice is partially heritable (Mosing et al., 2014). In a series of studies, Schellenberg and colleagues investigated the contribution of cognitive and personality variables to music training, showing that those who engage in music perform better on cognitive tasks, have better educated parents and describe themselves as more "open to experience" on personality scales (Corrigall et al., 2013). Findings are also beginning to accumulate in the music performance domain, indicating that learning outcomes can be predicted in part based on pre-existing structural or functional brain features (Herholz et al.; 2015). A convincing example of dysfunctional genetic predisposition is the inability to acquire auditory skills in congenital amusia, a hereditary condition characterized by absent or highly deficient pitch perception (Gingras et al.; 2015). In the sensory-motor domain, musician's dystonia, the loss of motor control in skilled movements while playing an instrument, has a strong genetic background in about one third of affected musicians (Schmidt et al.; 2009).

On the other hand, training is clearly necessary for musical expertise, with a large number of studies finding that the length of musical experience is strongly correlated with performance on a range of musical tasks, as well as with brain function and structure (Amunts et al., 1997; Bengtsson et al., 2005; Bermudez et al. 2008; Chen et al. 2008a; Oechslin et al.; 2010). Taken together, both, predisposition and experience contribute to musical expertise, and the relative balance between the two factors may differ in specific aspects of the many different musical subskills. Furthermore, it seems that there exist early sensitive periods during which musical stimulation or training of sub-skills has to take place in order to establish fertile ground for growing extra-ordinary expertise later in life. This is best illustrated by the **scaffold metaphor** (Steele et al., 2013): an early start to training develops the "scaffold" for building a "skyscraper-like" level of expertise later in life, whereas a late start of training allows only for moderate results even after long and intense training. Of course these scaffolds may differ from one domain to the next. For example an outstanding virtuoso like the legendary pianist Lang Lang, known for his breathtaking finger dexterity, may require both, highly relevant inherited traits and intense early sensory-motor training. Other musicians such as the late French singer Edith Piaf, known for her emotional expressivity but somehow lacking in technique, may have started technical exercises late in life but have genetic and biographical conditions allowing them to build up emotional depth, a character trait we feel and value, despite the difficulty in operationalizing it for precise study.

Performing music at a professional level relies on a range of sub-skills, which are represented in different, though overlapping brain networks. Auditory skills such as the above-mentioned perfect pitch, sensitivity to timing variations (e.g. "groove") and to micro-pitches (e.g. tuning of a violin), or auditory long-term memory (e.g. memorizing a 12-tone series), are mainly processed in the temporal lobes of both hemispheres with a right hemisphere bias. However, signs of auditory and musical expertise can already be detected in the ascending auditory pathway at the brainstem level (Skoe and Kraus, 2013). Sensory-motor skills, such as low two-point discrimination levels and high tactile sensitivity (e.g. left fifth finger in professional violinists), bimanual or quadrupedal coordination (e.g. for piano and organ playing), fast finger movements (e.g. right hand arpeggios on the classical guitar) or complex hand postures (e.g. left hand on the electric guitar), are represented in premotor, motor and parietal cortical areas, and in subcortical brain structures such as the basal ganglia and the cerebellum. Emotional and performance skills are supported by individualized prefrontal and orbitofrontal cortical regions and in the limbic system. Self-monitoring, anticipation of consequences of one's actions, motivation and focusing attention (all contributing to goal-directed "deliberate" practice), recruit a highly diverse network, including lateral prefrontal cortices, parietal cortices, limbic structures, and particularly motivational pathways, including the accumbens nucleus, and memory structures such as the hippocampus, deep on the base of the temporal lobe. All of these regions and the interconnecting nerve fibers are subject to modifications in function and structure in association with musical practice, a phenomenon termed "brain plasticity".

Brain plasticity denotes the general ability of our central nervous system to adapt throughout the life span to changing environmental conditions, body biomechanics and new tasks. Brain plasticity is most typically observed for complex tasks with high behavioral relevance and those which activate circuits involved in emotion and motivation. The continued activities of accomplished musicians are ideal for providing the prerequisites of brain plasticity (for a review see Schlaug, 2015). In musical expertise, the above-mentioned processes are accompanied by changes which take place not only in the function of the brain's neuronal networks, as a result of a strengthening of synaptic connections, but also in its gross structure. With respect to mechanisms and microstructural effects of plasticity, our understanding of the molecular and cellular processes underlying these adaptations is far from complete. Brain plasticity may occur on different time scales. For example, the efficiency and size of synapses may be modified in a time window of seconds to minutes, while the growth of new synapses and dendrites may require hours to days. An increase in gray matter density, which mainly reflects an enlargement of neurons due to increased metabolism, needs at least several weeks. White matter density also increases as a consequence of musical training. This effect is primarily due to an enlargement of myelin cells which wrap around the nerve fibres (axons) and dendrites, greatly contributing to the velocity of the electrical impulses travelling along them. Under conditions requiring rapid information transfer and high temporal precision these myelin cells adapt by growing, and as a consequence nerve conduction velocity increases. Finally, brain regions involved in specific tasks may also be enlarged after long-term training due to the growth of structures supporting nervous function, for example in the blood vessels that are necessary for oxygen and glucose transportation.

There are four main reasons why researchers believe that these effects on brain plasticity are more pronounced in music performance than in other skilled activities. First, the intensity of goal-directed training is extremely high: students admitted to a German state conservatory have spent an average of 10 years and 10,000 hours of deliberate practice in order to pass the demanding entrance examinations (Ericsson et al.,1993). Second, related to the above, musical training in those individuals who later become professional musicians usually starts very early, sometimes before age six when the adaptability of the central nervous system is at its highest. Third, musical activities are strongly linked to conditions of high arousal and positive emotions, but also to stressors such as music performance anxiety. Here, neuro-active hormones, such as adrenalin (arousal), endorphins (joy), dopamine (rewarding experience) and stress hormones (fear of failure) support neuroplastic adaptations. Fourth, performing music in public is frequently accompanied by strong social feelings best described as a sense of connectedness and meaning. As a consequence, increased release of oxytocin and serotonin will similarly enhance plastic adaptations.

However, we should be careful in claiming that music produces more prominent plastic adaptations in the brain compared to other skilled activities as the methodology of group comparisons in brain plasticity research might produce a bias. For example, group investigations into professional classical pianists compared to "non-musicians", such as in our study by Vaquero et al. (2015), might be influenced by differences in sample homogeneity. Pianists experience similar acculturation and take part in highly homogeneous activities due to the canonical nature of their training in comparison to non-musician groups, such as medical students. The former study similar etudes of Hanon, Czerny and Chopin for many years, and this may well produce more uniform brain adaptations, which dominate any individual changes. In other pursuits such as the visual arts, creative writing, architecture, jazz improvisation and music composition, individualized training may produce more diverse effects that are masked in group statistics.

Brain regions involved in performing music: A quick overview

As outlined above, playing a musical instrument or singing at a professional level requires highly refined auditory, sensory-motor, and emotional-communicative skills that are acquired over many years of extensive training, and that have to be stored and maintained through further regular practice. Auditory feedback is needed to improve and perfect performance, and emotion-related brain areas are required to render a performance vivid and touching. Performance-based music-making therefore relies primarily on a highly developed auditory-motor-emotion integration capacity, which is reflected on the one hand in increased neuronal connectivity and on the other hand in functional and structural adaptations of brain areas supporting these activities. In the following, we give a quick overview on the many brain regions involved in making music.

Music perception involves *primary and secondary auditory areas* (A1, A2) and *auditory association areas* (AA) in the two temporal lobes. The primary auditory area, localized in the upper portion of the temporal lobe in Heschl's Gyrus receives its main input from the inner ears via the ascending auditory pathway. It is mainly involved in basic auditory processing such as pitch and loudness perception, perception of time structures, and spectral decomposition. The left primary auditory cortex is specialized in the rapid analysis of time structures, such as differences in voice onset times when articulating “da” or “ta”. The right, on the other hand, deals primarily with the spectral decomposition of sounds. The secondary auditory areas surround the primary area in a belt-like formation. Here, more complex auditory features such as timbre are processed. Finally, in the auditory association areas, auditory gestalt perception takes place. Auditory gestalts can be understood, for example, as pitch-time patterns like melodies and words. In right-handers, and in about 95% of all left-handers, Wernicke's area in the left posterior portion of the upper temporal lobe is specialized in language decoding.

In contrast to the early auditory processing of simple acoustic structures, listening to music is a far more complex task. Music is experienced not only as an acoustic structure over time, but also as patterns, associations, emotions, expectations and so on. Such experiences rely on a complex set of perceptive, cognitive and emotional operations. Integrated over time, and frequently linked to biographic memories, they enable us to experience strong emotions, processed in structures of the limbic system such as the ventral tegmental area of the mesencephalon or the accumbens nucleus in the basal forebrain (Salimpoor et al., 2013). Memories and social emotions evoked during music listening and playing involve the *hippocampus*, deep in the temporal lobe, and the dorsolateral prefrontal cortex, mainly in the right hemisphere.

Making music relies on voluntary skilled movements which involve four cortical regions in both hemispheres: the *primary motor area* (M1) located in the *precentral gyrus* directly in front of the central sulcus; the *supplementary motor area* (SMA) located anteriorly to M1 of the frontal lobe and the inner (medial) side of the cortex; the *cingulate motor area* (CMA) below the SMA and above the corpus callosum on the inner (medial) side of the hemisphere; and the *premotor area* (PMA), which is located adjacent to the lateral aspect of the primary motor area (see Fig. 1).

SMA, PMA and CMA can be described as *secondary motor areas*, because they are used to process movement patterns rather than simple movements. In addition to cortical regions, the motor system includes the subcortical structures of the basal ganglia, and the cerebellum. Steady kinaesthetic feedback is also required to control any guided motor action and comes from the *primary somatosensory area* (S1) behind the central sulcus in the parietal lobe. This lobe is involved in many aspects of movement processing and is an area where information from multiple sensory regions converges. In the posterior parietal area, body-coordinates in space are monitored and calculated, and visual information is transferred into these coordinates. As far as musicians are concerned, this area is prominently activated during tasks involving multi-sensory integration, for example during sight-reading, the playing of complex pieces of music (Haslinger et al., 2005), and the transformation of musical pitch information into movement coordinates (Brown et al.; 2013) and of musical notation into corresponding motor actions (Stewart et al., 2003).

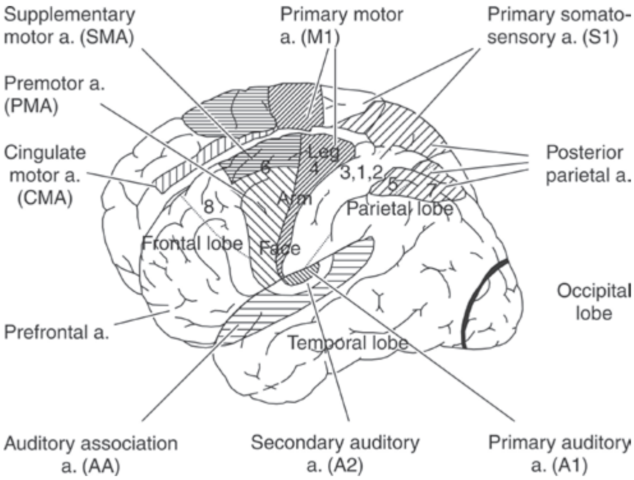

Fig. 1: Brain regions involved in sensory and motor music processing. (The abbreviation "a" stands for "area.") Left hemisphere is shown in the foreground; right hemisphere in the background. The numbers relate to the respective Brodmann's areas, a labelling of cortical regions according to the fine structure of the nervous tissue.

The **primary motor area** (M1) represents the movements of body parts distinctly, in systematic order. The representation of the leg is located on the top and the inner side of the hemisphere, the arm in the upper portion, and the hand and mouth in the lower portion of M1. This representation of distinct body parts in corresponding brain regions is called "somatotopic" or "homuncular" order. Just as the motor homunculus is represented upside-down, so too is the sensory homunculus on the other side of the central sulcus. The proportions of both the motor and the sensory homunculi are markedly distorted since they are determined by the density of motor and sensory innervations of the respective body parts. For example, control of fine movements of the tongue requires many more nerve fibres transmitting information to this muscle, compared to control of the muscles of the back. Therefore, the hand, lips and tongue require almost two-thirds of the neurons in this area. However, as further explained below, the relative representation of body parts may be modified by usage. Moreover, the primary motor area does not simply represent individual muscles: multiple muscular representations are arranged in a complex way so as to allow the execution of simple types of movements rather than the activation of a specific muscle. This is a consequence of the fact that a two-dimensional array of neurons in M1 has to code for three-dimensional movements in space (Gentner and Classen, 2006). Put more simply, our brain does not represent muscles but rather movements.

The **supplementary motor area** (SMA) is mainly involved in the sequencing of complex movements and in the triggering of movements based on internal cues. It is particularly engaged when the execution of a sequential movement depends on internally stored and memorized information. It therefore is also important for both rhythm and pitch processing because of its role in sequencing and the hierarchical organization of movement (Hikosaka and Nakamura, 2002). Skilled musicians and non-musicians engage the SMA either when performing music or when imagining listening to or performing music (de Manzano and Ullén, 2012; Herholz and Zatorre, 2012). This suggests that the SMA may be crucial for experts' ability to plan music segment-by-segment during performance.

The **premotor area** (PMA) is primarily engaged when externally stimulated behaviour is being planned and prepared. It is involved in the learning, execution and recognition of limb movements and seems to be particularly concerned with the integration of visual information, which is necessary for movement planning. The PMA is also responsible for processing complex rhythms (Chen et al., 2008b).

The function of the **cingulate motor area** (CMA) is still under debate. Electrical stimulation and brain imaging studies demonstrate its involvement in movement selection in situations when movements are critical to obtain reward or avoid punishment. This points towards close links between the cingulate gyrus and the emotion processing limbic system. The CMA may therefore play an important role in mediating cortical cognitive and limbic-emotional functions, for example in error processing during a musical performance (Herrojo-Ruiz et al., 2009a).

The **basal ganglia**, located deep inside the cerebral hemispheres, are inter-connected reciprocally via the thalamus to the motor and sensory cortices, thus constituting a loop of information flow between cortical and sub-cortical areas. They are indispensable for any kind of voluntary action and play a crucial role in organizing sequences of motor actions. The basal ganglia are therefore the structures mainly involved in automation of skilled movements such as sequential finger movements. Here, their special function consists of selecting appropriate motor actions and comparing the goal and course of those actions with previous experience. The middle putamen in particular seems to be involved in storing fast and automated movement programs. It is subject to plastic adaptations in professional musicians, as we will see below. Furthermore, in the basal ganglia the flow of information between the cortex and the limbic emotional systems, in particular the amygdala and the accumbens nucleus, converges. It is therefore assumed that the basal ganglia process and control the emotional evaluation of motor behavior in terms of expected reward or punishment.

The **cerebellum** is an essential contributor to the timing and accuracy of fine-tuned movements. It is thought to play a role in correcting errors and in learning new skills. The cerebellum has been hypothesized to be part of a network including parietal and motor cortex that encodes predictions of the internal models of these skills. The term "internal model" here refers to a neural process that simulates the response of the motor system in order to estimate the outcome of a motor command. The cerebellum is connected to almost all regions of the brain, including those important for memory and higher cognitive functions. Based on this, it has been proposed that this structure serves as a universal control system that contributes to learning, and to optimizing a range of functions across the brain (Ramnani, 2014).

The effects of musical training on brain function

The neural bases of **refined auditory processing** in musicians are well understood. In 1998, Pantev and colleagues provided a first indication that extensive musical training can plastically alter receptive functions (Pantev et al., 1998). Equivalent current dipole strength, a measure of mass neuronal activation, was computed from evoked magnetic fields generated in auditory cortex in response to piano tones and to pure tones of equal fundamental frequency and loudness. In musicians, the responses to piano tones (but not to pure tones) were ~25% larger than in non-musicians. In a study of violinists and trumpeters, this effect was most pronounced for tones from each musician's own type of instrument (Hirata et al., 1999). In a similar way, evoked neural responses to subtle alterations in rhythm or pitch are much more pronounced in musicians than in non-musicians (Münte et al., 2003). Even functions such as sound localization, that operate on basic acoustic properties, have shown effects of plasticity and expertise amongst different groups of musicians. A conductor, more than any other musician, is likely to depend on spatial localization for successful performance. For example, he might need to guide his attention to a certain player in a large orchestra. Consistent with this, in one study professional conductors were found to be better than pianists and non-musicians at separating adjacent sound sources in the periphery of the auditory field. This behavioral selectivity was paralleled by modulation of evoked brain responses, which were selective for the attended source in conductors, but not in pianists or non-musicians (Münte et al., 2001). These functional adaptations are not restricted to the auditory cortex, but can be observed in subcortical areas of the ascending auditory pathway: musically trained individuals have enhanced brainstem representations of musical sound waveforms (Wong et al., 2007).

Refined **somatosensory perception** constitutes another basis of high-level performance. Here, the kinaesthetic sense is especially important. It allows for control and feedback of muscle and tendon tension as well as joint positions, which enables continuous monitoring of finger, hand and lip position in the frames of body and instrument coordinates (e.g., the keyboard, the mouthpiece). Intensive musical training has also been associated with an expansion of the functional representation of finger or hand maps, as demonstrated in magnetoencephalography (MEG) studies. For example, the somatosensory representation of the left fifth digit in string players was found to be larger than that of non-musicians (Elbert et al., 1995). Musicians who had begun training early in life (<13 years) also demonstrated larger cortical representation of this digit compared to those who started to play their instruments later. This is behaviorally reflected in lower two-point discrimination thresholds at the finger tips of musicians who started their training earlier (Ragert et al. 2003).

In **motor brain function**, changes corresponding to the acquisition of musical expertise can also be observed with electrophysiological methods. These are mainly related to reduced motor excitability thresholds (Ridding et al., 2002, Pascual-Leone 2001), changes in motor receptive fields of trained motor patterns (Pascual-Leone et al., 1994), and changes in sensory-motor integration. For example, auditory and premotor cortices become co-activated when novices learn to play piano. In a longitudinal study, Bangert and Altenmüller (2003) showed that the formation of such multisensory connections between auditory and motor areas needs less than six weeks of regular piano training. This demonstrates how brain adaptations dynamically accompany musical learning processes. A further causal link between training and auditory-motor integration has been shown by findings of enhanced premotor recruitment in generating tonal patterns after specific training on the production of those patterns Lahav et al., 2007).

Activation of **motor co-representations** can occur in trained pianists not only by listening to piano tunes (Bangert et al. 2006), but also by observing pianists' finger movements. When pianists observed video sequences of a moving hand at the piano, activation was found in additional brain areas as compared to musically naïve subjects (Haslinger et al., 2005): in addition to the hand area in the primary motor cortex, secondary auditory cortices in the temporal lobe, and polymodal association cortices in the dorso-lateral premotor cortex and the parietal cortex were activated. Furthermore, the hand areas of the cerebellum were active. This extended neuronal network corresponds to a **"mirror neuron network"**, a group of functionally connected areas involved in imitation of movements and learning through observation (Rizzolatti et al., 1996). As a consequence for musical practice, it follows that careful demonstration at the instrument may enhance learning. Teaching methods based on demonstration and imitation are widely used at all levels of musical training, and would appear to be particularly effective in cases where teachers demonstrate an action or series of actions that are carefully and methodically observed by the student.

Practicing through listening and/or observation can be considered as special cases of **mental training**. Narrowly defined, mental training is understood as the vivid imagination of movement sequences without physically performing them. As with observation of actions, principally the same brain regions are active as if the imagined action is performed; that is, the primary motor cortex, the supplementary motor cortex and the cerebellum (Kuhtz-Buschbeck et al., 2003). In a study investigating mental training of finger movement sequences of different complexities, brain activation increased with the degree of difficulty of the imagined motor task. Furthermore, when continuing mental practice over a period of several days, the involved brain regions showed plastic adaptations. Although these adaptations were less dramatic than if the motor tasks were practiced physically, mental training produced a clear improvement in task performance as assessed by finger-tapping tests.

A large body of research has used functional magnetic resonance imaging (fMRI) to compare musicians and non-musicians. Taken together, differences in activity have been observed across many brain regions when individuals are asked to perform musical tasks involving discrimination (e.g., Foster and Zatorre, 2010) working memory (e.g. Gaab et al., 2006) or production (Bangert et al., 2006, Kleber et al., 2010). Despite the heterogeneity of the tasks used, an area that was commonly differentially activated in many of these studies was the posterior superior temporal gyrus, which is important for auditory gestalt perception, spectrotemporal processing and auditory-motor transformations (Warren et al., 2005). Indeed, a recent study identified the left superior temporal gyrus as the region that is most linked with musical training, in terms of cumulative practice hours (Ellis et al., 2013). As we will see below, morphometric studies have found larger amounts of gray matter in this region related to expertise and specific auditory skills, such as the possession of perfect pitch (Gaser and Schlaug, 2003).

The effects of musical training on brain structure

Since the age of phrenology, neuroscientists have tried to relate extraordinary skills to changes in brain anatomy. For example, at the beginning of the twentieth century, Auerbach (1906) reported that the middle and posterior thirds of the superior temporal gyrus were larger than normal in several postmortem studies of the brains of famous musicians. Modern brain-imaging techniques such as high-resolution magnetic resonance imaging (MRI), voxel based morphometry (VBM), and tensor based morphometry (TBM) allow precise determination of gray and white matter volume in predefined brain regions. A relatively new technique that can be used to study differences in fiber tract volume and direction is diffusion tensor imaging (DTI). This provides information about white matter microstructures by measuring diffusion properties of water molecules that move preferentially along the myelin sheets of axons. The degree of diffusivity is quantified as fractional anisotropy (FA), a measure allowing the assessment of orientation and direction of axons and their degree of myelination.

In the **auditory domain** functional adaptations, such as increased sensitivity to sounds, are accompanied by anatomical changes in primary or secondary auditory cortices of the superior temporal gyrus and the temporal plane (Bermudez et al., 2008; Gaser and Schlaug, 2003; Schneider et al., 2005; Zatorre et al., 2007). A study by Schneider and colleagues (2002) in professional musicians, amateurs and non-musicians is especially meaningful: they not only found an enlargement of the primary auditory cortex (Heschl's gyrus) related to increased cumulative life practice time in professional musicians, but also demonstrated that this enlargement was accompanied by more pronounced neuronal representations for pure tones in the same region, as reflected in the dipole size of evoked neuromagnetic fields. Behavioral tests in the same three groups of subjects revealed that the volume of Heschl's gyrus was positively related to improved auditory working memory and gestalt perception, as operationalized in a musical aptitude test. These behavioral, functional and anatomical changes have been shown to be causally linked to musical training in a longitudinal study with children (Hyde et al., 2009). Fifteen six-year old children received 15 months of piano training and showed not only improved auditory perception, but also enlarged gray matter of the right primary auditory cortex as compared to 16 age-matched controls.

In **absolute pitch possessors,** a pronounced leftward asymmetry of the temporal plane was found (Schlaug et al., 1995a). It was also demonstrated that in musicians with absolute pitch, the posterior superior temporal gyrus is connected to a region within the middle temporal gyrus which has been associated with categorical perception (Loui et al., 2010). Thus, the connections between the posterior part of the superior temporal gyrus and the middle temporal gyrus may play a role in determining whether or not someone develops absolute pitch, alongside early exposure to music.

In the **sensory-motor domain**, extensive musical practice during childhood and adolescence might have a strong effect on the maturation and the development of brain structures involved. Keyboard players have been a preferred group to study structural brain changes due to a high demand on bimanual dexterity and the possibility of assessing behavior such as speed and regularity of finger movements with MIDI-technology (Amunts et al., 1997; Bangert et al., 2006). In the first study that examined structural differences between musicians and non-musicians, Schlaug and collaborators (Schlaug et al., 1995b) showed that professional musicians (pianists and string-players) had a larger middle section of the **corpus callosum** compared to a non-musician control group. This was ascribed to an increase in myelination in the crossing fibers of the hand areas of both hemispheres, related to the high demands on bimanual coordination. Different research groups using a range of methodological approaches have replicated this finding (Öztürk et al., 2002, Gärtner et al., 2014). Again, a causal relationship between piano training and enlargement of the corpus callosum was established in the above longitudinal study by Hyde et al. (2009). Other fiber tracts have been investigated in musicians: in a diffusion tensor imaging (DTI) study with pianists, Bengtsson and colleagues (2005) found that the size of several white matter tracts correlated with the estimated amount of musical practice during childhood. These structures included the posterior limb of the internal capsule, a part of the corticospinal tract descending from the motor cortex to the spinal cord, and fiber tracts connecting the temporal and frontal lobes. Although the total number of practice hours during childhood was lower than in adolescence and adulthood, these adaptations support the idea that the central nervous system exhibits greater plastic capacities during early stages of development and maturation periods). However, some studies have reported lower fractional anisotropy in musicians in the corticospinal tract connecting primary motor areas with the spinal cord (Imfeld et al., 2009), and in the arcuate fasciculus, the fiber tract connecting auditory and pre-motor regions (Halwani et al., 2011). According to Schlaug (2015) these discrepant results may be explained by the fact that these fiber tracts are aligned in a less parallel manner than in non-musicians due to increased axonal sprouting and more branching of axons. Here, future imaging technologies may provide a more fine-grained picture of nervous tissues.

Concerning the size of **primary motor cortex**, various interesting findings have been obtained. In pianists, the depth of the central sulcus, often used as a marker of primary motor cortex size, was larger in both hemispheres but more pronounced on the right hemisphere compared to non-musicians (Amunts et al., 1997; Schlaug, 2001). It was argued that years of manual motor practice of the non-dominant left hand produced this effect. For the dominant right hand this effect was believed to be masked, since it undergoes some form of fine-motor training in everyone who writes and performs other skilled sensory-motor tasks with that hand. As was observed for the corpus callosum, there was a positive correlation between the size of the primary motor cortex and the onset of instrumental musical training. Again, a causal relationship was established in the above-mentioned longitudinal study in child piano novices, with an increase in gray matter density in the right motor hand area associated with 15 months of piano training (Hyde et al., 2009). A recent investigation into middle-aged pianists revealed some interesting details concerning the effect of ongoing expertise on life-long plasticity (Gärtner et al., 2014). Pianists who continued to give concerts and practice for a minimum of three hours a day showed not only larger motor hand areas, but also larger foot areas in the sensory-motor cortices of both hemispheres than pedagogues who had majored in piano performance, but who had practiced for less than two hours a day over the last ten years. This result relates to the important role of pedaling in piano performance. Pedaling is a highly refined skill requiring spatiotemporal control in the range of millimeters and milliseconds in order to adaptively modulate color, expressivity and loudness of the music.

Structural brain differences have been reported in musicians who play different instruments (Bangert and Schlaug, 2006). For keyboard players, the omega-shaped folding of the precentral gyrus, which is associated with hand and finger movement representation, was found to be more prominent in the left hemisphere for keyboard players, but was more prominent in the right hemisphere for string players. This structural difference is likely to reflect an adaptation to the specific demands of different musical instruments. Obviously, the rapid and spatiotemporally precise movements of the left hand in string-players are a stronger stimulus for plastic adaptations compared to the right hand bowing movements requiring the fine-tuned balance of fingers at the frog of the bow, and precise movements of wrist and arm. Gaser and Schlaug (2003) compared professional pianists, amateur musicians and non-musicians and reported increased gray matter (GM) volume in professional musicians not only in primary motor, somatosensory, and premotor areas, but also in multisensory parietal integration areas and in cerebellar brain regions. Modeling musical expertise with the same three-group population, James and collaborators (James et al., 2013) reported an intricate pattern of increased/decreased GM. In particular, musicians showed GM density increases in areas related to higher-order cognitive processes (such as the fusiform gyrus or the inferior frontal gyrus), whereas GM decreases were found in sensory-motor regions (such as perirolandic and striatal areas). These reductions in GM were interpreted as reflecting a higher degree of automaticity of motor skills in more expert musicians.

It is now well established that along with increasing expertise, not only enlargement but also reduction of neural structure can be observed. This was first established in a study of pianists targeting the middle putamen in the basal ganglia, a brain region involved in automation of motor programs. Granert and colleagues (2011) measured the skill level of piano playing via temporal accuracy in a scale-playing task. These authors found that the higher the level of piano playing, the smaller the volume of gray matter in the right putamen. This reduction was ascribed to an optimization process of neuronal networks within the putamen, leading to fewer, but more efficient and stable dendritic and axonal connections in this area of the motor basal ganglia loop.

Until recently, it remained an open question, the degree to which these structural and functional brain changes are influenced by age at onset of musical activity and by cumulative practice hours over particular periods of life. These factors have often been confounded and it was generally believed that early commencement of musical activity, along with increased life practice time, resulted in enlarged neural representations underpinning auditory or sensory-motor skills. Steele and colleagues (2013) were the first to investigate the morphology of the corpus callosum such that they could compare its white-matter organization in early- and late-trained musicians who had been matched for years of training and experience. They found that early-trained musicians had greater connectivity in the posterior part of the corpus callosum and that fractional anisotropy in this region was related both to age at onset of training and to sensory-motor synchronization performance. They concluded that training before the age of 7 years resulted in changes in white-matter connectivity that may serve as a scaffold upon which ongoing experience can build. Inspired by this work, and since in this study neither gray matter density nor the size of specific brain areas were analyzed, we designed a similar brain morphometry study in a group of 36 award-winning professional pianists (Vaquero et al. 2016). We kept cumulative life practice time constant, but split the group into 21 pianists who had started their musical training before age seven, and another group of 15 who had started after that age. We compared brain anatomy between these groups, and between musicians and age-matched medical students who were non-musicians. In addition, 28 pianists from the sample completed a scale-playing task, in order for us to obtain an objective measure of their pianistic abilities and temporal precision. Compared with non-musicians, pianists showed more gray matter in regions associated with learning (hippocampus), sensory and motor control and processing (putamen and thalamus), emotional processing and the reward system (amygdala), and with auditory and language processing (left superior temporal cortex). However, they also showed *less* gray matter in regions involved in sensory and motor control (postcentral gyrus) and processing of musical stimuli (right superior temporal cortex), as well as structures that have been related to music-score reading (supramarginal gyrus). Moreover, among the pianists it was observed that the size of the right putamen correlated significantly with the age at which music training began: the earlier they started to play the piano, the smaller the volume of gray matter in the right putamen (see Fig. 2). In keeping with the interpretation of the results of Granert et al. (2011) reported above, pianists who started earlier in life optimized functionality of neural structures involved in sensory-motor processing, motor learning and motor memory. This is reflected in the behavioral task: those pianists who had started their musical training before age seven played with higher regularity than those who started after that age, even though all of the pianists practiced for the same number of hours around the time of the study and had achieved the same level of proficiency. This is an important scientific proof of common knowledge, expressed in German the proverb “a tree must bend while it is young.” Neuroscientifically it is an interesting phenomenon, showing that even for highly complex motor tasks, sensitive periods in the nervous system exist (Furuya et al. 2014a). However, as we have seen, such windows of opportunity can depend on domain, genetics and continuing training.

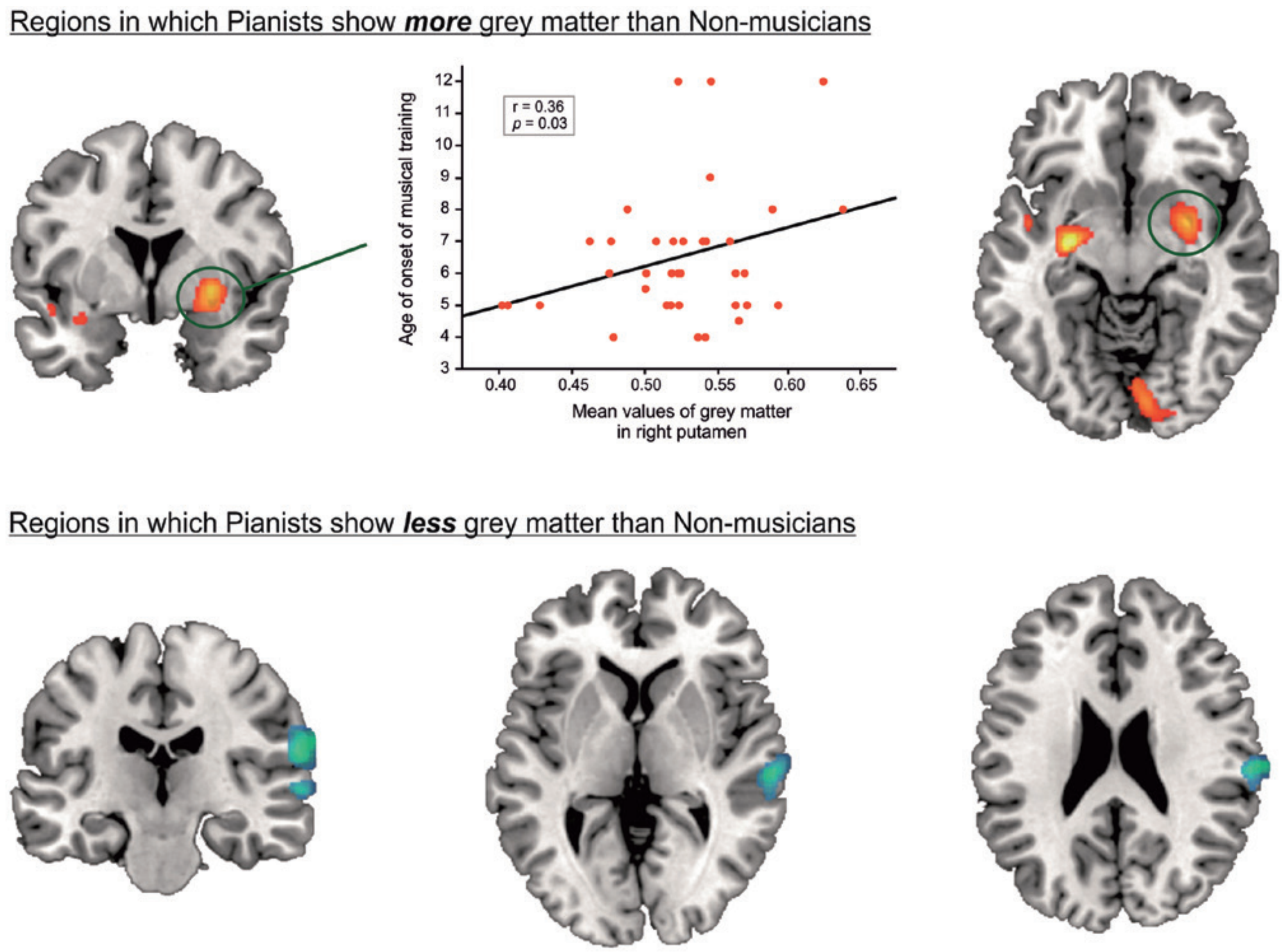

Fig. 2: Summary of the results of the study on pianists by Vaquero et al. (2016). Courtesy of Lucia Vaquero and Antoni Rodriguez-Fornells (with permission). Explanations are given in the text.

De-Expertise: Musician's Dystonia as a syndrome of maladaptive plasticity

Brain plasticity is not always beneficial. Overtraining, fear of failure, chronic pain and other stressors may trigger a deterioration of motor control and initiate a process of de-expertise. Approximately one or two in 100 professional musicians suffer from a loss of voluntary control of their extensively trained, refined, and complex sensory-motor skills. This condition is generally referred to as focal dystonia, violinists' cramp, or pianists' cramp. In many cases, focal dystonia is so disabling that it prematurely ends the artist's professional career (Altenmüller et al., 2015). The various symptoms that can mark the beginning of the disorder include subtle loss of control in fast passages, finger-curling (cf. Fig. 3), lack of precision in forked fingerings in woodwind players, irregularity of trills, fingers sticking on the keys, involuntary flexion of the bowing thumb in strings, and impairment of control of the embouchure in woodwind and brass players in certain registers. At this stage, most musicians believe that the reduced precision of their movements is due to a technical problem. As a consequence, they intensify their efforts, but this often only exacerbates the problem.

Musician's dystonia (MD) has been described for almost every instrument, including keyboard, strings, plucked instruments, woodwind, brass, percussion and folk instruments such as bagpipes and accordion. In a recent epidemiological study of 369 German professional musicians suffering from MD, keyboard players were most common with 27.1 %, followed by woodwinds (21.7%) and brass players (20.9 %). When subdividing these instrumental groups into single instruments, piano represented 22% of the total, guitar 15.2%, flute 9.7% and violin 7.6% (Lee et. al., 2017, submitted).

Fig. 3: Typical patterns of dystonic posture in a pianist, violinist, trombonist, and flutist

The relative rarity of certain instruments in these studies, even after accounting for the relative number of professionals playing each in the population, such as double bass, harp and cello, and the over-representation of piano, guitar, and flute suggests that the specific physical demands of the instrument constitute risk factors. For example, fast, fine and simultaneous finger placement in the latter instruments may be more likely to trigger the development of dystonia compared to forceful finger flexion at a lower tempo as required in the former group. It is likely that the distribution of affected hands in musician's dystonia is not random. Among pianists and guitarists the right hand is more frequently involved, among violinists the left hand. These trends correlate with differences in the technical demands imposed by each instrument. The virtuoso piano repertoire demands more from the right hand than the left, as the right hand must usually play faster trills, arpeggios and ornaments. It also often carries the treble melodic line with the 3rd, 4th and 5th fingers (Lehmann and Ericsson, 1996). On the violin the technical demands of the left fingering hand are more pronounced, requiring temporo-spatial precision in the millisecond and millimeter range for professional-level playing. Among woodwind players, both hands are equally likely to be affected. An exception is in flautists, for whom the left hand is more commonly problematic, due to the fact that the left index finger must support the weight of the instrument as well as depress the keys, and that the left thumb, ring and little fingers are extremely active compared to those of the right hand (Baur et al., 2011).

The interplay of predisposing and triggering factors in musician's dystonia has become a topic of intense research (Jabusch and Altenmüller, 2004; Jabusch et al., 2004; Ioannou and Altenmüller, 2015; Ioannou et al., 2016). As predisposing factors, male gender, genetic susceptibility and psychological traits such as elevated anxiety and obsessive-compulsive-disorder (OCD) have been documented. These may be partly interrelated: male gender and genetic susceptibility for malfunction of sensory-motor pathways may have a common origin, such as certain genes located on the X-chromosome. OCD and anxiety can in turn lead to dystonia-triggering behaviors, such as over-use of muscles and exaggerated, repetitive training. The following triggering factors have been identified: high motor demands, extra-instrumental activities, such as writing and typing (Baur et al., 2011), late onset of training, playing classical music with high demands on precise temporo-spatial control, increased general psychological and muscular tension, and destabilization of overlearned sensory motor programs due to imposed technique changes or sensory disturbances following nerve or soft-tissue injury (for a review see Altenmüller et al., 2015). The interplay of predisposing and triggering factors in the development of musician's dystonia is depicted in Fig. 4. According to our model, the emergence of musician's dystonia is a gradual process, starting with reversible tensions and dysfunctional movements termed "dynamic stereotypes", which are then gradually consolidated in sensory-motor memories and finally automated. Only at this stage would we speak of musician's dystonia, which is defined as a persistent muscular incoordination that is difficult to cure.

With respect to predisposing factors, demographic data demonstrate a preponderance of male musicians with a male/female ratio of about 4:1 (Lim et al., 2004). Hereditary factors play an important role, since a positive family history of dystonia in first-degree relatives can be found in up to 36% of affected musicians (Schmidt et al. 2009). Premorbid OCD and anxiety disorders are found in 40% of our patients (Ioannou and Altenmüller, 2014; Ioannou et al., 2016). The mean age at onset of dystonic symptoms is 35 years (Lee et al. 2016), however those musicians with elevated anxiety and stress levels develop dystonia on average ten years earlier (Ioannou et al. 2016). Furthermore, there is high variability, with the youngest patients developing dystonia at the age of around 18 and the oldest while in their sixties (Altenmüller, 2003).

Late onset of training is another important triggering factor. Musicians with dystonia start their training at an average age of around ten, whereas the mean starting age for healthy musicians is seven (Schmidt et al., 2013). This underlines the important role of early optimization of sensory-motor programs to allow the establishment of a stable scaffold for further improvements over the lifetime. The term **metaplasticity,** referring to sensitive periods in the lifetime during which general learning strategies in specific domains are best acquired, describes this

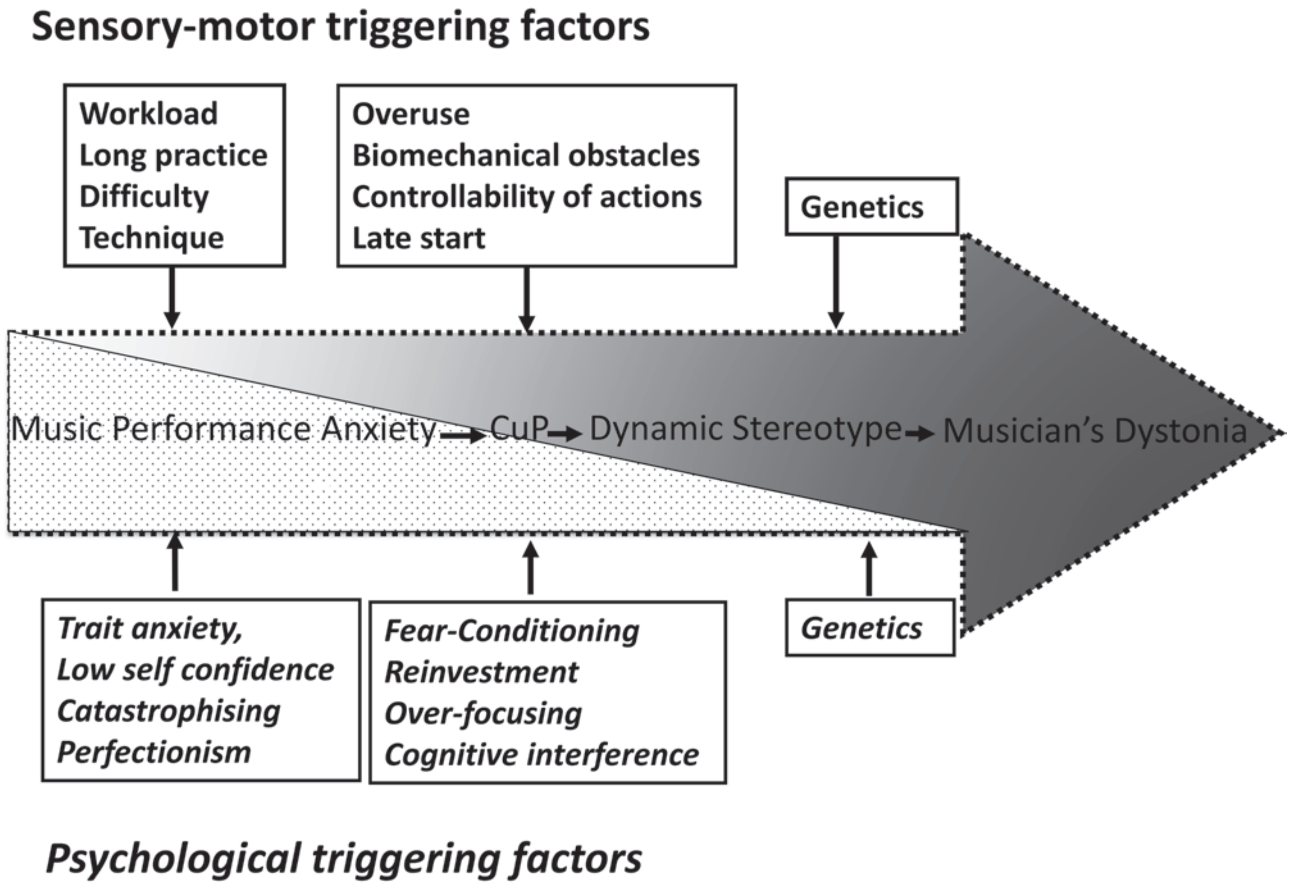

Fig. 4: Heuristic model demonstrating the proposed interplay of sensory-motor and psychological triggering factors and their contribution to the different motor disturbances. The assumed degree of "psychological" triggering factors is displayed as the dotted space; the increasing gray shade symbolizes the increasing degree of loss of motor control.

phenomenon (for a review see Altenmüller and Furuya, 2016). Metaplasticity may also account for the fact that alteration of playing technique at a later age, for example when changing teacher during the transition from school to university, may destabilize motor programs and trigger dystonia.

The genre in which the overwhelming majority of patients suffering from focal dystonia operate is classical music. In contrast to pop or jazz, with improvised structures and great freedom of interpretation, musical constraints are most severe in classical music. This genre requires maximal temporal accuracy (in the range of milliseconds), which is scrutinized by the performing musician as well as by the audience throughout the performance. As a consequence, public performances of classical music can involve a high level of social pressure: here the gap between success and failure is minimal.

Finally, physical and psychological traumata are frequently found in the history of musicians suffering from focal dystonia. With respect to physical traumata, we know that sensory disturbances and chronic pain may induce maladaptive plastic changes in the brain's sensory and motor networks, leading to a degradation of motor control. This is best documented in neural studies of the consequences of complex regional pain syndromes (Henry et al., 2011). Research on psychological trauma triggering musician's dystonia is in its infancy. Here, Jabusch and Altenmüller (2004) proposed that acute and chronic stress may promote dysfunctional motor memory formation via beta-adrenergic activation, stress hormone release, increased muscle tone and associative learning.

In summary, the association between the above-mentioned trigger factors and the development of focal task-specific dystonia is highly suggestive of a strong environmental contribution to the pathogenesis of musician's dystonia. However, the observation that the majority of performing artists fortunately do not develop musician's dystonia underlines the important role of underlying genetic predispositions.

Brain changes associated with loss of sensory motor control

The aetiology of focal dystonia is not completely understood at present, but is probably multifactorial. Most studies of focal dystonia reveal abnormalities in three main areas: a) reduced inhibition in the motor system at cortical, subcortical and spinal levels b) altered sensory perception and integration; and 3) impaired sensory-motor integration. All of these changes are believed to primarily originate from dysfunctional brain plasticity.

A **lack of inhibition** is a common finding in studies of patients with all forms of dystonia (for a review see Lin and Hallett, 2009). Fine motor control in general requires a subtle balance in neural circuits between excitation and inhibition. This is particularly important in allowing precise and smooth hand movements. For example, rapid individuated finger movements in piano playing require selective and specific activation of muscles to move the intended finger in the desired manner, and to inhibit movements of uninvolved fingers (Furuya et al., 2015). In patients suffering from hand dystonia, electromyographic recordings have revealed abnormally prolonged muscle firing with co-contraction of antagonistic muscles and overflow of activation to inappropriate muscles (Furuya and Altenmüller, 2013b). Lack of inhibition is found at multiple levels of the nervous system. At the spinal level, it leads to reduced reciprocal inhibition of antagonistic muscle groups producing co-contraction, for example of wrist flexors and extensor muscles. This in turn produces a feeling of stiffness and immobility, and frequently leads to abnormal postures with predominant flexion of the wrist due to the relative strength of the flexor muscles. Abnormal inhibition has also been demonstrated at the cortical level by using non-invasive transcranial magnetic stimulation to measure intracortical inhibition (Sommer et al. 2002). Interestingly, at this level abnormal inhibition is frequently seen in both hemispheres, despite unilateral symptoms. This points towards a more generalized form of inhibition deficit. Finally, lack of inhibition is also seen in more complex tasks, such as when movement preparation is required prior to scale playing, and for sudden movement inhibition following a stop signal in pianists (Herrojo-Ruiz et al., 2009b). The ubiquitous demonstration of deficient inhibition is suggestive of a common underlying genetic cause. However, it has to be emphasized that none of these electrophysiological effects allow diagnosis on an individual level, since the variability in both healthy and dystonic musicians is extremely large.

Altered **sensory perception** may also be a sign of maladaptive brain plasticity. Several studies have demonstrated that the ability to perceive two stimuli as temporally or spatially separate is impaired in patients with musician's dystonia, whether sensation is via the fingertips (in hand dystonia), or the lips (in embouchure dystonia). This behavioral deficit is mirrored in findings of the cortical somatosensory representation of fingers or lips. It has been demonstrated with various functional brain imaging methods that in somatosensory cortex the topographical location of sensory inputs from individual fingers overlap more in patients with musician's cramp than in healthy controls (Elbert et al., 1998). Similarly, lip representation may be altered in patients suffering from embouchure dystonia (Haslinger et al., 2010). Other abnormalities include elevated temporal discrimination thresholds, a marker of basal ganglia dysfunction found to be relevant to the pathogenesis of focal dystonia (Termsarasab et al., 2015). Since in healthy musicians an increase of the size of sensory finger representations has been interpreted as an adaptive plastic change to support the current needs and experiences of the individual (see above, Elbert et al., 1995), it could be speculated that these changes over-develop in musicians suffering from dystonia, shifting brain plasticity from being beneficial to maladaptive (Rosenkranz et al., 2005). In this context it is worth recalling that local pain and intensified sensory input due to nerve entrapment, trauma or muscle overuse have been described as potential triggers of dystonia. Interestingly, there are clear parallels of abnormal cortical processing of sensory information and cortical reorganization between patients with chronic pain and those with focal dystonia. An animal model of focal dystonia established in over-trained monkeys supports this: repetitive movements induced both types of symptoms – pain syndromes as well as dystonic movements. Mapping of neural receptive fields has demonstrated a distortion of cortical somatosensory representations (Byl et al., 1996), suggesting that over-training and practice-induced alterations in cortical processing may play a role in focal hand dystonia.

Impaired **sensory-motor integration** also plays an important role in the pathophysiology of musician's dystonia. This is best illustrated by the "sensory trick" phenomenon: some musicians suffering from dystonia show a marked improvement of fine motor control when playing with a latex glove, or when holding an object (such as a rubber gum) between the fingers, thus changing the somatosensory input. In experimental settings, vibrating stimuli lead to a worsening of musician's dystonia. In one study, when transcranial magnetic stimulation was used in conjunction with muscle vibration, motor evoked potentials decreased in agonist muscles and increased in antagonist muscles (Rosenkranz et al., 2002). These data again suggest an altered central integration of sensory input in musician's dystonia, which might be due to the failure to link the proprioceptive input to the appropriate motor cortical area. Reversing these effects of sensory-motor disintegration is the approach of several retraining therapies. Sensory retraining in the form of tactile discrimination practice can ameliorate motor symptoms, suggesting that the above-mentioned sensory abnormalities may drive the motor disorder. Interestingly, a positive response to the sensory trick phenomenon is linked to a better outcome in attempts to re-educate musicians with dystonia (Paulig et al., 2014).

Innovative brain imaging techniques recently demonstrated that musician's dystonia is also a **network disorder**. Assessment of changes in functional brain-networks and in neural connectivity between different brain regions revealed that patients with musician's dystonia show altered network architecture characterized by abnormal expansion or shrinkage of neural cell assemblies. These changes include the breakdown of basal ganglia–cerebellar interaction, loss of a pivotal region of information transfer in the premotor cortex, and pronounced reduction of connectivity within the sensory-motor and frontoparietal regions (e.g. Strübing et al., 2012, Battistella et al., 2015). These abnormalities have been further characterized by significant connectivity changes in the primary sensory-motor and inferior parietal cortices. Therefore, musician's dystonia likely represents a disorder of large-scale functional networks. However, the specific role of these networks and their inter-individual variability remain to be clarified.

There are currently several treatment methods available for musician's dystonia. Novel strategies aim to reverse the maladaptive plastic changes, for example with inhibition of over-active motor areas on the affected side, alongside activation of the contralateral "healthy" motor cortex, whilst musicians perform in-phase symmetrical finger exercises on a keyboard (Furuya et al. 2014b). Retraining may also be successful, but usually requires several years to succeed (van Vugt et al. 2013). Symptomatic treatment through temporary weakening of the cramping muscles by injecting Botulinum-toxin has proven to be helpful in other cases; however, since the injections need to be applied regularly every three to five months during one's career, this approach does not offer a good solution for young patients. Thus, the challenge is to prevent young musicians from acquiring such a disorder. The components of such a prevention program include reasonable practice schedules, economic technique, prevention of muscle overuse and pain, mental practice, avoidance of exaggerated perfectionism, and psychological support with respect to self confidence.

Brain plasticity as prerequisite and result of expert performance in musicians

In the preceding paragraphs, we have demonstrated how musical activities, such as learning to master an instrument and to perform in public, induce brain plasticity. These central nervous adaptations are in most cases beneficial but in some circumstances may be detrimental, as illustrated in musician's dystonia. Age at commencement of practice, amount and quality of practice, and accompanying conditions, such as stressors or muscular overuse, determine the quality and nature (adaptive or maladaptive) of these brain changes. Furthermore, the brain's "sensitive periods", when it is best shaped, seem not only to depend on hereditary factors but also to vary in different sensory, motor and cognitive domains. We propose the concept of metaplasticity, conceptualized above with a scaffold metaphor: early musical training stabilizes the sensory-motor system and provides neuroprotective effects with respect to the development of focal dystonia (see Fig. 5). Interestingly, these effects are maintained for the whole life span: those musicians who start early do not only develop superior auditory and sensory-motor skills, they also show less age-induced decline of sensory-motor and cognitive functions (Krampe and Ericsson, 1996; Meinz, 2000). Taken together, intense musical training in childhood can bring about lifelong change in both structure and functions of auditory, sensory-motor, and emotional systems. These not only enhance musical skill acquisition and guard against disorders triggered by extensive training, but also serve as ingredients for better shaping life-long neuronal development.

We would like to conclude our chapter with a general remark. As emphasized above, the complex neurophysiological processes involved in musical training and expert performance are not restricted to sensory-motor brain circuits, but also involve memory, imagination, creativity and – most importantly – emotional communicative skills. The most brilliant virtuosos will not move their listeners if imagination, color, fantasy and emotion are not part of their artistic expression. These qualities are often not trained solely within a practice studio, but depend on and may be linked to experience from daily life, human rela-

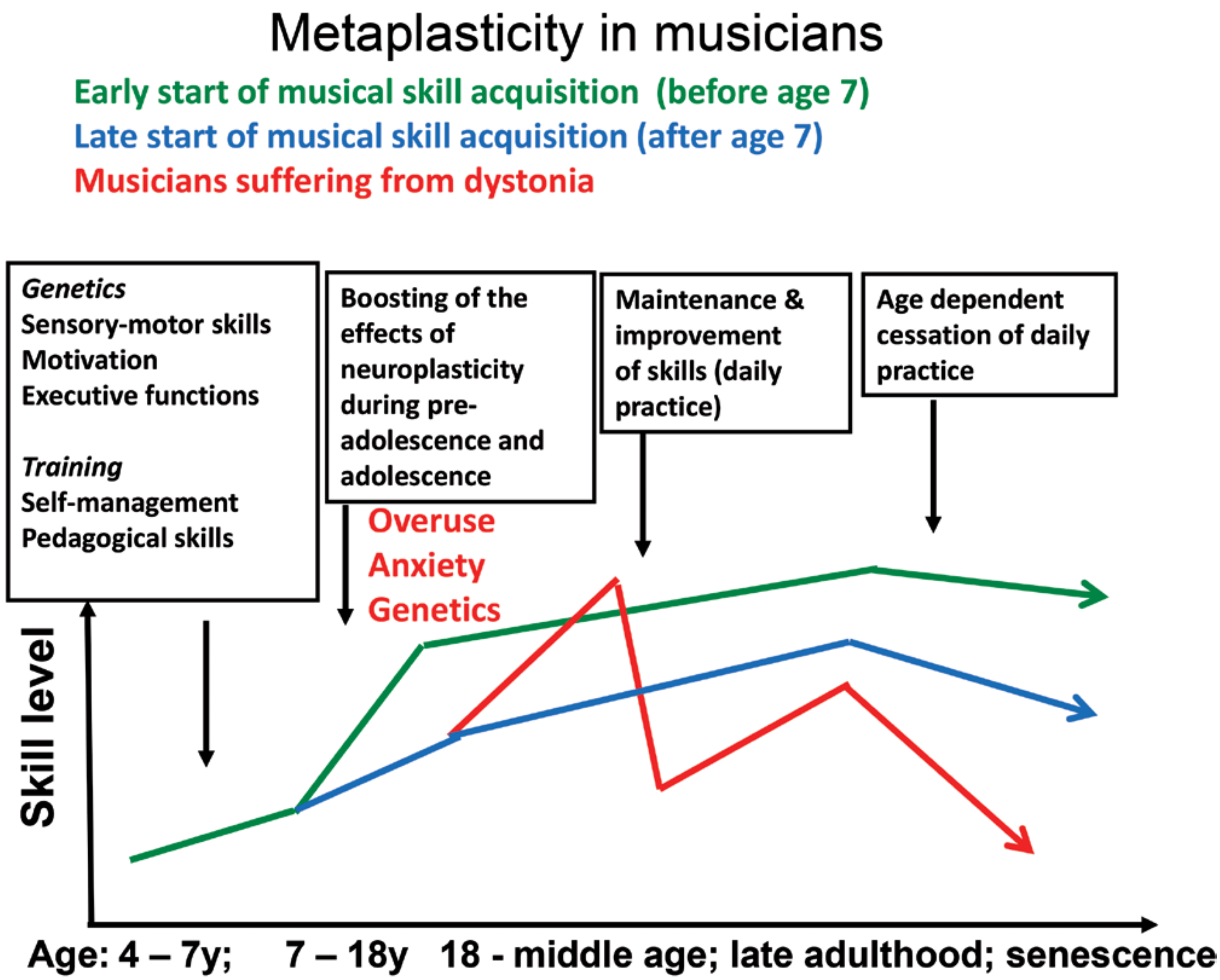

Fig. 5: Different time courses of skill acquisition in earlier and later "starters", and in musicians suffering from dystonia. Neuronal networks underpinning specific skills are optimized in childhood. This allows more effective acquisition during pre-adolescence and adolescence. Skill level continues to improve during adulthood, and stabilises as related activities cease. Early-optimized neuronal networks are more stable and less susceptible to maladaptive changes, such as occur in musician's dystonia. Here late inception of training and specific trigger factors may lead to a deterioration of sensory-motor skills.

tionships, a rich artistic environment, an empathetic outlook, and emotional depth. Such factors that profoundly influence the aesthetic quality of music performance can be subject to expertise research, however they are presently inaccessible to neuroscientific methodology. Important steps here will include the development of more fine-grained imaging technologies and the integration of findings from brain morphology, nerve-cell metabolism, connectivity measures and neurotransmitter activities, at the individual level (Amunts und Zilles, 2015). Along with experimental paradigms that include meaningful behavioural measures, such research may eventually enable us to uncover the secrets of musical creativity and its emotional power.

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