The plastic human brain

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Abstract. *Purpose* In this review I summarize and discuss reported findings of structural and functional plasticity in the intact human brain.

Methods The main focus is placed on research that uses musicians as a model to study brain plasticity. I summarize therefore mostly studies dealing with musicians or with the effect of music practice. In the first section, structural plasticity is described on the basis of modern neuroanatomical studies using magnetic resonance imaging (MRI) techniques. In the second part, emphasis is given to studies reporting functional plasticity on the basis of changed neurophysiological activation patterns. These studies are discussed in the context of two approaches employed to study plasticity in the human brain: the cross-sectional and longitudinal approaches.

Results The reviewed studies altogether indicate that experience can shape brain anatomy and brain physiology. Brain plasticity as demonstrated here is related to changed grey and white mater densities (and volumes) but also to changed activation patterns in the brain areas involved in controlling the expertise task.

Conclusions Taken together, all studies support the view that the human brain is much more plastic than had been anticipated 20 years ago.

1. Introduction

Since its very beginning experimental psychology has focused closely on the study of learning and memory processes in both humans and animals. The work of the early pioneers uncovered many basic principles of learning and memory that are still recognized today. One of the hallmarks of experimental and cognitive psychology is the detailing of learning and memory theories. Such is the importance attached to the mechanisms of learning and memory that the sustained endeavor of neuroscientists to shed light on the molecular and neurophysiological underpinnings of learning and memory can come as no surprise. The Polish neuroscientist Jerzy Konorski (1948) is regarded as being the first to introduce to the scientific literature the term *neuroplasticity* (variously referred to as brain plasticity, cortical plasticity or cortical re-mapping). This term refers to the changes that occur in the organization of the brain as a result of experience. Jerzy Konorski was a pupil of the famous Russian physiologist Ivan Pavlov, best known for his studies on classical conditioning. Konorski introduced a new direction of research and established original theories about the physiology of the brain. He also published many papers and authored two important books on learning. In the first book, he presented one of the earliest comprehensive theories of associative learning as a result of long-term neuronal plasticity. Konorski also proposed the idea of synapses that strengthen with use. In 1949, the Canadian neuropsychologist Donald O. Hebb published a book entitled "The Organization of Behavior" in which he also proposed his well-known Hebbian theory, later also referred to as "Hebbian learning" (Hebb, 1949). "Hebbian learning" is basically the same idea as Konorski had proposed (synapses strengthen with use), but Hebb specified this idea further, as best expressed in his book in his own words: "When an axon of cell A is near enough to excite cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased." This postulate is often paraphrased as "neurons that fire together wire together" and commonly referred to as

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Hebb's Law. But it should be pointed out that Konorski and Hebb proposed this mechanism independently of one another and together paved the way for modern neuroplasticity research.

Although these eminent researches highlighted the importance of neuroplastic processes, it took some time until this concept was widely accepted. The consensus several decades ago was that lower brain and neocortical areas are immutable after development, whereas areas related to memory formation, such as the hippocampus and dentate gyrus, are highly plastic. At that time, the concept of the "critical period" was widely accepted. This suggested strong plasticity until a specific age period, after which there would be some fixation of pathways and neural structures. However, neuroanatomical and neurophysiological studies have changed this picture substantially over the last 20 years, having shown that substantial changes occur in the entire brain of both humans and animals in response to experience. Interestingly, plastic changes have been demonstrated not only in the brain of children, adolescents, and younger adults, but also in mid-aged adults and more recently in the elderly (Boyke et al., 2008). Thus, the human brain is plastic throughout the entire lifespan. It is no exaggeration that one of the most important findings of neuroscientific research in the last 20 years is that the human brain is plastic and even more plastic than previously anticipated.

As mentioned above cortical plasticity research has its theoretical origin in the late 1940s. However, it has its experimental origins in animal research dating back to the late 1970s and early 1980s. During this period several groups began to explore the neurophysiological and neuroanatomical consequences of altered sensory and motor experience. In summary, these studies demonstrated that the neural assemblies change their firing pattern as a consequence of experience. Most interestingly, these studies also demonstrated that the cortical organization of neural assemblies changed due to experience (Jenkins et al., 1990; Merzenich et al., 1990; Nudo et al., 1990; Nudo and Milliken, 1996; Rauschecker, 2002; Nudo, 2006).

All the preceding studies explored cortical plasticity in animals. One of the main starting points for the study of brain plasticity in humans was Ramachandran's research on patients suffering from phantom limb pain (Ramachandran et al., 1992; Ramachandran et al., 1995). Phantom limb pain is most commonly found in people who have undergone amputations of hands, arms, and legs. It is thought that phantom limb pain results from disorganization in the somatosensory

cortex and the inability to receive input from the targeted area. Interestingly, it is more common after unexpected losses than planned amputations, and there is a high correlation between the extent of phantom limb pain and the extent of physical remapping. Phantom limb pain subsides when the somatosensory representation has adapted to the new situation. This adaptation is mostly accomplished when the neurons normally involved in processing the afferent information from the amputated limb are incorporated into the somatosensory control of body parts that are still functioning.

The advent of modern brain imaging methods enabled the study of cortical plasticity in healthy human subjects. The availability of this technique has boosted plasticity research in the last 20 years. Thus, the study of cortical plasticity in the human brain is one of the most challenging undertakings of current neuroscience research. In principle, three different approaches to studying plastic processes are possible: (1) the cross-sectional approach in which experts and non-experts are compared with respect to anatomical or functional brain measures. This approach has been widely used and has provided many interesting findings. But the basic caveat with it is that the uncovered differences are simply correlational, thus meriting caution in drawing overly strong causal inferences from the data. (2) Short-term longitudinal studies in which subjects have undergone a specific training intervention. These studies are typically designed according to a pre-post design and the subjects are enrolled in training programs lasting several hours to several months. (3) Long-term longitudinal studies in which subjects have undergone a longer (at least for years) training. In the following review I will summarize the findings of cross-sectional and longitudinal research on cortical plasticity, placing greater emphasis on structural and functional plasticity in one specific expert group, namely musicians.

2. Structural plasticity

The emergence of magnetic resonance imaging (MRI) technology and of improved mathematical methods for the analysis of the brain imaging data has given morphometric analysis a tremendous boost, because morphometric brain measures can now be conducted in vivo instead of post-mortem. In vivo human brain imaging allows the versatile measurement of brain structure in large samples of randomly or selectively collected subjects. In addition, and most importantly for the scope of the present paper, MRI-based

morphometry provides a valuable opportunity for repeated measurement of the brain. This opens the way for conducting longitudinal studies. But despite being the gold standard of brain plasticity research, MRI-based morphometry has not been used particularly frequently in the study of structural brain plasticity. The most common methodological approach thus far is the cross-sectional strategy, and I will begin reviewing this.

2.1. Cross-sectional studies

Professional musicians have been used over the last 15 years as a model for brain plasticity (Schlaug, 2001; Münte et al., 2002). Why are musicians so interesting for plasticity research? First of all, they are experts in playing musical instruments. For example, to play the demanding two three-second segments of the 11th variation from the 6th Paganini-Etude by Franz Liszt requires the production of 1800 notes per minute. A tremendous amount of training is needed to achieve this kind of finger movement speed. Ericsson was one of the first to show how much professional musicians do in fact practice (Ericsson et al., 1993; Ericsson and Lehmann, 1996). He showed that professional pianists and violinists practise for 7500 hours before reaching the age of 18 years, while music teachers can look back on a total practice time of approximately 3500 hours. This difference was unaffected by the quality of musical education, since all musicians in this study had passed the prestigious *Berlin Academy of Music*. Thus, the amount of practice is one of the most important factors influencing musical expertise, at least in terms of the skill required to play a musical instrument.

The first anatomical studies relating neuroanatomical markers to musical expertise and musicianship were published by the Dusseldorf group in the 1990s (Schlaug et al., 1995a; Schlaug et al., 1995b; Amunts et al., 1997). In the first study, Schlaug and colleagues measured the midsaggital size of the corpus callosum (CC) in professional musicians using T1-weighted MRI images. They uncovered a larger anterior surface of the CC in musicians who commenced with musical training before the age of 7 compared with those who started later in life. The authors took this finding as support for their idea that early motor training before the "critical age" would influence the maturation of the fiber tracts crossing through the anterior CC. Given that the fibers crossing the anterior CC connect motor areas (primary and premotor) as well as prefrontal areas of both hemispheres, this findings was understood as evidence for a stronger anatomical inter-hemispheric connection be-

tween the frontal brain areas in musicians who started with their musical training early in life (Schlaug et al., 1995a). In a further paper of this group, the authors reported substantial morphological differences in the hand motor area in professional musicians (Amunts et al., 1997). They measured the length of the posterior wall of the precentral gyrus bordering the central sulcus (intrasulcal length of the precentral gyrus, ILPG) in horizontal sections located in the hand motor area in consistent-right-handed professional musicians and non-musicians. They used this measure as an estimate of the size of each hand motor area that controls either the right or the left hand. This study uncovered several important findings: (1) The ILPG was larger on the left than on the right hemisphere demonstrating that handedness is strongly related to anatomical between-hemisphere differences in the hand motor area. (2) The ILPG was generally larger in professional musicians than in non-musicians. (3) In musicians the ILPG was disproportionately greater on the right hemisphere controlling the subdominant left hand than the ILPG of the left hemisphere that controls the dominant right hand. It is necessary to note that all musicians were either professional pianists or violinists who altogether have practiced their left sub-dominant hand intensively because they have to use the left hand for manipulating their instruments. Most important for the subject matter of this paper was the finding that the ILPG measures on both hemispheres correlated with the age of commencement of musical training, this supporting the notion that the earlier musical training starts the stronger is its impact on anatomical changes in the hand motor area.

Recently Bangert and Schlaug (2006) reported, that pianists atypically showed the "omega sign" (indicative of a larger hand motor area) on both hemispheres while violinists only showed the "omega sign" on the right hemisphere controlling the left hand. This specific anatomical feature possibly is related to the fact that pianists practice a lot with both hands while violinists practice a lot with their left hand (manipulating the strings) and their right arm (manipulating the bow). Thus, violinists might *drive* only the right-sided hand motor area while pianists *drive* the hand motor areas on both hemispheres.

Although not an anatomical study in a pure sense, the paper published by Thomas Elbert and colleagues from Konstanz (Elbert et al., 1995) has strong neuroanatomical implications. They used MEG to measure the cortical representation of the digits of the hand of string players. For this they stimulated each digit sep-

arately and measured the concomitant brain responses. The intracerebral sources of these brain responses were identified and the authors calculated on this basis the size of the somatosensoric representation of the stimulated hand. They found in string players a massive reorganization for the left hand (larger representation). Most interestingly and in accordance with the findings of Amunts et al. (1997), the amount of cortical reorganization was correlated with the age of commencement at which the person had begun to play. Thus, these two studies clearly suggest that age of commencement of musical training is an important variable determining the amount of cortical reorganization.

The preceding studies used the so-called classical region-of-interest (ROI) approach. One major problem associated with this is the fact that many anatomical regions are not appropriately defined and are in part difficult to detect in MRI scans. Furthermore, the ROIs in the majority of ROI-reliant morphometric studies are delineated on consecutive slices either manually, semi-automatically or automatically. This interactive approach not only introduces user bias, but it is also highly time-consuming. This generally leads to the analysis of a limited number of a-priori defined ROIs and in a restriction of the number of examined subjects. Recent morphometry studies have made use of voxel-based morphometry (VBM). The advantage of VBM is the increase in objectivity of measures of anatomical differences. In addition, the analysis is not restricted to a few anatomical areas as in classical ROI approaches. It is in fact possible to measure anatomical features and differences in the entire brain (for the technical and computational underpinnings of this approach see Jäncke, 2002).

Using this approach Gaser and Schlaug (2003) identified grey matter volume differences in motor, auditory, and visual-spatial brain regions when comparing professional musicians (in this study keyboard players) with a matched group of amateur musicians and non-musicians. Most interestingly, they found a strong association between structural differences (grey matter density), musician status, and practice intensity, supporting therefore the view that practice (in this case practicing to play a musical instrument) has an impact on brain anatomy. Most recently, a Swedish group used diffusion tensor imaging (DTI) to measure the fiber tracts in 8 professional pianists and found a strong positive correlation between the measure of fractional anisotropy (FA), indicating the integrity of the fiber system, and time spent practicing on the piano (Bengtsson et al., 2005; Han et al., 2008). Thus, the pianists

who practiced frequently showed higher FA values (indicating a higher integrity of the fiber system). This finding is of outstanding importance because it brings to light morphometric differences even within a highly specialized group of skilled pianists and that these differences are due to practice time ("specialization of the specialized").

In 2002, Schneider and colleagues from Heidelberg reported a remarkable anatomical finding in musicians. Using MEG and sophisticated anatomical analyses they found neurophysiological and anatomical differences between musicians and non-musicians. First, the neurophysiological activity in the primary auditory cortex 19–30 ms after tone onset was more than 100% larger. In addition, the gray matter volume of the anteromedial part of Heschl's gyrus was 130% larger in musicians. Both measures were also highly correlated with musical aptitude. This study is one of the first to indicate that both the morphology and neurophysiology of Heschl's gyrus have an essential influence on musical aptitude (Schneider et al., 2002). The second paper of the same group was even more spectacular (Schneider et al., 2005). In this paper they found a strong relationship between the used strategy in processing complex tones and anatomical features in the primary auditory cortex. Professional musicians who preferentially analyze the fundamental pitch[1] of complex tones were found to have a leftward asymmetry of gray matter volume in Heschl's gyrus, whereas those who prefer to analyze the spectral pitch of complex tones show a rightward asymmetry of gray matter volume of Heschl's gyrus. Thus, a marked anatomical feature of the auditory system correlated with a particular tone processing strategy within a group of professional musicians. For me, this is one of the most exceptional structure-function relationships ever published.

Patricia Sluming from Liverpool and colleagues published a paper in which they reported anatomical differences in Broca's area between musicians and non-musicians (Sluming et al., 2002). In particular, they reported increased gray matter in Broca's area in the left inferior frontal gyrus in musicians. In addition, and this is very important for aging research, they observed significant age-related volume reductions in cerebral hemispheres, dorsolateral prefrontal cortex bilaterally and gray matter density in the left inferior frontal gyrus in controls but not in musicians! In oth-

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[1]The fundamental tone (abbreviated f0 or F0), is the lowest frequency in a harmonic series.

er words, musicians showed no or a reduced decrease of gray matter density in the frontal cortex compared with non-musicians with increasing age. This anatomical study suggests that orchestral musical performance might promote use-dependent retention, and possibly expansion, of gray matter within Broca's area. In addition, this study emphasizes the significant point that shared neural networks (within Broca's area) are involved in the control of language and music. In a more recent study, the same group showed that Broca's area is also involved in the control of mental rotation but only in musicians (Sluming et al., 2007). They relate this extraordinary finding to the sight-reading skills of musicians. In sight-reading, visuospatial cognition is related to some kind of language decoding. Broca's area might be involved in the control of this specific interrelationship.

The most recent study to use DTI techniques was published by Imfeld et al. (2009). These authors measured the training effects on fractional anisotropy (FA) in the corticospinal tract (CST) of professional musicians and control non-musicians. They found significantly lower FA values in both the left and the right CST in the musician group. Diffusivity, a parameter indicating the amount of water which diffuses along and across the axon, was negatively correlated with the onset of musical training in childhood in the musician group. A subsequently performed median split into an early and a late-onset musician group (median = 7 years) revealed increased diffusivity in the CST of the early-onset group as compared with both the late-onset group and the controls. In conclusion, DTI was successfully applied in revealing plastic changes in white matter architecture of the CST in professional musicians. The present results challenge the notion that increased myelination induced by sensorimotor practice leads to an increase in FA, as has been suggested previously. Instead, training-induced changes in diffusion characteristics of the axonal membrane may lead to increased radial diffusivity reflected in decreased FA values. However, this issue deserves more intensive discussion about the methodological aspects associated with FA and diffusivity measurements.

A somewhat special case is the extraordinary ability of absolute pitch (AP) in musicians and the associated brain features. Absolute pitch (AP) is defined as the ability to identify accurately the pitch of a single tone without referring to a reference tone. Estimates of the prevalence of AP vary from 1 in 1,500 in amateur musicians to up to 15% in students at music schools. There is now consensus that AP relies on both a ge-

netic predisposition and early musical training (Levitin and Rogers, 2005). Anatomically, in vivo magnetic resonance imaging (MRI) studies of musicians have shown increased left-sided asymmetry of the superior bank of the temporal lobe, the planum temporale (PT), in individuals with AP. This asymmetry appears to be the result of a smaller-than-normal right PT in musicians with AP rather than an expansion of the left side (Schlaug et al., 1995b; Keenan et al., 2001) (A further neuroanatomical study emphasized specific anatomical features in the superior temporal cortex and the dorsolateral frontal cortex; Bermudez et al., 2009). A functional MRI study found that the intensity of hemodynamic responses to music pieces in the left rather than right PT correlates with both AP ability and the age at which musical training started (Ohnishi et al., 2001). Early training alone cannot account for the PT asymmetry, as musicians with relative pitch (RP) who started training early do not have such an asymmetry. One study found that blind AP musicians revealed greater variability in planum temporale asymmetry compared with the increased left-sided asymmetry described in sighted AP musicians (Hamilton et al., 2004). The authors suggest that the specific experience of blind AP musicians with a stronger focus on the auditory world might shape the architecture of the planum temporale area. A recently conducted fMRI study supported this proposal by demonstrating (in one blind AP musician) that the blind musician showed significantly more activation of bihemispheric visual association areas, lingual gyrus, parietal and frontal areas than the sighted musicians to tones (Gaab et al., 2006). These differences in the activation pattern indicate that a different neural network, which includes visual association areas, is recruited in this blind musician compared to sighted musicians when performing pitch categorization and identification.

What is the significance of AP ability in the context of this review about plasticity? As mentioned in the introduction of this chapter, it is now regarded as a matter of common understanding that both genetic and experience-related factors determine AP ability. For example, most AP musicians started their formal musical training before the age of 7 (approximately 70%). There is also a strong correlation between age of commencement of musical training and AP ability (Levitin and Rogers, 2005). Thus, anatomical features, which are specific for AP musicians, might also be influenced by learning experience, that is, in this specific case, by learning to identify and discriminate musical sounds.

While musicians have served as the model group for studying neuronal plasticity, similar findings have been

reported for other expert groups, including taxi drivers, typists, mathematicians, bilinguals, subjects with superior verbal proficiency, and professional golfers (Golestani et al., 2002; Mechelli et al., 2004; Aydin et al., 2007; Lee et al., 2007; Cannonieri et al., 2007; Jäncke et al., 2009). Besides using a cross-sectional approach most of these studies relate the specific anatomical features to retrospectively obtained behavioral measures (e.g., duration of practice, years of academic training, verbal proficiency measures etc.) and have uncovered strong correlations between these behavioral measures and the specific anatomical features. Thus, changed anatomy is not an exclusive feature found only in musicians, it can rather be found in all subjects with specific behavioral expertise.

2.1.1. Interim summary of cross-sectional studies on structural plasticity

Summarizing the above-mentioned findings there is considerable evidence that highly proficient subjects demonstrate specific neuroanatomical features in brain areas involved in the control of the particular task for which the subjects demonstrate their particular expertise. For example, professional (and semi-professional) musicians demonstrate specific anatomical features in the motor system (controling the hands with which the musicial instruments are manipulated), the entire auditory system (processing the musical sounds), and the cognitive system (controlling memory and attention functions). But not only musicians demonstrate specific neuroanatomical features, there are also considerable anatomical peculiarities in other groups with specific expertise. For example, professional golf players, academic mathematicians, professional London taxi drivers, subjects with long lasting bilingual experience, and even typists with long last lasting practice experience alltogether demonstrate specific neuroanatomical features which are strongly related to their particular expertise.

2.2. Longitudinal studies

Only few studies to date have used the longitudinal approach to investigate the influence of experience and practice on brain anatomy. All studies, which have been published so far (except one), have been conducted with non-musicians. Because longitudinal approaches are vital for understanding neuroplasticity I will summarize them here, too. The first study of this type was published by Draganski and colleagues (Draganski et al., 2004). They examined two groups of subjects ($n = 24$,

mean age $= 22$ years) all of whom were inexperienced jugglers. The subjects in the juggler group were given 3 months to practice juggling until they could successfully sustain juggling for at least 60 seconds with three balls. Before and after this training period, whole brain MRI scans were obtained. The authors identified two brain areas known to be strongly involved in controlling juggling that had changed in grey matter density during the course of practice, the intraparietal sulcus (IPS) and the human movement territory (hMT). The IPS is part of the dorsal visual stream and is involved in transforming retinotopic into body-centered information necessary to visually control movements. The hMT is a highly specialized brain area for analyzing visual movement information. A third scan was obtained 3 months after the second scan. During this follow-up period none of the jugglers practiced juggling. By the end of this period all subjects of the juggler group were found to have unlearned juggling and were unable to juggle the three balls for 60 seconds. Most interesting is the finding that the grey matter density increases following practice were reversed during the 3 months without practice. Thus, practice obviously drives structural plasticity in specific brain areas. When practise stops the anatomical changes returned to baseline level. Thus, use it or lose it is a metaphor bringing brain plasticity to the point.

In a very recent carefully controlled study published by Boyke and colleagues (2008), the authors observed that elderly persons (mean age 60 years) were also able to learn three-ball cascade juggling (with slightly less proficiency than the 20-year-old adolescents studied in afore-mentioned study). Similar to the young group studied in the preceding study, grey matter changes in the older brain related to skill acquisition were observed in area hMT/V5 (middle temporal area of the visual cortex), showing that in the elderly brain, structural plasticity occurs in a manner similar to that found in young brains. Beside this corresponding structural plasticity, there were some additional changes in the elderly, with transient increases in grey matter in the hippocampus on the left side and in the nucleus accumbens bilaterally. In summary, this latter study suggests that age is not in itself a limiting factor for structural plasticity that is driven by procedural learning.

The same group also demonstrated that explicit learning can drive structural plasticity (Draganski et al., 2006). In this study, MRI scans were obtained at three different time points while medical students learned for their final medical examination. The first scan was acquired three months before the examination, while

the second scan was made 1–2 days after the examination. The third scan was obtained 3 months after the examination. During this learning period, grey matter was shown to increase significantly in the posterior and lateral parietal cortex bilaterally. These changes reached their maximum after the second scan, but did not change significantly toward the third scan during the semester break 3 months after the examination. The posterior hippocampus showed a different pattern of change in grey matter over time. There was a linear increase of grey matter from the baseline until the third scan, even demonstrating an increase after the learning period. The anatomical locations of the structural changes are consistent with the literature showing that the posterior parietal cortex is part of a network of declarative network (Todd and Marois, 2004; Todd et al., 2005). Several studies have shown that this area is involved in encoding of visual information, but also in the retrieval of memory information (Wheeler and Buckner, 2004; Wheeler et al., 2006).

Recently, Hyde et al. (2009) published a paper strongly supporting my own interpretation of the brain's capability for experience-dependent influences on brain anatomy and function. In concrete, this study demonstrates that 6-year-old children receiving instrumental musical training for 15 months not only learned to play their musical instrument, they rather showed changed anatomical features in brain areas known to be involved in the control of playing a musical instrument. Most of these brain areas are part of the cortical motor system but there were also structural changes in the auditory system and in the corpus callosum. This is the first longitudinal study demonstrating brain plasticity in children in the context of learning to play a musical instrument.

These studies strongly support the idea that practice and experience shape specific anatomic features. Although the presented data are compelling, it is currently not entirely clear which specific neuroanatomical changes underlie the macroscopic changes. The anatomical measures reviewed above are taken from magnetic resonance images that mostly utilize spatial resolutions in the range of 1 mm^3. A voxel of that size contains thousands of neurons, but changes can only be demonstrated when many neurons or fibers in that cube change their anatomical features. It is known from animal experiments that synaptogenesis and dendritic expansion take place as a consequence of learning, and that these changes can happen quite early after learning (20 minutes) (Kempermann et al., 1997). Thickening of neurons and myelin sheets have also been identified as

possible candidates for neuroplastic processes. Beside these changes, higher metabolic efficiency, increased neurotransmitter production, release, and re-uptake are also possible factors. The human hippocampus (i.e., the dentate gyrus) is one of only two anatomical regions known for its life-long neurogenesis (the ability to generate neurons derived from local stem cells) (Eriksson et al., 1998). Work in mice and rats have shown that physical activity and enriched environment improve the rate of adult neurogenesis and maintenance of these new neurons (Kempermann et al., 1997; Gage, 2002; Pereira et al., 2007). Thus, there is at least the theoretical possibility that angiogenesis/neurogenesis underlie plasticity processes.

2.2.1. Interim summary of longitudinal studies on structural plasticity

The few longitudinal studies on structural plasticity, which have been published so far unisono come to the same conclusion. Practicing a particular task results in anatomical changes specifically in the brain areas involved in controlling the practiced task. The studied practice times ranged from several months to several years. Most interestingly is the finding that practice dependent alterations of brain anatomy are not stable. It has rather been shown that when the subjects stop practicing the anatomical measures returned to baseline levels. Thus, *use it or lose it* is the metaphor at best explaining the use-dependent alterations found in the context of longitudinal studies.

2.3. Open questions

The above reviewed studies support the idea that experience modifies specific anatomical features. However, although the above-mentioned findings seem to be appealing there are some unanswered questions left. For example, more neuroanatomical work is needed to uncover the microscopic underpinnings of GM and WM changes. For example, it is necessary to understand what GM and WM density and/or volume real indicate. Most importantly, there is also considerable discrepancy with respect to the meaning of FA values (measured with DTI) in the context of specific behavioral expertise. Some studies have reported both, decreased and increased FA values to be associated with more skilled behavior. In addition, in the study of Bengtsson et al. (2005) it is puzzling that a positive correlation between the amount of piano practice and FA is reported along with generally lower mean FA values (in many brain regions) in skilled pianist as compared to

controls. The reasons for these inconsistent results are manifold and, so far, not much effort has been put into a further discussion of this issue. FA reflects the proportion of axial and radial diffusion of water molecules in neural white matter. High FA values are measured in case of strong axial water diffusion (diffusion along the WM fibers). Therefore, reduced FA values in the group of musicians as compared to the control group suggest either (1) increased radial diffusion or (2) decreased axial diffusion or (3) a mix of both. Increased radial diffusion would indicate between-group differences with respect to myelin and axonal membrane structure (Beaulieu, 2002), e.g. increases in membrane permeability for water molecules. Also the axonal diameter has been shown to influence radial diffusion values (larger axonal diameter is associated with stronger radial diffusion) (Beaulieu, 2002). Decreased axial diffusion would rather be attributed to the growth of axonal neurofibrils, such as microtubules and neurofilaments (Kinoshita et al., 1999), which normally occurs during development (Haynes et al., 2005) but may also play a role in the context of practice.

3. Functional plasticity

In this section I will focus on functional plasticity. This is the change in neurophysiological activation (measured in terms of electric, magnetic and blood flow responses). I will also provide a brief review of some of the behavioral consequences associated with these neurophysiological changes. As in the section on structural plasticity, we can distinguish between (1) cross-sectional and (2) longitudinal studies. Most of the published papers have taken the cross-sectional approach in which highly skilled subjects are compared with less-skilled subjects in terms of specific neurophysiological parameters. In longitudinal studies, skilled and less-skilled subjects typically undergo some kinds of practice procedures and the associated neurophysiological and behavioral changes are monitored. In the following, I will place the emphasis of my review on musicians. As mentioned above, musicians are special in the sense that their musical training (generally) begins early in life and continues as a life-long undertaking. In the following, I briefly review the most important differences between musicians and non-musicians according to findings yielded by the cross-sectional and the longitudinal approaches.

3.1. Cross-sectional studies

3.1.1. Perception

Sensory and especially auditory information is very important for musicians. For example, hearing music can automatically evoke motor actions (even in non-musicians). The most obvious example is that of dancing or swaying to music. Thus, there must be a strong link between perception and motor action. We call this link sensorimotor association, and this is particularly important for skilled musicians. Playing in an orchestra requires ongoing synchronization with the performance of the orchestra. The musician has to play with the appropriate sound quality, rhythm, and tempo, while the composer needs to play a short musical phrase, evaluate the generated sound pattern by ear, and then put this on record by writing it up in musical notation. Human brain lesion and brain imaging studies show us that specific brain regions are specialized in analyzing pitch, timbre, contour relations, musical timing and rhythm. Most of these neural networks are functional in non-musicians, suggesting that these brain regions have evolved in the human brain independently of intensive practice or musical expertise. However, several studies show that these networks can be shaped by musical experience. For example, the timbre of a particular note is processed differently in musicians, as has been shown in a number of behavioral experiments in which musicians and non-musicians decide which of two tones is similar or dissimilar in pitch. When the pitch of the two tones was the same but the timbre varied (e.g., a guitar tone versus a piano tone), non-musicians made significantly more errors than musicians. In one study, there was even a strong correlation between accuracy of discrimination and performance in pitch – timbre discrimination ($r = 0.66$), indicating that musicians use pitch information to a greater extent than non-musicians (Pitt and Crowder, 1992). Beal (1985) tested musically trained and untrained subjects in their ability to discriminate changes in timbre. Akin to the aforementioned experiment, Beal found that discrimination accuracy was almost perfect (98%) when timbre and pitch information remained constant. But when pitch and timbre information varied (e.g., comparing tones of similar pitch but different timbres; guitar versus piano) the performance of the non-musicians dropped substantially; they were half as accurate as musicians. Pitt and Crowder claimed that timbre information, and not pitch, is the more salient acoustic dimension for non-musicians because timbre delivers more relevant information. However, analysis of pitch

should therefore require more formal musical training. Thus, in non-musicians differences in timbre between two tones should be distracting even if the pitches are identical, causing problems with pitch discrimination.

Recent brain imaging studies have revealed that timbre processing is different in the auditory cortex depending on the familiarity of the presented tone. Specifically, auditory cortical representations of tones of different timbre (violin and trumpet) are enhanced compared with sine wave tones in violinists and trumpeters, preferentially when hearing timbre tones of their own instrument (Pantev et al., 2001). These findings suggest that experience-dependent plasticity optimizes the auditory system in musicians. A further finding emphasizes the role of individual strategies used by musicians in processing pitch and timbre information. Schneider and colleagues (2005) showed that the relative pitch of harmonic complex sounds is perceived by decoding either the fundamental pitch or the spectral pitch of the auditory stimuli. Compared with fundamental pitch listeners, spectral pitch listeners demonstrated a pronounced rightward anatomical asymmetry of gray matter volume. They also showed an enhanced neural response 50 ms after tone presentation located in the right-sided pitch-sensitive lateral Heschl's gyrus (indicated by the magnetic P50m component). Those preferring to analyze complex tones using the spectral strategy showed an enhanced gray matter volume for the right-sided Heschl's gyrus and a concomitantly enhanced P50 generated by the right Heschl's gyrus. A chief point of interest is that these neurophysiological findings highly correlated with musical aptitude. Besides these timbre-specific findings, several neurophysiological studies using EEG, MEG, or fMRI have shown that musicians process musical information differently. The EEG and MEG studies have also demonstrated that these differences appear at every time point in the auditory processing stream and even when musicians imagine hearing music (Bhattacharya et al., 2001; Bhattacharya and Petsche, 2001a; Bhattacharya and Petsche, 2001b; Koelsch et al., 2003; Fujioka et al., Grell et al., 2009; Ruiz et al., 2009; 2004; Knosche et al., 2005; Fujioka et al., 2005; Patel et al., 2006; Fujioka et al., 2006; Meyer et al., 2006; Meyer et al., 2007; Patel and Iversen, 2007; Shahin et al., 2007; Besson et al., 2007; Baumann et al., 2008; Herholz et al., 2008; Zarate and Zatorre, 2008).

While the above-cited experiments describe a characteristic formation and specialization of a musician's auditory system for processing timbre, pitch, rhythm and musical contour, another principle of learning is

associated with the improved cognition of musicians. From the standpoint of cognitive psychology, optimization of musical perception is associated with the processing of larger perceptual chunks at hierarchically lower processing levels that typically have less processing capacity. Thus, musical perception is optimized during the course of musical training by making many steps more automatic. Perception of pitch contour and interval deviations in simple melodies is associated with a marked event-related brain response, termed mismatch negativity (MMN), which reflects automatic processing of incoming stimuli in skilled musicians. This has led to the suggestion that musical training enhances the ability to automatically register abstract changes in the relative pitch structure of melodies (van Zuijen et al., 2005). Besides improved musical perception, musicians also show some kind of changed memory processes for recognizing familiar tunes. This has recently been examined in an elegant experiment published by Bella et al. (2003). They used a specifically adapted recognition paradigm that involved sequentially presenting the tunes of a melody and requiring the subjects to provide a familiarity judgment or to recognize the melody. Interestingly, musicians judged the familiarity of the musical pieces on the basis of fewer notes than did non-musicians (after four notes in musicians and five notes in non-musicians). Familiarity therefore evolves slightly earlier in musicians, suggesting that perceptual memory (mostly working automatically) for melodies works faster in musicians. Taken together, musicians outperform non-musicians in several aspects of musical perception, including perception of pitch, timbre, and timing. In addition, they show improved performance in recognition of melodies. Altogether, these enhanced aspects of cognition are necessary for the performance of music even at moderate levels. These superior performance skills are all related to typical neurophysiological features.

3.1.2. Sight-reading

Reading musical scores is in many ways similar to reading words. The special ability to read musical scores while playing an instrument is called sight-reading. In order to sight-read music, a musician must translate written notes into appropriate motor commands that subserve specific movements. In addition, these notes should be interpreted and translated into aesthetically appealing signals. In order to accomplish sight-reading in a fast and efficient way, skilled musicians must use a strategy that allows them to look ahead in the score so as to anticipate what is coming next

in a way similar to how an experienced reader might read a book. Unfortunately, only a few experiments have studied this phenomenon empirically. Truitt et al. (1997) carried out sophisticated experiments using eye movement recordings and keystroke analysis. With their approach they analyzed the so-called *eye-hand span* and the *perceptual span*.

The *eye-hand span* is a measure of the distance between the note being looked at and the note being played. The *perceptual span* is the region around the note being looked at from which useful information is extracted. The authors found that the *perceptual span* of skilled and less skilled pianists was approximately the same, ranging between two and four beats. However, the *eye-hand span* differed between skilled and less skilled pianists. For the less skilled pianists, the *eye-hand span* was only about half a beat, indicating that the fixation point was less than one beat ahead of the hands. The *eye-hand span* for the skilled pianists was about on average two to three beats; thus, the fixation point was much further ahead of the hands than in non-skilled pianists. In a few instances the skilled pianist's point of regard was behind rather than in front of the note currently being played, suggesting that the player may have been reflecting on the note just played. These findings are in a way astonishing in that they show that the visual perceptual span is similar for skilled and less skilled pianists and that the *eye-hand span* of skilled pianists is not much different than that of less skilled pianists, although skilled pianists show a larger *eye-hand span*. Although the *eye-hand span* is larger in skilled pianists, this does not explain the virtuoso level at which accomplished pianists play their instrument. This highlights a point of discrepancy between these experimental data and the conventional wisdom that pianists might extract information from a wider region of vision than non-musicians. The reason for the apparent similarity (or small difference) between skilled and less skilled musicians is possibly due to the constraints of short-term memory. If the encoding process advances too far ahead of the motor output (i.e. when the *eye-hand span* becomes too large), there is probably a loss of information stored in short-term memory. However, the evidence that skilled musicians can perform at virtuoso levels emphasizes that some kind of optimization has been implemented on the motor rather than on the visual side of this complex sensorimotor process. Obviously, skilled pianists have developed the ability to translate complex visual information (e.g., several notes) into a complex motor program subserving the fast movements associated with piano playing.

A very recently published paper by Ruiz and colleagues (2009) elegantly demonstrated this efficient sensory-motor association in pianists. They demonstrated that playing a wrong note is identified in advance or in other words before the pianist becomes aware of his error. Thus, playing notes on a piano is controlled by highly automized motor control mechanisms generating feedforward control loops.

3.1.3. Motor functions

Performing music at a professional level is arguably among the most complex of human accomplishments. A pianist, for example, has to bimanually coordinate the production of up to 1800 notes per minute. Similar motor control demands are placed on violinists who additionally have to cope with unusual biomechanical constraints to hold the violin. A further point demonstrating the superiority of the motor system of professional musicians is their extraordinary ability to use both hands (or arms) in a coordinated manner. For example, during piano playing one hand plays the melody (mostly the dominant right hand manipulating the high pitches) while the other hand (the subdominant hand) plays the rhythm. For the violin the case is different. While the left hand is manipulating the strings in a way partly similar to playing the piano, the right arm swings the bow. Here the right arm has to generate a fast spatial – temporal pattern coordinated with fast finger movements of the left hand (Wurtz et al., 2009). Thus, both instruments place different demands on bimanual coordination. Many researchers have tried to delineate specific motor functions in musicians on the basis of sophisticated behavioral experiments. One of the simplest motor tasks is tapping with the index finger and measuring the maximum tapping frequency with one target finger. To obtain the maximum tapping frequency, subjects are required to tap as fast as possible with one finger (e.g. the index finger) within a pre-determined period (e.g. 20 s). The inter-tap interval as well as the maximum number of taps is counted using simple computer software and keys registering the taps. The maximum tapping speed has been shown to indicate basic neurophysiological properties of the primary motor cortex that controls the particular finger and to be significantly faster for the dominant hand when tapping with the index finger. That is, right-handers exhibit faster tapping speeds for the right than for the left hand while left-handers show the opposite pattern. This asymmetry in hand skills is relatively stable during the course of short-term hand-skill training (Peters, 1976; Peters and Durding, 1978). It

is argued that the primary hand motor area controls maximum tapping speed. Several positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) experiments have shown that the rate of finger tapping correlates with the intensity or spatial extent of activation within the sensorimotor cortex (including M1 and S1) (e.g. Jancke et al., 2000). In addition to this, single-cell recording studies in monkeys have shown that the discharge activity of M1 motoneurons maximally correlates with the force and velocity of the movement (Hepp-Reymond, 1988). Since fast finger tapping requires high movement velocities, one might conclude that fast finger tapping is mainly controlled by M1 motoneurons.

Pianists and string players differ substantially from non-musicians in that the latter tap much more slowly. The tapping rate of the musician's dominant hand is about 14% greater and the rate of the non-dominant hand about 20% greater than the corresponding rates of normal controls (right hand; musicians 128 taps/20 s, 6.4 Hz; non-musicians 110 taps/20 s, 5.5 Hz; left hand, musicians 120 taps/s., 6 Hz; non-musicians 95 taps/s, 4.75 Hz). The non-dominant left hand demonstrates a slightly larger performance gain compared with the dominant hand, a fact resulting in a decreased asymmetry between both hands in musicians. Typical hand asymmetry scores are calculated by dividing the performance difference of both hands by the performance sum of both hands, $(R - L)/(R + L)$. The obtained asymmetry score is significantly lower in musicians than in non-musicians (Jancke et al., 1997). The tapping rates are also different for string and keyboard players, with pianists outperforming string players with a tapping speed approximately 8% faster, although string players are far better than normal controls. A similar finding has recently been published for drummers (Fujii and Oda, 2006).

In view of the preceding findings, many authors conclude that this performance gain is related to the extraordinary amount of training that musicians accumulate through practicing their particular instrument. This argument of use-dependent plasticity is supported by the fact that the tapping asymmetry in musicians is related to the age at which they begin their musical training. Musicians starting their musical training very early in life revealed the smallest tapping asymmetry compared with musicians starting later in life (Jancke et al., 1997, but see also Kopiez et al., 2009). Recently, Jabusch and colleagues (2009) demonstrated that motor skill in pianists can be best explained by accumulated practice time. In addition, several studies have shown that even

non-musicians can improve their motor skills and especially their tapping to a substantial degree during the course of a one-week motor training (Schulze et al., 2002; Koeneke et al., 2006). Thus, there is strong evidence that this simple motor measure indicating basic motor control mechanisms depends on practice effects and on the age when practicing started. Obviously, the motor system (here M1) is tuned to effectively control finger movements.

Besides the fact that pianists and string players tap with a faster speed, several studies have shown that pianists generate the taps with decreased variability, that is, their tapping is more stable. This stability has been found not only for regular beats but also for rhythms generated unimanually or bimanually. Using mathematical models, some authors suggest that this timing stability is due to superior peripheral motor implementations (inserting a motor program from central processing centers to the executing organs) and timekeeper executions (e.g. using an internal clock more efficiently) (Krampe et al., 2002).

A further superior aspect of movement control is that when asked to tap along with the rhythm of the music, musicians' tapping is slower the more familiar the specific piece of music is. This slowing of sensorimotor response is thought to be associated with a different way of integrating motor and sensory functions. In fact, it is thought that with increasing familiarity with the musical piece, musicians tend to synchronize their tapping with the perceived rhythm, relying hereby on higher hierarchical levels (Drake and Ben El Heni, 2003). Recent work by Drost et al. (2005) uncovered an additional and very important specificity of the motor system of musicians. These authors found evidence from behavioral experiments that musicians implicitly anticipate a specific motor program when required to play a musical chord in response to an imperative visual stimulus congruent with the chord. However, when this association between visual stimulus and motor response was disturbed by a concurrent task (e.g. playing an auditory stimulus which is congruent with the chord) the performance in playing the chords (reaction time) diminished in the musicians only. This reveals that the musicians appear to anticipate implicitly the appropriate motor program (playing a chord) when seeing the imperative stimulus and when hearing the concurrent auditory stimulus. Of course, both stimuli have their own associations with motor programs which might interfere. Taken together, these (and other) behavioral experiments clearly demonstrate that musicians (pianists in particular) have developed a

specialized and highly tuned sensorimotor system that enables them to perform at a high level of skill.

An interesting and impressive example of the adaptive nature of the sensorimotor system of pianists has been described by the Harvard psychologists Bruno Laeng and Anne Park (1999). They examined how right- and left-handed novice pianists adapt to playing a reversed piano with the high pitches on their left and the low on their right. The left-handers had fewer problems with learning on a reversed piano, while right-handed learners experienced some difficulty with this task. But when experienced pianists were tested on the reversed piano, they were basically unable to play even if they were strong and consistent left-handers. This study demonstrates that pianists acquire strong associations between their motor responses and visual cues (arrangement of keys on the keyboard) that are difficult to rearrange or inhibit once they have been established (see also Ruiz et al., 2009).

In the previous sections the findings from classical behavioral studies were discussed. Interestingly, there are only a few studies that have directly investigated neurophysiological functions in musicians during various music-related tasks and compared performance with normal controls. One of the earliest studies examining musicians on the basis of electroencephalography (EEG) measurements was published by Lang et al. (1990). They recorded direct current (DC) potentials in musicians before and during the execution of bimanual motor sequences. Unfortunately, they did not examine normal control subjects, permitting therefore no direct comparison between musicians and control subjects. A more recent study using a somewhat similar technique has been published by Kristeva et al. (2003). These authors used EEG measurements as the basis of their investigation of the temporal sequence and time course of brain activation while violin players (two advanced musical students and five professional players) executed or imagined a musical sequence on a violin. Using modern methods to analyze and to cortically map current source densities (CSD), the authors showed that three of seven violinists revealed strong activation bilaterally in the frontal opercular region earlier than the motor areas (M1), while a further violinist showed simultaneous activations in these regions. The frontal opercular regions were also strongly activated throughout musical execution or imagining. And, the supplementary motor area and the left primary sensorimotor area were involved in the preparation and termination of the musical sequence, both for execution and imagination. The main finding of this study is that the frontal oper-

culum (which is part of the ventral pre-motor cortex) is bilaterally involved in the preparation, execution, and imagination of playing a musical piece with the violin. Thus, the ventral pre-motor cortex, which has been suggested to house the human homologue of the so-called 'mirror neurons', is strongly active during complicated motor actions like playing a violin. This suggestion complements findings obtained from studies conducted with non-musicians in which the ventral pre-motor cortex was shown to be involved in the preparation and execution of various (non-music-related) complicated motor tasks. Most of these tasks have investigated the observation, imagination, and execution of every-day activities like grasping, squeezing, modeling, and tapping (Hoshi and Tanji, 2007). The new finding reported in the Kristeva et al. study is that the ventral premotor cortex is also involved in music-related activities. Thus, the ventral pre-motor cortex can be trained to participate in the control of complex movements like violin playing.

Lotze et al. (2003) examined professional and amateur violinists during actual and imagined performance of Mozart's violin concerto in G major (KV216) using fMRI. Because a violin can not be played in a fMRI scanner the authors asked their subjects to perform corresponding finger movements on their chests. According to the authors, the violinists encountered after a short training session no difficulty whatsoever in executing this task as a substitute for real violin playing. The main finding of this study is that professional musicians revealed focused cerebral activations in the contralateral primary sensorimotor cortex, the bilateral superior parietal lobes, and the ipsilateral anterior cerebellar hemisphere. In addition, the authors found that professional musicians exhibited higher activity of the right primary auditory cortex during execution. Interestingly, a similar pattern of cortical activation was found during the imagination of violin-playing movements. But there was no activation within the auditory cortex during imagination of movement. These results support the assumption that musicians execute music-relevant finger sequences with higher motor control economy than amateur musicians. The reported absence of activation of the auditory cortex during imagined movements was interpreted as evidence for the view that auditory cortex activation is only present when the interconnected motor areas are activated in order to control real music-relevant movements.

A recent study applied a similar logic to examine musicians during motor tasks that can only be performed by musicians (Meister et al., 2004). In this fMRI study,

the authors investigated the cortical network that mediated music performance compared with music imagery in 12 music academy students. The subjects' task was to execute or imagine playing the right-hand part of a Bartok piece. There were two important findings in this study: first, during imagery and execution a similar bilateral frontoparietal network was active comprising the pre-motor areas, the pre-cuneus, and the medial part of the superior parietal lobe (SPL); secondly, during music performance (but not during imagery) the contralateral primary motor cortex and the posterior parietal cortex (PPC) were active bilaterally. This shows that while both imagery and actual execution of a musical piece partly evoke activation in a similar cortical network, imagination of movement does not activate the primary motor cortex and the PPC, thus indicating that these areas are probably more involved in the actual execution of music performance.

As mentioned above, although these studies have shown that distributed brain areas are involved in the control of playing a musical instrument, they do not directly help us to understand what is different or special in the motor system of musicians. This highly interesting question is however difficult to examine. This is because many of the motor activities that are relevant for musical performance are so special and well-tuned that only musicians are able to generate them. This means that one has to develop tasks that are as similar as possible to musical tasks but which can also be performed (in principle) by non-musicians. Three fMRI-based studies have been published thus far, in which pianists were compared with non-musicians during different motor tasks. Irrespective of the used motor task, these studies demonstrated that trained pianists use smaller neural networks within the primary and secondary motor areas in order to control unimanual and bimanual movements (Krings et al., 2000; Jancke et al., 2000; Meister et al., 2005). Two additional studies employed TMS techniques to directly study the excitability of the motor system (Ridding et al., 2000; Nordstrom and Butler, 2002). Both uncovered different neural activation patterns in the motor system of one hemisphere and between the motor areas of both hemispheres, this suggesting that trained pianist's neural control of finger movements is not only different but also more efficient.

The findings of the preceding studies let assume that professional pianists or violinists control their movements much more efficiently. One reason for increased efficiency of motor control might be related to the 'degrees of freedom problem'. According to this theoretical view, different muscles are functionally linked together and controlled conjointly. In this context, it is speculated that with increasing motor skill more and more effectors are linked together, thus reducing the number of 'degrees of freedom' to be controlled via motor commands. In this sense, highly trained pianists most likely control fewer 'degrees of freedom' for these tasks, this enabling them to control uni- and bimanual movements much more efficiently with smaller neural networks than non-musicians. This in turn should increase the control capacity of pianists because they can then control more 'degrees of freedom' or more motor programs with a given network. Considering the fact that highly trained musicians also have larger hand motor areas, this would suggest that they have an efficiently organized neural network as well as a generally larger network at their disposal in the hand motor area.

3.1.4. Interim summary of cross-sectional studies on functional plasticity

There is considerable evidence that experts show different neurophysiological activations in brain areas involved in controlling the particular expertise task. These different neurophysiological activations come along with particular differences in performing the expertise tasks. For example, musicians process auditory information (tones, rhythms, and melodies) differently than non-musicians. They also have a different eye-hand span in the context of sight-reading and their motor behavior is also different. All behavioral differences are accompanied with particular differences in terms of neurophysiological activations within the brain areas involved in controlling the expertise task. Most of these activation differences point to the fact that musicians process specific auditory, visual and motor information faster and more efficiently. Some of the afore-mentioned studies support the idea that musicians use different neurophysiological control strategies. These behavioral-functional differences speak for use-dependent reorganizations in those brain areas involved in controlling the expertise task.

3.2. Longitudinal studies

Only a small number of longitudinal studies has examined practice-induced musical expertise, including a few motor studies, one of which was published by Hund-Georgiadis and von Cramon (1999). These authors investigated hemodynamic responses in several motor areas during short-term motor learning of the dominant right hand in 10 piano players (PPs) and 23 non-musicians (NMs), using a complex finger-tapping

task. In summary, they found the following: (1) All subjects achieved considerably increased tapping frequency during the training session of 35 min in the scanner; (2) PPs, however, performed significantly better than NMs and showed increasing activation in the contralateral primary motor cortex throughout motor learning in the scanner. At the same time, the involvement of secondary motor areas, such as the bilateral supplementary motor area, the pre-motor, and the cerebellar areas, diminished in relation to the NMs throughout the training session. (3) Extended activation of primary and secondary motor areas in the initial training stage (7–14 min) and rapid attenuation were the main functional patterns underlying short-term learning in the NM group; attenuation was particularly marked in the primary motor cortices as compared with the PPs. (4) When tapping of the rehearsed sequence was performed with the left hand, transfer effects of motor learning were evident in both groups. Involvement of all relevant motor components was smaller than after initial training with the right hand. Ipsilateral pre-motor and primary motor contributions, however, showed slight increases of activation, indicating that dominant cortices influence complex sequence learning of the non-dominant hand.

The major new finding of this study is that experience (motor skill) influences the contribution of secondary motor areas in the motor learning of simple sequential unimanual tasks. In concordance with the studies mentioned above, this study also demonstrates minor involvement of the SMA in the PP group and shows attenuation effects in both groups during motor learning. Modern brain imaging studies have demonstrated that the mesial motor areas (especially the SMA proper and the pre-SMA) are strongly involved in the acquisition and execution of complex unimanual and bimanual tasks. Thus, the stronger the activation in these areas the more complex or the more demanding is the movement control. With increasing level of skill the complexity of movement control and the demands of movement control diminish.

This means that with increasing levels of skill fewer neurons in these areas are recruited during the control of unimanual or bimanual movements, as in the case of professional musicians. The above-mentioned fMRI studies have shown that the motor system of musicians has specifically adapted to the demands of playing a musical instrument. Although these studies have considerably furthered our understanding of these adaptive processes, fMRI data has one particular disadvantage: it is basically impossible to infer

from increased or decreased hemodynamic responses whether these changes are due to cortical excitation or inhibition. In order to know more about the particular neurophysiological processes underlying these hemodynamic changes more direct neurophysiological data are needed.

A further study of this type has been published by Bangert and Altenmüller (2003). They recorded changes in cortical activations (using DC-EEG) induced by short- (20 min) and long-term (5 week) piano practice using auditory and motor tasks. Two groups that were both new to piano playing were trained. One group was allowed to learn the standard piano key-to-pitch map (the 'map' group) and the other (the 'no-map' group) experienced a random assignment of keys to tones that prevented such a map. On the basis of the EEG obtained during the training session, the authors calculated the EEG coherence and DC intensity. They found marked changes in the EEG (both for EEG coherence and EEG DC intensity) even after a short training period of only 20 min. This effect was enhanced after 5 weeks of training. The increased DC changes were most prominent in the left central and right anterior regions when the training was conducted with the right hand. The right anterior activation was only present for the 'map' group in which the association of auditory cues (the notes) with a particular motor action was possible. Obviously, the frontal EEG activity captures the neural activations of pre-motor areas that are known to associate sensory cues with motor programs. Interestingly, these associations are generated very early during motor learning.

A very important study that explored the influence of musical training on the neurophysiological underpinnings of auditory processing in music-naive subjects was published by Fujioka et al. (2006). They measured basic neural responses in children to tones over a 1-year period using magnetoencephalography (MEG). Half of the examined children participated in musical lessons throughout the year; the other half had no music training. Significant changes in the peak latencies were found over time for nearly all auditory evoked responses. There were also larger amplitudes for the responses measured 100–450 ms after tone presentation. A very specific and clear musical training effect was found in a larger and earlier response (the N250m) in the left hemisphere in response to the violin sound in musically trained children compared with untrained children. Similar findings have been reported by Moreno et al. (2005). They observed that relatively short exposure (eight weeks) of musical training improved pitch pro-

cessing in language. A further study of the same group revealed that the amplitude of a late positive ERP component was reduced after training but only in the music group (Moreno and Besson, 2006). A still more recent study of the same group reported identical findings in the context of much better controlled experiments (Moreno et al., 2008).

3.2.1. Interim summary of longitudinal studies on functional plasticity

The above reviewed studies demonstrate that short- and long-term training of a particular musical task results in changed neurophysiological activations in those brains areas involved in controlling the expertise task. Thus, the human brain can quickly adapt to new control challenges associated with the performance of well-trained tasks.

4. Conclusions

As demonstrated in this chapter, several neuroanatomical and neurophysiological studies support the idea that intensive practice with a musical instrument stimulates cortical adaptations. These adaptations can be seen at macro-anatomical levels, as reflected in increased volume and grey matter density of those brain areas involved in the control of the practiced task. They can also be seen at the level of neurophysiological activation as indexed by changed hemodynamic responses and EEG-MEG-based measures originating from the involved brain areas. A major finding of plasticity research is, that experience dependent anatomical changes can disappear when practicing stops, indicating that plasticity is possible in all direction. This leads to the metaphor "use it or lose it" emphasizing the reliance on use-dependent influences. In this context one has to consider the hypothesis that age-dependent neuroanatomical and neurophysiological alterations are at least partly related to decreased environmental input (e.g., less implicit learning). On the other hand these new findings might offer a new perspective on use-dependent alterations of the older brain and opens the route for education and training even for the elderly.

In this review, I have focused exclusively on the systemic view of cortical plasticity. The concept of plasticity can also be applied to many levels of organization involving molecular, neuronal or chemical events, this fact serving to demonstrate just how complex the phenomenon of plasticity is. To some extent, the term itself has lost its explanatory value because almost any changes in brain activity can be attributed to some sort of "plasticity". For example, the term is now used prevalently in studies of axon guidance during development, short-term visual adaptation to motion or contours, maturation of cortical maps, recovery after amputation or stroke, and changes that occur in normal learning in the adult. Plasticity describes also a property of the central nervous system, the term reorganization being used to introduce the specific types of changes observed including axonal sprouting, long-term potentiation or the expression of plasticity related genomic responses. Although it is time to sharpen the focus and refine the experimental methodologies toward a more detailed understanding of plasticity, the partly reviewed findings to date have had a significant impact on cognitive neuroscience and have drawn a great deal of attention toward this fascinating new areas of research. Future studies should endeavor to show whether these plastic changes occur or can occur across the entire life span or are restricted to critical periods of life.

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