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CHAPTER 12

Adaptation and maladaptation: insights from brain plasticity

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Abstract: Evolutionary concepts such as adaptation and maladaptation have been used by neuroscientists to explain brain properties and mechanisms. In particular, one of the most compelling characteristics of the brain, known as neuroplasticity, denotes the ability of the brain to continuously adapt its functional and structural organization to changing requirements. Although brain plasticity has evolved to favor adaptation, there are cases in which the same mechanisms underlying adaptive plasticity can turn into maladaptive changes. Here, we will consider brain plasticity and its functional and structural consequences from an evolutionary perspective, discussing cases of adaptive and maladaptive plasticity and using examples from typical and atypical development.

Keywords: crossmodal plasticity; maladaptive plasticity; phantom limb pain; tinnitus; cochlear implants; evolution.

Lessons from evolution

A number of terms used to characterize the evolutionary process have also been adopted by neuroscientists to define brain mechanisms, processes, and abilities. The following short definitions of fundamental evolutionary terms will aid in understanding the context which "inspired" neuroscientists in defining their own terms. In drawing some parallels between these commonly adopted terms, our attempt will be to put the brain, and its particular adaptive properties, into a broader evolutionary perspective, according to which some structural and functional properties of an individual's brain are considered to be the result of natural selection. In this context, we will discuss the capacity of the brain to change its functional and structural organization (called plasticity or neuroplasticity) and particularly the resulting beneficial (adaptive) as well as possible detrimental (maladaptive) outcomes.

Adaptation defines a dynamic process in structure, function, and behavior by which a species or individual improves its chance of survival in a specific environment as a result of natural

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selection. While the term adaptation speaks for the evolutionary process, an *adaptive trait* is an aspect of the developmental pattern of the organism that enables or enhances the probability of that organism to survive and reproduce during certain stages of the lifespan (Dobzhansky, 1956). Adaptation became the root concept of Darwin's theory (1859), in that it provided the mechanism to explain why things change in the course of time, and how these affect all aspects of the life of an organism.

Natural selection acts on phenotypes (i.e., an observable trait of an organism, which includes physiological as well as behavioral changes), and a particular trait will survive if best suited to the environment. Most importantly, though, only a change in genotype (i.e., the complete set of genes within an organism) will define evolution. Natural selection typically produces *fitness*, a commonly used but nonetheless controversial term that describes how successful an organism has been at passing its genes.

Adaptive traits have continuously evolved as a response to environmental demands. The mechanism underpinning all environmentally induced phenotypic variations is called *phenotypic plasticity* (Via et al., 1995). This mechanism allows a single genotype to produce more than one response (in terms of morphology, physiological state, etc.) to environmental changes, including learned behaviors as well as reaction to diseases. When an organism produces a phenotype that can continuously change as a function of environmental change (e.g., the ability of the marine snail to increase shell thickness in response to new predators; see Trussell and Smith, 2000), the relationship between these two is termed reaction norm. These reactions can be flexible or more inflexible with the term flexible indicating the ability of the phenotypic trait to change throughout the organism's lifespan. In contrast, the term inflexible indicates an inability to change so that any determined characteristic remains fixed. Phenotypic plasticity likely evolved to allow different organisms a greater chance of survival in their ever-changing surroundings. Finally, it is as a result of plasticity that the environment directly influences which phenotypes are exposed to selection.

In our view, brain plasticity can be seen as an example of phenotypic plasticity. In particular, its many possible outcomes can be seen as phenotypes that react to the environmental changes. Changes in behavior occur at an ontogenetic level, but plasticity itself may have evolved phylogenetically. At the same time, the importance of phenotypic plasticity in driving genetic evolution (Price et al., 2003) suggests the importance of considering brain plasticity within the larger framework of evolutionary processes.

The vision from the brain

The term plasticity, as is true of most scientific terms, has undergone debates and revisions for the past 100 years (Berlucchi and Buchtel, 2009). In his seminal paper entitled "Réflexions sur l'usage du concept de plasticité en neurobiologie," Paillard (1976; see Will et al., 2008 for the English translation and commentaries) stated that not every change in the neural system should be considered plastic. Only those resulting from a structural and functional change should be considered as such. Also, structural and functional changes should be long-lasting and not transient events (to distinguish plasticity from "elasticity"). Finally, only changes resulting from an adaptation of the system to environmental pressures should be considered plastic, therefore excluding those mechanisms responsible for the "natural" maturation of the early developing system.

Recently, Lövdén et al. (2010), presenting a new theoretical framework for the study of adult plasticity and inspired by Paillard's ideas, has proposed that plasticity occurs as a consequence of a prolonged mismatch between supply (i.e., the actual capacities of the brain resulting from biological constraints and environmental influences) and environmental demands. Plasticity is then the ability of the brain to react to this mismatch

undergoing anatomical as well as functional changes to best fit an adaptive demand.

In this view, the resulting structural and functional change that accompanies plasticity can be seen as a phenotypic plastic change.

Adaptation

In referring to brain mechanisms, adaptation commonly refers not only to plasticity, which is the capacity of the brain to change to suit external environmental as well as inner changes, but also to any experience acquired throughout development (for reviews, see Kolb et al., 2003; Pascual-Leone et al., 2005).

Adaptive plasticity is also known as *experience-dependent plasticity* (Greenough et al., 1987). This type of plasticity refers to the ability of the brain to learn throughout its lifespan by means of processes involving structural and functional changes. Although experience-dependent plasticity refers to the ability to learn any new perceptual, motor, or cognitive skill, a particularly spectacular example is provided by musicians, whose extensive practice on a particular task (i.e., playing an instrument) has been shown to modify tactile, motor, and auditory brain regions (for reviews, see Johansson, 2006; Münte et al., 2002).

Most of these studies were conducted on adult musicians, leaving the question of whether these structural brain changes could be innate (therefore predisposing the individual to learn music) or acquired through training (i.e., "real" plastic adaptation of the brain to the greater use of particular regions). Recently, some studies (Hyde et al., 2009; Moreno et al., 2009) have precisely addressed this question by investigating structural brain and behavioral changes in children trained on music skills compared to nontrained children. Hyde et al. (2009) trained fifteen 6-year-old children for 15 months on playing the keyboard, while the control group consisted of age-matched children who only had weekly music classes in school. Both groups were tested on behavioral tasks as well as scanned with MRI before and after training. Results showed that trained children had increased activity in motor hand areas and primary auditory areas compared to controls, which correlated with behavioral improvements on motor and auditory-musical tasks. The fact that no structural brain difference was found between the two groups before training strongly suggests that training itself triggers adaptive changes.

Although studies on adults and children have not directly tested whether these plastic changes can persist longer in life even if musical training is suspended, there may be a sensitive period (which refers to the limited period during development in which effects of experience are particularly strong in shaping the brain, see Knudsen, 2004) in childhood in which musical practice may result in long-lasting benefits in performance later in life. For example, brain-imaging studies highlighting plastic changes occurring as a consequence of musical training have found that the degree of these changes appears to decrease as a function of age, so that musical training experienced very early in life triggers larger plastic changes (Elbert et al., 1995). Given the particular nature of early developmental plasticity (Greenough et al., 1987; Knudsen, 2004), it could be hypothesized that musical training early in life changes the brain structurally and functionally in a hierarchical and long-lasting fashion.

Although only investigated by means of a behavioral task, Watanabe et al. (2007) addressed this question by comparing performance of two groups of adults who started their musical training at different ages: early (i.e., before 7 years of age) or late (i.e., after 7 years of age). Participants of the two groups were matched for years of musical experience and practice, so that they only differed in the age when training began. The task consisted in learning to reproduce a temporally complex motor sequence by tapping in synchrony with sequentially presented visual stimuli. Results showed that early-trained musicians had an overall better performance compared to late-trained

musicians, suggesting that musical training started early in life (i.e., during sensitive periods) can have long-term effects on the ability to learn novel motor tasks.

While the case of musicians speaks for the ability of the typically developing brain to change as a function of increased demand, there are cases in which changes in supply (i.e., the brain) cause plasticity to take place to functionally adapt to the new environment. In other words, in the case of direct or indirect brain insult (i.e., brain lesions or sensory loss, respectively), plasticity will act to reorganize the brain. In particular, plastic changes after sensory deafferentation (i.e., blindness, deafness) trigger the system to reorganize in a compensatory fashion to enable sensory-deprived individuals to better suit new environmental pressures. The following section will discuss this particular type of plasticity mechanism, which we will compare to an evolutionary concept known as *exaptation*.

Crossmodal plasticity after sensory deafferentation: a case of exaptation?

Exaptation refers to the shifts in functions of a trait during evolution, so that one trait originally serving a particular function may evolve and serve another one, achieving complete fitness for that trait (Gould, 1991; Gould and Lewontin, 1979). The classical example is bird feathers, which initially evolved for temperature regulation and only later were adapted for flight. Moreover, Gould (1991) suggested that there are two types of exaptation. The first type characterizes features that evolved by natural selection to process one function but are then co-opted for another function (i.e., the example of the bird's feathers); the second type refers to features that did not evolve as adaptations through natural selection but are rather side effects of adaptive processes, features that Gould defined *spandrels*. Arguing against the rigidity of concepts such as adaptation and natural selection, which cannot fully explain the complexity of some human behaviors, he described the concept of spandrels making a parallel from the architectural spandrels present in the church of San Marco in Venice: "Every fan-vaulted ceiling must have a series of open spaces along the midline of the vault, where the sides of the fans intersect between the pillars. As the spaces must exist, they are often used for ingenious ornamental effect." In other words, those spaces between vaults, which originally had purely structural functions, ended up being used to enhance esthetic characteristics (i.e., a by-product of their original function).

Spandrels in the brain

The term exaptation, if considered in its conceptual form, well suits a particular type of plasticity called *crossmodal plasticity*. The term crossmodal plasticity has been adopted particularly when describing compensatory plasticity that emerges in some cases of sensory deprivation, such as blindness and profound deafness (Bavelier and Neville, 2002; Pascual-Leone et al., 2005). In particular, some studies have suggested that the absence of the stream of information coming from one sensory modality causes the brain to reorganize in a crossmodal fashion, so that the deafferented cortex responds to input coming from the intact sensory modalities. These types of changes have been also called *intermodal changes* in both animal (Rauschecker, 1995) and human studies (Röder et al., 1999) because of their "between-senses" interactions. In this view, intermodal changes share commonalities with the concept of exaptation, in that regions subserving the deafferented modality take over new functions originally exclusively mediated by other brain areas. Specifically, a subset of the neurons that are usually responsive to a particular stimulation in a region of the brain will now respond to stimulation of another modality or in the context of a new function.

The rationale behind drawing parallels between crossmodal plasticity after sensory deprivation and the concept of exaptation is that the former

has been enthusiastically advanced as the mechanism responsible for the enhanced performance found, for example, in tactile and auditory tasks in blind individuals (Amedi et al., 2010; Gougoux et al., 2005; Röder et al., 1999). However, this explanation has been challenged by the diversity of tasks eliciting visual cortex activation after congenital blindness (differing in modality and complexity, see, e.g., Pavani and Röder, 2011) and by studies that found similar crossmodal activity in sighted individuals blindfolded a few days only (Pascual-Leone and Hamilton, 2001), suggesting that this process may not exclusively emerge as a consequence of early sensory deprivation *per se*. Where does the idea of functional crossmodal plasticity come from?

Around 20 years ago, animal studies began to address the question of whether the functional properties of cortical tissue are determined by the inputs they receive rather than being innate. In these experiments, input from one sensory modality was rerouted to the primary cortex of another modality (Sur et al., 1990; von Melchner et al., 2000). For instance, Sur et al. (1990) rerouted retinal axons of newborn ferrets into the auditory pathway by removing ascending auditory projections through deafferentation of the medial geniculate nucleus (MGN) (and by removing the visual cortical targets by ablating visual cortex). This caused retinal fibers to innervate the MGN, so that MGN was now "invaded" by visual input. These inputs were then transferred to auditory cortex via intact MGN projections. The physiological and anatomical consequence of this rerouting was the development of visual networks in auditory cortex, so that a map of visual space emerged in the auditory cortex (i.e., a change in receptive field properties including the development of visual orientation-selective cells). How were these structural changes then interpreted by the animal? In other words, were the rewired projections interpreted as a visual input or an auditory one? If the behavioral role of a cortical area is independent of its input, then activation of the auditory cortex by any stimulus would be interpreted as auditory. In contrast, if the nature of the input has a role in determining the function of a cortical area, then rewired animals should interpret visual activation in the auditory cortex as a visual stimulus.

Von Melchner et al. (2000) addressed this question by training neonatal ferrets to discriminate between visual and auditory stimuli. A group of ferrets were "rewired" by directing their retinal axons to the left MGN, thus providing visual information to the auditory cortex in the left hemisphere. When the auditory cortex in the left hemisphere was lesioned, these animals were no longer able to discriminate visual stimuli, indicating that they became blind in the right visual field because the auditory cortex had mediated visual processing for this part of visual field. These experiments suggest that visual inputs routed to the auditory thalamus are capable of inducing auditory pathways to mediate vision, which crucially means that cortical areas process their functions under the input control.

The fact that rewired cortices functionally mediate functions originally belonging to another region leads to the suggestion that even after sensory deprivation (i.e., without artificial rerouting), crossmodal plasticity may take place. In addition, would crossmodal plasticity correspond to an enhancement in performance in some behavioral tasks? To address this issue, Rauschecker and Kniepert (1994) tested visually deprived cats in a localization task in which animals had to walk toward a target sound source that was continuously manipulated in azimuth location. Deprived cats showed better auditory localization abilities compared to nondeprived cats, particularly for lateral and more peripheral locations, suggesting that compensatory plastic changes could underlie enhanced performance in the intact modality after sensory deprivation. Similar findings also come from King and Parsons (1999), who investigated auditory spatial acuity in visually deprived ferrets and documented improved performance in the lateral sound field for both juvenile and adult animals that were deprived early in life. However, these

studies might also be partially explained by intramodal changes, for example, by a higher functionality of cortical networks associated with the auditory system. Therefore, they did not provide complete answers to the functional meaning of the deafferented cortical activity.

Recently, in reviewing their experiments on deaf cats conducted over several years, Lomber et al. (2010) have advanced a new hypothesis on crossmodal reorganization after sensory deprivation. In a number of experiments, the performance of congenitally deaf cats and hearing controls was compared for a number of visual psychophysical tasks (i.e., visual localization, movement detection, orientation and velocity discrimination, and visual acuity). Deaf cats were found to have enhanced performance only on the visual localization task (particularly for peripheral locations) and on the movement detection task. To investigate which cortical area could mediate the enhanced visual abilities, portions of auditory cortex were deactivated by means of a cryoloop device, which applied cold temperatures to a specific region of the brain and temporarily inactivated its functions. Interestingly, results showed that cooling of different areas could undermine the enhanced performance of deaf cats selectively for one task only, suggesting that perceptual enhancements were processed in specific cortical areas. In sum, crossmodal reorganization does not seem to be a unitary process involving reorganization of the whole (auditory) cortex; rather, it seems to involve changes in specific cortical loci. What are the characteristics of these reorganized loci? Why should they be so "special"? Lomber et al. (2010) suggested that only those regions subserving supramodal functions might undergo reorganization, while leaving modality-specific functions unaltered. In other words, skills that are shared across senses have greater potential to undergo enhancement and reorganization. For example, while color discrimination is an exclusively visual ability, and pitch discrimination an exclusively auditory ability, information on the spatial location of an object is provided by both vision and audition. In this supramodal view, auditory deprivation will lead to crossmodal changes in those regions that "naturally" engage multisensory processing, thus leaving unchanged regions that functionally process a modality-specific feature (such as color or tone).

Interestingly, crossmodal plasticity after auditory deprivation in humans appears to have a similar behavioral pattern as shown in Lomber et al. (2010). For instance, from a behavioral point of view, deaf individuals show enhanced performance in highly task-specific contexts, suggesting that not all aspects of the visual system are reorganized following sensory loss (for reviews, see Bavelier et al., 2006). In particular, deaf individuals have proven to have comparable performance to hearing controls in most visual tasks involving accuracy and sensitivity thresholds. These include brightness discrimination (Bross, 1979), visual contrast sensitivity (Finney and Dobkins, 2001), luminance change detection (Bavelier et al., 2000, 2001), motion direction (Bosworth and Dobkins, 2002a, b), motion velocity (Brozinsky and Bavelier, 2004), and temporal order perception (Nava et al., 2008). By contrast, deaf individuals appear to have enhanced performance for detection or discrimination of stimuli presented in the periphery of the visual field (Bavelier et al., 2000; Loke and Song, 1991; Neville and Lawson, 1987; but see Bottari et al., 2010 for contrasting results). In addition, found enhanced tactile sensitivity in congenitally deaf individuals when detecting suprathreshold tactile changes within a monotonous sequence of vibratory stimuli (Levänen et al., 1998; Levänen and Hamdorf, 2001).

In contrast, studies in blind individuals have shown more consistent results with regards to enhanced performance compared to sighted controls in several different domains (Amedi et al., 2010; Collignon et al., 2009; Gougoux et al., 2009; Röder et al., 1996), For example, blind individuals outperform sighted controls on tactile tasks (Amedi et al., 2010; Sadato et al., 1996), auditory tasks (Rauschecker, 1995; Röder et al., 1996), sound localization tasks (Collignon

et al., 2009; Rauschecker, 1995; Voss et al., 2004), spatial imagery (Röder et al., 1997; Vanlierde et al., 2003), voice perception (Gougoux et al., 2009), and language perception (Röder et al., 2002).

Some studies have put forward the possibility that the enhanced performance in deaf and blind individuals may be a result of recruitment of the deafferented sensory cortices by the intact senses to functionally compensate for the loss (Cohen et al., 1997; Levänen et al., 1998; Sadato et al., 1996). However, these studies remain very controversial due to several possible confounding factors (i.e., different experimental paradigms, individuals' high variability). The most important factor concerns the limited spatial resolution of the employed neuroimaging techniques, which may not be sufficiently precise to identify the subregions of the deafferented cortex involved.

In sum, the data discussed above show that the functional meaning of the cortical activity in the sensory-deprived cortex still needs to be further investigated. However, they also suggest that at least a portion of the cortical tissue that has become dominated by the intact senses may reorganize to now subserve functions of the intact modalities.

In this sense, the possibility that brain regions that originally evolved to process specific modalities may partially take on new functions to better suit the environment can be seen as a case of exaptation; namely, as a mechanism that has new biological functions different from the ones that caused the original selection of that mechanism.

The following section will discuss how these same spandrels can sometimes lead to maladaptive changes, therefore suggesting that plasticity may have mixed consequences: "positive" ones and "negative" ones.

Maladaptation

So far, plasticity has been viewed as a highly evolved feature of the brain to allow the organism to best adapt to the challenges imposed by the environment. However, the same mechanisms that promote adaptation can sometimes turn into maladaptive changes in structure and behavior.

In evolutionary biology, maladaptation has been defined as a deviation from adaptive peaks (Crespi, 2000). *Adaptive peaks* refer to the notion of an adaptive landscape introduced by Sewell Wright in 1931. The metaphor of the adaptive landscape was adopted to graphically summarize a theory concerning population genetics, by which "hills" represent the fittest populations (in terms of combination of genes) and the "valleys" represent the less fit populations. Natural selection tends to move the populations toward the peaks of the hills, but as the environment continuously changes, the populations are forced to adapt to these changes to maintain or build fitness.

Assuming, hypothetically, that plasticity may be encoded in a group of genes, its phenotypic expression can be either adaptive or maladaptive. In this view, maladaptive plasticity can be seen as a phenotype placed in a valley of the adaptive landscape. Thus, it could be hypothesized that adaptive plasticity has evolved while leaving behind maladaptive plasticity. However, the following paragraphs will show that in some cases, the same mechanisms allowing adaptive changes can sometimes lead to maladaptive changes, thus narrowing the border between adaptive and maladaptive plasticity.

Maladaptive brain plasticity, the other side of the coin

Adaptive plastic changes in the cases we have described in the previous paragraph have a positive nature, in that they aid typically and atypically developing brains to functionally best fit the environment. However, there is also the other side of the coin of plasticity, which Elbert and Heim (2001) called "the dark side" of cortical reorganization, and what is commonly known as maladaptive plasticity. This can be seen as an excess of brain reorganization but might actually

consist of only a small structural change. In both cases, the outcomes are highly dysfunctional. If seen in the perspective of the mismatch between supply and demand, maladaptive changes even go beyond this mismatch, in that the supply (i.e., the brain) abnormally interprets the environmental demands and does not adjust to a more suitable and optimal condition. Curiously, in some cases, the same adaptive plastic changes that have aided the brain to best suit the environment are also those that can lead to maladaptive changes. For example, musicians, whose differences in brain structure with respect to nonmusicians may likely represent plastic brain adaptations in response to skill acquisition and repetitive rehearsal of those skills, can also sometimes develop the so-called musician's cramp, which is very similar to the well-known "writer's cramp" (Quartarone et al., 2003). Both maladaptive syndromes lead to focal dystonia, a movement disorder that causes the muscles to contract and spasm involuntarily. This debilitating disease finds its explanation in a dysfunctional reorganization of the brain (Tamura et al., 2009), particularly in the reorganization of the digits in the primary somatosensory cortex in these cases. More precisely, the topographic map represented in the somatosensory cortex is altered during the learning of sensorimotor skills, and those parts of the body (i.e., fingers, hand) that are stimulated the most drive the homologous cortical representations to expand (for classical animal studies, see Kaas, 1991).

In support of the findings that cases of focal dystonia are triggered by maladaptive plastic changes, Candia et al. (2003) have developed a new treatment for focal hand dystonia in musicians based on the assumption that if the dysfunction arises as a consequence of maladaptive shifts of cortical reorganization, retuning the sensorimotor representations could likely treat these patients. During this training, dystonic patients have one or more nondystonic fingers immobilized in a splint device. The therapy consists in making sequential movements of two or three digits in extension, including the dystonic finger, for a prolonged period and increasing time of training each day. In particular, in their fMRI experiment, Candia et al. (2003) showed a reduction in distances between cortical finger representations, suggesting a normalization of functional topography associated with the therapy. Most importantly, this cortical shift correlated with behavioral motor benefits, thus corroborating the notion that the underlying maladaptive mechanisms of dystonia may find their roots in cortical reorganization.

The following paragraphs will focus on three particular cases for which plasticity operates in a maladaptive fashion: pain following amputation, tinnitus following hearing loss, and absence of benefits following cochlear implantation. While for the first two cases, the notion of maladaptive plasticity has a more intuitive connotation, maladaptive plasticity after cochlear implantation has a different nature. Nonetheless, all three cases represent the other side of the coin of beneficial adaptive changes, suggesting that plasticity can exert its influence in different ways.

Phantoms after sensory deafferentation: phantom limb pain and tinnitus

Phantom limb pain and tinnitus share common characteristics that allow, to some extent, for a direct comparison. First of all, both syndromes are characterized by a "phantom" sensation, sometimes very painful, arising from a lesion (in case of amputation) or a disease (in some cases of tinnitus following hearing loss). This, in turn, results in perceived pain although no stimulus is actively triggering it. Also, both maladaptive sensations are subjective and can change in quality throughout life, and for both conditions, similar recent training procedures have been shown to provide beneficial effects (Flor and Diers, 2009). In particular, the rationale behind the training is the assumption that pain is triggered, in both cases, by a reorganization of cortical maps, and by an "expansion" of some frequencies (in tinnitus) or somatosensory representations (in phantom pain) at the expense of others.

Phantom limb pain

After amputation of a body part, the sensation of the presence of the missing part is reported by almost all amputees. The reported prevalence of phantom pain varies considerably in the literature, but most studies agree that around 60–80% of all amputees experience phantom pain following amputation. Phantom pain seems to be independent of age, gender, and cause of amputation. Very interestingly, phantom limb pain mostly occurs in late-amputated individuals (i.e., amputated in adulthood), being instead very infrequent in amputated children and almost absent in congenital amputees (for reviews, see Flor, 2002; Flor et al., 2006).

The mechanisms underlying phantom limb pain are not fully understood and may involve complex interactions between morphologic, physiologic, and chemical changes at central and/or peripheral levels (Flor et al., 2006). However, similarly to the musicians' case, the experience of pain correlates with reorganization of the somatosensory map. The possibility that pain, the maladaptive component following amputation, could be directly related to cortical reorganization of the primary somatosensory cortex, has only recently found major acceptance in the literature. As plastic reorganization has commonly been seen (as discussed in the previous paragraphs) as a beneficial and functional response of the brain to adaptive needs, the possibility that the same mechanism could trigger maladaptive outcomes has somehow been viewed as counterintuitive.

However, nearly 15 years ago, along with other causal mechanisms that can explain phantom limb pain, the possibility that this maladaptive plastic change could additionally result from cortical reorganization started emerging (Birbaumer et al., 1997; Flor et al., 1995; Knecht et al., 1996). The relationship between cortical reorganization and phantom limb pain started with the notion that deafferentation of digits or the hand leads to plastic changes in the somatosensory cortex (Pons et al., 1991). In addition, findings on chronic back pain revealed a strong correlation between cortical alteration and pain (Flor et al., 1997), with patients exhibiting more cortical reorganization as a function of felt pain. These two factors led researchers to point to cortical reorganization as a structural correlate of phantom limb pain.

For example, Flor et al. (1995) and Birbaumer et al. (1997) determined cortical reorganization in a group of adult amputees by means of neuroelectric source imaging (a technique that combines evoked potential recordings with structural magnetic resonance imaging). In particular, Birbaumer et al. (1997) compared the representations of hand and mouth in both hemispheres of the somatosensory cortex. As amputees without pain were found to have mirrored representations of mouth and hand, any asymmetry found in amputees with pain would become a marker of cortical reorganization. As hypothesized, the cortical representation in amputees with pain showed a shift of the lip representation into the cortical region, which previously belonged to the amputated hand.

An intriguing explanation of phantom limb pain has also been put forward, namely, the possibility that the maladaptive outcome could be elicited by the memory of the pain experienced prior to amputation (Flor, 2002; Katz and Melzack, 1990). In other words, if the pre-amputated limb had received prolonged and intense noxious input, it would have developed enhanced excitability for pain and therefore exhibited an alteration in cortical somatosensory processing. Subsequent amputation and invasion of the cortical region by neighboring inputs would then activate cortical neurons coding for pain, leading to the perception of pain. In support to this view, Nikolajsen et al. (1997) have shown that pain experienced before amputation can sometimes even predict phantom limb pain after deafferentation, supporting the importance of the memory of pain in making the phantom persist over time.

A particularly interesting finding concerns the lack of reorganization of somatosensory cortical maps in congenital amputees, which also correlates with their lack of reported pain (though the sensation of the missing limb persists in many cases). However, only in recent times has this correlation been investigated. So, for example, Flor et al. (1998) investigated cortical reorganization in primary somatosensory cortex in a group of congenital amputees and a group of traumatic amputees with or without pain determined by neuromagnetic source imaging. Results showed that the most cortically reorganized individuals were the traumatic amputees reporting pain. In contrast, the congenital amputees and amputees without pain presented very little reorganization and the small amounts of reorganization observed in each case were similar. In addition, phantom limb pain was found to positively correlate with cortical reorganization and with no other factor (i.e., time as amputation) or sensation (i.e., phantom limb sensation *per se*). The fact that congenitally limb-deprived individuals do not experience pain and do not present cortical reorganization opens an additional issue concerning adaptive and maladaptive plasticity that should be further explored, namely, the possibility that these two outcomes are influenced by development. In other words, while congenital or early deprivation may favor overall adaptation, deprivation experienced in adulthood may lead to maladaptation. Curiously, the presence or absence of beneficial versus detrimental cortical reorganization differs between types of developmental deprivations, as the following section will suggest.

Adaptation early in life: a comparison between congenitally deprived sensory modalities

While congenital amputees have been shown to have a lack of cortical reorganization compared to late amputees, some studies in blind individuals show the opposite pattern (Cohen et al., 1999; Sadato et al., 2002). For example, Fieger et al. (2006) compared his results in late-blind individuals with the findings of Röder et al. (1999) in congenitally blind individuals and showed that despite comparable performance, the brain mechanisms differed between the two groups. While a more precise spatial tuning of early auditory processes was observed in the congenitally blind (indexed by the event-related potential (ERP) called N1), later processing stages (indexed by the ERP called P3) seemed to mediate the improved behavior in the late blind. Overall, these results showed that the neural mechanisms underlying crossmodal changes differ in the developing and adult brain, further corroborating the notion that plastic changes that occur early in life can lead to functional advantages throughout life.

In sum, in congenital blindness, the *presence* of crossmodal reorganization appears to be functionally adaptive, while in congenitally limb-deafferented individuals, the *absence* of crossmodal reorganization appears to be one of the preconditions for avoiding maladaptive outcomes (i.e., pain). What can this differential pattern of plasticity suggest? A hypothesis could be that plastic changes early in life as a consequence of congenital deafferentation may be more adaptive compared to changes at later developmental stages. In other words, the flexibility of the brain after either direct or indirect damage during early development may be the expression of normal ontogenetic mechanisms that instead of "repairing" (as in the case of adult brains) simply make the young brain optimally adjust to the insult. The fact that positive adaptive plasticity is expressed differentially (i.e., reorganization vs. nonreorganization) in the two cases (i.e., blindness vs. phantom limb pain) could possibly be due to the specific type of damage or exceptional experience.

Tinnitus

Tinnitus can be "objective" or "subjective." The former refers to a perceived sensation of sound

elicited by internal stimulation (i.e., abnormal blood flow pulsations or muscle contraction) that can be heard (therefore objectively measured) by a clinician (e.g., by placing a stethoscope over the patient's external auditory canal). Here, we will focus on subjective tinnitus, which causes the affected person to experience "phantom sounds," commonly reported to be ringing noises, buzzes, clicks, pure tones, and even songs. Tinnitus has many different causes, otologic, neurologic, and drug related, making the understanding and treatment of the disease difficult to handle (for a clinical review of tinnitus, see Lockwood et al., 2002; Møller et al., 2010).

The prevailing opinion is that tinnitus is generated as a consequence of altered patterns of intrinsic neural activity generated along the central auditory pathway following damage to peripheral auditory structures (Eggermont and Roberts, 2004), making it a prevailing symptom following hearing loss. But what does this altered neural activity precisely refer to?

Electrophysiological recordings in animals have identified three types of abnormal activity in the auditory system following sensory deprivation, which could also account for causes of tinnitus when associated with hearing loss (for a comparison between animal and human studies, see Adjamian et al., 2009). The first type refers to changes in the spontaneous neural firing rate, by which neurons at rest fire even in the absence of sound stimulation (Seki and Eggermont, 2003). The second type refers to changes in the temporal firing pattern of a single neuron as well as the synchronous activity between neurons. After high-noise exposure or hearing loss, their impulses tend to become pathologically synchronous. This synchronic firing would then become more salient compared to more dispersed firing and be interpreted by the brain as a real sound. Moreover, it is precisely this prolonged synchronization that would induce the perception of tinnitus (Noreña and Eggermont, 2003; Seki and Eggermont, 2003; Weisz et al., 2005, 2007). Weisz et al. (2007) have proposed that gamma band activity, which is increased in tinnitus patients, may reflect the synchronous firing of neurons within the auditory cortex and constitute the neural code of tinnitus. The reason why gamma band activity has been viewed with such excitement in explaining tinnitus is because a series of previous studies have shown that gamma band synchronous oscillations of neuroelectrical activity may be a mechanism used by the brain to generate and bind conscious sensations to represent distinct objects (for a review, see Sauvé, 1999). This functional significance of gamma band activity would, therefore, explain why tinnitus patients consciously experience a phantom sensation.

Finally, the third type of abnormal activity in the auditory system following sensory deafferentation has been shown to result in reorganization of the cortical tonotopic representation. This third type clearly parallels mechanisms of cortical reorganization reviewed for phantom limb pain. As in the latter case, the tonotopic map becomes distorted for those sound frequencies where the hearing loss occurred. This results in an expansion of the representation of the frequencies that border on the lost frequencies, so that the deprived neurons now become responsive to frequencies adjacent to those at which hearing loss has taken place.

To investigate this issue, Mühlnickel et al. (1998) used magnetoencephalographic recordings on 10 individuals with tinnitus to establish whether there could be any reorganization of the tonotopic map in the auditory cortex. The rationale was to observe whether tinnitus could be related to a shift of frequency representations in the auditory cortex. To this end, four sets of pure tones above an individual's hearing level were selected and presented to each ear to form a trajectory representing the tonotopic map in healthy controls. For tinnitus patients, three tones were distant from the tinnitus frequency and the fourth was close to the tinnitus frequency. The three tones served to reconstruct the tonotopic map of each patient. Results showed that the tinnitus frequency had "invaded" the neighboring

frequency regions. Further, this invasion correlated with tinnitus strength, so that patients reporting more symptoms were also the ones who presented more cortical reorganization.

It is worth noting that the three types of changes described seldom occur independently of each other, as suggested by animal (Seki and Eggermont, 2003) and human studies (Weisz et al., 2005, 2007), pointing to their correlational rather than causal nature. That these three factors may be simultaneously present has been highlighted in studies that are investigating which treatments can exert the most beneficial and prolonged effects on tinnitus. In other words, several studies have particularly manipulated cortical reorganization with the assumption that, as in the case of dystonic patients, retuning the tonotopic maps could relieve patients of the phantom sensation.

Recently, Okamoto et al. (2010) exposed eight chronic tinnitus patients to music they chose themselves and which they were asked to listen to for 12 months regularly. The music was then frequency modified, so that it did not contain frequencies in the range neighboring the tinnitus frequency. After a 1-year exposure, tinnitus patients reported a reduction in tinnitus loudness. There was also a corresponding decrease in evoked activity in auditory cortex areas corresponding to the tinnitus frequency. The authors speculated that lateral inhibition from the neighboring parts of the tonotopic map were responsible for the beneficial effects on tinnitus.

"Rewiring" cortical reorganization through prostheses: to what extent is plasticity malleable?

Considering the lessons learned from maladaptive plastic changes strictly linked to cortical reorganization, one could ask whether restoring sensory input to the deafferented region by means of a prosthesis would provide substantial relief to tinnitus and phantom limb pain patients. The rationale behind reafferentation is that either tactile (for phantom limb pain) or auditory (for tinnitus) stimulation will expand the cortical representation of the stimulated body region, thus "rewiring" cortical maps back to their original state. According to this view, prostheses for phantom limb pain and cochlear implants for tinnitus patients could potentially help in "blocking" or even "rewiring" the effects of maladaptive plasticity.

A cochlear implant is a neuroprosthetic device consisting of a microelectrode array inserted in the cochlea that directly stimulates the auditory nerve (for reviews, see Moore and Shannon, 2009; Rauschecker and Shannon, 2002). Although limb prostheses and cochlear implants cannot be directly compared because they are based on different principles (i.e., on somatosensory feedback in the former case, and on nerve stimulation in the latter), they nonetheless represent good models to investigate how and to what extent the brain learns to interpret new information. In particular, several studies have shown that these devices can, in some cases, relieve phantom limb pain and tinnitus. For example, Lotze et al. (1999) examined the effects of the use of a myoelectric device in a group of unilateral amputees using fMRI. The groups were split into myoelectric versus nonmyoelectric users based on the extent of wearing time and average usage. The myoelectric users showed a symmetrical lip representation in the somatosensory cortex (in accordance with previous studies showing that symmetrical body representations are an index of a lack of cortical reorganization), which correlated with a reduction of phantom limb pain. In contrast, the nonmyoelectric users showed the exact opposite pattern, namely, a reported intense pain that correlated with massive cortical reorganization. Similarly, for tinnitus patients, several studies have documented a reduction of tinnitus after cochlear implantation (Miyamoto et al., 1997; Ruckenstein et al., 2001). However, it should be noted that results for both treatments are controversial, in that not all patients have systematically reported benefits. To date, it is not

known whether this difficulty in "undoing" or "rewiring" previous plastic changes relates to the technical limits of the devices and/or to the limits of plasticity itself. It is likely, though, that both factors interact to make reafferentation a challenging issue.

The particular case of cochlear implants failing to suppress and reduce tinnitus leads to our discussion of the last example of maladaptive plasticity.

In which sense can a cochlear implant be maladaptive?

As cochlear implantation has become routine therapy for partially restoring auditory function in profoundly deaf individuals, most studies have emphasized the beneficial outcomes of this device following auditory deprivation (Litovsky et al., 2006; Svirsky et al., 2000; Van Hoesel, 2004). The extent to which a cochlear implant exerts its benefits on single individuals appears to be determined by several factors. These factors include the age at which implantation takes place (Sharma et al., 2002, 2005), and the previous experience with auditory cues (Nava et al., 2009a,b).

Clearly, cochlear implantation *per se* does not create any phantom sensation, so that a direct comparison to tinnitus and phantom limb pain is not feasible. However, the outcome of a cochlear implant is related to the amount of cortical reorganization that has taken place prior to implantation. In other words, precisely what we have defined as "spandrels" after sensory deafferentation may be detrimental in case of reafferentation. The following examples show that some plastic changes can be maladaptive because they do not allow the brain to "rewire" once the reafferented sensory cortices have been taken over by other modalities.

Lee et al. (2001) were the first to suggest such a possibility by examining glucose metabolism (used as an index of brain activity) in a group of prelingually deafened individuals before cochlear implantation. The degree of hypometabolism before implantation correlated with the hearing abilities achieved after implantation, so that those patients with higher hypometabolism in temporal areas (including auditory cortex) were also the ones who gained more from auditory restoration. Conversely, those with lower hypometabolism did not achieve the same auditory capabilities, as measured with a speech perception test administered at several follow-up sessions after implantation. Results were interpreted as a being related to a possible increase in visual or somatosensory afferents to these temporal regions due to auditory deafferentation. Therefore, if crossmodal plasticity takes place in the auditory cortex before implantation, improvement in hearing after implantation will be less pronounced.

Beneficial outcomes after cochlear implantation have commonly been measured by evaluating speech recognition over time (for review, see Peterson et al., 2010). Reasoning that responses to visual stimulation in cochlear implant recipients may be related to their speech recognition abilities; Doucet et al. (2006) compared visual processing in two groups of cochlear implant recipients. The subjects were divided into "good" and "bad" performers according to their auditory speech perception skills, in that the former were able to recognize speech without visual cues, and the latter only relied on sign language and lip-reading to communicate efficiently. All participants were simply asked to fixate a visual stimulus presented several times while evoked potentials were recorded. Results showed that, while "good" performers had similar activation compared to hearing controls (i.e., evoked activity measured with ERPs was circumscribed around the primary visual cortex), "bad" performers exhibited extended cortical activity, suggesting recruitment of auditory cortical areas for visual processing. This result further suggests that once crossmodal plastic changes have taken place, speech perception performance after cochlear implantation might be undermined as a consequence of cortical reorganization.

The fact that crossmodal changes can undermine the good outcome of cochlear implants is relevant to the issue of *when* (in terms of age) plastic changes take place, and therefore *when* a device should be implanted. In this view, the existence of sensitive periods early in life for the typical development of the auditory system suggests that crossmodal plasticity may occur within these phases, and only to a lesser extent, or not at all, later in life. For example, Sharma et al. (2002) examined P1 latencies in congenitally deaf children who received a cochlear implant and found that those implanted before 3.5 years of age had normal P1 latencies, while children who received their implant after 7 years of age had abnormal latencies. This suggests a sensitive period for central auditory development that persists up to 3.5 years of age. In a further study, Sharma et al. (2005) assessed the time course of central auditory development in early and late congenitally deaf children implanted unilaterally either before 3.5 years of age or after 7 years of age. The results showed a different pattern of P1 development for early and late implanted children. While early implanted children reached almost normal P1 latencies within a week of implant use, late implanted children showed atypical response that remained atypical until the 18-month follow-up. Overall, these results suggest that, in line with what we have previously mentioned for congenitally blind individuals, plastic changes that occur within sensitive periods early in life might be particularly strong and long-lasting, therefore preventing the brain from reorganizing at a later time. In this sense, some plastic changes can be maladaptive from the perspective of reafferenting the auditory pathways later in life.

Finally, it should be mentioned that, comparable to the case of phantom limb pain after amputation later in life, crossmodal changes in the auditory cortex can occur also as a function of years of deprivation. For example, Lee et al. (2003) showed that there is a correlation between years of auditory deprivation and cortical reorganization that goes beyond sensitive periods. In his study (Lee et al., 2003), a group of postlingually deafened adults with years of auditory deprivation ranging from 2 months to 23 years underwent PET scans to evaluate their regional cerebral metabolism (similar to Lee et al., 2001). Results showed that glucose metabolism in the auditory cortex decreased after auditory deprivation, but increased as a function of years of deprivation, suggesting that functional crossmodal reorganization also takes place in the adult brain. What does this study suggest? First, it is compatible with the view that plasticity and crossmodal changes can also occur during adulthood (Pascual-Leone and Hamilton, 2001; Voss et al., 2004). Second, it corroborates the criterion expressed by Lövdén et al. (2010) by which adult plasticity is driven by a prolonged mismatch between supply and demand. The longer the mismatch is, the higher the probability that the change will result in a plastic change.

Final remarks

We started this review by defining some evolutionary terms adopted by neuroscientists to highlight some properties, mechanisms, and behaviors of the brain. As much as phenotypic plasticity represents an important factor in evolution, has a genetic basis, and may be altered by natural selection (Price et al., 2003), we suggest that brain plasticity could mimic this evolutionary pattern, so that it becomes worth asking why and how this characteristic of the brain has evolved.

Here, we have discussed how adaptive plasticity can lead the brain to structural and functional changes, in typical and atypical development, to best suit environmental demands. However, we have also challenged the view that plasticity consists only of beneficial adaptive changes, by emphasizing how it can sometimes result in highly dysfunctional outcomes that we have generally described here as being maladaptive.

From an evolutionary perspective, maladaptive plasticity arises as a phenotype that has reduced

fitness or is distant from an adaptive peak (Ghalambor et al., 2007). Brain plasticity has likely evolved to accommodate continuous environmental changes, suggesting that what we define as adaptive or maladaptive at any given time could also exchange roles as a function of changing environmental demands.

An additional important consideration is whether in the modern era making a distinction between adaptive and maladaptive plasticity is actually relevant. Advances in technology and medicine have clearly increased our chances of survival and have, therefore, changed the pressure of natural selection on our genes by changing the extent to which we must adapt to environmental demands. In this context of less selective pressures, an adaptive landscape may be more difficult to draw, as "hills" and "valleys" effectively become less distinct. In conclusion, the environmental manipulations carried out by humans may slowly shape natural selection, may even change the rate of evolutionary dynamics, and finally also the trait of plasticity.

References

Adjamian, P., Sereda, M., & Hall, D. A. (2009). The mechanisms of tinnitus: Perspectives from human functional neuroimaging. *Hearing Research*, *253*, 15–31.

Amedi, A., Raz, N., Azulay, H., Malach, R., & Zohary, E. (2010). Cortical activity during tactile exploration of objects in blind and sighted humans. *Restorative Neurology and Neuroscience*, *28*, 143–156.

Bavelier, D., Brozinsky, C., Tomann, A., Mitchell, T., Neville, H., & Liu, G. (2001). Impact of early deafness and early exposure to sign language on the cerebral organization for motion processing. *The Journal of Neuroscience*, *21*, 8931–8942.

Bavelier, D., Dye, M. W. G., & Hauser, P. C. (2006). Do deaf individuals see better? *Trends in Cognitive Sciences*, *10*, 512–518.

Bavelier, D., & Neville, H. J. (2002). Cross-modal plasticity: Where and how? *Nature Reviews. Neuroscience*, *3*, 443–452.

Bavelier, D., Tomann, A., Hutton, C., Mitchell, T., Corina, D., Liu, G., et al. (2000). Visual attention to the periphery is enhanced in congenitally deaf individuals. *The Journal of Neuroscience*, *20*, 1–6.

Berlucchi, G., & Buchtel, H. A. (2009). Neuronal plasticity: Historical roots and evolution of meaning. *Experimental Brain Research*, *192*, 307–319.

Birbaumer, N., Lutzenberger, W., Montoya, P., Larbig, W., Unertl, K., Töpfner, S., et al. (1997). Effects of regional anesthesia on phantom limb pain are mirrored in changes in cortical reorganization. *The Journal of Neuroscience*, *17*, 5503–5508.

Bosworth, R. G., & Dobkins, K. R. (2002a). The effect of spatial attention on motion processing in deaf signers, hearing signers, and hearing non-signers. *Brain and Cognition*, *4*, 152–169.

Bosworth, R. G., & Dobkins, K. R. (2002b). Visual field asymmetries for motion processing in deaf and hearing signers. *Brain and Cognition*, *49*, 170–181.

Bottari, D., Nava, E., Ley, P., & Pavani, F. (2010). Enhanced reactivity to visual stimuli in deaf individuals. *Restorative Neurology and Neuroscience*, *28*, 167–179.

Bross, M. (1979). Residual sensory capacities of the deaf: A signal detection analysis of a visual discrimination task. *Perceptual and Motor Skills*, *48*, 187–194.

Brozinsky, C. J., & Bavelier, D. (2004). Motion velocity thresholds in deaf signers: Changes in lateralization but not in overall sensitivity. *Cognitive Brain Research*, *21*, 1–10.

Candia, V., Wienbruch, C., Elbert, T., Rockstroh, B., & Ray, W. (2003). Effective behavioral treatment of focal hand dystonia in musicians alters somatosensory cortical organization. *Proceedings of the National Academy of Sciences of the United States of America*, *100*, 7942–7946.

Cohen, L., Celnik, P., Pascual-Leone, A., Corwell, B., Faiz, L., Dambrosia, J., et al. (1997). Functional relevance of cross-modal plasticity in blind humans. *Nature*, *389*, 180–183.

Cohen, L. G., Weeks, R. A., Sadato, N., Celnik, P., Ishii, K., & Hallett, M. (1999). Period of susceptibility for cross-modal plasticity in the blind. *Annals of Neurology*, *45*, 451–460.

Collignon, O., Voss, P., Lassonde, M., & Lepore, F. (2009). Cross-modal plasticity for the spatial processing of sounds in visually deprived subjects. *Experimental Brain Research*, *192*, 343–358.

Crespi, B. J. (2000). The evolution of maladaptation. *Heredity*, *84*, 623–629.

Darwin, C. (Ed.), (1859). *On the origin of species by means of natural selection, or the preservation of favoured races in the struggle for life*. Albemarle Street, London: John Murray.

Dobzhansky, T. (1956). What is an adaptive trait? *The American Naturalist*, *90*, 337–347.

Doucet, M. E., Bergeron, F., Lassonde, M., Ferron, P., & Lepore, F. (2006). Cross-modal reorganization and speech perception in cochlear implant users. *Brain*, *129*, 3376–3383.

Eggermont, J. J., & Roberts, L. E. (2004). The neuroscience of tinnitus. *Trends in Neurosciences*, *27*, 676–682.

Elbert, T., & Heim, S. (2001). A light and a dark side. *Nature*, *411*, 139.

Elbert, T., Pantev, C., Wienbruch, C., Rockstroh, B., & Taub, E. (1995). Increased cortical representation of the fingers of the left hand in string players. *Science*, *270*, 305–307.

Fieger, A., Röder, B., Teder-Sälejärvi, W., Hillyard, S. A., & Neville, H. J. (2006). Auditory spatial tuning in late-onset blindness in humans. *Journal of Cognitive Neuroscience*, *18*, 149–157.

Finney, E. M., & Dobkins, K. R. (2001). Visual contrast sensitivity in deaf versus hearing populations: Exploring the perceptual consequences of auditory deprivation and experience with a visual language. *Cognitive Brain Research*, *11*, 171–183.

Flor, H. (2002). Phantom-limb pain: Characteristics, causes, and treatment. *Lancet Neurology*, *1*, 182–189.

Flor, H., Braun, C., Elbert, T., & Birbaumer, N. (1997). Extensive reorganization of primary somatosensory cortex in chronic back pain patients. *Neuroscience Letters*, *224*, 5–8.

Flor, H., & Diers, M. (2009). Sensorimotor training and cortical reorganization. *NeuroRehabilitation*, *25*, 19–27.

Flor, H., Elbert, T., Knecht, S., Wienbruch, C., Pantev, C., Birbaumer, N., et al. (1995). Phantom-limb pain as a perceptual correlate of cortical reorganization following arm amputation. *Nature*, *375*, 482–484.

Flor, H., Elbert, T., Mühlnickel, W., Pantev, C., Wienbruch, C., & Taub, E. (1998). Cortical reorganization and phantom phenomena in congenital and traumatic upper-extremity amputees. *Experimental Brain Research*, *119*, 205–212.

Flor, H., Nikolajsen, L., & Jensen, T. S. (2006). Phantom limb pain: A case of maladaptive CNS plasticity? *Nature Reviews. Neuroscience*, *7*, 873–881.

Ghalambor, C. K., McKay, J. K., Carroll, S. P., & Reznick, D. N. (2007). Adaptive versus non-adaptive phenotypic plasticity and the potential for contemporary adaptation in new environments. *Functional Ecology*, *21*, 394–407.

Gougoux, F., Belin, P., Voss, P., Lepore, F., Lassonde, M., & Zatorre, J. R. (2009). Voice perception in blind persons: A functional magnetic resonance imaging study. *Neuropsychologia*, *47*, 2967–2974.

Gougoux, F., Zatorre, R. J., Lassonde, M., Voss, P., & Lepore, F. (2005). A functional neuroimaging study of sound localization: Visual cortex activity predicts performance in early-blind individuals. *PLoS Biology*, *3*, e27.

Gould, S. J. (1991). Exaptation: A crucial tool for an evolutionary psychology. *Journal of Social Issues*, *47*, 43–65.

Gould, S. J., & Lewontin, R. C. (1979). The sprandels of San Marco and the Panglossian Paradigm: A critique of the adaptationist programme. *Proceedings of the Royal Society of London*, *205*, 581–598.

Greenough, W. T., Black, J. E., & Wallace, C. S. (1987). Experience and brain development. *Child Development*, *58*, 539–559.

Hyde, K. L., Lerch, J., Norton, A., Forgeard, M., Winner, E., Evans, A. C., et al. (2009). Musical training shapes structural brain development. *The Journal of Neuroscience*, *29*, 3019–3025.

Johansson, B. B. (2006). Music and brain plasticity. *European Review*, *14*, 49–64.

Kaas, J. H. (1991). Plasticity of sensory and motor maps in adult mammals. *Annual Review of Neuroscience*, *14*, 137–167.

Katz, J., & Melzack, R. (1990). Pain 'memories' in phantom limbs: Review and clinical observations. *Pain*, *43*, 319–336.

King, A. J., & Parsons, C. (1999). Improved auditory spatial acuity in visually deprived ferrets. *The European Journal of Neuroscience*, *11*, 3945–3956.

Knecht, S., Henningsen, H., Elbert, T., Flor, H., Hohling, C., Pantev, C., et al. (1996). Reorganizational and perceptional changes after amputation. *Brain*, *119*, 1213–1219.

Knudsen, E. I. (2004). Sensitive periods in the development of the brain and behavior. *Journal of Cognitive Neuroscience*, *16*, 1412–1425.

Kolb, B., Gibb, R., & Robinson, T. E. (2003). Brain plasticity and behavior. *Current Directions in Psychological Science*, *12*, 1–5.

Lee, D. S., Lee, J. S., Kim, S. H., Kim, J. W., Chung, J. K., Lee, M. C., et al. (2001). Cross-modal plasticity and cochlear implants. *Nature*, *409*, 149–150.

Lee, J. S., Lee, D. S., Oh, S. H., Kim, C. S., Kim, J. W., Hwang, C. H., et al. (2003). PET evidence of neuroplasticity in adult auditory cortex of postlingual deafness. *Journal of Nuclear Medicine*, *9*, 1435–1439.

Levänen, S., & Hamdorf, D. (2001). Feeling vibrations: Enhanced tactile sensitivity in congenitally deaf humans. *Neuroscience Letters*, *301*, 75–77.

Levänen, S., Jousmaki, V., & Hari, R. (1998). Vibration-induced auditory-cortex activation in a congenitally deaf adult. *Current Biology*, *8*, 869–873.

Litovsky, R. Y., Johnstone, P. M., & Godar, S. P. (2006). Benefits of bilateral cochlearimplants and/or hearing aids in children. *International Journal of Audiology*, *45*, 78–91.

Lockwood, A. H., Salvi, R. J., & Burkhard, R. F. (2002). Tinnitus. *The New England Journal of Medicine*, *347*, 904–910.

Loke, W. H., & Song, S. (1991). Central and peripheral visual processing in hearing and nonhearing individuals. *Bulletin of the Psychonomic Society*, *29*, 437–440.

Lomber, S. G., Meredith, M. A., & Kral, A. (2010). Cross-modal plasticity in specific auditory cortices underlies visual compensations in the deaf. *Nature Neuroscience*, *13*, 1421–1427.

Lotze, M., Grodd, W., Birbaumer, N., Erb, M., Huse, E., & Flor, H. (1999). Does use of a myoelectric prosthesis prevent cortical reorganization and phantom limb pain? *Nature*, *2*, 501–502.

Lövdén, M., Bäckman, L., Lindenberger, U., Schaefer, S., & Schmiedek, F. (2010). A theoretical framework for the study of adult cognitive plasticity. *Psychological Bulletin*, *136*, 659–676.

Miyamoto, R. T., Wynne, M. K., McKnight, C., & Bichey, B. (1997). Electrical suppression of tinnitus via cochlear implants. *The International Tinnitus Journal*, *3*, 35–38.

Møller, A. R., Langguth, B., DeRidder, D., & Kleinjung, T. (Eds.), (2010). *Textbook of Tinnitus*. Springer: New York, USA.

Moore, D. R., & Shannon, R. V. (2009). Beyond cochlear implants: Awakening the deafened brain. *Nature Neuroscience*, *12*, 686–691.

Moreno, S., Marques, C., Santos, A., Santos, M., Castro, S. L., & Besson, M. (2009). Musical training influences linguistic abilities in 8-year-old children: More evidence for brain plasticity. *Cerebral Cortex*, *19*, 712–723.

Mühlnickel, W., Elbert, T., Taub, E., & Flor, H. (1998). Reorganization of auditory cortex in tinnitus. *Proceedings of the National Academy of Sciences of the United States of America*, *95*, 10340–10343.

Münte, T. F., Altenmüller, E., & Jäncke, L. (2002). The musician's brain as a model of neuroplasticity. *Nature Neuroscience. Reviews*, *3*, 473–478.

Nava, E., Bottari, D., Bonfioli, F., Beltrame, M. A., & Pavani, F. (2009a). Spatial hearing with a single cochlear implant in late-implanted adults. *Hearing Research*, *255*, 91–98.

Nava, E., Bottari, D., Portioli, G., Bonfioli, F., Beltrame, M. A., Formigoni, P., et al. (2009b). Hearing again with two ears: Recovery of spatial hearing after bilateral cochlear implantation. *Neuropsychologia*, *47*, 928–932.

Nava, E., Bottari, D., Zampini, M., & Pavani, F. (2008). Visual temporal order judgment in profoundly deaf individuals. *Experimental Brain Research*, *190*, 179–188.

Neville, H. J., & Lawson, D. S. (1987). Attention to central and peripheral visual space in a movement detection task: An event related potential and behavioral study. II. Congenitally deaf adults. *Brain Research*, *405*, 268–283.

Nikolajsen, L., Ilkjaer, S., Kroner, K., Christensen, J. H., & Jensen, T. S. (1997). The influence of preamputation pain on postamputation stump and phantom pain. *Pain*, *72*, 393–405.

Noreña, A. J., & Eggermont, J. J. (2003). Changes in spontaneous neural activity immediately after an acoustic trauma: Implications for neural correlates of tinnitus. *Hearing Research*, *183*, 137–153.

Okamoto, H., Stracke, H., Stoll, W., & Pantev, C. (2010). Listening to tailor-made notched music reduces tinnitus loudness and tinnitus-related auditory cortex activity. *Proceedings of the National Academy of Sciences of the United States of America*, *107*, 1207–1210.

Pascual-Leone, A., Amedi, A., Fregni, F., & Merabet, L. B. (2005). The plastic human brain cortex. *Annual Review of Neuroscience*, *28*, 377–401.

Pascual-Leone, A., & Hamilton, R. (2001). The metamodal organization of the brain. *Progress in Brain Research*, *134*, 427–445.

Pavani, F., & Röder, B. (2011). Crossmodal plasticity as a consequence of sensory loss: Insights from blindness and deafness. In B. E. Stein (Ed.), *The new handbook of multisensory processes.* Cambridge, MA: MIT Press.

Peterson, N. R., Pisoni, D. B., & Miyamoto, R. T. (2010). Cochlear implants and spoken language processing abilities: Review and assessment of the literature. *Restorative Neurology and Neuroscience*, *28*, 237–250.

Pons, T. P., Garraghty, P. E., Ommaya, A. K., Kaas, J. H., Taub, E., & Mishkin, M. (1991). Massive cortical reorganization after sensory deafferentation in adult macaques. *Science*, *28*, 1857–1860.

Price, T. D., Qvarnström, A., & Irwin, D. E. (2003). The role of phenotypic plasticity in driving genetic evolution. *Proceedings: Biological Sciences*, *270*, 1433–1440.

Quartarone, A., Bagnato, S., Rizzo, V., Siebner, H. R., Dattola, V., Scalfari, A., Morgante, F., Battaglia, F., Romano, M., & Girlanda, P. (2003). Abnormal associative plasticity of the human motor cortex in writer's cramp. *Brain*, *126*, 2586–2596.

Rauschecker, J. P. (1995). Compensatory plasticity and sensory substitution in the cerebral cortex. *Trends in Neurosciences*, *18*, 36–43.

Rauschecker, J. P., & Kniepert, U. (1994). Auditory localization behaviour in visually deprived cats. *The European Journal of Neuroscience*, *6*, 149–160.

Rauschecker, J. P., & Shannon, R. V. (2002). Sending sound to the brain. *Science*, *295*, 1025–1029.

Röder, B., Rösler, F., & Henninghausen, E. (1997). Different cortical activation patterns in blind and sighted humans during encoding and transformation of haptic images. *Psychophysiology*, *34*, 292–307.

Röder, B., Rösler, F., Henninghausen, E., & Näcker, F. (1996). Event-related potentials during auditory and somatosensory discrimination in sighted and blind human subjects. *Cognitive Brain Research*, *4*, 77–93.

Röder, B., Stock, O., Bien, S., Neville, H., & Rösler, F. (2002). Speech processing activates visual cortex in congenitally blind humans. *The European Journal of Neuroscience*, *16*, 930–936.

Röder, B., Teder-Sälejärvi, W., Sterr, A., Rösler, F., Hillyard, S. A., & Neville, H. J. (1999). Improved auditory spatial tuning in blind humans. *Nature*, *400*, 162–166.

Ruckenstein, M. J., Hedgepeth, C., Rafter, K. O., Montes, M. L., & Bigelow, D. C. (2001). Tinnitus suppression in patients with cochlear implants. *Otology & Neurotology*, *22*, 200–204.

Sadato, N., Okada, T., Honda, M., & Yonekura, Y. (2002). Critical period for cross-modal plasticity in blind humans: A functional MRI study. *Neuroimage*, *16*, 389–400.

Sadato, N., Pascual-Leone, A., Grafman, J., Ibañez, V., Deiber, M. P., Dold, G., et al. (1996). Activation of the primary visual cortex by Braille reading in blind subjects. *Nature*, *380*, 526–528.

Sauvé, K. (1999). Gamma-band synchronous oscillations: Recent evidence regarding their functional significance. *Consciousness and Cognition*, *8*, 213–224.

Seki, S., & Eggermont, J. J. (2003). Changes in spontaneous firing rate and neural synchrony in cat primary auditory cortex after localized tone-induced hearing loss. *Hearing Research*, *180*, 28–38.

Sharma, A., Dorman, M. F., & Kral, A. (2005). The influence of a sensitive period on central auditory development in children with unilateral and bilateral cochlear implants. *Hearing Research*, *203*, 134–143.

Sharma, A., Dorman, M. F., & Spahr, A. J. (2002). A sensitive period for the development of the central auditory system in children with cochlear implants: Implications for age of implantation. *Ear and Hearing*, *23*, 532–539.

Sur, M., Pallas, S. L., & Roe, A. (1990). Cross-modal plasticity in cortical development: Differentiation and specification of sensory neocortex. *Trends in Neurosciences*, *13*, 227–233.

Svirsky, M. A., Robbins, A. M., Iler Kirk, K., Pisoni, D. B., & Miyamoto, R. T. (2000). Language development in profoundly deaf children with cochlear implants. *Psychological Science*, *11*, 153–158.

Tamura, Y., Ueki, Y., Lin, P., Vorbach, S., Mima, T., Kakigi, R., et al. (2009). Disordered plasticity in the primary somatosensory cortex in focal hand dystonia. *Brain*, *132*, 749–755.

Trussell, G. C., & Smith, L. D. (2000). Induced defenses in response to an invading crab predator: An explanation of historical and geographic phenotypic change. *Proceedings of the National Academy of Sciences of the United States of America*, *97*, 2123–2127.

Van Hoesel, R. J. M. (2004). Exploring the benefits of bilateral cochlear implants. *Audiology & Neurotology*, *9*, 234–246.

Vanlierde, A., De Volder, A. G., Wanet-Defalque, M. C., & Veraart, C. (2003). Occipito-parietal cortex activation during visuo-spatial imagery in early blind humans. *Neuroimage*, *19*, 698–709.

Via, S., Gomulkiewicz, R., De Jong, G., Scheiner, S. M., Schlichting, C. D., & Van Tienderen, P. H. (1995). Adaptive phenotypic plasticity: Consensus and controversy. *Trends in Ecology & Evolution*, *10*, 212–217.

Von Melchner, L., Pallas, S. L., & Sur, M. (2000). Visual behaviour mediated by retinal projections directed to the auditory pathway. *Nature*, *404*, 871–876.

Voss, P., Lassonde, M., Gougoux, F., Fortin, M., Guillemot, J. P., & Lepore, F. (2004). Early- and late-onset blind individuals show supra-normal auditory abilities in far-space. *Current Biology*, *14*, 1734–1738.

Watanabe, D., Savion-Lemieux, T., & Penhune, V. B. (2007). The effect of early musical training on adult motor performance: Evidence for a sensitive period in motor learning. *Experimental Brain Research*, *176*, 332–340.

Weisz, N., Müller, S., Schlee, W., Dohrmann, K., Hartmann, T., & Elbert, T. (2007). The neural code of auditory phantom perception. *The Journal of Neuroscience*, *27*, 1479–1484.

Weisz, N., Wienbruch, C., Dohrmann, K., & Elbert, T. (2005). Neuromagnetic indicators of auditory cortical reorganization of tinnitus. *Brain*, *128*, 2722–2731.

Will, B., Dalrymple-Alford, J., Wolff, M., & Cassel, J. C. (2008). The concept of brain plasticity—Paillard's systemic analysis and emphasis on structure and function (followed by the translation of a seminal paper by Paillard on plasticity). *Behavioral Brain Research*, *192*, 2–7.