



Representational Plasticity in Response to a Changing Environment

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Abstract

A wealth of research has been conducted with the aim of further understanding the role of somatosensory, visual, and auditory cues in creating a neuronal representation of the organisms the surrounding environment. Evidence from many studies suggests that there exist universal underlying mechanisms behind the adaptation, stability, and complex integration of sensory modalities. Sensory networks were once believed to be fixed, but recent evidence has confirmed that the brain is highly malleable, especially at sensory cortices (Collignon, Voss, Lassonde, & Lepore, 2009). The present review aims to consolidate the literature investigating both intact sensory maps and the adaptations of these maps in response to peripheral nerve changes. Observed cross-modal plasticity suggests a hierarchical preservation that conserves the most vital information while efficiently utilizing available neural networks. Although there is much evidence to support the notion of sensorimotor plasticity, there have been few studies that attempt to elucidate the inherent components of this reorganization. This paper discusses possible theories to explain the development and mechanisms behind sensory maps. Several experiments to test these theories are proposed.

Introduction

Spatial representations of sensory cues present a model of learning at a neuronal level. Learning is an “experience-dependent generation of enduring internal representations or experience-dependent lasting modifications in such representations” (Dudai, 1989). Commonly held theories posit that critical periods are more flexible than previously thought. Highly malleable, internal maps of sensory cues present an accurate and traceable model of the brain’s reactions to external change. The interactions of neurons both within and between different sensory cortices have served as a foundation for and continue to shape our understanding of neuroplasticity in the adult brain. In addition, these maps have been described and localized, which facilitates experimental investigations.

Neuroplasticity is often used as an umbrella term to describe all types of learning in the brain. Both structural and physical changes have been found to underlie this important process. Neurogenesis, the growth of and incorporation of new neurons, plays an important role in developmental plasticity. Furthermore, Hebbian plasticity describes the differential strengthening of synapses that occurs as a result of both long-term potentiation and long-term depression. Long-term potentiation refers to the physiological changes that underlie the strengthening of a synapse that occurs when two neurons fire simultaneously. Long-term depression refers to the physiological changes that underlie the weakening of a synapse between two neurons.

Cortical Re-mapping Within Distinct Sensory Modules

Somatosensory cortex. Although neuroplasticity occurs in many areas of the brain, one of the most remarkable locations of isolated cortical re-mapping is in the sensory modules of the brain. Although many studies have demonstrated cross-modal plasticity, this section will focus on plasticity that occurs within distinct

sensory modalities¹. Research on the presence of phantom limbs, or the persistence of feeling in an amputated limb, in humans suggests somatosensory remapping occurs in response to peripheral nerve loss or injury (Ramachandran, Brang, & McGeoch, 2010). The somatosensory cortex is organized topographically, such that neurons responding to sensory input from the hand are adjacent to neurons responding to input from the cheek nerves. Individuals with the feeling of phantom limb in an amputated arm or hand have reported that when their face is touched they experience the sensory input in their absent hand; this phenomena is referred to as residual phantom pain (Flor, Nikolaisen, & Jensen, 2006). This topographic remapping is behavioral evidence that the neurons previously responding to sensory input from the hand have shifted to respond to sensory input from the cheeks.

Technological advances have allowed for better understanding of somatosensory plasticity on a neuronal level. Merzenich et al. (1984) used microelectrode-mapping techniques to determine cortical representations of the hand in adult owl monkeys in response to digit amputation. Successive maps were taken over time to determine the precise receptive field changes. The representations of skin surfaces surrounding the amputated digit in the somatosensory cortex expanded topographically, explaining the described behavioral changes in human amputees. Several amputation studies demonstrate that the changes in receptive fields in monkeys, raccoons, and rats mimic the time course of changes in sensory acuity in human amputees. This suggests that re-mapping resulting from a change in sensory inputs leads to modifications in sensory capabilities (Merzenich et al., 1984; Halligan, Marshall, & Wade, 1994; Calford, 2002).

Just as the existence and alteration of phantom limbs is suggestive of cortical remapping, neural responses to other external changes are indicative of neuroplasticity of the somatosensory system. Tinazzi et al. (1998) recorded cortical, brain stem, and spinal tactile-evoked potentials in response to ulnar nerve stimulation in patients afflicted with carpal tunnel syndrome. Their result suggests that a chronic modification of peripheral inputs, such as carpal tunnel syndrome, results in changes in neural activity at multiple sites of the somatosensory system. This conclusion was made through a direct comparison of the tactile-evoked potentials on the affected side with those on the unaffected side. Tinazzi et al. (1998) postulated that the expansion of receptive fields in the somatosensory cortex is mediated by GABA receptors. Calford (2002) claims that the research conducted by Tinazzi (1998) suggests plasticity resulting from disruption of peripheral nerves occurs only at the cortical level. More data should be collected to confirm this argument.

Visual cortex. The plasticity evident in the somatosensory cortex in response to external change is not unique to that region of the brain. Similar changes have been observed in the visual cortex in response to abnormal visual input. Through their research on ocular dominance in kittens, Hubel and Wiesel (1998) demonstrated visual cortical plasticity. The study blocked visual input from one side by stitching an eye shut and used microelectrodes to record activity from neurons in the primary visual cortex. The results indicate that the neurons previously receiving input from the blocked eye had begun to receive input from the other side of the visual field. In addition, the results suggest that this plasticity, like somatosensory reorganization, decreases with age. This process mimics the process seen in cortical remapping in the somatosensory cortex.

Many studies investigating the effects of visual input manipulation during the critical learning period have demonstrated that a selectively competitive process underlies normal developmental plasticity in the visual cortex (Gordon & Stryker, 1996). Studies utilizing transgenic and gene-targeting technologies have opened up the potential to determine the synaptic and cellular basis of this developmental plasticity in mice. One such study beautifully illustrates the contrast between developmental plasticity and experience-dependent plasticity in the mouse primary visual cortex. In this study, while monocular lid sutures induced a maximal loss in responsiveness of cortical neurons to the deprived eye, this decreased responsiveness was not seen after binocular lid suture. Taken in conjunction, these data suggest that experience-dependent plasticity relies upon competitive synaptic plasticity (Gordon & Stryker, 1996).

On a cellular level, the remodeling of dendritic arbors in GABAergic interneurons is responsible for the routine cortical reorganization seen in the adult visual cortex (Lee et al., 2006). This study used multiphoton microscopy to image and reconstruct neurons in the rodent cerebral cortex over a period of multiple months. While pyramidal neurons remained stable, GABA-positive non-pyramidal interneurons could be observed modifying existing dendritic branches, which is important as it indicates that cortical remapping of an adult brain is restricted by cell-type. This finding is significant as it supports the theory that dendritic structural remodeling is the backbone of adult plasticity. In contrast to the large-scale age-related plasticity decline shown by Hubel and Wiesel (1998) this research suggests plasticity is still occurring in the adult brain as a result of

¹ Cross-modal plasticity is a broad term that refers to the adaptive reorganization of neurons in order to integrate the function of two or more sensory systems. It often occurs after sensory deprivation. There is a large range of types of cross-modal plasticity, depending on the degree of sensory deprivation.

anatomical changes, albeit on a smaller scale. It is important to note that this study does not account for the fact that these dendritic changes might be universal aspects of a day-to-day change in cortical structure. Although this implies adult plasticity occurs, it is still unclear as to what anatomical changes occur in response to abnormal visual input. In fact, many studies have concluded that cortical plasticity in the visual cortex happens as a result of physiological changes, not anatomical changes (Calford, 2002).

Auditory cortex. Unlike somatosensory cues and visual cues, auditory cues do not have an inherent spatial component in their transmission to the brain. This means the brain must rely upon computations to create a topographic map of auditory cues. The existence of a topographic map coding for sound localization has been shown to exist through microelectrode recordings in the auditory cortex of the barn owl (Knudsen & Konishi, 1979). Similarly, a tonographic map, which differentiates between sound frequencies, has been found to exist in the brain. These auditory maps are universal across species, and thus the inferior colliculus and the auditory cortex offer universal models of cortical plasticity in response to changing auditory inputs. One study showed that sensory input directs both spatial and temporal plasticity in the primary auditory cortex. In this study, basal forebrain stimulation was paired with auditory stimulus. Basal forebrain activity has been linked with the release of acetylcholine, a neurotransmitter that enhances cortical plasticity (Froemke, Merzenich, & Schreiner, 2007). Receptive fields were determined through microelectrode recordings taken from the auditory cortex. By varying the frequency and duration of the auditory stimulus and the temporal coincidence of the forebrain activation and the stimulus, the receptive fields of auditory cortex neurons could be manipulated (Kilgard et al., 2001). This finding indicates the brain modulates learning through precise control of cortical plasticity.

Similar to ocular deprivation studies, cochlear damage results in changes in auditory input. Harrison, Ibrahim and Mount (1998) examined the response in the brain to changes in auditory input in the chinchilla brain. Bilateral lesions were made on the cochlea of newborn pups. Subsequent studies determined the degree of the hair cell lesions. After the animals reached maturity, single unit electrophysiological mapping was performed to delineate tonotopic representation in the inferior colliculus. The mapping showed tonotopic overrepresentation of frequencies slightly below and slightly above the frequency that was coded for by the lesioned part of the cochlea. In much the same way as somatosensory re-organization temporarily increases the representation of certain digits in response to digit amputation, auditory receptive field expansion temporarily increases the resolution of certain frequencies (Harrison et al., 1998). Calford (2002) reviews several similar studies that have reproduced cortical reorganization in different organisms auditory cortex, suggesting similar mechanisms occur in the human brain.

In addition to the above evidence indicating that there are universal mechanisms, which underlie auditory cortex re-organization in the human brain, further studies confirm these similarities. Gilley, Sharma and Dorman (2008) observed cortical reorganization in children with cochlear implants. Congenital deafness leads to atypical organization of the auditory nervous system. In this study, cortical auditory evoked potentials were recorded in normal hearing children and in congenitally deaf children fitted with cochlear implants. Through high density EEG and source modeling, normal activity was observed in the auditory cortex of children implanted with a cochlear implant at an early age. Children who received an implant after a critical period has ended showed activity from the parietotemporal cortex in response to auditory input. This study suggests topographic and tonographic mapping is experience-expectant for a certain period but can still occur in a different area of the brain past that period. Although this study does not necessarily determine the nature of cortical plasticity, it demonstrates that the presence of auditory stimuli is necessary for auditory cortex plasticity.

The above studies illustrate the universal principles that underlie cortical re-mapping in the somatosensory, visual, and auditory cortex. All cortices have experience-expectant critical periods that guide their topographic organization. The sensory modalities respond to deprivation through topographic re-organization that results in temporary overrepresentation of certain stimuli. In this re-mapping, neural networks and space are conserved and used efficiently. In addition, preliminary evidence suggests specific cell types drive cortical plasticity. Inhibitory interneurons have been identified as playing a key role in sharpening resolution of sensory stimuli (Froemke, et al., 2007). Recordings were taken over a period of time of inhibitory post-synaptic currents in the auditory cortex in response to the coincidence of auditory stimuli and nucleus basalis stimulation have indicated modulation of inhibition plays an important role in synaptic plasticity (Froemke et al., 2007). Calford (2002) argues that disinhibition underlies all synaptic plasticity in the sensory modalities, as it is the balance between excitation and inhibition that maintains receptive fields. Further studies should be conducted to understand the specific role of inhibition and specific neurotransmitters in modulating cortical plasticity, which are discussed later in this paper.

Cross-Modal Plasticity

Although intriguing examples of cortical plasticity can be found within individual cortices, a full consideration of neuroplasticity is not complete without an examination of how these distinct cortices interact. Cross-modal plasticity studies demonstrate how malleable the brain is and that this plasticity exists both within specific cortices as well as between distinct sensory cortices. The conservation and hierarchical preservation seen in individual modalities in response to partial sensory deprivation is also seen across cortices in response to complete deprivation of a certain type of stimuli.

Plasticity seen in the adult auditory cortex of deaf ferrets suggests cross-modal plasticity can occur after a critical period of sensory system maturation. Allman, Keniston and Meredith (2009) deafened several adult ferrets for a significant period of time and made electrode recordings from sixty-nine places in the auditory cortex. The neurons previously responding to auditory stimuli now responded to somatosensory stimuli. The conversion of the auditory cortex to somatosensory cortex indicates that learning in the sensory modalities is experience-dependent and can occur at any time. This sensory conversion is similar to the plasticity that occurs in response to partial sensory deprivation in the individual cortices.

Several studies on congenitally blind humans suggest that a critical period does not exist for cross-modal plasticity. Collignon et al. (2009) review several studies to unravel the basis of cross-modal plasticity in blind organisms. Taken in conjunction, several studies offer evidence that enhanced auditory perception seen in the congenitally blind results from conversion of the occipital areas in the brain into areas that respond to auditory stimuli. Furthermore, these studies show that cross-modal recruitment follows the same mechanisms and organizational principles that occur within individual cortices. Several experiments have shown that normal synaptic pruning during development eliminates projections from the auditory cortex towards the occipital cortex. For example, in kittens deprived of vision at birth, these connections are not modified, indicating that pruning is an experience-dependent process (Bavelier & Neville, 2002). A functional MRI (fMRI) study conducted by Sadato, Okado, Honda and Yonekura (2002) found that past a critical developmental period, cross-modal plasticity would not occur in blind humans. The primary visual cortex in congenitally blind humans has been shown to be involved in tactile discrimination tasks. Through fMRI studies, brain activity in the primary visual cortex was measured while subjects performed passive tactile discrimination tasks. The fMRIs indicate that the primary visual cortex was converted in subjects who became blind before sixteen years of age but, it was not converted in subjects who became blind past that critical period (Sadato et al., 2002).

Although many studies have confirmed the existence of enhanced responses to auditory and tactile stimuli in the visual cortex of blind humans, little is known about the principles that drive this reorganization. Many scientists claim that the cross-modal plasticity seems to be monitored by subcortical pathway plasticity (Calford, 2002; Collignon et al., 2009; Tinazzi et al., 1998). In an intriguing study, Lewis, Saenz and Fine (2010) found that cross-modal plasticity within blind subjects does not originate from either an increasing or unmasking of existing cross-modal sensitivities found in sighted subjects. This study used functional imaging of the visual, auditory, and somatosensory cortices to create three-dimensional anatomical images of the brain. The subjects were presented with auditory and tactile tasks for ten seconds followed by a period of two seconds for data acquisition. The enhanced cross-modal responses found in the auditory cortex, described as an “additive shift” indicates that new connections are responsible for the responses.

The existence of cross-modal plasticity indicates that the topographic organization of cortices occurs even in the absence of a certain type of sensory stimuli. Normal topographic organization depends upon the presentation of normal sensory stimuli during a critical period, indicating that complete sensory organization is experience-expectant learning. In the absence of normal stimuli, topographic organization still occurs in a highly structured manner, albeit different cortices often lie in different locations. It seems that experience-dependent learning can occur after a critical period to encode for and distinguish between distinct sensory stimuli. The similarities between normal cortical plasticity and cross-modal plasticity are vast. The conservation of information seen in individual cortices is clearly the basis for cross-modal plasticity. In addition, the competition that drives the normal development of the visual cortex seems to drive the normal development of cross-modal connections. These similarities indicate the organization within individual cortices mimics the organization between cortices.

Analysis and Future Directions

Topographic maps have adaptive values in the brain. Topographic organization enables cortical plasticity, which preserves receptive fields and thus maintains accurate interpretations of sensory input. Calford (2002) claims that the rapidity and reversibility of cortical plasticity indicate that mechanisms that respond to change in peripheral input are inherent in the circuitry of the topographic representations in the brain. The adaptive importance of universal mechanisms explains their existence, but it is still unclear what process

mediates the cortical changes within and across sensory modalities. As described before, the similarities in cortical plasticity both within and between modalities are vast. Therefore, this theoretical analysis will treat all plasticity mechanisms as identical.

Many studies have shown that cortical plasticity in response to sensory stimuli lacks a critical period. As mentioned, Sadato et al. (2002) showed that, in blind human subjects, conversion of the primary visual cortex to a tactile discrimination cortex would not occur after age sixteen. One fault of this study is that it only looks at tactile discrimination tasks. Although cortical conversion of this type might have a critical period in the visual cortex, this is not sufficient evidence to suggest that cross-modality plasticity of the visual cortex has a universal critical period. A need-based cross-modal plasticity mechanism might control the analogous conversion of the primary auditory cortex in the absence of visual stimuli. Three experiments that would further identify the factors that modulate cross-modal plasticity in the visual cortex are proposed below.

First, a study examining the conversion of the primary visual cortex in human subjects who lost their sight at different ages would determine if the visual cortex responds to other sensory stimuli after age sixteen. Through functional MRIs studies it is possible to determine which stimuli activate the visual cortex in these subjects. This would determine if the cortical area had converted to become responsive to other types of stimuli.

A study on mice could determine whether the presence of acetylcholine in the primary auditory cortex of blinded mice regulates the conversion of the visual cortex to a tactile discrimination cortex as determined by microelectrode recordings. Acetylcholine has been shown to enhance cortical plasticity in all sensory modalities thus it is a good choice of neurotransmitter to potentially induce cross-modal plasticity (Froemke et al., 2007). By comparing the conversion that occurs in the auditory cortex of mice treated with acetylcholine with the conversion that occurs in the auditory cortex without acetylcholine would indicate the role of acetylcholine in this type of conversion.

Some studies suggest that attention to particular stimuli enhance the representation of those stimuli in the brain. Thus, an obvious question follows: would attention towards tactile discrimination tasks result in a greater change of conversion of the primary auditory cortex towards a tactile discrimination cortex in the absence of visual stimuli? A third study would involve training blind mice in tactile discrimination tasks while recording from the primary visual cortex, which would indicate whether or not this conversion is experience-expectant or experience-dependent.

Another factor that might regulate both the magnitude and the existence of representational plasticity is age. Age-related plasticity declines have been documented in many learning and memory studies that illustrate how an older brain loses its potential to learn new information. It remains unclear whether age-related decline of representational plasticity occurs. Results from Flor et al. (2006) suggest that because phantom limb pain is proportional to age, it indicates that maladaptive plasticity increases with age. This increased pain might be a result of more solidified somatosensory maps such that a disturbance causes more pain than in younger somatosensory maps. It is hypothesized that representational plasticity does not decline but differs as a function of age. With age comes a need to discriminate between more stimuli. For example, as one gets older their repertoire of different colors is much greater thus their need to distinguish between them is greater. Does topographic re-organization in response to changes in peripheral input accurately reflect these age-based needs? Experiments that examine cross-modal plasticity as a function of time will shed light on the relationship between age and representational plasticity changes. An experiment to test this idea could utilize the somatosensory conversion of the auditory cortex in deaf ferrets. Allman et al. (2009) used adult deafness to examine cortex conversions but an experiment that looked at the conversions in the auditory cortex of ferrets deafened at different ages could determine how age affects representational plasticity.

Inhibition and disinhibition have been shown to modulating receptive fields in the sensory modalities. Because this review argues cross-modality plasticity is similar to representational plasticity, it is hypothesized that inhibition also plays a role in controlling cross-modal plasticity and cortex conversions. Friedel and Hemmen (2008) conducted a complex study that demonstrated that inhibition is the key to multimodal sensory integration. In this study, supervised spike-timing-dependent plasticity was measured to gauge input from distinct sensory modalities. In the barn owl, audio-visual spatial integration learning was found to rely upon inhibition. Although multi-modal integration relies upon different mechanisms than multi-modal plasticity, the role of inhibition in controlling two distinct modalities suggests that inhibition could easily play a role in cross-modal plasticity.

One of the great dichotomies presented in representational plasticity studies is the role of structural and functional changes. Calford (2002) claims in his review that physiological changes underlie all cortical plasticity and that there are no structural changes that underlie cortical re-mapping changes. Although modulation of receptive fields is controlled by neurotransmitters and current changes, it seems hard to believe

that no structural changes mediate the long-term connections. GABAergic interneurons control normal axonal growth. Preliminary research suggests that GABA responsive cells play an important role in solidifying new circuits in response to changes in sensory input. The importance of structural changes in facilitating cortical plasticity could be determined through studies that examine cortical plasticity in the presence of compounds that halt activity of GABA responsive cells. If normal cortical plasticity occurred and was maintained then that would be preliminary evidence that structural changes do not underlie the initiation and sustainment of cortical re-mapping. The physiological components of neuroplasticity require long-term potentiation. Thus, it is important to note that NMDA receptors must be present in the cortical receptors. This theory is confirmed by several studies presented in Calford's (2002) review. Furthermore, the induction of long-term potentiation produces long-term changes in sensory neurons. The existence of long-term physiological changes implies there is no need for structural changes to maintain changed receptive fields, the foundation of representational plasticity.

In the visual cortex, competition between inputs from each eye is shown to maintain normal topography. Evidentially, in the absence of input from one eye, the lack of competition helps drive cortical plasticity. As mentioned, the connections between distinct sensory modalities are pruned during normal development. It can be hypothesized that competition controls the pruning of these connections and in the lack of competition, cross-modal plasticity is enabled by the presence of these connections. Finding a methodology to monitor the developmental and learned components of these connections would shed light on what influence these connections play in enabling cross-modal plasticity. Through multiphoton microscopy the connections between sensory modalities can be visualized. If these connections were modified while cross-modal plasticity was induced through blindness or deafness, their role in the plasticity could be determined. Lewis et al. (2010) argued that their study suggested that cross-modal plasticity did not occur as a result of unmasking. The proposed experiment might confirm this belief.

Conclusion

The studies presented in this paper use a range of different animal models with different capabilities. It is important to note that this analysis is not claiming these adaptations, patterns of learning, or coding mechanisms are identical across species or sensory cortices. But, there is evidence to suggest that there is comparative relevance due to many similarities across both species and neurons in distinct sensory cortices. These parallels are indicative of universal mechanisms of all nervous systems and sensory areas in adjusting to changing sensory inputs. All nervous systems of organisms represented in this paper are complex enough to represent localized sensory input in the brain.

Topographic maps are malleable and present a great model for quick sustainable learning. Deprivation studies provide the basis for research on neuroplasticity in the sensory modalities. Localization of plasticity in the sensory modalities offers a great starting point for studying universal mechanisms. Chemical analysis and imaging techniques have opened the doors to finally understanding what underlies this amazing capacity of the brain to respond instantaneously to changes in the environment. More research needs to be done to better understand the mechanisms that modulate cortical plasticity. Once these mechanisms are found further studies will hopefully illuminate the effects of inhibition, age, competition, and physiological/anatomical changes in the plasticity of the sensory modules.

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