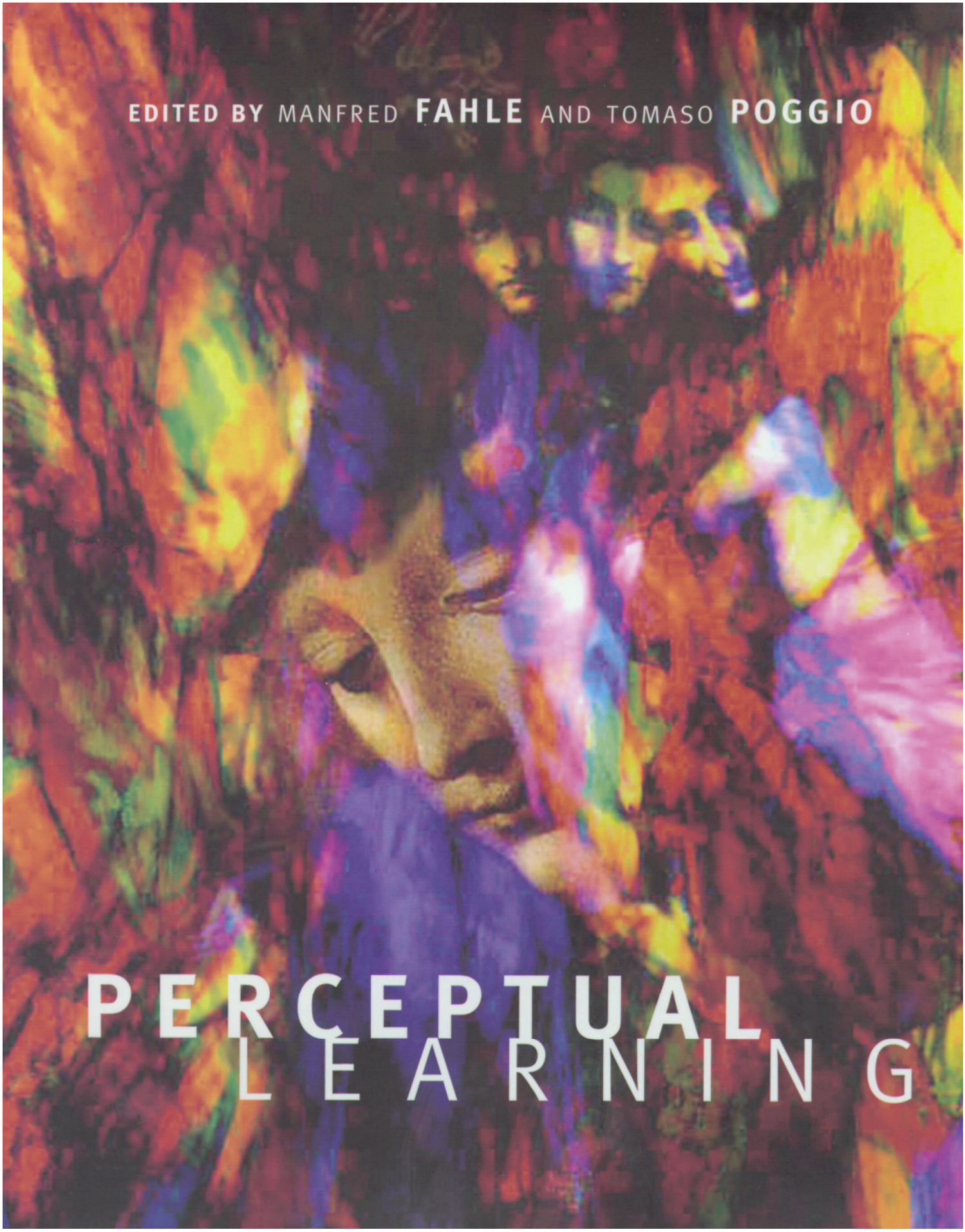

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PERCEPTUAL LEARNING

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Chapter 2

Adaptation of Inputs in the Somatosensory System

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Adaptation of Inputs in the Somatosensory System

2

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Abstract

This chapter summarizes evidence that cortical maps and cortical response properties are in a permanent state of use-dependent fluctuations, where "use" includes training- and learning-induced changes. In their simplest form, use-dependent changes are input driven. Although attention and other high-level processes may contribute and enhance use-dependent neural changes by specific pathways conveying top-down information, reorganization can occur in the absence of high-level processes. The current experimental data imply that altered performance is based on altered forms of neural representations, and that all forms of perceptual learning can therefore be assumed to operate within the framework of cortical adaptivity.

2.1 Introductory Remarks

2.1.1 Two Forms of Plasticity

Postontogenetic plasticity describes the capacity of adult brains to adapt to internal or environmental changes. It is useful to distinguish between two different forms of adult plasticity:

1. Lesion-induced plasticity, which subsumes cortical reorganization after injury or lesion, induced either centrally or at the periphery, refers to compensation for and repair of functions acquired before the injury or lesion.

2. Training- and learning-induced plasticity, often called "use-dependent plasticity," refers to plastic changes that parallel the acquisition of perceptual and motor skills.

Because, for example, amputation changes the pattern of use entirely, a more accurate distinction would be between "lesion-induced" and "non-lesion-induced" plasticity. To what extent the two forms are based on different or perhaps even on similar mechanisms is a matter of ongoing debate.

In contrast to developmental plasticity, adaptations of adult brains do not rely on maturation or growth. For learning-induced alterations, there is agreement on the crucial role played by so-called functional plasticity based on rapid and reversible modifications of synaptic efficacy, although large-scale amputations have been shown to involve sprouting and outgrowth of afferent connections into neighboring regions at cortical and subcortical levels (Florence, Taub, and Kaas 1998; Jain et al. 2000).

2.1.2 Sites of Changes

Perceptual learning is often highly specific to stimulus parameters such as the location or orientation of a stimulus, with little generalization of what is learned to other locations or to other stimulus configurations (see chapters 9, 11, 12, 14). Selectivity and locality of this type implies that the underlying neural changes are most probably occurring within early cortical representations that contain well-ordered topographic maps to allow for this selectivity (see chapter 1). In addition, a transfer of the newly acquired abilities is often considered an important marker of the processing level at which changes are most likely occur: limited generalization is taken as evidence for high locality of effects in early representations. In

contrast, transfer of learned abilities is taken as evidence for the involvement of higher processing levels often observed in task and strategy learning (see chapters 13, 14). There is increasing evidence that changes in early cortical areas might be more directly linked to perceptual learning than previously thought (Karni and Sagi 1991; Recanzone, Jenkins, et al. 1992; Schoups, Vogels, and Orban 1995; Crist et al. 1997; Fahle 1997, chapter 10).

In fact, most of what we know today about adaptation of the somatosensory system comes from the investigation of the somatosensory areas characterized by extended and ordered neural representations of the body surface (box 2.1). In contrast, less is known about both the role of higher areas and the interaction between sensory association areas for perceptual learning. In any case, the conjecture that perceptual learning affects early areas provides an important conceptual link to somatosensory adaptational processes (see chapters 9–14).

2.1.3 Driving Forces That Lead to Adaptational Changes

What factors might induce changes in neural representations? Let us assume a dynamically maintained steady state of representations emerging from learning during development and adulthood that reflects the adaptation history to a "mean environment," defined as the accumulated and idiosyncratic experience of an individual. Adaptational processes are assumed to operate on these representations, and long-lasting changes are likely to occur when sensory input patterns are altered such that they deviate from the mean environment. The average steady state can be altered in three principal ways:

1. By changing the input statistics. Specifically effective in driving adaptational changes are simultaneity, repetition, and, more generally, spatiotemporal proximity (see chapters 14, 20). Because these changes in input do not involve attention or processing for meaning, they induce a class of noncognitive adaptations based largely on bottom-up processing.

2. By drawing attention to certain aspects of a stimulus, thereby selecting it in comparison to others. The relevance of a stimulus can also change, depending on context, history, and behavioral task, thereby modifying how physically defined attributes are processed. There is general agreement that modification of early sensory processing by attention and stimulus relevance reflects top-down influences arising from cognitive processes (see chapters 13, 14, 20).

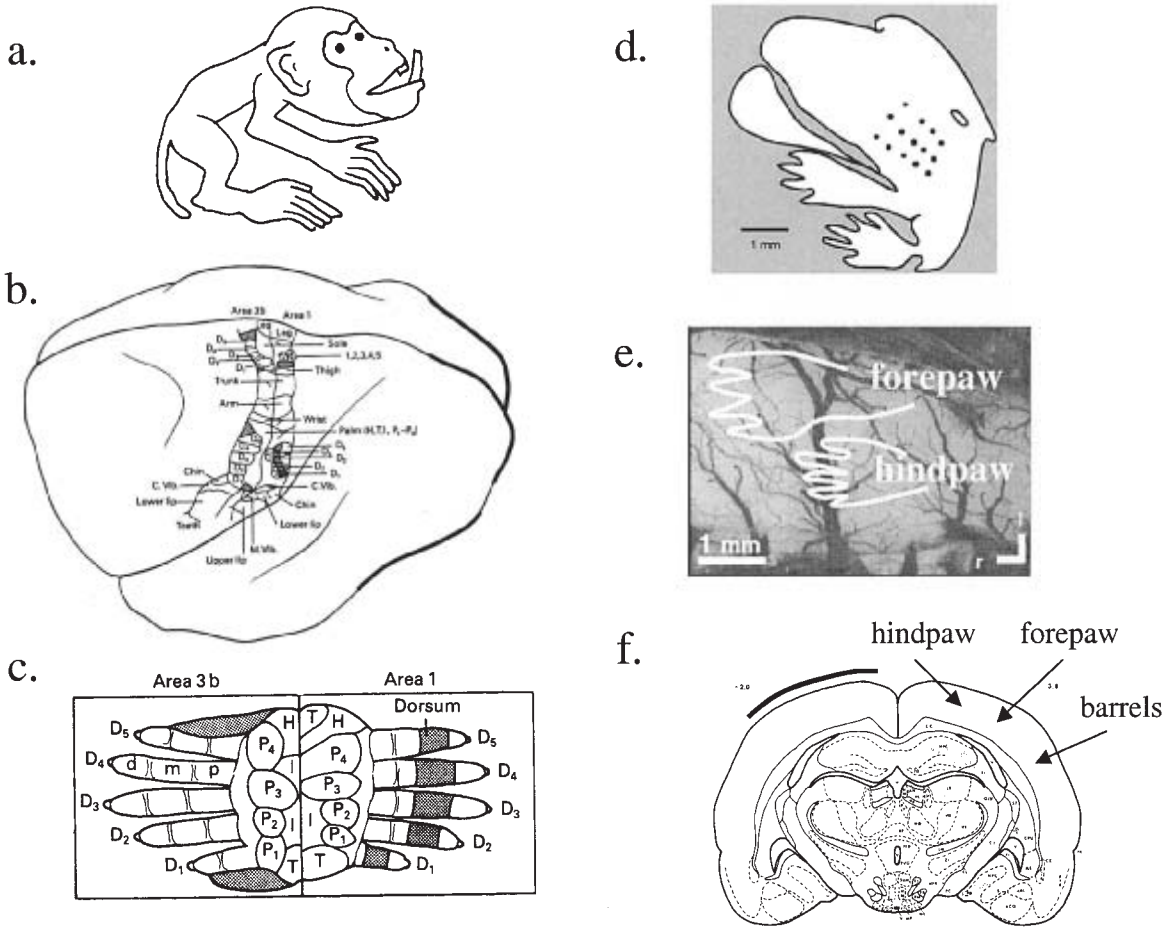
3. By using reward or punishment to reinforce learning. Such influences usually accelerate adaptational processes and are assumed to be mediated by specific brain regions modifying early sensory processing (see chapter 20).

2.1.4 The Hebbian Metaphor

A central paradigm in the description and analysis of cortical plasticity is built around the Hebbian concept (1949): episodes of high temporal correlation between pre- and postsynaptic activity are prerequisite for inducing changes in synaptic efficacy. Historically, the idea that cooperative processes are crucially involved in generating long-lasting changes in excitability can be traced back to the nineteenth century (James 1890).

Indeed, since Hebb, the aspect of simultaneity has become a metaphor in neural plasticity, although the exact role of Hebbian mechanisms in use-dependent plasticity remains controversial (Carew et al. 1984; Fox and Daw 1993; Granger et al. 1994; Montague and Sejnowski 1994; Joublin et al. 1996; Buonomano and Merzenich 1996; Edeline 1996; Cruikshank and Weinberger 1996a,b; Ahissar et al. 1998). It has been suggested that the definition of Hebbian mechanisms

Box 2.1



Higher mammals contain complete and ordered topographic maps of the skin of the body surface giving rise to a "homunculus." Adjacent locations on the skin are represented at adjacent locations in the cortex. Exceptions such as face-hand border arise from the problem of mapping a three-dimensional object onto a two-dimensional surface. (*a*, *d*) Examples of "homunculi" for monkey and rat. Monkeys are characterized by "multiple" representations. (*b*) Mirror-like arranged body surface representations of areas 3b and 1 in an owl monkey. (*c*) Detailed map of the hand representation often used for assessment of adaptational changes. In rats, most of our knowledge about the body representation is from primary somatosensory cortex that is mapped along the dorsolateral aspect of the cortex. (*f*) Locations of hind paw, forepaw, and barrel system. (*e*) Video image of the dorsal surface of the brain, as indicated by the thick dark line in panel *f*, with the locations of the hind and forepaws marked in white. (Panels *a*–*c* reprinted with permission from Kandel et al. © [1992] McGraw-Hill Companies; *f* reprinted with permission from Pellegrino et al. [1986]).

must be extended beyond simultaneity in the sense of strict coincidence to cover all facets arising from learning processes. Such a definition must include a large number of pre- and postsynaptic patterns as well as a broad time window of what neural systems regard as "simultaneous."

2.1.5 Use-Dependent Plasticity as a Basis of Perceptual and Motor Skills

One of the striking features of use-dependent plasticity is the correlation of cortical changes with performance. The acquisition of skills has often been used as an index for the buildup of implicit memories. There are a number of crucial properties that distinguish implicit from explicit memory. Implicit memories are acquired automatically and unconsciously. Many repetitions over a long time without higher-level cognitive processes are sufficient to improve perceptual and motor skills. That the repetitions are noncognitive and many represents an important aspect of use-dependent neural plasticity. It has therefore been speculated that use-dependent plasticity might be strongly related to, if not a substrate for, implicit memory function.

2.1.6 Input Statistics versus Attention

As outlined above, attention plays an important role in learning and adaptational processes (Ahissar and Hochstein 1993; Recanzone, Merzenich, et al. 1992; Goldstone 1998; Buchner et al. 1999). It has been suggested that specific high-level attentional mechanisms modify early sensory processing levels (Ahissar and Hochstein 1993), although recent experiments (Ito, Westheimer, and Gilbert 1998) indicate that attentional mechanisms themselves can be changed by practice (see also chapter 14). Similarly, researchers (Sireoteanu and Rettenbach 1995) have shown that training can transform a serial search to a parallel search task (see chapters 13, 14, 20).

On the other hand, there is little doubt about the significant contributing role of input statistics. Many studies have demonstrated that neural changes and parallel improvement of performance can be evoked by a specific sensory input pattern without involving attentional mechanisms, provided the statistics are sufficiently altered (see also section 2.4.2).

2.1.7 Top-Down Modulation of Plasticity

There are many brain centers that play a role in modulating cortical responsiveness. The major source of cholinergic inputs long implicated in learning and memory comes from several groups of neurons within the basal forebrain, which receives inputs from limbic and paralimbic structures. For example, in animal experiments, pairing of sensory stimulation with electrical stimulation of the nucleus basalis has been shown to result in rapid and selective reorganization (Rasmusson and Dykes 1988; Edeline et al. 1994; Bakin and Weinberger 1996; Bjordahl, Dimyan, and Weinberger 1998; Kilgard and Merzenich 1998). On the other hand, lesion of the cholinergic system has been shown to prevent plastic reorganization (Baskerville, Schweitzer, and Herron 1997; Sachdev et al. 1998). Consequently, cholinergic inputs have been assumed to represent one example of a top-down system providing modulatory information of higher-order, presumably cognitive processes (cf. chapters 13, 14 and 20).

2.1.8 Synopsis

The present chapter summarizes recent work on somatosensory adaptations with special emphasis on behavioral and perceptual consequences of use-dependent plasticity as defined above. (For reviews

covering all facets of cortical plasticity, see Merzenich et al. 1988; Kaas 1991; Garraghty and Kaas 1992; Sameshima and Merzenich 1993; Donoghue 1995; Weinberger 1995; Cruishank and Weinberger 1996a; Edeline 1996; Merzenich, Wright, et al. 1996; Dinse et al. 1997; Kaas and Florence 1997; Sanes and Donoghue 1997; Buonomano and Merzenich 1998a; Nicolelis, Katz, and Krupa 1998.)

We first survey studies of training and use in a variety of animal models, then discuss recent studies of somatosensory adaptations in humans by researchers using noninvasive imaging technologies. These imaging studies provide compelling evidence for the relevance of adaptational changes to everyday life. Next, we consider approaches that, by varying input probability, explore how "driving factors" induce adaptational changes. We review the increasing evidence for "maladaptive" aspects of neuroplasticity and touch on the role of "subcortical" plasticity. Finally, we critically examine what is changed during adaptations, as this relates to the coding and decoding of sensory information during adaptations needed to alter perceptual and motor performance.

2.2 Role of Training, Differential Use, and Behavior

It is common wisdom that perceptual skills improve with training (see Gibson 1953). Recent studies in "perceptual learning" have focused on problems and questions associated with skill acquisition. One of the most stimulating questions in cortical plasticity is how cortical changes are linked to changes in performance, a question requiring simultaneous assessment of both neurophysiological and behavioral changes.

For example, Recanzone, Jenkins, and coworkers (1992) showed that tactile frequency discrimination training in adult owl monkeys over several months leads to a significant reduction of frequency discrimination threshold. When the cortical areas representing the skin of the trained fingers were mapped, large-scale cortical reorganization became apparent, which included changes in receptive fields and in the topography of cortical representational maps (Recanzone, Merzenich, et al. 1992). After training, sinusoidal stimulation of the trained skin elicited larger-amplitude responses, peak responses earlier in the stimulus cycle, and temporally sharper responses, than did stimulation applied to control skin sites. Analysis of cycle histograms for area 3b neuron responses revealed that the decreased variance of each stimulus cycle could account for behaviorally measured frequency discrimination improvements (Recanzone, Merzenich, and Schreiner 1992). These studies demonstrated for the first time a direct relation between cortical plasticity and improvement of performance (see also figure 2.1), establishing a tight link between neurophysiological experiments and psychophysical tasks and making it possible to correlate precisely defined aspects of use with plastic changes.

A related approach was taken by Xerri et al. (1999), in which monkeys were trained to pick up food pellets from wells of different sizes. Although all monkeys exhibited a gradual improvement in digital dexterity, each monkey developed an individual retrieval strategy. In area 3b, the cortical magnification of the differentially engaged glabrous fingertip surfaces was nearly twofold larger than it was for control digits. Receptive fields of neurons representing the engaged digital surfaces were less than half as large as those representing the corresponding surfaces of control digits. These results confirmed that behaviorally important skin surfaces are represented in a much finer representational grain than normal.

Use-dependent plasticity has been investigated in a more natural context as well, where the link between behavior and cortical reorganization is often

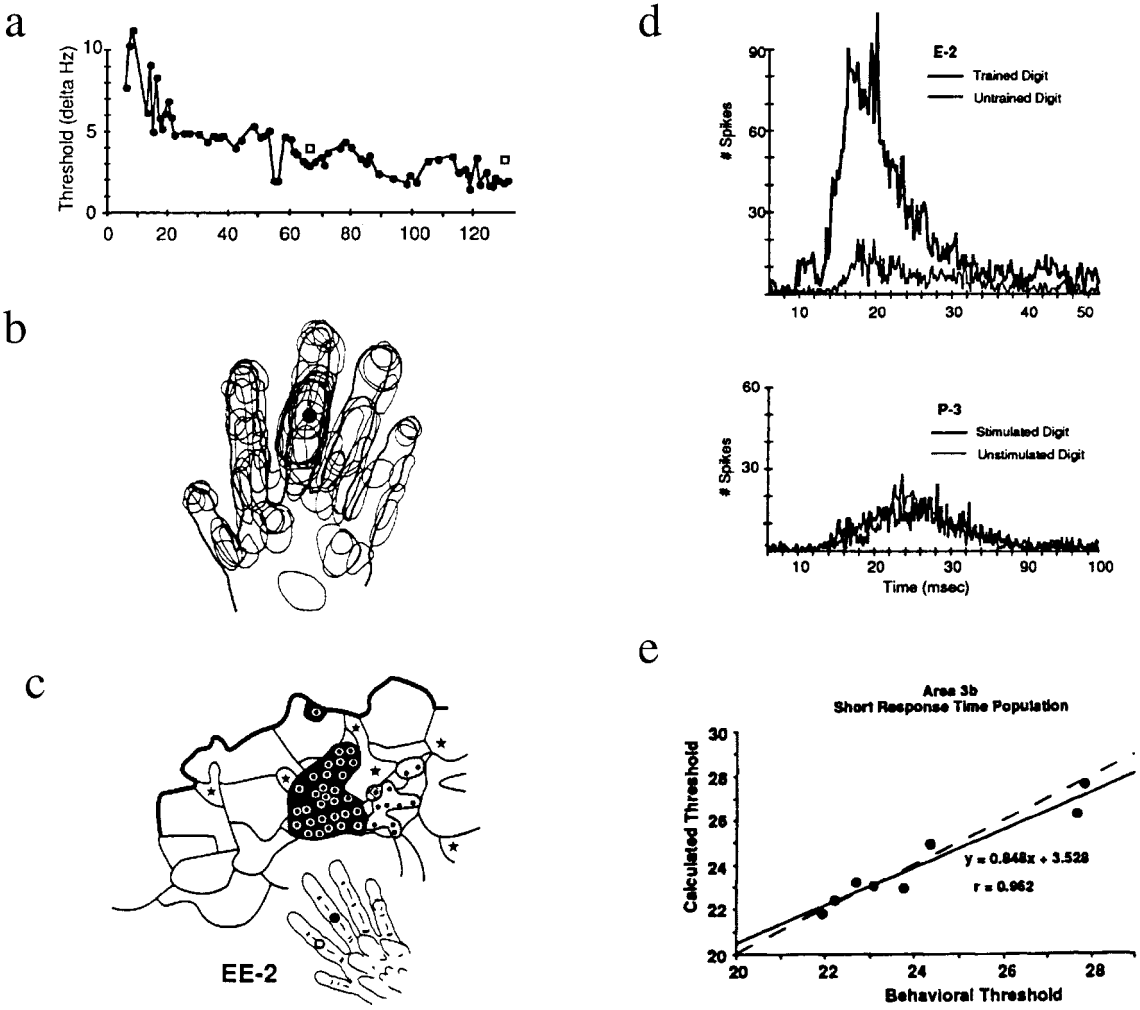


Figure 2.1

Adult owl monkeys were trained to detect differences in the frequency of a tactile flutter vibration stimulus above a 20 Hz standard. All stimuli were delivered to a constant skin site on a small segment of one finger. (*a*) Changes of psychophysical performance in terms of threshold over successive sessions indicate progressive improvement with training that was highly selective for the trained skin site. (*b*) Representative receptive fields defined in area 3b on the trained hand of the same monkey shown in panel a. Filled circle denotes the area of skin trained in the behavioral task. The size of receptive fields increased in the zone of representation of the trained digit as compared to adjacent digits or the control hand. (*c*) Cortical representational map highlighting all penetrations that included some or all of the trained skin (dark stipple), the homologous skin on the adjacent digit (light stipple) or both skin surfaces (hatched). The inset shows the stimulated skin site (black dot) and its equivalent on the adjacent finger (stippled dot). This analysis revealed that the representation of the stimulated skin was larger than the control skin site. (*d*) To study the temporal response characteristics, neurons were stimulated using

less quantifiable, although still intuitively obvious. In their study of lactating rats, Xerri, Stern, and Merzenich (1994) showed the implications of episodic differential use following normal nursing behavior: the area SI representation of the ventral trunk skin was significantly larger in lactating rats than in matched postpartum nonlactating or virgin controls. The greatest representational change was a twofold increase of the cortical representation of the nipple-bearing skin between the forelimbs and hind limbs.

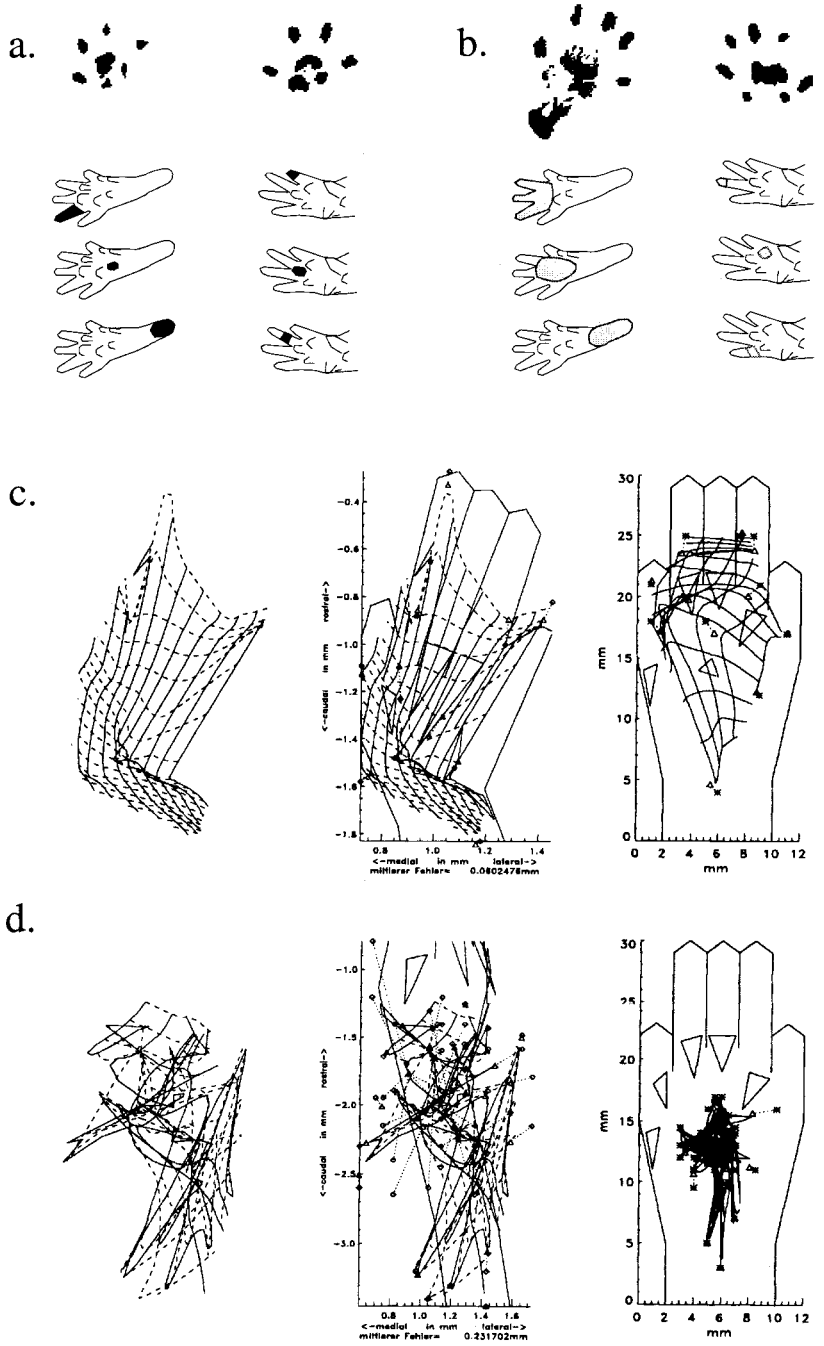
Housing rodents in an enriched environment has been shown to inhibit spontaneous apoptosis, prevent seizures, and produce general neuroprotective effects (Young et al. 1999). Furthermore, in the hippocampus of even senescent mice, an enriched environment induced neurogenesis (Kempermann, Kuhn, and Gage 1997). The areal extent of the forepaw cutaneous representation was significantly larger in rats housed in enriched environments promoting differential tactile experience (EE rats) for 71–113 days from weaning than in control rats housed under standard conditions (Coq and Xerri 1998). In addition, the receptive fields tended to progress in more orderly fashion across the digit glabrous skin of EE rats than they did in control rats, corroborating the view that cortical cutaneous maps are maintained in a permanent state of use-dependent fluctuation.

In adult rats, a tendon of a hind limb was cut, leading to slight changes in walking behavior. Analysis of receptive fields (RFs) and cortical representational maps of the hind paw revealed an increase of RF size and a shrinkage of the cortical map within a few days. Both behavioral effects and cortical changes were reversible within weeks (Jürgens and Dinse 1997a; Zepka, Jürgens, and Dinse 1996), demonstrating that even modest modification in behavior can lead to rapid and large-scale cortical changes. These findings extend the results of Fox and coworkers (1994), who studied adult rats under space flight conditions after complete prevention from use or hind limb suspension. Both approaches resulted in modified posture and gait, which returned to normal after about two weeks. Behavioral adaptations were paralled by a reduction in the number of GABA-immunoreactive cells (D'Amelio et al. 1996).

For the human motor system, similar fast adaptational regulations have been reported. Using transcranial magnetic stimulation (TMS) mapping, Licpert, Tegenthoff, and Malin (1995) have shown that, in patients who had unilateral immobilization of the ankle joint without peripheral nerve lesions, the area of motor cortex representing the tibial anterior muscle was significantly smaller for the immobilized than for the unaffected leg. The reduction in area was correlated with the duration of immobilization, an effect rapidly reversed by voluntary muscle contractions.

The framework of modified use as a determinant of cortical organization has been tested in an in-

sinusoidal tactile stimuli in the range of 20 to 26 Hz corresponding to the frequency range tested behaviorally. Upper population cycle histogram (E-2) was constructed from summing neural responses of trained and stimulated digits (heavy line) recorded at all area 3b locations, superimposed with histograms for stimulation of adjacent untrained digits (thin line), in the monkey shown in panels a–c; bin width was 0.1 msec. Note entrained and faster response characteristics for the trained digit, an effect missing for the passively trained monkey shown in lower population cycle histogram (P-3). (*e*) Regression analysis for the calculated threshold based on the overlap of the second cycle in the cycle histograms as a function of behaviorally threshold, indicating that the training-induced temporal processing characteristics can explain behavioral performance to a considerable degree. (Modified from Recanzone, Jenkins, et al. 1992; Recanzone, Merzenich, et al. 1992; Recanzone, Merzenich, and Schreiner 1992. Reprinted with permission from the American Physiological Society.)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vestigation of age-related modifications of cortical representational maps in old rats, known to show a number of age-related changes. The characteristic impairment of the sensorimotor state is most strikingly expressed in a walking impairment of the hind limbs (Schuurman et al. 1987; Ingram 1988; Stoll et al. 1990). Using electrophysiological recordings, researchers (Jürgens and Dinse 1995; Spengler, Godde, and Dinse 1995) demonstrated that behavioral changes in old rats were paralleled by massive reorganization of the somatosensory cortex (figure 2.2). Age-related changes were characterized by an enlargement of receptive fields of the hind paw representation, an increase of RF overlap and a deterioration of the topography of the cortical maps. It has been suggested (Dinse et al. 1995) that certain aspects of these age-related behavioral changes reflect plastic changes resulting from prolonged disuse of the hind limbs rather than from age-related cortical degeneration. Sensorimotor behavior of the forelimbs remains largely unaffected even in animals of high age. Accordingly, in the case of neural degeneration, one would expect comparable changes to occur in both the forepaw and the hind paw representation. Indeed, analysis of RFs in the cortical forepaw representation of animals of high age revealed no alterations (Jürgens and Dinse 1997b). The results imply that age-related changes can be regionally very specific, thereby arguing against an unspecific origin for such changes, and that age-related neural changes and specific age-related behavioral alterations are linked.

Interestingly, enriched environment has been shown to prevent age-related decrease in synaptic density in the aged brain (Saito et al. 1994); indeed, when old rats were kept in an enriched environment for several months, no comparable age-related alterations of sensory (Churs et al. 1996) and motor hind paw representations (Reinke and Dinse 1999) were found. These results indicate that the beneficial outcome of an enriched environment, namely, reinforced mobility and agility, occurs even in animals of high age.

Figure 2.2

Specific effects of age on receptive fields of the hind paw recorded in somatosensory cortex of aged rats. (*a*, *b*) Representative examples of behavioral changes of walking pattern derived from footprint analysis for young, control animal, left hind paw and right forepaw and for old animal, left hind paw and right forepaw, respectively. Note selectivity of walking impairment restricted to hind leg. Examples of receptive fields (RFs) recorded in the hind paw representation (panels a and b, lower left) and in the forepaw representation (panels a and b, lower right) in young and old animal, respectively. Age-related changes are limited to the behaviorally impaired extremity. To visualize the effects of aging on the topography of the underlying cortical maps, we reconstructed somatosensory maps using a computer-based interpolation algorithm based on a linear least square approximation of sampling coordinates of penetration sites and corresponding receptive field centers. (*c*, *d*) Reconstructions of a cortical hind paw representation are shown for control and for old rat, respectively. Examples of cortical topographies represented as a regular lattice within somatosensory cortex (*left*). Extrapolated cortical representation of a schematic and standardized drawing of the hind paw (*middle*). Dashed lines indicate horizontal, and solid lines the vertical, components of the lattice. One square of the lattice represents 1 mm^2 skin area. Diamonds indicate penetration sites; squares give the interpolated RF centers. Dotted lines give the deviation between them. Backprojection of the regular lattice of the cortical map onto the hind paw (*right*). Squares give the interpolated, and stars the measured, RF centers. One square of the lattice represents the skin portions that is represented by 0.01 mm^2 cortical area. According to these reconstructions, maps of the hind paw representation recorded in old animals, characterized by a selective impairment of the hindlegs show a dramatic distortion of their representational maps and a loss of topographic order. (Modified from Spengler, Godde, and Dinse 1995; Jürgens and Dinse 1997b. Panels *c* and *d* reprinted with permission from Spengler et al. © [1995] Lippincott Williams & Wilkins.)

Taken together, these studies suggest that small alteration in behavior due to special demands imposed in everyday life alters early cortical representations rapidly and reversibly. The summarized studies imply that wearing a cast for some weeks due to a broken limb should be sufficient to alter associated maps of somatosensory and motor cortex (for discussion of perceptual consequences, see section 2.3).

From a more general point of view, the findings on age-related changes in the somatosensory system extend the concept of use-dependent plasticity to high age. There is growing evidence from human studies that sensorimotor processing is more closely related to cognition than previously thought (Grady and Craik 2000). Aging gives rise to an increasingly strong association between sensory and cognitive functioning (Baltes and Lindenberger 1997).

2.3 Relevance of Adaptational Changes from Noninvasive Imaging Studies in Humans

The recent development of noninvasive imaging techniques has made it possible to study the impact of modified use and practice in humans. (For an overview of the modern imaging techniques currently employed in human studies, see, chapter 7, this volume.) Imaging studies have provided overwhelming evidence that extensive use and practice result in substantial changes of associated cortical representations in blind Braille readers (Pascual-Leone and Torres 1993; Sterr et al. 1998a,b), in players of string instruments (Elbert et al. 1995), in other musicians (Pantev et al. 1998), and in subjects given long-term perceptual training in tactile discrimination (Spengler et al. 1997). Of particular interest are findings on cross-modal plasticity in blind subjects (Sadato et al. 1996; Cohen et al. 1997, 1999; Röder, Rösler, and Neville 1999; Röder et al. 1999). Furthermore, cortical reorganization of the finger representation extending several millimeters was observed in adults studied before and after surgical separation of webbed fingers (syndactyly; Mogilner et al. 1993), a finding reminiscent of what had been reported some years ago for artificial induction of syndactyly in monkeys (Clark et al. 1988).

Taken together, human studies confirm the close relation between intensified use and enlargement of associated cortical representational maps thus supporting the relevance of the concept of cortical plasticity for everyday life.

What are the functional implications of these changes? Although, as discussed above (see section 2.1.5), the observed effects are assumed to be the substrate mediating the altered performance, there is controversy about the specificity of the neural changes that accompany perceptual changes. According to one view, the adaptational changes are highly specific, allowing for improvement of the trained motor or perceptual skill only: neural changes arising during training are assumed to have little effect on information processing beyond that skill. According to an alternative view, neural changes result in a widespread modification of sensory processing overall; changes in perceptual and cognitive skills generalize widely beyond the trained task. In other words, there is controversy over whether a specific improvement is paralleled by other perceptual changes, independent of the trained performance. There is evidence, for example, that many aspects of auditory processing in blind subjects are superior to those in normally sighted subjects (see Hollins 1989; see also Röder, Rösler, and Neville 1999, 2000). Pascual-Leone and Torres (1993) reported increased sensory representation of the reading finger in blind Braille readers, but no change in their spatial two-point discrimination abilities, whereas Axelrod (1959) found evidence of improved discrimination perfor-

mance in such readers. More studies are needed to resolve this controversy and to clarify how far perceptual changes extend across different forms of specific adaptations and skills (see also section 2.8).

Although extremely beneficial in revealing signatures of cortical plasticity, human studies of the type discussed cannot determine the "driving factors" behind cortical reorganization. The exact nature of inputs in a physical stimulus pattern is difficult, if not impossible, to assess. What is needed, therefore, are complementary studies that investigate cortical reorganization induced by a systematic variation of input pattern.

2.4 Role of Input Statistics

Although many lines of evidence have shown that the somatosensory system adapts to input pattern of different probabilities, whether—without cognitive processes—variation of input statistics alone suffices to reorganize cortical maps is a matter of long-standing debate. Accordingly, studies that directly address the role of input probabilities for adaptational processes are needed to provide insight into principles and constraints governing adaptational processes.

2.4.1 Intracortical Microstimulation

A technique to evoke selective motor responses by applying current through microelectrodes inserted into defined regions of motor representations, intracortical microstimulation (ICMS) has more recently been employed to study short-term and reversible plastic changes in motor, somatosensory, auditory, and visual cortex as well as thalamic relay nuclei of the somatosensory system (Nudo, Jenkins, and Merzenich 1990; Dinse, Recanzone, and Merzenich 1990, 1993; Recanzone, Merzenich, and Dinse 1992; Spengler and Dinse 1994; Sil'kis and Rapoport 1995; Gu and Fortier 1996; Kimura, Melis, and Asanuma 1996; Maldonado and Gerstein 1996a,b; Joublin et al. 1996; Xing and Gerstein 1996; Dinse et al. 1997). ICMS allows researchers to investigate the properties of functional plasticity locally—independently of the peripheral and subcortical pathways and independently of the constraints provided by particularities of a sensory pathway and its preprocessing. In a typical ICMS experiment, repetitive electrical pulse trains of very low currents (usually less than 10 μA) are delivered via a microelectrode. Based on theoretical calculations, ICMS of that intensity was assumed to activate a cortical volume of only 50 microns in diameter (Stoney, Thompson, and Asanuma 1968) supporting the locality of the changes. Synchronized discharges are generated, which are assumed to play a crucial role in mediating plastic changes. The short timescale and reversibility of ICMS effects supported the hypothesis that modulations of synaptic efficiency in neuronal networks occur very rapidly without necessarily involving anatomical changes.

In the rat motor cortex, border shifts in movement representations exceeding 500 microns were observed after a few hours of ICMS (Nudo, Jenkins, and Merzenich 1990). Application of ICMS in the hind paw representation of the adult rat somatosensory cortex caused an overall but selective expansion of receptive field size (Recanzone, Merzenich, and Dinse 1992; Dinse, Recanzone, and Merzenich 1993; Spengler and Dinse 1994). Receptive fields close to that of the stimulation site were enlarged, and comprised large skin territories always including the RF at the ICMS site, revealing a distance-dependent, directed enlargement toward the ICMS receptive field. Early ICMS-related reorganization could already be detected after 15 minutes of ICMS, and much greater effects emerged after 2 to 3 hours. Changes were reversible within 6 to 8 hours after

termination of ICMS (Dinse, Recanzone, and Merzenich 1993; Spengler and Dinse 1994).

Neural groups and assemblies are thought to be subject to modification during reorganizational processes. Using ICMS, researchers can directly address the question of dynamic changes of neural assembly membership (cf. 2.7). ICMS resulted in a significant enhancement of correlated, synchronized neural activity that paralleled changes of cortical RFs and cortical maps (Dinse, Recanzone, and Merzenich 1990, 1993). Similar results have been obtained for plastic changes in auditory cortex (Maldonado and Gerstein, 1996a,b). Where cortical neurons exhibited highly synchronous oscillatory firing patterns that were enhanced by ICMS, depending on the anatomical distance between the two neurons: ICMS changed the strength and the local number of such correlations. Overall, the results obtained with intracortical microstimulation demonstrated the capacity for cortical plasticity in the absence of peripheral stimulation.

2.4.2 Coactivation Studies

To study the effects of input statistics systematically, a number of protocols have been introduced in which the neural activity needed to drive plastic changes was generated by simultaneous, associative pairing (Diamond, Armstrong-Jones, and Ebner 1993; Wang et al. 1995; Godde, Spengler, and Dinse 1996; Godde et al. 2000). In a pioneering study by Frégnac et al. (1988), functional persistent changes in response properties of single neurons of cat visual cortex were induced by a differential pairing procedure, during which iontophoresis was used to artificially increase the visual response for a given stimulus and decrease the response for a second stimulus. In contrast, the protocols described below used a pairing of adequate (tactile) stimuli.

In Diamond, Armstrong-Jones, and Ebner 1993, sensory experience was altered by a few days of "whisker pairing": whiskers D2 and either D1 or D3 were left intact, whereas all other whiskers were trimmed. Reorganizational changes were assessed in terms of response amplitude evoked by single neurons recorded in the corresponding barrel field representations of somatosensory cortex. During the period of whisker pairing, the RFs of cells in barrel D2 changed in distinct ways: the response to the center RF, whisker D2, increased. The response to the paired surround RF whisker nearly doubled, and the response to all trimmed, unpaired surround RF whiskers decreased. After whisker pairing, the response to the paired neighbor of D2 was more than twice as large as the response to the trimmed neighbor of D2. These findings indicate that a brief change in the pattern of sensory activity induced by pairing of tactile stimuli can alter the configuration of cortical RFs of adult animals.

To test the hypothesis that consistently noncoincident inputs may be actively segregated from one another in their distributed cortical representations, monkeys were trained to respond to specific stimulus sequence events (Wang et al. 1995). Animals received temporally coincident inputs across fingertips and fingerbases, but distal versus proximal digit segments were noncoincidentally stimulated. Electrophysiological mapping experiments in area 3b showed that synchronously applied stimuli resulted in integration of inputs in the cortical maps, whereas stimuli applied asynchronously were segregated. In contrast to those in normal control animals, cortical maps in trained animals were characterized by two bandlike zones in which all neurons had multiple digit RFs representing the stimulated skin surfaces. These two zones were separated by a region containing normal single-digit RFs. This segregation was further augmented by a band of units responding

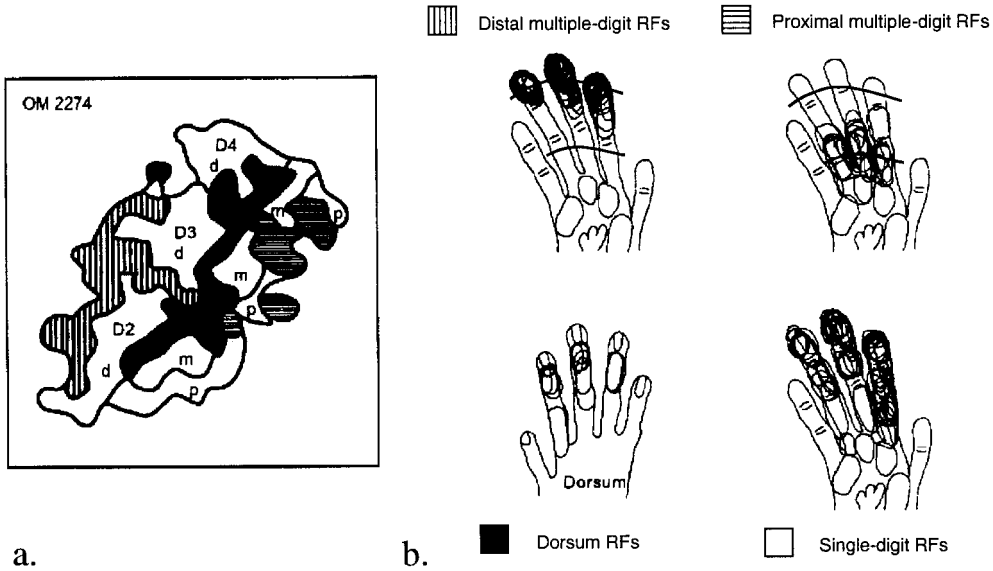


Figure 2.3
Typical reorganized cortical map of a hand in area 3b and receptive fields derived in an owl monkey engaged in a behavioral training to discriminate tactile stimulus sequences delivered to the hand by two narrow bars. One bar stimulated a narrow line of skin across the distal segments of the digits 2, 3, and 4; the second bar excited a narrow line of skin crossing the proximal segments of the same three digits (thin lines in panel b). The training resulted in temporally coincident inputs across fingertips and finger bases, whereas the distal versus proximal digit segments were noncoincidentally stimulated. (*a*) The reorganized map shows that in contrast to normal maps, a significant portion of the map exhibited multiple receptive fields that were specific to either the proximal (horizontal striping) or distal (vertical striping) portions of the digit. Interestingly, both regions representing the trained skin surfaces became segregated by a band of single-digit receptive fields (white) and a band of receptive fields located on the dorsum of the hand (black). (*b*) The corresponding receptive fields are sorted according to the four classes observed: distal multiple-digit, proximal multiple-digit, dorsum, and single-digit receptive fields. (Modified from Wang et al. 1995; Buonomano and Merzenich 1998a. Reprinted with permission from the *Annual Review of Neuroscience*, vol. 21 © 1998 by Annual Reviews www.AnnualReviews.org. Physiological Society. Reprinted by permission from *Nature* © 1995 Macmillan Magazines Ltd.)

to dorsal skin inputs, both features are normally not present in area 3b finger representations (figure 2.3). Interestingly, maps derived in the ventroposterior portion of the thalamus (VPL) were not equivalently reorganized suggesting that this particular type of representational plasticity appears to be cortical in origin.

In Godde, Spengler, and Dinse 1996, non- or only partially overlapping receptive fields on the hind paw of adult rats were used for coactivation in order to study effects of simultaneous stimulation. The authors reported reversible reorganization, namely, selective enlargement of the cortical territory and of the receptive fields representing the stimulated skin fields, as well as emergence of a large representation that included a joint representation of both sites (figure 2.4). A control protocol of identical stimulus patterns applied to only a single skin site evoked no changes,

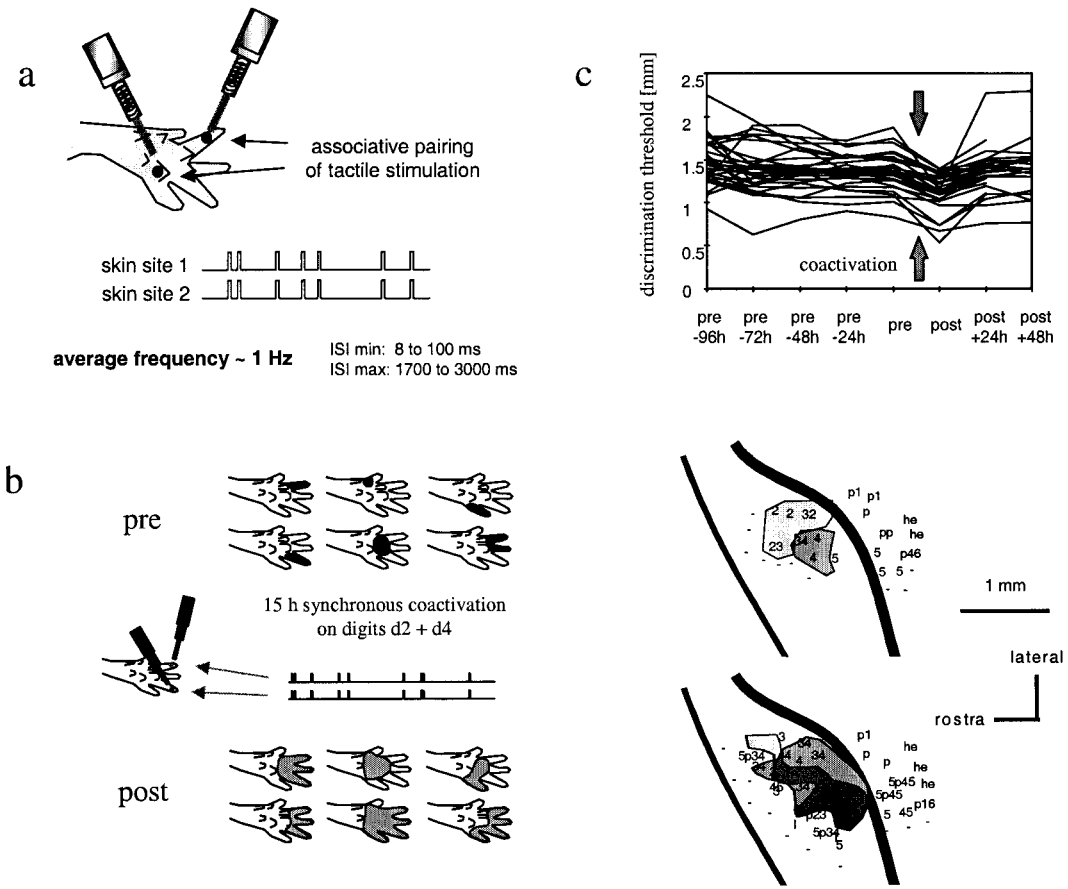


Figure 2.4

Scheme of the tactile coactivation protocol as utilized by Godde et al. (1996, 2000). (*a*) Two locations on the skin were simultaneously stimulated for several hours with computer-controlled tactile stimulators. Example of the time course of stimulation is shown. Average frequency is about 1 Hz. (*b*) Changes of receptive fields (RFs) as compared to control condition (*top left*) after coactivation (*bottom left*) performed on d2 and d4 are characterized by a dramatic enlargement of RF size. Note that, after coactivation, digit RFs cover always all of the skin surface of the coactivated digits d2 and d4. Cortical maps derived before (*top right*) and after (*bottom right*) coactivation on d2 and d4. Black lines indicate blood vessels, penetration sites are marked. Numbers indicate digits 1 to 5, p, pads; he, heels. Bars indicate locations where cells could not be driven by low threshold cutaneous inputs. Cortical territories representing d2 or d4 are denoted by different grays. Dark gray indicates zone of overlap between both representations, that is, a common representation of d2 and d4. After coactivation, cortical territory representing the coactivated skin sites increased significantly; new skin representations containing the stimulated skin fields emerged up to 400 microns beyond the control boundaries, whereas recording sites that were more rostral maintained their unresponsiveness. Note also the emergence of a large common representation of both skin sites not present under control conditions. (*c*) Tactile two-point discrimination thresholds of the index finger of the right hand as measured in a two-alternative forced-choice discrimination experiment in thirty-five right-handed human subjects. Thresh-

indicating that coactivation was essential for induction. The selective and local changes within the cortical map imply that early sensory cortical processing was affected: only those areas undergoing a specific alteration in input reorganized.

To demonstrate the perceptual relevance of neural changes induced by the coactivation protocol, Godde et al. (2000) investigated spatial discrimination performance in human subjects given similar passive costimulation of the tip of the index finger. Using discrimination thresholds to mark reorganizational effects due to variation of input statistics on human perception, they found that two hours of coactivation sufficed to drive a significant improvement of the spatial discrimination performance. These results demonstrated the potential role of pure input statistics in inducing cortical plasticity without involving cognitive factors such as attention or reinforcement (figure 2.4; see also section 2.8). A combined assessment of discrimination thresholds and recording of somatosensory evoked potentials in human subjects revealed that the individual gain of discrimination performance was correlated with the amount of cortical reorganization in primary somatosensory cortex as referred from the shifts of the location of the N20 dipole (Pleger et al. 2001).

The coactivation protocol allows complete control of timing and amount of stimulation. Using asynchronous rather than synchronous stimulation resulted in reorganizations characterized by a large separation of both stimulated skin sites (Zepka, Godde, and Dinse 2000).

Similarly, Liepert, Terborg, and Weiller (1999) reported that about an hour of synchronous movements of the thumb and foot resulted in a reduction of the distance of the center of gravity of their respective output maps in area MI as measured by TMS, whereas asynchronous movements evoked no significant changes, indicating that similar principles of coactivation hold for both the sensory and motor system.

Recanzone, Merzenich, et al. (1992) recorded only modest increases in topographic complexity in cortical hand representations for passively stimulated hands and no effects on RF size or overlap. On the other hand, the coactivation studies discussed above showed a clear effect on both cortical and perceptual levels, even though attention was not involved. In the human discrimination experiments, subjects were instructed not to attend the stimulation; indeed, during the several hours of coactivation all subjects continued their normal business work. Conceivably, the engagement in normal day work had not been possible without the simultaneous attentive engagement in other perceptual and motor tasks. One explanation is that during the coactivation protocol, which was, on average, applied at a rate of 1 Hz for several hours, selected skin regions were stimulated 10,000 times or more, a much higher frequency of stimulation than that given the monkeys during the passive discrimination training. Conceivably, the intensity of the stimulation protocol might be the crucial factor responsible for its effectiveness. As stated in section 2.1.6, adaptational changes and parallel improvement of performance can be evoked by changes in input statistics provided the statistics are sufficiently altered.

Coactivation studies of this type are instrumental in providing insight into the role of timing parameters

olds were measured five days before and immediately after coactivation (arrows) and on two subsequent days. In all subjects, thresholds were reduced immediately after coactivation but returned to control values one day after coactivation, revealing a time course of reversibility similar to that described for the electrophysiological reorganizational changes in rats. Control experiments performed on the index finger of the opposite hand, which received no coactivation, showed no changes. (Modified from Godde, Spengler, and Dinse 1996. Reprinted with permission. © [1996] Lippincott Williams & Wilkins.)

that control reorganization in animals and humans: they allow researchers to experimentally assess the time window that defines simultaneity; to relate neural changes as measured in animals with psychophysical performance as assessed in humans; and thereby to explore the perceptual relevance of simple paradigms that successfully induce adaptational changes at the neuron level.

2.5 Therapeutic Consequences of Somatosensory Adaptations

The final outcome of reorganizational process need not be beneficial. There is increasing evidence that abnormal perceptual experiences such as the phantom limb sensation arise from reorganizational changes induced by the amputation of the limb. A strong relationship has been reported, but not for nonpainful phantom phenomena experienced after arm amputation, implying that these changes are maladaptive rather than adaptive (Flor et al. 1995). By contrast, neuromagnetic source imaging revealed minimal reorganization of primary somatosensory cortex in congenital amputees and in traumatic amputees not suffering from phantom limb pain (Flor et al. 1998). These data indicate that phantom limb pain is related to, and may be a consequence of, plastic changes in primary somatosensory cortex. Interestingly, recent studies reported a decrease of phantom limb pain associated with prosthesis-induced use of the stump (Weiss et al. 1999) and with less related reorganization in the motor cortex (Lotze et al. 1999). The precise topographic mapping of the phantom limb onto the face area was explained in terms of the topography of the border of the face-hand maps (Ramachandran, Stewart, and Rogers-Ramachandran 1992; Halligan et al. 1993; Aglioti et al. 1997).

The power of the early evoked magnetic field elicited by painful stimulation was elevated in patients with chronic pain relative to that elicited by painful back stimulation in healthy controls. Furthermore, this enlargement showed a linear increase with chronicity of pain (Flor et al. 1997), suggesting that the cortical reorganization that accompanies chronic pain may serve an important function in its persistence.

Repetitive strain injuries including occupationally induced focal dystonia have a high prevalence in workers who perform heavy schedules of rapid alternating movements or repetitive, sustained, coordinated movements. It has been hypothesized that use-dependent plastic changes such as those reviewed above may cause repetitive strain injuries characterized by sensory dysfunction and impairment of motor control (Byl, Merzenich, and Jenkins 1996; Byl et al. 1997). This view is supported by studies showing that monkeys trained in repetitive hand closing and opening developed typical movement control disorders indicated by a 50% drop in motor performance. Electrophysiological mapping within the primary somatosensory cortex revealed a dedifferentiation of cortical representations of the skin of the trained hand, manifested by receptive fields 10 to 20 times larger than normal, as well as by a breakdown of the receptive field topography (Byl, Merzenich, and Jenkins 1996). Thus repetitive, highly stereotypic movements can actively degrade cortical representations of sensory information guiding fine motor hand movements. Using MEG, Elbert et al. (1998) found a smaller distance between the representations of the digits in somatosensory cortex for the affected hand in musicians suffering from focal hand dystonia than for the hands of nonmusician control subjects, indicating that central reorganization develops as a consequence of repetitive strain injuries in humans as well (see also chapter 7).

The maladaptive consequences of cortical plasticity have become increasingly acknowledged as a major factor in various forms of dysfunctions. For example,

a negative outcome of neuroplasticity may play a major role in some forms of age-related changes. Jürgens and Dinse (1997b) found that walking impairments that develop in rats of high age as a secondary response to muscle atrophy and to other factors promoting limited agility were the result of maladaptive cortical reorganizations.

2.6 Subcortical Plasticity

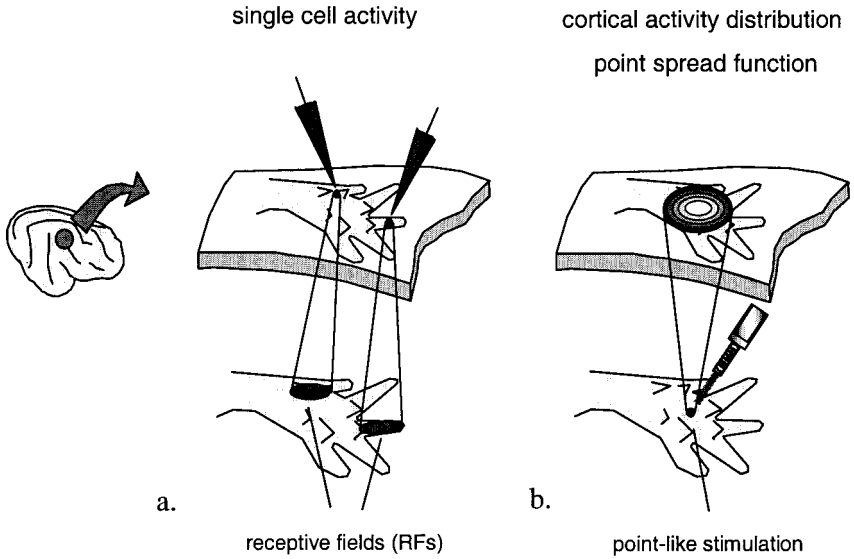
Studies of subcortical and brain stem structures have clearly shown that reorganizational changes occur along the entire sensory pathway (Wilson and Snow 1987; Garraghty and Kaas 1991; Nicolelis et al. 1993; Pettit and Schwark 1993; Florence and Kaas 1995; Faggin, Nguyen, and Nicolelis 1997; Jones and Pons 1998; Nicolelis, Lin, and Chapin 1997; Hubscher and Johnson 1999; Xu and Wall 1997, 1999; Woods et al. 2000). On the other hand, cortical changes have been reported in the absence of parallel subcortical changes. Accordingly, there are still many open questions about the role of subcortical substrates. For example, Wang and coworkers (1995) did not find topographic changes in the thalamic relay nucleus comparable to those in area 3b after coactivation, as described in section 2.4.2. Similarly, Tinazzi et al. (1997) could not find parallel subcortical changes after transient deafferentation in humans. Dinse et al. (1997) found that applying microstimulation in the thalamus had little effect on RF size when compared to applying such microstimulation directly in cortex.

Of course, the central question behind these studies is exactly what role cortices play in the overall processes of reorganization (Darian-Smith and Gilbert 1995; Fox 1994; Florence, Taub, and Kaas 1998; Kaas and Ebner 1998; Kaas 1999; Kaas, Florence, and Jain 1999). Much of the plasticity encountered at a subcortical level may depend on feedback connections from the cortex (Ergenzinger et al. 1998; Krupa, Ghazanfar, and Nicolelis 1999). Furthermore, the usually extensive cortical reorganizations may in part depend on activation of the widespread horizontally connected network that is lacking in thalamic nuclei.

2.7 Beyond Receptive Fields

Earlier work on cortical reorganization concentrated largely on the analysis of receptive fields and on the areal extent of representational maps. Both variables still figure widely in current research, and abundant data have allowed researchers to make valuable comparisons between different species and modalities (box 2.2). In addition, new imaging techniques, such as fMRI, have allowed them to study adaptational changes in humans more precisely, to describe changes in neural representations in terms of the activation size of cortical maps, and thereby to link human and animal studies. Temporal aspects of coding have become increasingly prominent; consequently, synchronicity and correlated activity have been intensively studied (see 2.4.1, figure 2.5). There is now substantial evidence that cooperativity among many neurons is subject to modification during plastic reorganization, implying that changes in temporal coding are important or even crucial to use-dependent plasticity. This evidence supports the hypothesis that neural assembly membership is organized along primarily dynamic lines (for theoretical work, see Edelman and Finkel 1984; Braitenberg 1986; von der Malsburg 1987; Aertsen et al. 1989; Abeles 1991; Shenoy et al. 1993; for experimental work, see Dinse, Recanzone, and Merzenich 1990, 1993; Ahissar et al. 1992, 1998; Nicolelis et al. 1993; Nicolelis, Lin, and Chapin 1997; Maldonado

Box 2.2



Two different ways to assess cortical maps, activity distributions, and receptive fields. (*a*) Action potentials from single neurons or from small clusters of neurons are measured by inserting microelectrodes into the middle layers of the cortex. The receptive field on the skin surface is defined as that region where stimulation evokes action potentials. This procedure maps activity recorded in the cortex into the stimulus space that allows an easy and systematic way of parametric analysis. When moving the electrode to an adjacent location in the cortex, a systematic shift in the corresponding receptive field location will be encountered. A complete topographic map can be obtained when a large number of electrode penetrations are combined such that the penetration coordinates are related to the corresponding receptive field coordinates. (*b*) Cortical activity distributions are measured. In contrast to panel *a*, a fixed stimulus, ideally a small, "pointlike" stimulus, is applied, and the entire activity in the cortex evoked by that stimulus is measured. This type of activity distribution if often referred to as "point spread function" (PSF). Technologies used for this kind of analysis are optical and functional magnetic resonance imaging. It should be noted, however, that the PSF can be obtained using microelectrodes, in which case the activity of single or multiple neurons evoked by the "pointlike" stimulus is recorded and its spatial distribution is derived from a systematic mapping of that response at different locations.

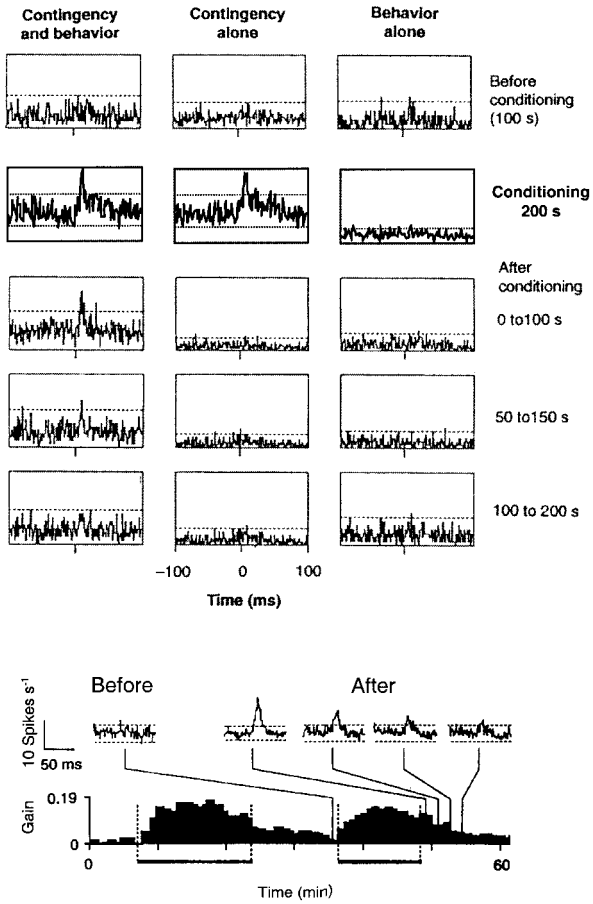


Figure 2.5
Pairs of neurons were recorded in a monkey performing an auditory discrimination task. The dependence of functional plasticity on the contingency between activities of two neurons and on behavior was tested by a combination of cellular conditioning and behavioural paradigms. The activity of one neuron in each pair (CS neuron) was regarded as the conditioned stimulus (CS); the activity of the other neuron (CR neuron), as the conditioned response (CR). An auditory stimulus capable of eliciting or suppressing activity in the CR neuron was used as unconditioned stimulus (US), which was used both for pairing the activities of the two neurons and for guiding the monkeys performance in an auditory discrimination task. There were three conditions: conditioning with behavior (contingency and behavior), conditioning without behavior (contingency alone), and pseudoconditioning (behavior alone) that occurred when the monkey performed the task but the contingency between neurons was not affected. *Top*, cross-correlograms (top) show effect of modification of functional connections between neuron pairs. Uppermost row shows control condition, with no significant correlations between the shown neuron pair; second row shows conditioning condition, with correlated activity both for contingency and behavior and for contingency alone. Interestingly, persistent changes in functional connectivity require the establishment of contingency together with behavior. *Bottom*, example of functional plasticity as a function of time, with periods of conditioning indicated by the filled horizontal bars. Cross-correlograms before and after the second conditioning are presented above to indicate changes in functional plasticity. Gain of connection was defined as peak area in correlograms. As shown, the gain was enhanced during the first conditioning period (left) and remained strong after conditioning was stopped (right). The potentiation was extinguished during the next minutes of spontaneous activity; the second conditioning was then applied, yielding similar results. (Modified from Ahissar et al. 1992.) Reprinted with permission. © [1992] American Association for the Advancement of Science.)

and Gerstein 1996a,b; Faggin, Nguyen, and Nicolelis 1997; Ghazanfar, Stambaugh, and Nicolelis 2000; Laubach, Wessberg, and Nicolelis 2000).

Nevertheless, temporal processing, that is, the computation of sequential events, is still poorly understood. The severe temporal constraints imposed by timing and sequencing modulate neuron responses and reveal response properties not apparent under steady state conditions using solitary stimulation: moreover, the analysis of timing and order effects allows researchers to directly link cortical with behavioral studies. Indeed, there is clear experimental evidence that repetitively applied stimuli evoke cortical responses that differ from those evoked by a single stimulus isolated in time (Gardner and Costanzo 1980; Lee and Whitsel 1992; Dinse 1994;

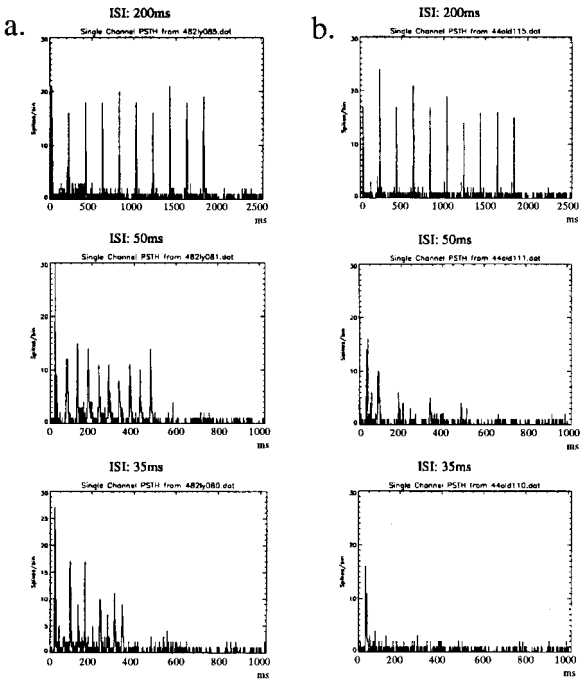


Figure 2.6
The effect of aging on temporal sequence representation was investigated using trains of 10 tactile stimuli of variable interstimulus intervals (ISIs). (*a*, *b*) Examples of post-stimulus-time histograms (PSTHs) recorded in young and in old rat, respectively. ISIs used were 200 msec, 50 msec, and 35 msec. Bin size was 1 msec; neural activity in spikes per bin is plotted on the ordinate, time on the abscissa. Each PSTH gives the response accumulated over 32 trials; pause between each single trial was 5 sec. For a slow repetition rate of tactile stimuli, neurons recorded in young and old rats follow truthfully each stimulus, which evoked about the same peak activity. Whereas neurons recorded in the young rat can still represent the sequence of stimuli delivered at an ISI of 50 msec, those recorded in the old rat manifest a significant deterioration in their ability to follow this sequence. This failure to represent fast sequences becomes even more dramatic at an ISI of 35 msec. In addition to massive changes of topography developing during aging (see figure 2.2), there is also a significant deterioration of temporal processing abilities, which are also correlated to the behavioral status of the hind limb: the temporal deficits can be ameliorated by housing the animals in an enriched environment. (Modified from Jürgens and Dinse 1995; Churs et al. 1996.)

Merzenich et al. 1993; Tommerdahl et al. 1996, 1998; Polley, Chen-Bee, and Frostig 1999a).

Thus far, few researchers have related changes in temporal processing to parallel changes in perception. Recanzone, Merzenich, and Schreiner (1992) demonstrated that behavioral training of a frequency discrimination task affected entrainment of repetitive stimuli (see figure 2.1). Jürgens and Dinse (1995; see figure 2.6), using trains of repetitive tactile stimuli of variable interstimulus intervals (ISIs), observed dramatic impairment of repetition coding and input sequence representations in the hind paw representation of old rats as compared to young controls. They found comparable changes of the neural input sequence representation in rats with artificially induced walking alterations (Jürgens and Dinse 1997a). Other researchers (Buonomano 1999; Buonomano and Merzenich 1998b), in their in vitro studies, demonstrated a different susceptibility between first and later excitatory postsynaptic potentials (EPSPs) to time-varying stimuli for neocortical slices, indicating that the balance of different time-dependent processes can modulate the state of networks in a complex manner.

It has been suggested that a dysfunction in normal phonological processing, which is critical to the development of oral and written language, may derive from difficulties in perceiving and producing basic sensorimotor information in rapid succession. Indeed, children with language-based learning impairments of this type, when given adaptive training in temporal processing, showed marked improvement in their ability to recognize brief and fast sequences of non-

speech and speech stimuli, suggesting that the reorganizational changes are specifically sensitive for temporal parameters of the input. (Tallal, Miller, and Fitch 1993; Merzenich, Jenkins, et al. 1996; Tallal et al. 1996).

Thus adaptational processes alter both spatial and temporal aspects of sensory processing, which has implications for all forms of perceptual learning, and specifically for tasks involving spatiotemporal proximity such as interval or saltation learning (Geldard and Sherrick 1972; Cholewiak 1976; Kilgard and Merzenich 1995).

2.8 Coding of Adaptational Changes

Changes in receptive fields, cortical maps, correlated activity, and temporal sequence processing (see figure 2.7) clearly suggest that use and training alters cortical processing. Yet, in most cases, the causal link between neural changes and changes in performance remains to be clarified. Recanzone, Merzenich, and coworkers (1992) pointed out that there was no correlation between increased RF size and performance. In contrast, the enhancement of temporally coherent responses correlated strongly with the discriminative performances (Recanzone, Merzenich, and Schreiner 1992).

Indeed, many studies have reported an increase in receptive field size in response to a broad spectrum of different forms of induction of adaptational changes. This frequently observed phenomenon makes it difficult to attribute a specific coding aspect to RF size. It could be that strengthening of synapses during a Hebbian learning process inevitably leads to RF enlargement with little bearing on behavior. From a methodological point of view, assessment of RF size is usually done by hand-plotting techniques that provide scant information about the internal organization of receptive fields and their spatial substructures. Accordingly, subtle but highly task-specific and more complex changes in RF organization that are easy to miss experimentally may contribute to an improvement of perceptual performance. On the other hand, several potential mechanisms can result in RF enlargement: downregulation of inhibitory surrounds; strengthening of excitatory, previously subthreshold RF regions; enhanced, synchronized discharge resulting in lowering of thresholds; or a mixture of all these putative mechanisms. In any event, monitoring RF size without monitoring the mechanisms underlying changes in RFs will yield only limited insight into the meaning of the changes.

For the tactile coactivation protocol described above, Godde and coworkers (Godde, Spengler, and Dinse 1996; Godde et al. 2000) observed an RF increase in rats and a lowering of the discrimination threshold in human subjects. Assuming that the coactivation protocol results in comparable changes in both man and rat, the enhancement of the discrimination performance appears at first sight to contradict the reported receptive field enlargement. A discrepancy between perceptual thresholds and single-neuron properties is not a new finding, however. For example, Westheimer (1979) found that hyperacuity could not be explained in terms of the receptive field sizes of single cells. Coactivation-induced plasticity included enlargement of receptive fields, accompanied by increased receptive field overlap and enlargement of the representational maps, which, in turn, reflected an increase in the total number of neurons activated by the stimulation and thus of processing resources. Temporal aspects of neuron responses were also changed in terms of response duration and paired pulse behavior. It appears reasonable that all these changes, in concert, enable cortical networks to perform a faster and more elaborate decoding and processing of information.

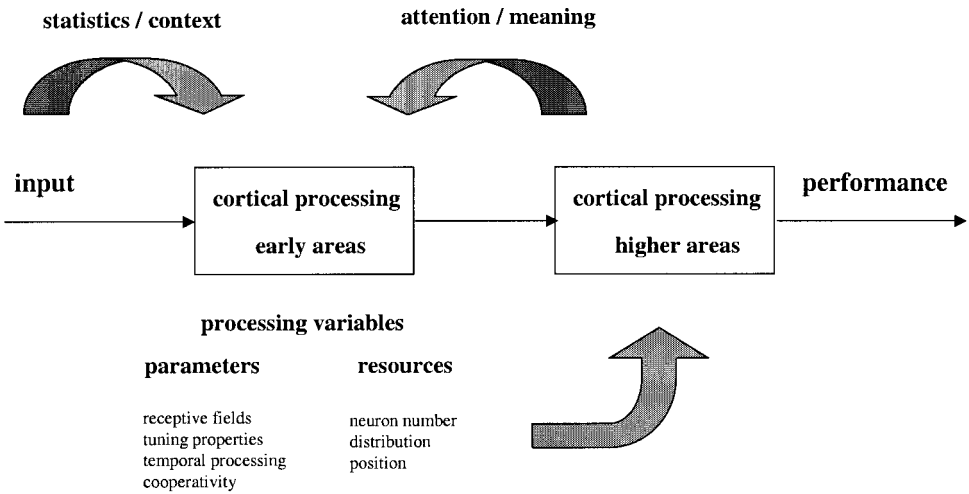


Figure 2.7
Scheme of adaptational processes and interaction with information processing. The main driving forces of adaptations are input statistics and context, on the one hand, and attention and meaning, on the other; by acting bottom-up and top-down, respectively, these modify information processing. Among the parameters subject to modification by adaptational processes are the typical descriptors of cortical processing such as receptive fields, tuning properties, and various aspects of temporal processing and cooperativity among many neurons. In addition to training- or use-specific alteration of such parameters, processing resources can be adjusted according to the requirements of the behavioral status.

In the psychophysical experiments performed by Godde and coworkers (2000), spatial discrimination, but not localization abilities were tested. Evidence for a trade-off between localization and discrimination can be inferred from Sterr et al. 1998a, which reported that stimuli were more often mislocalized on the reading fingers of three-finger Braille readers than on control fingers (see chapter 7). This finding suggests that spatial discrimination performance might benefit from enlarged receptive fields at the expense of localization performance. Thus further understanding of what is coded requires not only detailed analysis of neural changes, but also a broad battery of psychophysical and behavioral tests to find out what really is changed, what is improved, and what may become impaired.

From a theoretical point of view, the "coarse coding" principle (Hinton, McClelland, and Rumelhart 1986; Baldi and Heiligenberg 1988; Eurich and Schwegler 1997; Eurich et al. 1997) has been used to explain high-resolution performance by a population of neurons with broad tuning characteristics: given sufficient overlap between tuning curves, each desired resolution can be achieved. If we assume that it is not the property of a single cell that determines behavior, the coarse coding principle can be considered a variant of the more general population coding approach. Neural population analysis implies that large ensembles of neurons contribute to the cortical representation of sensory or motor parameters. Early formulations of this idea postulated that complex stimuli are represented by the simultaneous activation of elementary feature detectors (see Erickson 1974). In primary motor cortex, ensembles of neurons broadly tuned to the direction of movement have been shown to accurately represent the current

value of that parameter (Georgopoulos, Schwartz, and Kettner 1986). When Nicolelis and coworkers (1998) used simultaneous multisite neural ensemble recordings to investigate the representation of tactile information in areas 3b, SII, and 2 of the primate somatosensory cortex, they found that small ensembles consisting of 30–40 broadly tuned somatosensory neurons were able to identify correctly the location of a single tactile stimulus in a single trial. Similarly, for visual cortex, Jancke et al. (1999) showed that a population of neurons represented the actual position of a stimulus with deviations several times smaller than average receptive field size. Recently, it has become evident that a critical step in learning how distributed cell assemblies process behaviorally relevant information is identifying functional neuronal interactions within high-dimensional data sets (see Nicolelis 1999). By chronically recording neuronal ensembles in the rat motor cortex throughout the period required for rats to learn a reaction time task, Lauberg, Wessberg, and Nicolelis (2000) demonstrated an increase in the experimenter's ability to predict a correct or incorrect single trial based on measures such as firing rate, temporal patterns of firing, and correlated firing.

Thus there appears to be at least one simple rule of thumb: extensive use leads to an enlargement of representational areas, whereas limited or no use leads to a reduction in such areas, indicating a form of proportionality between representational area and use (see figure 2.8). As discussed above, representational size correlates with the number of neurons activated by a given task or stimulation, which suggests that enhanced performance is at least partially achieved by recruitment of processing resources.

Recent animal studies have challenged this view, however. Combining electrophysiological mapping and optical imaging of rat somatosensory cortex, Polley, Chen-Bee, and Frostig 1999b observed a large-scale expansion of a single whisker's functional

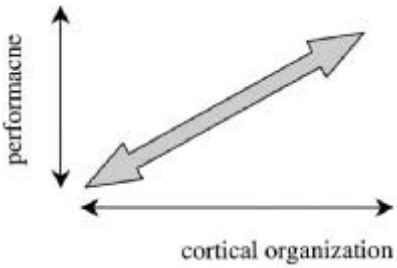


Figure 2.8
According to the summarized experimental evidence, there appears to be a proportionality between changes in behavioral performance and cortical organization, although the exact mapping of cortical changes into performance remains unclear.

representation after innocuous removal of all neighboring whiskers, but a large-scale contraction of the representation after the same procedure when the animal was given a brief opportunity to use its whiskers for active exploration of a different environment. Thus allowing the animal to use its deprived receptor organ in active exploration can determine the direction of plasticity in the adult cortex. Further studies are needed to explore whether a similar potential for a use-dependent direction of reorganizational changes holds true in normal (non-deprived) animals. From a more general point of view, this study suggests that the outcome of adaptations in the somatosensory system might depend on far more subtle constraints imposed by the individual task than previously thought.

Of course, part of the problem is the simple fact that even under normal conditions—without involving adaptive processes—sensory processing and the coding of performance are only poorly understood. That is why it is not clear what receptive field size means. Is it "good" when a tuning curve gets sharper? "Good" for what? The exploration of adaptivity should help us, not only to unravel the

mechanisms of learning, but also to better understand sensory coding and processing.

2.9 Conclusions

It is now well acknowledged that use-dependent plasticity can have a significant "negative" impact. Many forms of maladaptive consequences of cortical reorganization have been described. There are more and more examples of highly successful therapeutical intervention based on these findings about use-dependent plasticity. Yet many open questions remain. Among them are the origin and contributing role of subcortical plasticity, the link and interaction between cortical and higher cortical adaptations, and, most important, the coding and decoding of adaptational processes. Comparison of adaptations taking place in auditory and visual systems may shed light on how far somatosensory adaptations generalize in the typical learning processes of the adult brain.

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