Is there a thalamic component to experience-dependent cortical plasticity?

Kevin Fox^{*}, Helen Wallace[†] and Stanislaw Glazewski[‡]

School of Biosciences, Cardiff University, Museum Avenue, Cardiff CF10 3US, UK

Sensory deprivation and injury to the peripheral nervous system both induce plasticity in the somatosensory system of adult animals, but in different places. While injury induces plasticity at several locations within the ascending somatosensory pathways, sensory deprivation appears only to affect the somatosensory cortex. Experiments have been performed to detect experience-dependent plasticity in thalamic receptive fields, thalamic domain sizes and convergence of thalamic receptive fields onto cortical cells. So far, plasticity has not been detected with sensory deprivation paradigms that cause substantial cortical plasticity. Part of the reason for the lack of thalamic plasticity may lie in the synaptic properties of afferent systems to the thalamus. A second factor may lie in the differences in the organization of cortical and thalamic circuits. Many deprivation paradigms induce plasticity by decreasing phasic lateral inhibition. Since lateral inhibition appears to be far weaker in the thalamus than the cortex, sensory deprivation may not cause large enough imbalances in thalamic activity to induce plasticity in the thalamus.

Keywords: somatosensory; barrel cortex; ventro-posterior medial

1. INTRODUCTION

Synaptic plasticity is now regarded as one of the basic cellular properties underlying the normal function of the brain. Neuronal circuits employ synaptic plasticity during sensory processing (Fregnac & Schulz 1999) as well as for specialized functions such as memory storage and recall (Bliss & Collingridge 1993). To what degree is plasticity a property of intracortical circuits as opposed to thalamocortical circuits or purely thalamic circuits?

The results of a variety of experiments lead to the view that the thalamus plays a limited part in adult plasticity whereas it plays a prominent part in developmental plasticity. In the cat visual cortex, the geniculocortical afferents segregate into eye-specific ocular dominance domains during the first 2–6 weeks of life (LeVay *et al.* 1978). This process is controlled by the amount of visually driven activity coming from each eye, so that monocular deprivation leads to the geniculocortical afferents for the open eye occupying a greater territory than that occupied by those for the closed eye (Antonini & Stryker 1993). However, geniculocortical afferent plasticity shows a clear critical period ending at *ca.* six weeks in the cat (*Felis domesticus*) and two months in the monkey (*Macaca mulatta*) (Olsen & Freeman 1980; LeVay *et al.* 1980). At later ages, ocular dominance plasticity is restricted to intracortical circuits and the thalamic afferents remain stable (see Fox 1996).

A similar age dependency is seen in the rodent somatosensory system. During early postnatal development the thalamocortical afferents are plastic while they are still forming the barrels (Van der Loos & Woolsey 1973). However, plasticity decreases during the first four postnatal days (Woolsey & Wann 1976) and the thalamic afferents show no detectable plasticity to whisker deprivation beyond *ca.* four weeks of age (Fox 1996). At later ages, whisker deprivation plasticity does occur in the rat cortex indicating that the locus of plasticity has changed from thalamocortical to intracortical pathways (Fox 1994; Wallace *et al.* 2001).

So does this mean that the thalamus is not capable of plasticity in adulthood? There is certainly evidence for thalamic plasticity, or at least subcortical plasticity, in cases where the periphery sustains some injury or nerve inactivation. For example, upper limb deafferentation can lead to plasticity in VPI (Jones & Pons 1998) and acute inactivation of primary afferents can cause rapid cortical and thalamic remapping (Nicolelis *et al.* 1993) although even here, the thalamic remapping appears to depend on cortical feedback (Krupa *et al.* 1999).

In none of the experiments performed to date has it been shown that a change purely in sensory experience without peripheral nerve injury can produce thalamic plasticity in adults (Wang *et al.* 1995; Glazewski *et al.* 1998a). It may be that the thalamus does show experience-dependent plasticity in adult animals but the appropriate test has not yet been performed. Alternatively, it may be that the thalamus is not plastic beyond a certain age except under conditions of severe peripheral trauma, a condition that is likely to induce primary afferent and brainstem plasticity anyway (Li *et al.* 1995; Jones & Pons 1998). In this review, we consider some of the experiments aimed at measuring experience-dependent plasticity in the thalamus and compare thalamic and cortical responses to sensory deprivation paradigms.

^{*} Author for correspondence (foxkd@cf.ac.uk).

[†] Present address: Institute of Child Health, Alder Hey Children's Hospital, Eaton Road, Liverpool L12 2AP, UK.

[‡] Present address: McKay Institute of Communication and Neuroscience, Keele University, Staffordshire ST5 5BG, UK.

One contribution of 22 to a Discussion Meeting Issue 'The essential role of the thalamus in cortical functioning'.

2. METHODS OF INDUCING EXPERIENCE-DEPENDENT PLASTICITY

In the visual system, the methods used traditionally to induce plasticity cause experience-dependent plasticity without damage to any of the supporting neural system. For example, monocular deprivation in the cat, where an eye lid is sutured closed (Wiesel & Hubel 1965), or orientation deprivation in the cat, where the view of the world is restricted to a striped environment (Sengpiel *et al.* 1999), alter the range of visual experience without damage to the nervous system. Both methods produce profound plasticity within a critical period of development. As mentioned in § 1, in the rat and monkey somatosensory system, the methods used traditionally to induce plasticity lead to direct and indirect damage to the peripheral and central nervous system. For example, peripheral nerve transection or dorsal column lesions are used to induce somatotopic map plasticity (see Kaas *et al.* 1983). These studies are of great importance for understanding the changes that occur following injury, but they clearly involve at least two factors that simultaneously influence the plasticity of the nervous system:

- (i) the abrupt cessation of activity from the denervated sensory receptors; and
- (ii) the primary and in some cases, transynaptic degeneration of the afferent sensory pathways.

In order to disentangle these two factors, a number of studies have employed manipulations that just affect the sensory experience component without causing injury. These methods have usually been employed in adult or adolescent animals by contrast to the monocular deprivation studies that have been performed in immature animals. In the monkey, a procedure known as syndactyly involves fusing the skin surfaces from two adjacent fingers so that the animal is obliged to use them as a single digit (Clark *et al.* 1988; Wang *et al.* 1995). Syndactyly changes the receptive fields of the cortical neurons in the hand representation of the somatosensory cortex from predominantly single digit fields to ones that represent surfaces on both fingers. Similarly, univibrissae experience involves depriving a rodent of all its whiskers save one so that the animal is obliged to sense the world using a single whisker. This method produces an increased representation of the spared whisker in areas of the rodent somatosensory cortex that previously responded only weakly to that whisker (Hand 1982; Glazewski & Fox 1996).

It has been shown that univibrissae experience leads to a change in experience without any detectable damage to the ascending somatosensory pathways. The peripheral nerves show the same number of myelinated and unmyelinated axons before and after whisker deprivation and the somata of those nerves in the trigeminal ganglion show none of the classic signs of nerve damage normally associated with nerve injury such as changes in neuropeptide expression levels (Li *et al.* 1995). Consequently, if the whiskers are allowed to regrow, the responses of cells recorded in the trigeminal ganglion are identical before and after whisker deprivation (Glazewski *et al.* 1998a). By contrast, the responses of cells in the somatosensory cortex to stimulation of the regrown whiskers are very differ-

ent before and after deprivation, indicating that plasticity has occurred somewhere in the pathway between peripheral nerve and cortical cell.

In order to study where plasticity occurs and, in particular, to see if any experience-dependent plasticity might occur in the thalamus, other studies have employed a different form of whisker deprivation known as chessboard-pattern deprivation. Chessboard-pattern deprivation involves removal of every other whisker from the face of the animal. As a result, each deprived whisker is surrounded by four adjacent spared whiskers and every spared whisker is surrounded by four adjacent deprived whisker follicles. The pattern is therefore similar to the disposition of black and white squares on a chessboard.

Chessboard-pattern deprivation causes plasticity in the somatosensory cortex after just a few days (Wallace & Fox 1999). The responses to the spared whiskers are potentiated and the responses to the deprived whiskers, once they have been allowed to regrow, are depressed. Intracortical transmission between spared and deprived columns is accelerated, while transmission in the opposite direction, between deprived and spared columns, is retarded (Wallace & Fox 1999). Both potentiation and depression are dependent on cortical activity during the deprivation period. If cortical activity is blocked by chronic muscimol application neither potentiation nor depression occur (Wallace *et al.* 2001).

This result strongly indicates that experience-dependent plasticity occurs in the cortex and that one need not postulate the existence of subcortical plasticity to explain the effects of whisker deprivation on cortical receptive fields. Nevertheless, it is conceivable that subcortical plasticity occurs but that the effect is not relayed on to the cortex. If this idea is correct, it should be possible to measure plasticity in the thalamus.

3. TESTING FOR PLASTICITY IN THE THALAMUS

(a) *Average receptive-field responses*

When neurons are recorded in the VPM component of the thalamus to assess the size of their principal whisker response, it is found that the principal whisker evokes an average response of just over one spike per stimulus in normal rats (1.12 ± 0.08 spikes per stimulus, figure 1). Several investigators have made the same measurement independently and found almost identical values (Armstrong-James & Callahan 1991; Glazewski *et al.* 1998a; Wallace *et al.* 2001). Remarkably, where studies have measured the principal whisker response in VPM for animals undergoing chessboard-pattern deprivation, the responses appear to be almost identical to control values. Responses to the spared and deprived whiskers are again about one spike per stimulus (1.12 ± 0.04 spikes per stimulus for spared whiskers and 1.0 ± 0.04 spikes per stimulus for deprived whiskers, figure 1). This represents a 0% change in the spared whisker response and a statistically insignificant 11% decrease in the deprived whisker response.

In contrast to the lack of change in thalamus, studies have shown the same deprivation method leads to substantial changes in the cortex. In layer IV of the cortex, the responses evoked by spared whisker stimulation increase by 17% while responses to the deprived whiskers

Figure 1. Sensory responses to principal whisker stimulation before and after chessboard-pattern whisker deprivation in the rat. Left, thalamic responses to a standard one-degree whisker deflection are shown for spared (grey) and deprived then regrown (white) whiskers. The average thalamic responses for spared and deprived whiskers are not significantly different from one another nor are either different from values measured in control animals (undeprived, dashed line). Average responses for neurons recorded in layer IV of the cortex are very different for stimulation of their principal whisker dependent on whether it has been deprived or spared. The responses to deprived whiskers are substantially smaller than control values (dashed line) in the principal barrel whereas responses to spared whiskers are slightly greater (adapted from Wallace *et al.* (2001)).

decrease by 35%. The effect on the spared whisker responses is even greater outside the principal barrel in the near neighbouring barrel where responses increase by 120% (Wallace & Fox 1999). Similarly, the effect on the deprived whisker responses is even greater in layers II/III (one stage beyond the cortical input layer) where responses are 48% lower than control (Wallace & Fox 1999).

The fact that thalamic responses are not affected by deprivation while their target cells in layer IV are affected indicates that plasticity occurs at the cortical or thalamo-cortical level rather than within the thalamus. These results would appear to rule out a role for the primary thalamic nucleus in expression of this form of cortical plasticity. However, it is possible that while individual thalamic cells show similar responses before and after deprivation, the number of cells responding within the thalamus changes and this would still represent plasticity. To check this possibility, it is necessary to measure the area over which responses to spared and deprived whiskers can be recorded in the thalamus.

(b) Thalamic domains

It is possible to test whether the number of cells in the thalamus responding to stimulation of the whiskers is equivalent in deprived and undeprived animals by measuring the distance between the spared vibrissal representations and the distance between the deprived

representations. In chessboard-deprived animals, if spared and deprived domains occupy similar areas, then the distance between the centres of spared whisker domains should be the same as the distance between the centres of deprived whisker domains (figure 2). In addition, the width of a spared whisker domain should be the same as the width of a deprived whisker domain.

In practice, the size of spared and deprived whisker domains is similar in the thalamus (Wallace 2000). The distance between the centre of spared whisker domains varies from 100 to 500 μm (median 200 μm) for different cases as does the distance between the centres of deprived domains (median 150 μm). It has been found that the width of domains varies from 100 to 500 μm for spared cases and that the median width of the domains are close at 250 μm for spared whiskers and 200 μm for deprived whiskers (figure 2). The width of the domains is measured as the total distance over which the whisker response can be detected irrespective of whether it was the whisker giving the greatest response. The distance measured therefore includes both locations where the whisker studied was the principal whisker and areas where it was the surround receptive-field whisker. These findings make it difficult to attribute changes that occur in the cortex to changes in domain size in the thalamus.

4. THE THALAMOCORTICAL TRANSFER FUNCTION AND THE ORIGIN OF CORTICAL SURROUND RECEPTIVE FIELDS

So where does plasticity occur if not in the thalamus? One possibility is that plasticity occurs due to changes in cortical pathways. This view is supported by evidence showing an increase in the amount of the plasticity induced as one moves from thalamus (where no plasticity can be detected) to layer IV where some plasticity occurs, to layer II/III and neighbouring cortical columns where substantial plasticity occurs. Further evidence that plasticity occurs in cortical pathways comes from studies where cortical plasticity can be blocked by blocking cortical activity. Blocking cortical transmission with muscimol during the deprivation period prevents both depression and potentiation of cortical responses without altering thalamic responses (Wallace *et al.* 2001). Also, ablating a spared whisker's cortical barrel after induction of plasticity prevents expression of plasticity in the cortex (Fox 1994).

However, the question arises of whether some of the change in the cortical receptive fields can be attributed to changes in the convergence or divergence of thalamic receptive fields onto cortical receptive fields. To answer this question it is necessary to look at the normal relationship between the thalamic input and cortical surround receptive fields. Thalamic neurons are normally driven by one main whisker that dominates the receptive field and one or several other surround whiskers that can also elicit a response. The secondary and tertiary whiskers have been shown to activate the cell at *ca.* 20% and 10% of the level of the principal whisker, respectively. These surround components could potentially converge to produce surround receptive-field responses in cortical neurons, but do they?

Figure 2. Thalamic domain sizes for whiskers of rats undergoing chessboard-pattern whisker deprivation. (a) The diagram illustrates four theoretical barreloid domains within the thalamus as four elliptical areas. In a chessboard pattern of deprivation, adjacent domains are alternately spared (white) or deprived (shaded). Two measurements are made, the distance between the centres of the domains (either spared to spared as illustrated or deprived to deprived) and the distance across one domain (the distance across a deprived domain is illustrated). (b–e) The distances between the centres of domains are the same for deprived (b) and spared whiskers (d). The width of the domains is similar for the deprived (c) and spared (e) whisker domains (adapted from Wallace (2000)).

In order to see the effect that thalamic inputs have on cortical cells in the absence of intracortical transmission, studies have been performed where the cortex is suffused with muscimol, which diffuses in directly from a reservoir on the pial surface (Fox *et al.* 2001). To see sensory responses, an iontophoretic electrode then releases bicuculline locally within layer IV where the thalamic afferents terminate. Normally iontophoresis of bicuculline would

produce a large increase in response from centre and surround receptive-field components in a normal cortex. However, in a cortex where intracortical activity is blocked, only one whisker is able to drive the cells (figure 3). This implies that individual cells in cortical barrels do not receive any surround receptive field components from thalamic neurons. Somehow, the principal whisker response is passed on but the surround is stripped away.

Figure 3. Normalized receptive-field responses for whiskers composing the centre and surround receptive field in rat cortex. (a) Responses to a standard one-degree deflection of the whisker are shown for cells located in layer IV of the barrel cortex. Responses have been normalized so that the principal whisker (1') response is unity. Four surround receptive-field whiskers are shown. (b) Following a block of intracortical activity with muscimol, local application of bicuculline restores the principal whisker responses but reveals that almost the entire surround receptive field has been lost (from Fox *et al.* (2001)).

Since cortical cells do exhibit surround receptive fields, the obvious conclusion is that they derive their surround receptive fields by intracortical communication. This view is supported by the finding that selective lesions of a particular barrel in the cortex removes the corresponding whisker from the surround receptive fields of cells in neighbouring barrels (Armstrong-James & Callahan 1991; Fox 1994). Similarly, blocking activity in a single barrel by iontophoresis of muscimol will also selectively block responses to the corresponding whisker in a neighbouring barrel (Fox *et al.* 2001). Therefore, if experience-dependent plasticity in the cortex manifests itself as a change in surround receptive field structure, and those surround receptive fields are generated intracortically, then experience-dependent plasticity represents plasticity of intracortical pathways.

5. PLASTICITY INDUCTION

If we accept the argument that experience-dependent plasticity measured in the cortex is due to changes in intracortical pathways and not to changes in thalamic receptive-field properties, thalamic convergence or thalamic domain size, it raises a number of questions about why the cortex should be more adaptive to changes in sensory input than the thalamus. As illustrated in § 4, at least part of the explanation may come from differences in the circuitry of the two areas. Even if changes in the surround receptive fields of thalamic cells did occur in response to sensory deprivation, the surround receptive fields appear to be stripped away from the information the thalamic afferents can present to the cortex by the very nature of the thalamocortical transfer function.

A second explanation comes from the way the neuronal apparatus is engaged by the sensory stimulus during deprivation. When a rodent investigates an object it whisks its whiskers back and forth ensuring that several whiskers pass across the surface of the object within a few milliseconds of one another (Welker 1964; Carvell & Simons

1990). The response of a cortical barrel neuron to such a stimulus is due to the feed-forward excitation from the thalamus generating its centre receptive field moderated by the lateral inhibition produced by the whiskers surrounding its principal whisker. Removing the surrounding whiskers removes the lateral inhibition and therefore generates a greater response to stimulation of the whisker than it did before (Kelly *et al.* 1999). Therefore, deprivation techniques that involve removing surround whiskers, such as chessboard deprivation or univibrissal experience, result in stronger activation of layer IV cells in the spared whisker's principal barrel than occurs under control conditions. One of the consequences of the increased activation is an increase in CRE-mediated gene expression in the spared barrel (Barth *et al.* 2000) and this may trigger several changes in cell metabolism and growth. Another consequence is that second-order cells receiving their input from the spared barrel such as layer II/III cells are also driven at higher rates than before (Kelly *et al.* 1999), which could provide the activity-dependent trigger for plasticity in these pathways (figure 4). It is known that layer IV to layer II/III pathways show tetanus-induced and spike-timing-induced LTP and LTD (Glazewski *et al.* 1998b; Feldman 2000).

The thalamic neurons, however, far from being driven more powerfully by the spared whisker in the absence of its surrounding whiskers, respond at a slightly lower rate than before deprivation (Kelly *et al.* 1999). This strongly implies that the lateral inhibition responsible for moderating the layer IV responses occurs at the cortical level rather than the thalamic level or earlier in the pathway. Indeed, layer IV shows the strongest GABA_A receptor staining and a high density of GABA-ergic terminals, so the substrate certainly exists in the cortex for inhibition (Houser *et al.* 1984; Kossut *et al.* 1993). Indeed, it has recently been shown that lateral inhibitory connections occur between barrels (Schubert *et al.* 2001). One candidate for this role is the large basket cell that has vertically oriented dendrites and axons that project laterally (Wang *et al.* 2002). Such a cell would therefore tend to pick up input primarily from a single column and inhibit neighbouring columns. Therefore, not only does the evidence point to intracortical lateral inhibition but the substrate for such a mechanism is known to exist.

It is less clear why the thalamic neurons are not also subject to release from the lateral inhibition produced during whisking. One possibility is that the inhibition generated by feedback from the thalamic reticular neurons tends to produce in-field inhibition rather than surround inhibition. This subject has not been investigated thoroughly, but if feedback inhibition is focused on the centre receptive field, then removing surround whiskers would not alter the responses of the thalamic neurons to spared whisker stimulation and therefore would not produce an impetus for activity-dependent plasticity to occur in the thalamus. There is physiological and anatomical evidence that reticularis projects back exclusively to the barreloid corresponding to its principal whisker (Barthélemy *et al.* 2002) and that inhibition is restricted to a single whisker (Shosaka 1986), but it is conceivable that some cross whisker inhibition could be mediated via dendrites that cross barreloid boundaries (Barthélemy *et al.* 2002).

Figure 4. Theoretical model of how whisker deprivation in rodents initiates changes in cortical firing patterns that subsequently induce plasticity. (a) Three barrels are shown with input (arrows) from the thalamus carrying excitatory drive from the C1, D1 and E1 whiskers. The output of the layer IV cell (arrows and dotted line arrows) is partly dependent on the excitatory drive from the principal whisker (D1 in this case) but is tempered by the lateral inhibition between barrels generated by surround whisker stimulation (C1 and E1 in this case). (b) Following whisker deprivation the deprived surround whisker no longer generate lateral inhibition within the D1 barrel and therefore the excitatory drive from the thalamus evokes a greater response in the layer IV neuron.

6. CONCLUSIONS

Experience-dependent plasticity is a distinct and separate component of the plasticity evoked by nerve injury. Changes in activity may contribute to injury-induced plasticity but they are not the sole mechanisms involved. The cortex seems far more sensitive to changes in experience than the thalamus. This may be due to inherent differences in the synaptic plasticity of pathways terminating in

the thalamus, or it may be due to inherent differences in cortical versus thalamic circuitry. If the latter, it may be that the appropriate change in experience has not yet been tried that would reveal thalamic experience-dependent plasticity. For the moment, however, we have to say that it has not yet been demonstrated!

REFERENCES

- Antonini, A. & Stryker, M. P. 1993 Rapid remodelling of axonal arbors in the visual cortex. *Science* **260**, 1819–1821.
- Armstrong-James, M. & Callahan, C. A. 1991 Thalamocortical processing of vibrissal information in the rat. II. Spatiotemporal convergence in the thalamic ventroposterior medial nucleus (VPM) and its relevance to generation of receptive fields of S1 cortical 'barrel' neurones. *J. Comp. Neurol.* **303**, 211–224.
- Barth, A. L., Glazewski, S., McKenna, M., Hill, P., Impey, S., Storm, D. & Fox, K. 2000 Upregulation of CRE-mediated gene expression during experience-dependent plasticity in adult neocortex. *J. Neurosci.* **20**, 4206–4216.
- Barthélemy, D.-R. B., Varga, C., Lavallée, P. & Deschênes, M. 2002 Substrate for cross-talk inhibition between thalamic barreloids. *J. Neurosci.* **22**, RC218 (1–4).
- Bliss, T. V. & Collingridge, G. L. 1993 Synaptic model of memory, long-term potentiation in the hippocampus. *Nature* **361**, 31–39.
- Carvell, G. E. & Simons, D. J. 1990 Biometric analyses of vibrissal tactile discrimination in the rat. *J. Neurosci.* **8**, 2638–2648.
- Clark, S. A., Allard, T., Jenkins, W. M. & Merzenich, M. M. 1988 Receptive fields in the body-surface map in adult cortex defined by temporally correlated inputs. *Nature* **332**, 444–445.
- Feldman, D. E. 2000 Timing-based LTP and LTD at vertical inputs to layer II/III pyramidal cells in rat barrel cortex. *Neuron* **27**, 45–56.
- Fox, K. 1994 The cortical component of experience-dependent synaptic plasticity in the barrel cortex. *J. Neurosci.* **14**, 7665–7679.
- Fox, K. 1996 The role of excitatory amino acid receptors in developmental plasticity of sensory neocortex. In *Excitatory amino acids and the cerebral cortex*, chap. 21 (ed. F. Conti & T. P. Hicks), pp. 229–244. Cambridge, MA: MIT Press.
- Fox, K., Wallace, H., Glazewski, S. 2001 The origin of surround receptive fields in barrel cortex. *Soc. Neurosci. Abstr.* **27**, Prog. No. 393.16.
- Fregnac, Y. & Shulz, D. E. 1999 Activity-dependent regulation of receptive field properties of cat area 17 by supervised Hebbian learning. *J. Neurobiol.* **41**, 69–82.
- Glazewski, S. & Fox, K. 1996 The time-course of experience-dependent synaptic potentiation and depression in barrel cortex of adolescent rats. *J. Neurophysiol.* **75**, 1714–1729.
- Glazewski, S., McKenna, M., Jacquin, M. & Fox, K. 1998a The nature and origins of experience-dependent depression of vibrissae responses in rat barrel cortex. *Eur. J. Neurosci.* **10**, 2107–2116.
- Glazewski, S., Herman, C., McKenna, M., Chapman, P. F. & Fox, K. 1998b Long-term potentiation *in vivo* in layer II/III of rat barrel cortex. *Neuropharmacology* **37**, 581–592.
- Hand, P. J. 1982 Plasticity of the rat cortical barrel system. In *Changing concepts of the nervous system* (ed. A. R. Morison & P. L. Strick), pp. 49–68. New York: Academic.
- Houser, C. R., Vaughn, J. E., Hendry, S. H., Jones, E. G. & Peters, A. 1984 GABA neurons in the cerebral cortex. In *Cerebral cortex*, vol. 2 (ed. E. G. Jones & A. Peters). New York: Plenum.
- Jones, E. G. & Pons, T. P. 1998 Thalamic and brainstem con-

- tributions to large-scale plasticity of primate somatosensory cortex. *Science* **282**, 1121–1125.
- Kaas, J. H., Merzenich, M. M. & Killackey, H. P. 1983 The reorganization of somatosensory cortex following peripheral nerve damage in adult and developing mammals. *A. Rev. Neurosci.* **6**, 325–356.
- Kelly, M. K., Carvell, G. E., Kodger, J. M. & Simons, D. J. 1999 Sensory loss by selected whisker removal produces immediate disinhibition in the somatosensory cortex of behaving rats. *J. Neurosci.* **19**, 9117–9125.
- Kossut, M., Glazewski, S., Suicinska, E. & Skangiel-Kramska, J. 1993 Functional plasticity and neurotransmitter receptor binding in the vibrissa barrel cortex. *Acta Neurobiol. Exp.* **53**, 161–173.
- Krupa, D. J., Ghazanfar, A. A. & Nicolelis, M. A. 1999 Immediate thalamic sensory plasticity depends on cortico-thalamic feedback. *Proc. Natl Acad. Sci. USA* **96**, 8200–8205.
- LeVay, S., Stryker, M. P. & Shatz, C. J. 1978 Ocular dominance columns and their development in layer IV of the cat's visual cortex, a quantitative study. *J. Comp. Neurol.* **179**, 223–244.
- LeVay, S., Wiesel, T. N. & Hubel, D. H. 1980 The development of ocular dominance columns in normal and visually deprived monkeys. *J. Comp. Neurol.* **191**, 1–51.
- Li, X., Glazewski, S., Lin, X., Elde, R. & Fox, K. 1995 The effect of vibrissae deprivation on follicle innervation, neuropeptide synthesis in the trigeminal ganglion and S1 barrel field cortical plasticity. *J. Comp. Neurol.* **357**, 465–481.
- Nicolelis, M. A., Lin, R. C., Woodward, D. J. & Chapin, J. K. 1993 Induction of immediate spatiotemporal changes in thalamic networks by peripheral block of ascending cutaneous information. *Nature* **361**, 533–536.
- Olson, C. R. & Freeman, R. D. 1980 Profile of the sensitive period for monocular deprivation in kittens. *Exp. Brain Res.* **39**, 17–21.
- Schubert, D., Staiger, J. F., Kotter, R., Zilles, K. & Luhmann, H. J. 2001 Cell-type specific circuitry of cortical layer IV spiny neurons. *Soc. Neurosci. Abstracts* **313**, 15.
- Sengpiel, F., Stawinski, P. & Bonhoeffer, T. 1999 Influence of experience on orientation maps in cat visual cortex. *Nat. Neurosci.* **2**, 727–732.
- Shosaku, H. 1986 Cross-correlation analysis of a recurrent inhibitory circuit in the rat thalamus. *J. Neurophysiol.* **55**, 1030–1043.
- Van der Loos, H. & Woolsey, T. A. 1973 Somatosensory cortex, structural alterations following early injury to sense organs. *Science* **179**, 395–398.
- Wallace, H. L. 2000 The role of pre and post-synaptic activity in experience-dependent synaptic plasticity in barrel cortex. PhD thesis, Cardiff University, Wales.
- Wallace, H. & Fox, K. 1999 The effect of chessboard deprivation pattern on potentiation and depression of vibrissae responses in rat barrel cortex. *Somatosens. Mot. Res.* **16**, 122–138.
- Wallace, H., Liming, K., Glazewski, S. & Fox, K. 2001 The role of cortical activity in experience-dependent potentiation and depression of sensory responses in barrel field. *J. Neurosci.* **21**, 3881–3894.
- Wang, X., Merzenich, M. M., Sameshima, K. & Jenkins, W. M. 1995 Remodelling of hand representation in adult cortex determined by timing of tactile stimulation. *Nature* **378**, 71–75.
- Wang, Y., Gupta, A., Toledo-Rodriguez, M., Wu, C. Z. & Markram, H. 2002 Anatomical, physiological, molecular and circuit properties of nest basket cells in the developing somatosensory cortex. *Cerebral Cortex* **12**, 395–410.
- Welker, W. I. 1964 Analysis of sniffing in the albino rat. *Behaviour* **12**, 223–244.
- Wiesel, T. N. & Hubel, D. H. 1965 Comparison of the effects of unilateral and bilateral eye closure on cortical unit responses in kittens. *J. Neurophysiol.* **28**, 1029–1040.
- Woolsey, T. A. & Wann, J. R. 1976 Areal changes in mouse cortical barrels following vibrissal damage at different post-natal ages. *J. Comp. Neurol.* **170**, 53–66.

GLOSSARY

CRE: cyclic-AMP response element
 GABA: gamma-amino butyric acid
 LTD: long-term depression
 LTP: long-term potentiation
 VPI: ventro-posterior lateral
 VPm: ventro-posterior medial