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Structural changes in the cerebral cortex upon modification of the periphery: barrels in somatosensory cortex

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In the primary somatosensory cortex of the mouse there are approximately 35 cytoarchitectonic units, named 'barrels' (Woolsey & Van der Loos 1970), per hemisphere. There are also about 150 similar, but smaller, barrels. Each of the 35 large barrels is held to be the cortical end-station of the projections from one of the similar number of mystacial vibrissae on the animal's contralateral muzzle. These barrels are arranged in a pattern that is topologically equivalent to the pattern of the whiskers. There are five rows of whiskers and of barrels, named A, B, C, D and E, and four whiskers and barrels that straddle the ends of the rows named α, β, γ and δ. Morphological data obtained from mice (Woolsey & Van der Loos 1970; Van der Loos & Woolsey 1973) together with physiological data obtained from the rat (Welker 1971) contributed to the recognition of the relation between whiskerpad and barrelfield. A whisker and its corresponding barrel bear the same letter-number combination rather as on a chessboard. (For a review, see Van der Loos (1976*b*).) In what follows, analyses referred to are on mice, unless otherwise stated.

A whisker is part of a complex receptor organ. The hair-shaft is implanted in a tall papilla containing a large number of various sorts of receptor. Exhaustive morphological descriptions exist for the rat (see Vincent (1913) for light microscopy and Andres (1966) for electron microscopy). From a papilla leads a 'vibrissal nerve' that contains about 100 myelinated fibres (Lee & Woolsey 1975). Caudal whiskers and papillae are larger than rostral ones.

A barrel occupies the entire thickness of layer IV and consists of a 'side' of high perikaryon density and of a 'hollow' that is less densely packed. Barrels are separated by a continuum of 'septa', likewise of low cell density. A barrel is usually oblong and measures about 400 μm by 200 μm; it contains approximately 2000 neurons (Lee & Woolsey 1975). Medial barrels are larger than lateral ones. Lorente de Nó (1922) used Golgi and Nissl techniques and described many details of the barrelfield (which he believed to be part of the auditory cortex), and concluded that the specific thalamo-cortical fibres branched and terminated within what we now call barrels. This was confirmed by Killackey & Leshin (1975) who, in the rat, damaged the ventro-basal nucleus in thalamus and observed terminal degeneration in barrel-shaped clusters. Steffen (1976) produced some convincing photographs of Golgi-impregnated axonal arborizations that are confined to individual barrels with very little or no exchange of axons between barrels. Lorente de Nó (1922) and Woolsey, Dierker & Wann (1975) presented detailed Golgi-anatomy of barrel neurons. A large majority of neurons whose perikarya belong to a given barrel have their dendrites confined to that barrel. Both hollows (White 1976) and septa (Perentes, in preparation) have a synapse-rich neuropil, but the hollows, not the septa, seem to receive thalamo-cortical axons (see above).

As man bears his cortical homunculus, so mouse bears its musculuus. The barrelfield seems to be but part of that. As stated above, there are an additional 150 or so *small*, more or less circular, barrels in the barrelfield at large. The large oblong barrels, that are the subject of this résumé, lie postero-medial to the small ones and constitute the so-called postero-medial barrel subfield (Woolsey & Van der Loos 1970). (Small sinus hairs situated on the anterior end of the face and on the 'furry buccal pad' of the animal project to these small barrels; see Welker 1971.)

Whiskers are, for mice, important sense organs. Mice whisk their whiskers and thus palpate the world that is in front of them (Welker 1964). The whisking is due to the innervation, by the infraorbital branch of the facial nerve, of well-developed musculature associated with the papillae. The whisker is like a blind man's stick: it extends the somatosensory world.

The presence of barrels is related to whiskers but not to whisking. In a recent comparative study Woolsey, Welker & Schwartz (1975) pointed out that of the cavimorph rodents, the chinchilla whisks and the guinea pig does not. Both have barrels. And of myomorph rodents, rats whisk and muskrats do not and, again, both species have barrels. Beyond rodents, barrels, as defined in the present paper, have not been seen.

Between whiskerpad and barrel cortex there are two stations: the principal sensory nucleus of the trigeminal nerve and the ventro-basal nucleus of the thalamus. With respect to their significance in this particular pathway, these nuclei have been analysed (in rat) by physiological means only.

In the analysis of the trigeminal nucleus (Shipley 1974) emphasis was on neuronal encoding of stimulus parameters; in that of the thalamus (Waite 1973), on the topography of the responses evoked by stimulation of the individual whiskers. But in the dorsal part of the ventrobasal nucleus, pars medialis (VBm), I recently found an array of 'barreloids', topologically equivalent to the patterns of whiskers and of barrels (Van der Loos 1976*a*). VBm had been delineated, in an axon degeneration study by Smith (1973), as the major, and solely contralateral, thalamic projection field from the principal trigeminal nucleus.

The barrelfield can be modified by injury to the whiskerpad: in the brain of a mouse 12 days of age or older, the barrels whose corresponding papillae were damaged at birth are not there (Van der Loos & Woolsey 1973). The barrelless land is smaller than the territory occupied by the corresponding normal barrels. Oddly, it is bordered by an apparently normal septum, and a rim of high perikaryon density that resembles a barrel side. The barrels adjacent to barrelless land have grown larger, and into it. When the papillae are not damaged but, after whisker removal, glued shut at birth, the effect in cortex is milder: the corresponding barrels are a bit smaller. 'Compensatory' growth of adjacent barrels is, without rigorous quantification, difficult to assess. Whereas the injury (usually a small electrolytic lesion preceded by whisker removal) results in disappearance of the papilla, the glue treatment allows it to remain intact. An injury at 5 days of age has no effect (Weller & Johnson 1975). Also, a lesion at birth affects the barreloid array, but in a fashion that is less clear cut than in S I.

Killackey, Belford, Ryugo & Ryugo (1975) prepared rats by injuring certain papillae at birth. After the animals grew up they received lesions in VBm. Terminal degeneration was not only in the intact barrels, as Killackey & Leshin (1975) found before, but also in the area rendered barrelless by the earlier injury to the periphery. A fine-grained physiological unit analysis is indicated to find how the barrelless area and the overgrown adjacent barrels are related to the periphery.

The changes I report here are colossal: they can be observed with a hand-lens in Nissl preparations. Ryugo, Ryugo & Killackey (1975), using subtler techniques, found that, upon damage to whisker receptors at birth, the number of spines – as seen in Golgi preparations – is much reduced on apical dendrites in layer IV, i.e. apical dendrites that belong to certain pyramids of layer V.

With regard to the observations on the abnormal distribution of cell bodies – at least three synapses away from the site of injury – one may postulate three mechanisms: (i) barrels do not exist at the time of the lesion and the deranged cell distribution is a consequence of the lesion; (ii) barrels do not exist at the time of lesion but they form afterwards and then disappear; (iii) barrels do exist at the time of lesion and then disappear.

On the basis of the finding that barrels do not appear before the 4th postnatal day (Rice 1975) the third postulate can be ruled out. Preliminary observations (Jeanmonod, Rice & Van der Loos) make the second most unlikely. As to the first, further work by Rice (1975) indicates that the lesion cannot have an impact on the proliferation of cells destined for barrels: that process is completed 4 days before birth. Rice found also that while layers IV–VI are already laid down at birth, neuroblasts destined for layers II and III are still travelling at that time. Therefore a lesion at birth can influence migration of neurons and thus have a disruptive influence on the formation of barrels. Also, local modifications in cell rearrangement and/or cell death may play a role. I am totally in the dark about the physicochemical nature of the message that informs the cortex about the status of the periphery.

Two urgent questions about the deranged gross anatomy of the cortex are: (i) did the successful lesion affect the number of neurons in the altered part of the barrelfield, and (ii) are there among the neurons of the enlarged barrels – the barrels that border the barrelless land – cells that were destined for the barrels whose appearance was thwarted by the injury? These questions must be answered if we are to understand better the system's plasticity, and particularly that of its thalamo-cortical link.

For this, as for other analyses of neuronal plasticity, the great advantage of the mouse somatosensory system is in its visible topology.

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