CHAPTER 7

Geometrical and topological characteristics in the dendritic development of cortical pyramidal and non-pyramidal neurons

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Introduction

The literature indicates that in the cerebral cortex neuronal development in general and dendritic growth in particular, do not simply involve a progression in size. For instance, cortical neurons are generated at different times, for the most part according to an inside-out pattern, i.e. the majority of neurons in the upper layers are generated later than those in the lower layers (see Miller, 1988). In rat cerebrum, nearly all neocortical neurons are generated between embryological day 11 (E11) and E21 in the ventricular and subventricular zones (Fig. 1) (Uylings et al., 1990). They begin to proliferate dendrites mainly after they have reached the plexiform primordium (preplate) and cortical plate (Fig. 1). However, during normal development some neuronal death occurs in the neocortex at different stages (for review see Finlay, 1992; Ferrer et al., 1992). In addition, we know that several surviving neurons show an overgrowth, with a clear regression in the dendritic field, which even leads to a different morphological appearance in some cell types, e.g. Cajal-Retzius neurons, subplate neurons, and the small layer V pyramidal neurons.

In this chapter we will first deal with regression or reduction in the size of dendritic fields in some cell types during normal development, while the general developmental characteristics of cortical neurons will be discussed in greater detail. This part of the chapter will be illustrated using data from layer II/III pyramidal neurons, layer IV multipolar non-pyramidal neurons, small layer V pyramidal neurons and large layer V pyramidal neurons in rat visual cortex. These neurons show some different developmental characteristics.

Regression of dendrites during normal development

The outgrowth of individual, living cortical neurons in vivo (i.e. a longitudinal study) cannot be followed throughout their development. Therefore such phenomena as the occurrence of regression and spatial reorientation of dendritic fields can only be derived from tissues taken from different animals and at different ages. Thus, due to interneuronal and interanimal variability only relatively large-scale regression phenomena can be reliably detected.

For neocortical neurons such regression has so far been reported for a number of neuronal types, i.e. Cajal-Retzius cells, subplate neurons, and
layer V callosal pyramidal neurons. Marin-Padilla (1990) has shown that the dendrites and the axonal field of Cajal-Retzius cells transform the Cajal-Retzius cell in the marginal zone (Fig. 1) into a large horizontal multipolar neuron during ontogenesis in human neocortex. In the rat, Parnavelas and Edmunds (1983) have found also cellular transformation of the Cajal-Retzius cells, while Derer and Derer (1990), in their EM study have observed that some Cajal-Retzius cells die during normal development in mouse neocortex. In this respect it is important to note that the cell density measures mentioned in some studies will not be sufficient to detect the occurrence of cell death. They can even be misleading, especially during early development, when the tissue volume increases considerably (Swaab and Uylings, 1987).

Another clear example of neuronal shape transformation is seen in the group of subplate neurons. The subplate is a prominent zone situated below the cortical plate in the human brain (e.g. Kostović and Rakic, 1990; Mrzljak et al., 1990) (see Fig. 1). This zone is also clearly present in cat cortex (Shatz et al., 1988) and in rat cortex (Uylings et al., 1990). In the human brain the subplate is prominent during the third quarter of the gestation, when it reaches its peak (± 26–30 weeks of gestation), and is then about five times as thick as the cortical plate (Mrzljak et al., 1990). After that age the subplate diminishes or stretches to a thin layer which is difficult to discern 1 year after birth in Nissl-stained sections. The studies of Kostović and Rakic (1980), Luskin and Shatz (1985) and Wahle and Meyer (1987) indicate that many subplate cells die, but that a significant number remains, albeit in a more diluted fashion, in the white matter and in layer VI. With immunocytochemical staining, using neuropeptide Y (NPY) antibodies, it appears that the persisting NPY-positive subplate neurons in the human cortex become smaller during the first year and reorient their dendritic fields tangentially, i.e. parallel, to the direction of the axonal fibers of the white matter (Uylings and Delalle, 1994). The period of reshaping and reorientation is also the period in which degeneration features of other subplate neurons are observed (Uylings and Delalle, 1994). There is some suggestion that this also takes place in other mammalian species.

A third example of an obvious dendritic regression and reshaping is the apical dendritic field in the callosal, small layer V pyramidal cell (Koester and O’Leary, 1992). Parnavelas et al. (1977) and Wise and Jones (1977) described the presence of
different pyramidal cell forms in layer V and other lower layers in rat visual cortex. Later studies in rat and cat cortex (Hübener and Bolz, 1988; Hallman et al., 1988; Mason and Larkman, 1990; Chagnac-Amitai et al., 1990; Hübener et al., 1990; Vercelli and Innocenti, 1993) showed that the subdivision of layer V pyramidal neurons, based upon dendritic criteria, corresponds to subdivisions made using either their axonal connections or their electrophysiological properties. Small layer V pyramidal neurons have an apical dendrite which does not reach the superficial layers I and II, and these neurons appear to give rise to callosal or to ipsilateral intracortical projections. Electrophysiologically, the regular-spiking neurons are included among the small layer V pyramidal cells (Chagnac-Amitai et al., 1990; Mason and Larkman, 1990). Large layer V pyramidal neurons have a large apical dendrite which reaches the superficial layers I and II. These neurons appeared to project to subcortical structures. Electrophysiologically, the intrinsically bursting cells of layer V are included among the large layer V pyramidal neurons (Chagnac-Amitai et al., 1990; Mason and Larkman, 1990; Kawaguchi, 1993).

Koester and O'Leary (1992) and Vercelli et al. (1992) indicate that during normal development the callosal layer V neurons lose a superficial part or even whole apical dendrites during the first week of postnatal life. Taking literature data into consideration (Finlay, 1992; Ferrer et al., 1992), this period of regression coincides with the period of reported cortical cell death in the rodent cortical layers I–VI. The partial regression of the callosal apical dendrite is nicely demonstrated for rat cortex in the study of Koester and O'Leary (1992), which showed that all apical dendrites of all layer V pyramidal neurons reach layer I until postnatal day 4. After day 4, however, the apical dendrites of callosal pyramidal neurons regress so that they lose their contact with the superficial layer I (see Fig. 2). From this age on, dendritic differences in forms of apical dendrites distinguish the cortical projection pyramidal neurons from the subcortical projection neurons. Regression in their basal dendrites has so far not been noted, but was nevertheless also examined in our data on postnatal development (see section below).

Extensive dendritic regression during normal development is typical only for some neocortical neuronal types. Pronounced dendritic regression appears to be the exception rather than the rule for the neocortical neurons. This will be obvious from our data on pyramidal and non-pyramidal cortical neuronal development, given in the next two sections.

### Geometrical development

Several hypotheses on the maturation sequence in dendritic development have been proposed in the past: (a) earlier generated neurons located in ontogenetically older layers mature earlier; (b) projection neurons mature earlier than local circuit neurons; (c) larger cells differentiate earlier than smaller cell types (e.g. Jacobson, 1978; Lund, 1978). Several qualitative and quantitative studies on cortical development, mostly carried out in rat visual cortex (Parnavelas et al., 1978; Juraska and Fifkova, 1979; Parnavelas and Uylings, 1980; Juraska, 1982; Hedlich and Winkelmann, 1982; Uylings et al., 1983, 1990; Miller, 1988; Petit et al., 1988), have led to considerable modification of these hypotheses (e.g. Uylings et al., 1990).

In 120 μm thick Golgi-Cox stained sections of the visual cortex in female Sprague–Dawley rats we studied the large and the small layer V pyramidal neurons separately, since they make up distinct subpopulations. On postnatal day 6 (the earliest age at which measurements were done) these two different groups of neurons were easily discernible (Fig. 2). In addition, layer IV multipolar non-pyramidal and layer II/III pyramidal neurons were examined. From this study we noted a different time course for the branching of basal dendrites (Fig. 3), the increase in somatic size (Fig. 4) and the total dendritic length per neuron (Fig. 5). In her rapid-Golgi study of 100-μm thick sections of the visual cortex of male and female hooded rats, Juraska (1982) indicated that no
further increase in branching occurs after day 15 for layers III and V pyramidal neurons. We found no significant increase in branching of the two layer V pyramidal groups after day 10, but a decrease between days 10 and 14 in the large layer V pyramidal neurons and a decrease after day 18 in the small layer V pyramidal neurons (Fig. 3). After day 10, the number of basal dendrites reached a stable figure (i.e. mean values of 5.2 for layer II/III neurons, 5.0 for small layer V neurons, and 6.2 for the large layer V pyramidal neurons). After day 14, the number of dendrites per layer IV multipolar neurons reached the stable mean value of 6.0. These data on dendrite

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**Callosal**

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**Corticotectal**

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Fig. 2. An example of large dendritic regression during normal postnatal development in rat. Apical dendrites in callosal, small layer 5 pyramidal neurons regress in size between postnatal days (P) 4 and 7, whereas this does not occur in the large layer 5, long distance projection, pyramidal neurons. The borders of pial surface, layer I and layer 5/6 are indicated. Scale bar is 100 μm (reproduced with permission from Koester and O'Leary, 1992).
Fig. 3. Number of basal dendrite segments per pyramidal neuron: L.II + III: layer II/III neurons (total number of cells studied 135); L.Vs: small layer V neurons (total number of cells studied 143); L.VL: large layer V neurons (total number of cells studied 124). The number of dendritic segments per multipolar non-pyramidal neuron (MPNP) is indicated by the uninterrupted line (total number of cells studied is 220).

Fig. 4. The surface of the Golgi-Cox stained somata, projected on to the section-plane is indicative of somatic size, given the 3-D shape. Abbreviations as given in legends of Fig. 3.

number are comparable with those of Miller (1988) who also studied Sprague-Dawley rats.

The lengthening of dendrites, however, continues until a later age, day 18 (Fig. 5), at which time the maximal values are reached for both types of layer V pyramidal cells. This maximum is reflected in the individual segment length values (Fig. 6) as well as in the developmental curve of the radial distance from terminal tips (Fig. 7), so that we can assume that cutting did not interfere with our interpretation (Uylings et al., 1989b). The same assumption, i.e. that cutting does not complicate the interpretation of Fig. 5, holds for the increase in length through 90 days in multipolar non-pyramidal neurons and layer II/III pyramidal neurons (see Figs. 5, 6, 7). Our data on total dendritic lengths are comparable with, and an extension of, the data of Juraska (1982), who did not distinguish small from large layer V pyramidal neurons. Our data, however, differ from the developmental curves given for the large ('giant') layer V pyramidal neurons by Petit et al. (1988). In their study of 90-μm thick rapid Golgi stained sections of the visual cortex of male hooded rats they observed no clear maximal value on day 18. They reported that after day 15 the layer V 'total length of basal dendrites' values increase, but not significantly so. Their values for the 'giant' layer V pyramidal neurons are comparable only with our much lower values for the small layer V neurons. This holds also for their values of the individual terminal segments.

As reported earlier (Uylings et al., 1989b), no strong positive correlation exists in adulthood between somatic size (or projected somatic surface) and total dendritic length of basal dendrites. This is even weaker during development, probably
due to an unequal pattern in the development of axonal, apical and basal dendritic processes) (see Figs. 4 and 5). Our developmental curves for somatic sizes are compatible with those shown in Miller (1988) in rat and Ramirez and Kalil (1985) with the exception of the single very low value for large layer V pyramidal neurons on day 30.

In our data from Golgi-Cox stained sections the length of terminal segments accounts for 80–90% of the total length of (basal) dendrites per neuron. This is similar to the data on HRP-stained, fully reconstructed pyramidal neurons in young adult rats, as obtained by Larkman (1991). The large increase in the length of individual terminal segments of the basal dendrites in layer II/III pyramidal is noticeable after day 30, in contrast to those of the two layer V pyramidal cell groups (Fig. 6). This increase is thus also present in the total dendritic length per neuron and the radial distance of terminal tips of basal dendrites (Figs. 5, 7). On day 90 the length of the individual terminal segments of layer II/III does not differ significantly from those of the large layer V pyramidal neurons. Larkman (1991) reported that in young adult rats the values for both layer II/III and the large layer V pyramidal neurons are comparable, but that those for the small layer V were even larger. We did not find the latter result for the small layer V pyramidal neurons in our own data (Fig. 6; Uylings et al., 1990). Our data show a noticeable decline after day 18 in the curve for total length of basal dendrites per layer II/III neuron, whereas further growth has been detected even after day 30 (Figs. 5, 6, 7). This is further illustrated in the orientation-density analysis with the method of Ruiz-Marcos (1983) (see also Ruiz-Marcos and Ipiña, 1986 and Uylings et al., 1989b).
Fig. 7. The radial distance of terminal tips to center of soma in basal dendrites and in multipolar non-pyramidal dendrites. The number of terminal tips varies with cell type and age, but is larger than 200, frequently over 400 and twice over 700, per age per cell type. Reproduced with permission from Uylings et al., 1990.

The developmental alterations in extension and relative density of all of the pyramidal neurons examined is shown in Fig. 8. Statistical comparison of the homologous matrix elements (see Fig. 9) shows a slight decline in density for the two layer V and layer II/III pyramidal cell types after day 18, but also a clear increase in the extension and density of the layer II/III pyramidal neurons between days 30 and 90. The pictorial 2-D orientation-density analysis method of Ruiz-Marcos deepens our insight into the total length data presented above. It shows that minor dendritic regression in basal dendritic fields of pyramidal ages. The basal dendritic fields have been projected on to a grid or matrix with $15 \times 15 \, \mu m$ square elements. This matrix is parallel to the plane of sectioning. Per cell type and per age, the mean dendritic length value per $15 \times 15 \, \mu m$ is indicated by six rank numbers visualized by six different sizes of dots, respectively. The arrow points to the pial surface (see Ruiz-Marcos, 1983 for a detailed description of the method).
occurs after day 18, and that this is distributed over different parts of the basal dendritic field. However, in the layer II/III pyramidal neurons the regression is apparently reversed after day 30.

Dendritic regression of cortical pyramidal neurons is not generally reported in the rat studies (Wise et al., 1979; Petit et al., 1988) or else the reported trend did not reach statistically significant values (Juraska, 1982). Some regression is also indicated in the developmental study of layer V pyramidal neurons in rabbit visual cortex of Murphy and Magness (1984). In our human studies (Koenderink and Uylings, 1994; Koenderink et al., 1994), however, we do not observe a clear-cut maximal peak-decline pattern during development in the basal dendritic field of the layer IIIc and V pyramidal cells.

As mentioned above, this kind of study is hampered by the fact that a longitudinal study of particular neurons is presently impossible. In contrast to human studies, animal studies have the advantage that they can be designed so that the genetic and environmental conditions are under control, so that inter-individual variations can be minimized. In addition, it appears to be of importance in animal studies to examine a rather extensive and sufficiently fine-graded age series in order to avoid missing periods of rapid growth or decline. In addition, the possibility is not excluded (indeed for particular brain regions even likely: Greenough et al., 1977; Goldstein et al., 1990; Sasaki and Arnold, 1991; Cherry et al., 1992) that the developmental pattern differs for male and female animals (Muñoz-Cueto et al., 1991). Hemispheric asymmetry can also influence the developmental pattern in particular cortical areas but, viewing the possible alterations in asymmetry

and lower dendritic length value, respectively, per square element according to a two-tailed t-test ($P < 0.05$; see Uylings et al., 1986 for interpretation of statistical differences). In this pictorial test a single significant matrix element is not meaningful; only clusters of significantly differing matrix elements are relevant and indicative of a significant development in a particular direction.

Fig. 9. The comparison of the density of the basal dendritic fields of the set of layer II/III (A), of small layer V (B) and of large layer V (C) pyramidal neurons at successive ages studied. The size of each square element is 15 × 15 μm. The plane of projection is the coronal plane, and the arrow points to the pial surface. A + and a − indicate a significantly higher
during volumetric development of cortical areas, a study of this kind will require that many more animals and neurons be examined (Van Eden et al., 1984; Uylings et al., 1990).

So far, the data indicate that in the rat visual cortex the dendritic outgrowth of cortical neurons reach a plateau at the same age, i.e. 18 days, irrespective of layer, birth date of neuron, type of neuron or initial differences in maturation. After this age, dendritic fields either stay the same size or decline, without or with subsequent regrowth. Examples of these categories in the rat visual cortex are, respectively, (1) the multipolar layer IV neurons, (2) the two layer V pyramidal types, and (3) the layer II/III pyramidal neurons. A pattern of growth, decline and regrowth has also been detected in cerebellar Purkinje cells (Sadler and Berry, 1984; Pentney, 1986; Quakenbush et al., 1990; Wildenberg et al., 1993).

Mode of growth derived from segment length data

When no longitudinal data on growing trees are available, the analysis of growth pattern can best be performed with tree topology methods (e.g. Van Pelt and Verwer, 1986; Uylings et al., 1989a; Van Pelt et al., 1989, 1992; Verwer et al., 1992). The distribution of length values for individual segments, however, can also indicate to some extent how dendrites grow and bifurcate. The large differences between lengths of terminal segments and intermediate segments during development (Fig. 6) and for stimulated growth in adulthood (Uylings et al., 1978) indicate that branching occurs mainly in terminal segments, but not necessarily at their tips, due to 'dormant' or laterally induced growth cones; see for this aspect also the outgrowth model based on microtubule dynamics in the chapter by Van Veen and Van Pelt in this volume (Van Veen and Van Pelt, 1994).

The frequency distributions of terminal segment lengths are fairly symmetrical and show only a few values lower than 40 μm, whereas the frequency distributions of intermediate segments are skewed with a modal value around 10 μm and have relatively few values over 40 μm (see figures of these distributions in Uylings et al., 1978; Larkman, 1991). Segment length distributions can be simulated on the basis of growth algorithms (Nowakowski et al., 1992; Van Veen and Van Pelt, 1993). From the analysis of Van Veen and Van Pelt (1993) it appears that the difference in length between terminal and intermediate segments can be understood by (a) assuming a Poisson process for the occurrence of branch points along dendrites, i.e. assuming a constant branching probability per unit length of a neurite, (b) elongation at the terminal tip, and (c) branching at terminal tips or 'dormant' growth 'cones' along the terminal segments. In our previous review (Uylings et al., 1986) we described that, in nearly all neuronal types studied, the terminal segments are (considerably) longer than those of intermediate segments. In addition, we noted that the mean values for different types of intermediate segments vary widely among multipolar non-pyramidal neurons (Uylings et al., 1986), neocortical pyramidal neurons and hippocampal granule cells (Uylings et al., 1989b). The frequency distributions for different types of intermediate segments of cortical pyramidal and non-pyramidal neurons, respectively, show that these groups mainly differ in the tails towards higher values (Figs. 10 and 11). The longest tail is present in the segments of degree-2, i.e. segments which branch into two terminal segments. The modal value for all the different types is around 7–12 μm. This indicates the possibility of branching at long segments of degree-2. This is suggested by the following: (a) the mode and mean values for the group of intermediate segments with four or more terminal tips ahead (i.e. degree ≥ 4) remains about the same for all of the pyramidal cell types as well as for the multipolar non-pyramidal type after day 6; (b) the developmental increase in intermediate segments displayed in Fig. 6 for some types up to about day 18 is mainly due to the increase in degree-2 segment values (especially due to a longer and thicker tail of higher values) whereas the modal values for each cell type remain the
Fig. 10. The frequency distribution of the length of individual intermediate segments of basal dendrites in large layer V pyramidal cells (age: 10 days). The class width is 5 \( \mu m \), the points in the graph are the class-midpoints. The open circles represent the degree-2 intermediate segments, i.e. segments branching into two terminal segments. Their number is 239 and mean length value is 15.0 \( \mu m \). The open triangles display the degree-3 intermediate segments; \( n = 127 \) and the mean value is 11.3 \( \mu m \). The open squares represent the degree equal to and larger than four segments; \( n = 247 \) and the mean value is 9.7 \( \mu m \).

Fig. 11. The frequency distribution of the length of individual intermediate segments of layer IV multipolar non-pyramidal dendrites (age: 16 days). Class width is 5 \( \mu m \) and class values are displayed by class midpoints. The open circles display the values for degree-2 segments; \( n = 225 \) and the mean length is 28.8 \( \mu m \). The open triangle values represent the degree-3 segments; \( n = 97 \) and the mean value is 20.0 \( \mu m \). The open square values display the degree \( \geq 4 \) segments; \( n = 165 \), and the mean value is 9.7 \( \mu m \). Note the large variability in length values of the non-pyramidal neurons as compared with pyramidal neurons.

same. Another possible hypothesis is that especially degree-2 segments have a length frequency distribution with a long tail of high value due to incidental delayed branching, especially when the branching probability becomes reduced.

A characteristic difference between the frequency distributions of all the pyramidal cell types and the non-pyramidal cell types (e.g. multipolar, bitufted) is the low variability and the more clearly peaked modal values in the degree-2 and degree-3 segments in pyramidal neurons (see e.g. Figs. 10 and 11). The larger variability in length values for the intermediate segments of multipolar non-pyramidal neurons (Fig. 11), in comparison with those of pyramidal neurons, can be explained (using the model of Van Veen and Van Pelt, 1993) by a lower branching probability per unit length for the multipolar non-pyramidal neurons. This explanation is also compatible with the significantly lower mean number of terminal segments (which is equivalent to the number of bifurcations) per dendrite of multipolar non-pyramidal cells. These values make up nearly half of the values found in the basal dendrites of layer II/III pyramidal neurons after day 10.

**Topological analysis of dendritic growth**

When no longitudinal data are available for individual growing trees, topological analysis is the method of choice for examining the mode of
branching. A topological description of a tree defines how its different segments are interconnected, irrespective of metrical dimensions; each unique description is called a topological tree type (Van Pelt and Verwer, 1984a; Uylings et al., 1989a; Verwer et al., 1992). The topological size of a rooted tree, i.e. the number of segments, is directly related to the number of terminal segments per tree (e.g. Uylings et al., 1989a) or number of branching points per tree (Verwer et al., 1992). The topological analysis cannot be applied to one tree alone, since a given topological tree type can occur after different ways of branching. The frequencies of different topological tree types of a group of neurons, however, are indicative of the mode of branching (Van Pelt and Verwer, 1984a, 1986), even when some trees are cut due to sectioning (Van Pelt and Verwer, 1984b; Van Pelt, in preparation). A major difficulty in topological analysis is that, with increasing size of a tree, the number of topological tree types becomes unmanageably large: e.g. for trees with 14 terminal tips 2179 topological tree types exist, and for trees with 20 terminal tips (degree = 20) 293,547 topological tree types exist (Van Pelt et al., 1989; Uylings et al., 1989a). For large trees (degree \( n \geq 100 \)) there are roughly \( 2.4^n \) different topological tree types (Van Pelt et al., 1992).

For a long time we have been looking for topological measures which make a statistical and topological analysis of groups of observed trees manageable (Uylings et al., 1989a; Van Pelt et al., 1989; Verwer et al., 1992). We think we have managed to develop a practical measure, 'tree asymmetry' (Verwer and Van Pelt, 1986; Van Pelt et al., 1992), which has a strong discriminative power for topological differences (Van Pelt et al., 1989) and is very suitable for comparing sets of branching patterns (almost independent of topological size) as well as for indicating the mode of branching, since the mean and variance of tree asymmetry of a group of neurons depend on the mode of growth (Van Pelt et al., 1992). At each bifurcation, the number of terminal tips is partitioned. When they are partitioned into two equal sets the bifurcation is symmetrical and the asymmetry value is then zero. The 'tree asymmetry' is defined as the mean value of asymmetry of all bifurcations in a tree. This 'tree-asymmetry' measure has been normalized so that it ranges between 0 and the limit 1 (see for further details Van Pelt et al., 1992). To obtain a qualitative impression, Fig. 12 illustrates different 'tree-asymmetry' values for some trees with eight terminal tips.

Analysis of growth models shows that the mean 'tree asymmetry' values differ significantly for sets of trees grown under different branching rules (Van Pelt et al., 1992). For a set of trees with a number of terminals between 4 and 15 per tree, grown according to the random segmental branching model, mean tree asymmetry is equal to 0.59, whereas according to the random terminal branching model it is equal to 0.45 (see Table 3 in Van Pelt et al., 1992). These and other branching models predict a much larger variability in 'tree asymmetry' values for trees with less than 15 terminal tips (i.e. degree \( \leq 15 \)) in comparison with large trees (e.g. Purkinje cell trees with a degree between 150 and 800). This is observed for cortical pyramidal and non-pyramidal neurons in which almost all the dendrites have less than 15 terminal tips. Therefore, in groups of these small trees, testing of a slightly differing branching mode is relatively difficult (see Van Pelt et al., 1992). Still, the available data on

Fig. 12. Topological 'tree asymmetry' values are shown for six of the 23 different topological tree types of degree 8 trees (i.e. trees with 8 terminal tips) in order to illustrate the practical meaning of this variable.
TABLE I
Mean tree asymmetry ($\bar{A}$) during development (for trees with degree $\geq 4$)

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>Layer II/III pyr.</th>
<th>Small layer V pyr.</th>
<th>Large layer V pyr.</th>
<th>Layer IV multipolar nonpyramidal</th>
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<tr>
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<td>$\bar{A}$</td>
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<td>(no.)</td>
<td>$\bar{A}$</td>
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<td>6</td>
<td>—</td>
<td>—</td>
<td>(5)</td>
<td>—</td>
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pyr., pyramidal neurons.

different types of cortical pyramidal and nonpyramidal neurons (see Table I) point clearly to a topological mode of branching which is (1) similar for the layer II/III pyramidal and layer IV nonpyramidal multipolar neurons during the various developmental stages in rat visual cortex, and (2) consistent with the random terminal branching model. This model predicts a mean ‘tree asymmetry’ of 0.45 and a variance which is similar to the observed variances. The values of the two layer V pyramidal cell types are more variable during the different ages, although in general these values are also consistent with a model which assumes branching randomly at terminal segments. The lower values at some ages for the layer V pyramidal neurons are below the expected values according to the random terminal branching model and reflect a non-random regression in such a way that the trees become topologically more symmetrical. This needs to be tested in further research.

Conclusions

We may conclude from the data available concerning cortical dendrite development that, irrespective of birth date or an earlier start of dendritic maturation, the phase of rapid dendritic growth ends around the same age for all types of cortical pyramidal and non-pyramidal neurons. In rat cortex this is around postnatal day 18; at that age the electrophysiological development of rat cortex, though quite advanced, is not yet finished (e.g. Corner and Mirmiran, 1990; Hamill et al., 1991; Corner et al., 1992; Connors, 1994). After day 18 this is true also for dendritic development: the basal dendrites of layer II/III pyramids continue to grow at later ages, after a small decline, while a persisting minor regression can be noted in the basal dendrites of both types of layer V pyramidal neurons. No further large alteration has been found in the layer IV multipolar non-pyramidal neurons.

In general, the mode of branching appears to be the same for all the types of cortical neurons examined at the various ages studied, i.e. mainly random branching at the terminal segments. However, the branching probability per dendritic unit of length is lower in non-pyramidal neurons, resulting in fewer bifurcations per dendrite.

Dendritic regression during the period of normally occurring cell death (apoptosis) is large in only a few neuronal types. In addition, our results indicate the occurrence of some regression in the basal dendrites of pyramidal cell types during normal development and puberty. The major part of dendritic development appears to follow an intrinsic ‘program’ which can be modified; however, by environmental influences without altering the mode of branching (e.g. early malnutri-
tion, and exposure to an enriched environment, even in adulthood (Uylings et al., 1978; Juraska et al., 1980). In cases of major pathology, on the other hand, such intrinsic ‘programs’ of dendritic development may be drastically changed.

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References


