Postnatal Development of Radial Glia and the Ventricular Zone (VZ): a Continuum of the Neural Stem Cell Compartment

Anthony D. Tramontin, José Manuel Garcia-Verdugo1,
Dan A. Lim and Arturo Alvarez-Buylla

Department of Neurosurgery Research, University of California, San Francisco, CA 94143, USA, 1Universidad de Valencia, Burjassot-46100, Spain

The germinal neuroepithelium, or ventricular zone (VZ) of the developing fetal brain, was once thought to transform into the non-germinal ependymal zone of the postnatal and adult brain. Persistence of neural stem cells and neurogenesis throughout postnatal life, however, suggests a continuum between embryonic and adult germinal brain centers. Here, we suggest that developmental changes in anatomy and molecular marker expression in the ventricular walls (the principal germinal centers of the brain) may have misled us into current interpretations of VZ transformation from a germinal to a non-germinal epithelium. We review previous studies and present new data indicating that a germinal layer with characteristics similar to those of the embryonic VZ persists in lateral ventricular walls of the postnatal mouse brain, a region where the adult subventricular zone (SVZ) develops and where neurogenesis persists into adult life. The early postnatal VZ is largely composed of radial glial cell bodies that remain proliferative, display interkinetic nuclear migration and serve as progenitors of new neurons. Ependymal cells then progressively populate the walls of the lateral ventricle but a subpopulation of astrocytes, derived from radial glia, remain in contact with the ventricle lumen, into which they extend a single cilium similar to that found on neuroepithelial cells and radial cells. We propose that a VZ ‘compartment’ is retained postnatally and that this niche may be essential for stem cell function.

Introduction

Almost all of the cells in the developing mammalian brain are produced within two closely associated germinal zones located next to the ventricle walls (Jacobsen, 1991). The ventricular zone (VZ) is a pseudostratified epithelium containing multi-potent neural stem cells. The anatomy of this germinal region breaks down during perinatal development. The classical view, based largely on studies of the developing mammalian cerebral cortex, held that as the VZ disappears, the brain loses its germinal potential. The VZ was thought to transform into the ependymal layer, a non-germinal epithelium largely composed of multi-ciliated cells (The Boulder Committee, 1970). The second germinal zone, the subventricular zone (SVZ), is located adjacent to the VZ along the lateral ventricular wall. It is most prominent in the medial and lateral ganglionic eminences (MGE and LGE) of the embryonic brain (Anderson et al., 1999; Wichterle et al., 1999, 2001; Parnavelas, 2000). Importantly, neurogenesis persists in this part of the brain throughout an animal’s adult life. This postnatal SVZ (sometimes referred to as the subependymal layer in adults) is thought to develop from the fetal SVZ and to possess precursor cells with similar properties (Wichterle et al., 1999). The developmental origin of the adult SVZ is, however, poorly understood. Specifically, it is critical that the locations of primary (stem cells) and secondary progenitors are examined to determine how these cells are related to their developing counterparts. In the embryo, proliferating SVZ progenitors (secondary progenitors) are thought to derive from primary precursors or stem cells in the VZ. In the adult brain, the VZ is thought to disappear, but cells that retain properties of stem cells have been shown to persist in the lateral ventricular walls (Morshead et al., 1994; Reynolds and Weiss, 1996; Weiss et al., 1996; Doetsch et al., 1999a,b).

The identification of neural stem cells during development and in adults is essential to understanding the compartment in which these cells reside. Radial glia have been shown to be primary precursors of new neurons and astrocytes in the embryonic mammalian brain (Malatesta et al., 2000; Miyata et al., 2001; Noctor et al., 2001; Tamamaki et al., 2001) and the adult avian brain (Alvarez-Buylla et al., 1990, 1998). The somata of radial glia reside in the VZ, but these cells possess long processes that penetrate the underlying brain parenchyma and contact the pial surface of the brain. In adult mammals, however, radial glia are absent from the brain and astrocytes serve as stem cells in adult germinal regions (Doetsch et al., 1999a; Laywell et al., 2000; Skogh et al., 2001). We have previously suggested that cells within what was once considered the lineage of macroglia are neural stem cells (Alvarez-Buylla et al., 2001).

Here we discuss data suggesting that a VZ persists in the walls of the neonatal lateral ventricle between the ventricle lumen and the SVZ. We also present some new data showing that the postnatal VZ is formed by cell bodies of radial cells that continue to display interkinetic nuclear migration. Finally, we review the recent finding that radial glia give rise to neurons, and perhaps other cell types in the brain.

Postnatal Development of the Lateral Ventricular Wall

Proliferation and neurogenesis continues in the lateral walls of the lateral ventricle in the postnatal and adult rodent brain (Altman, 1969; Luskin, 1993; Lois and Alvarez-Buylla, 1994). However, the anatomy of this region changes dramatically during postnatal development (Fig. 1). The periventricular germinal regions are much larger and contain many more cells in neonates than in adults (Peretto et al., 1999) (Fig. 1). Between postnatal days 0 and 7, these regions shrink dramatically and by P15 the lateral ventricular wall appears grossly similar to that observed in the adult brain (Fig. 1). In neonates the ventricular walls comprise two distinct cellular zones, the VZ and the SVZ. Under the light microscope, the VZ contains elongated cells with light cytoplasm and nuclei. Cells in the SVZ have mixed morphologies and much darker nuclei. These two zones can be distinguished by the differential expression of two peptides, Noggin and DLX2. To illustrate this point, we killed Noggin:lacZ reporter mice (a kind gift from R.M. Harland) and DLX2:lacZ reporter mice (a kind gift from G. Fishell) (Corbin et al., 2000) as neonates and adults. Noggin binds bone morphogenetic protein (BMP) and thereby prevents the activation of BMP receptors (McMahon et al., 1998). DLX2 is a transcription factor expressed in neurogenic progenitors (Panganiban and
Rubenstein, 2002). At P0, Noggin is expressed mainly by cells in the VZ while DLX2 is expressed primarily in SVZ cells (Fig. 1). In the adult brain, Noggin protein is primarily expressed in the ependymal cells that line the ventricle (Lim et al., 2000).

Occasionally, SVZ astrocytes that contact the ventricle also express Noggin protein (unpublished observation). DLX2 continues to be expressed by SVZ cells throughout adult life (Fig. 1). Recent work has shown that in the adult brain SVZ DLX2

**Figure 1.** Germinal compartments in the neonatal brain. The VZ and SVZ compose the germinal region surrounding the lateral ventricle in newborn mice (A). The number of cells in these regions decreases progressively from P0 (A), through P7 (B), until adult numbers are achieved at P30 (C). Two molecular markers distinguish these two zones from one another. (D–G) are thin 1 µm plastic section from reporter mice expressing LacZ under the control of Noggin (D and E) and Dlx2 (F and G) promoters. The aqua blue perinuclear precipitate corresponds to the β-galactosidase staining revealing LacZ expression; the violet–blue is Toluidine blue counterstaining. Noggin is expressed primarily by VZ cells that contact the ventricle in the newborn brain (D), the inset shows a semithin section without counterstaining. Black arrows in the inset of D show the boundary between the VZ and SVZ. In the adult noggins is expressed primarily by ependymal cells in the adult brain (G). DLX2 is a transcription factor that is expressed by SVZ cells in the newborn (F) and adult brain (G). This marker, however, is not expressed in the VZ or the ependymal layer. Scale bar for panels A–C = 0.4 mm. Scale bar for panels D–G = 10 µm.
staining is limited to Type C cells (transit amplifying cells) and young neuroblasts, but it is not expressed by the primary progenitors (SVZ astrocytes). This suggest that DLX2 is primarily expressed in secondary precursors, which is consistent with the embryonic expression pattern.

Cellular Characteristics of the Postnatal VZ

In embryos, the VZ is a pseudostratified epithelium within which stem cells undergo interkinetic nuclear migration. These cells replicate their DNA deep in the VZ after which their nuclei translocate toward the ventricle lumen to divide (Sauer, 1935; Chenn and McConnell, 1995). To determine if these ‘elevator’ movements might occur in the postnatal VZ, we performed electron microscopy on histological sections prepared from neonatal mice (Fig. 2). We observed mitotic figures in the VZ demonstrating that cell division continues in this region after birth. Importantly, the somata of mitotic VZ cells were almost always observed immediately adjacent to the ventricle lumen. This observation suggested that cells in the neonatal VZ move toward the ventricle before they divide. To test this hypothesis directly, we injected neonatal mice with \[^{3}H\]thymidine and killed them either 1, 3, 5, 7 or 11 h later \(n = 4\) per treatment group; for methods see (Doetsch et al., 1997). In sections prepared from these animals, we measured the distance between \[^{3}H\]labeled cells in the VZ and the ventricle lumen. \[^{3}H\]thymidine is incorporated into the DNA of dividing cells during the S-phase of cell division. Accordingly, 1 h after \[^{3}H\]thymidine injection, labeled cell nuclei were located deep in the VZ (Fig. 2). Between 1 and 7 h after \[^{3}H\]thymidine injection, the somata of labeled cells in the VZ moved progressively closer to the ventricle lumen. At 11 h post-injection, labeled cells began to return to their positions deeper in the VZ. From these observations, we concluded that proliferative VZ cells behave similarly in embryos and neonates.

To determine the identity of the cells in the neonatal VZ, we examined sections of neonatal VZ using electron microscopy [for methods see Doetsch et al. (Doetsch et al., 1997)]. VZ cells possessed soma that were elongated orthogonally to the surface of the ventricle. Their cytoplasm contained abundant smooth endoplasmic reticulum, consistent with their ongoing proliferation. These cells also contained intermediate filaments that were aligned along the long axis of the cell. These filaments were abundant at the base of these cells from which a long radial process extended into the underlying parenchyma. The nuclei of these cells were elongated perpendicularly to the surface of the ventricular lumen and contained lax chromatin and one or two nucleoli. These cells were attached to one another by tight junctions near their apical surface. All of the cells examined made contact with the ventricle lumen, and many of them extended into the lumen a single cilium that possessed a 9 + 0 microtubule organization (Fig. 3). Together, these ultrastructural

![Figure 2](http://cercor.oxfordjournals.org/)

Figure 2. Interkinetic nuclear migration in the postnatal VZ. The VZ in the newborn brain is a pseudostratified epithelium containing the cell bodies of radial glia (A). When these cells divide, the mitotic figures are found immediately adjacent to the ventricle lumen (B). We tested for interkinetic nuclear migration in the newborn VZ by injecting \[^{3}H\]thymidine and killing mice 1, 3, 5, 7 or 11 h later \(n = 4\) per treatment group; for methods see (Doetsch et al., 1997). In sections prepared from these animals, we measured the distance between \(^{3}\text{H}\)labeled cells in the VZ and the ventricle lumen. \[^{3}H\]thymidine is incorporated into the DNA of dividing cells during the S-phase of cell division. Accordingly, 1 h after \[^{3}H\]thymidine injection, labeled cell nuclei were located deep in the VZ (Fig. 2). Between 1 and 7 h after \[^{3}H\]thymidine injection, the somata of labeled cells in the VZ moved progressively closer to the ventricle lumen. At 11 h post-injection, labeled cells began to return to their positions deeper in the VZ. From these observations, we concluded that proliferative VZ cells behave similarly in embryos and neonates.

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characteristics identify these cells as radial glia (Hinds and Ruffett, 1971).

The distinct anatomy of the VZ breaks down during postnatal development. To examine this process, we killed mice at P0, 7, 15 and 30 and performed VZ cell counts at the electron microscope [for methods see Doetsch et al. (Doetsch et al., 1997)]. At P0, the vast majority of cells in the VZ were radial glia (Table 1), but some immature ependymal cells were also observed. At P7, the proportion of radial glia had decreased while the proportion of immature ependyma increased by a similar percentage. This observation suggested that some radial glia might give rise to multi-ciliated ependymal cells. At P15 and P30, radial glia were completely absent from the VZ, which was predominantly composed of mature and immature ependyma. A significant percentage of the cells contacting the ventricle at these ages, however, possessed the ultrastructural characteristics of SVZ astrocytes. Similarly to radial glia at earlier developmental stages, adult astrocytes that contact the ventricle extend single 9 + 0 cilia into the ventricular lumen. These observations suggest that a subset of radial glia transform into SVZ astrocytes. Note that an earlier report suggested that ependymal cells could also function as neural stem cells (Johansson et al., 1999). Further studies from multiple laboratories, however, have not supported this interpretation (Chiasson et al., 1999; Doetsch et al., 1999a,b; Laywell et al., 2000; Capela and Temple, 2002).

Radial Glia Transformation

Studies of the developing cortex have used a variety of approaches to demonstrate that radial glia give rise to GFAP+ astrocytes, thus establishing a lineage between these two cell types (Schmechel and Rakic, 1979; Voigt, 1989; Gaiano et al., 2000). Our electron microscopy data discussed above are consistent with this hypothesis. To investigate this process in more detail in the lateral ventricular wall, we killed mice at P0, P7 and P15, and stained their brains with RC2 antibodies which specifically recognize radial glial cells (Missan et al., 1988; Gadiesseux et al., 1989) and antibodies directed against glial fibrillary acidic protein (GFAP) which stains astrocytes (Bignami and Dahl, 1974). RC2 staining was abundant in newborn mice, decreased over the first two postnatal weeks, and was absent in P15 mice (Fig. 3). The disappearance of RC2+ cells from the telencephalon correlated with the appearance of GFAP+ astrocytes. At P0, the lateral ventricular wall contained no GFAP+ cells. These cells began to appear at P7 and by P15 GFAP staining was abundant in the lateral ventricular wall that contains the SVZ. Our observations of RC2 and GFAP staining in the postnatal mouse brain were consistent with previous reports (Gates et al., 1995).

Although radial glia and SVZ astrocytes possess different morphologies and express different molecular markers, they do share some interesting structural features. Most intriguing is the single short cilium that both cells extend into the ventricular lumen (Doetsch et al., 1997, 1999a,b). This cilium has also been described in embryonic neuroepithelial stem cells (Sotelo and Trujillo-Cenóz, 1958; Stensaas and Stensaas, 1968; Cohen and Meiningner, 1987).

Radial Glia As Neural Stem Cells

The similarities between radial glia and stem cells in the embryonic and adult brain have been extended beyond mere anatomical features. In the adult avian brain radial glial cells function as progenitors for new neurons (Alvarez-Buylla et al., 1990). More recent studies have demonstrated that radial glia in the embryonic mammalian cortex are neurogenic and gliogenic precursors (Malatesta et al., 2000; Tamamaki et al., 2001; Noctor et al., 2001; Miyata et al., 2001). Between embryonic days 13 and 16, cortical radial glia in the dorsal (pallial) ventricular wall proliferate to produce neurons. After embryonic day 16, the dorsal wall of the ventricle loses its neurogenic potential as radial cells in this region give rise to cortical astrocytes. In contrast to the dorsal ventricular wall, the lateral (striatal) wall does not lose its neurogenic potential perinatally. Here, radial glia continue to produce neurons well into postnatal life (Tramontin et al., 2002) (Fig. 4). Furthermore, preliminary data suggest that radial glia in the lateral ventricular wall also give rise to ependymocytes, oligodendrocytes and SVZ astrocytes as function as adult neural stem cells (Doetsch et al., 1999a; Tramontin et al., 2002). These studies suggest that VZ cells in the developing brain become displaced into the underlying SVZ and that their morphology changes form radial to stellate. Thus the VZ radial cells that undergo interkinetic migration may correspond to the in vivo neural stem cells of the early postnatal brain. While these cells maintain the ability to generate neurons and glial cells, it is not known if their differentiation potential is as extensive as their embryonic counterparts.

The observations indicating that ‘glial’ cells function as stem cells challenges the widespread notion that these differentiated cells are lineage-restricted. Virchow introduced the term ‘glia’ to denote a cell type that served as ‘glue’ for neurons and neural circuits (see Jacobson for a historical review (Jacobson, 1991)). This term has become widely used to refer to non-neuronal cells that merely serve support functions in the CNS. It is difficult for many neurobiologists to see the term ‘glia’ used to denote a progenitor cell type that can generate neurons and it has been suggested that a different name should be used for progenitor cells. Conceptually, however, glial functions could be extended to that of a progenitor cells (Barres, 1999). In fact, radial glia, SVZ astrocytes and hippocampal astrocytes (Seri et al., 2001) all possess characteristics of differentiated glia with complex processes suggesting that they function as support (or ‘glue’) cells in addition to their stem cell duties. This changes our views of glial cells, but the above discussion does not imply that all glial cells are stem cells. In fact, only a subpopulation of adult astrocytes may have this potential. Future research should develop methods to identify those glial cells that function as stem cells and distinguish these from glia that only serve in support functions.

The Continuum of Proliferation in Germinal Brain Centers

The data discussed in this paper demonstrate a link between germinal brain regions during development and adulthood. The VZ persists into postnatal life and contains radial glial cell bodies with some properties of embryonic neural stem cells. Within the first two postnatal weeks, radial cells of the lateral wall transform into astrocytes. Some of the astrocytes derived from radial glia appear to remain within the SVZ where they retain stem cell properties (Doetsch et al., 1999a,b). The transformation of radial glia in the lateral ventricular wall is similar to that previously described for cortical radial glia (Schmechel and Rakic, 1979; Voigt, 1989). This morphological change is accompanied by changes in the expression of molecular markers. This morphological and molecular transformation is not, however, associated with terminal differentiation for a subpopulation of adult astrocytes. Some of the properties of embryonic germinal cells are retained. Note that the generalized use of molecular markers as infallible indicators of cell identity, differentiation
Figure 3. Postnatal development of the VZ, characterization of radial glia and astrocytes. Immunolabeling in panels A–F is in red and cell nuclei are labeled green (CyQuant). RC2 immunocytochemistry (ICC) labels a large cohort of radial glia in the newborn brain (A). Seven days after birth (B) radial glia are still present in the brain, but they are less abundant and appear somewhat disorganized. By P15 (C), radial glia are largely absent. The disappearance of RC2+ radial glia correlates with the appearance of GFAP+ astrocytes in the SVZ. At P0 (D), there are no astrocytes in the lateral ventricular wall. Seven days later (E), many GFAP+ cells are present in the medial ventricular wall (arrow) and the corpus callosum (cc), but only a few can be found in the SVZ. By P15 (F), many GFAP+ astrocytes are present in the SVZ (arrowheads), which appears similar to that observed in the adult brain. These data suggest that GFAP+ SVZ astrocytes develop from VZ radial glia. In support of this supposition, these two cell types share some interesting anatomical characteristics. Both VZ radial glia (G) and SVZ astrocytes (H) contact the ventricle lumen and extend a single short 9 + 0 cilium into the cerebrospinal fluid (arrows). The inset H1 shows the entire cell which has the cilium shown in H. Note how this SVZ astrocyte is squeezed into an SVZ location by two neighboring ependymal cells (*). This cilium has been previously described in the neuroepithelial stem cells of the embryonic mammalian brain and the adult avian brain (see text). Panel I shows the cilium at a higher magnification. Note the centriole at the base of this structure (arrow). Panel J shows a scanning electron micrograph of a cilium in the neonatal ventricular wall. Scale bar for panels A–F = 200 µm. Scale bar for panel G = 2.0 µm. Scale bar for panel H = 0.7 µm. Scale bar for panel I = 0.2 µm. Scale bar for panel J = 0.4 µm.
status and lineage has been misleading in the case of radial glia and astrocytes. In fact these markers are as dynamic as the morphological changes, and in the case of intermediate filaments are probably more related to cell physiology and cell cycle than to cell lineage identity.

Contact with the ventricle, movement of the nuclei during the cell cycle, and a single cilium are properties of early neuroepithelial cells and radial glia, whose cell bodies occupy the VZ during development. As postnatal development progresses, the ventricular surface becomes largely populated by ependymal cells, which may force the cell bodies of stem cell astrocytes away from the ventricle lumen. Many SVZ astrocytes, however, extend a thin process between ependymal cells suggesting that contact with the ventricle may be important for stem cell function (Doetsch et al., 1999b). Other astrocytes that lose this early epithelial attribute may lose exposure to signals required for stem cell competence. Thus, the idea that the VZ function ends perinatally may be inaccurate. Another problem with the current notion that the VZ disappears during development to transform into the ependymal epithelium is that it is very difficult, if not impossible, to accurately define when this transformation occurs. In fact the present results indicate that immature ependymal cells coexist with proliferating germinal cells during extended periods of development. This may also vary depending on the species. In birds and reptiles ependymal cells and germinal cells coexist within a VZ throughout the life of the animal (Goldman and Nottebohm, 1983; Alvarez-Buylla et al., 1990; Garcia-Verdugo et al., 2002). In mammals the ‘adult VZ’ is largely composed of non-proliferative ependymal cells,

Table 1
Proportions (%) of VZ cell types present throughout postnatal development

<table>
<thead>
<tr>
<th></th>
<th>P0 (n = 4)</th>
<th>P7 (n = 5)</th>
<th>P15 (n = 6)</th>
<th>P30 (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astrocyte touching ventricle</td>
<td>0</td>
<td>0</td>
<td>22.1</td>
<td>16.7</td>
</tr>
<tr>
<td>Mature ependymal</td>
<td>(0)</td>
<td>(0)</td>
<td>(100)</td>
<td>(73)</td>
</tr>
<tr>
<td>Immature ependymal</td>
<td>(0.1)</td>
<td>(0.41)</td>
<td>(0.306)</td>
<td>(0.355)</td>
</tr>
<tr>
<td>Radial glia</td>
<td>(1.6)</td>
<td>(31.5)</td>
<td>(10.2)</td>
<td>(2.3)</td>
</tr>
<tr>
<td>Mitotic</td>
<td>(0.8)</td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
</tr>
<tr>
<td>Unidentified</td>
<td>(2.0)</td>
<td>(2.9)</td>
<td>(0)</td>
<td>(0)</td>
</tr>
<tr>
<td>Cells sampled</td>
<td>(132)</td>
<td>(1652)</td>
<td>(452)</td>
<td>(438)</td>
</tr>
</tbody>
</table>

Numbers in parentheses represent the number of cells sampled.

Figure 4. Specifically labeled radial glia in the newborn brain generate neurons. The box in A shows the location of D, E and F in a horizontal section of a mouse brain. We injected an adenovirus expressing cre recombinase into the lateral striatum of cre reporter mice. In these animals, all infected cells and their progeny express the hPLAP reporter gene. By injecting into the striatum, we initially infect a cohort of non-proliferative striatal cells and also radial glia in the VZ that extend radial processes through the injection site. Two days after viral injection, the only labeled cells in the VZ were radial glia (B). Six days after injection (C), labeled migratory neuroblasts were found in the SVZ and the rostral migratory stream (E). Panel C shows an example of these migratory cells. Eight days after radial glia labelling, labeled neurons have migrated to the granule and periglomerular layers of the olfactory bulb (F). Scale bar in panel B = 100 µm. Scale bar in panel C = 50 µm.
but the presence of intercalated processes from stem cell astrocytes suggests some similarity to birds and reptiles.

The properties of the VZ microenvironment that permit radial glia and SVZ astrocytes to maintain stem cell potential are not fully understood. An environment rich in noggin is thought to release some progenitor cells from BMP inhibition, which in turn permits neurogenesis (Lim et al., 2000). As discussed earlier, noggin expression is found primarily in cells that contact the ventricle. In adults, these cells are ependymal and astrocytic, in neonates they are radial glia. The stem cell niche may be entirely linked to the epithelial nature of the early brain. Cells in the early neuroepithelium contact both the ventricular surface and the surface of the brain. As other epithelial cells, the end feet of neuroepithelial cells contact the basal lamina that separates the neuroepithelium from the surface mesoderm. These early epithelial contacts with mesoderm may be maintained in the adult through contacts with blood vessels. Both radial glia and astrocytes are known to make such contacts. Interestingly a close interaction has also been found between progenitor cells in the subgranular layer (SGL) of the hippocampus and blood vessels (Palmer et al., 2000). The recent identification of the primary progenitors of the SGL as radial astrocytes (Seri et al., 2001) and the demonstration that these cells too are derived from radial glia (Eckenhoff and Rakic, 1984) suggests similarities with the development of the SVZ described here. In the case of the SGL, however, it is interesting that the progenitor astrocytes have been displaced away from the ventricular wall. It will be interesting to determine in this hippocampal germinal zone what substitutes for the VZ niche.

Concluding Remarks
The data presented here indicate that the VZ persists postnatally in the lateral ventricle walls in the region where the adult SVZ develops and where neurogenesis persists into adult life. The neonatal VZ is composed largely of proliferative radial glial cell bodies that display interkinetic nuclear migration. Previous examinations of the VZ have been performed almost exclusively in embryos where experimental manipulations are difficult. The presence of the VZ in the more accessible postnatal animals may facilitate future studies of the cellular and molecular mechanisms that control stem cell proliferation and differentiation in the VZ. Preliminary data suggest that these neonatal VZ cells generate multiple brain cell types and ultimately give rise to the parenchymal and SVZ astrocytes of the adult brain (Fig. 5). The present work suggests that there is a continuum of germinal activity that links neuroepithelial stem cells to radial glia and ultimately to the astrocytes that are stem cells in the adult brain. The link between embryonic and adult neurogenesis may reveal significant breakthroughs in understanding how the brain matures and ages.

Notes
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Address correspondence to Anthony D. Tramontin, University of California, San Francisco, Neurosurgery Research, Box 0520, Koret Laboratories, K130, 10 Kirkham Street, San Francisco, CA 94143, USA.

Email: tonyt@itsa.ucsf.edu.

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