
Cell Migration in the Rostral Migratory Stream

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Abstract

Adult neurogenesis in the olfactory bulb of rodents is provided by cells which migrate tangentially from their site of genesis into the forebrain subependymal layer (SEL). This migration involves 'chains' of neuroblasts sliding into a meshwork of astrocytic cells and processes (glial tubes). The analysis of this process in postnatal rodents and in adult rabbits reveals different types of relationships occurring both among the migrating cells and between these cells and the glial structures of the SEL.

Tangential migration characterizes the subependymal layer (SEL) of adult rodents. Within the SEL, chains of migrating cells are ensheathed by a meshwork of astrocytes (glial tubes) that continue into the olfactory bulb, wherein single neuroblasts spread radially (Peretto *et al.*, 1999). This striking structural plasticity is the model of choice to unravel mechanisms that allow neurogenesis and cell migration to persist into the adult mammalian brain. Understanding these mechanisms is crucial from the perspective of repair of the mature nervous tissue. The unique organization of glia along the migration pathway led to the hypothesis that they have a scaffolding function in cell migration and guidance, as previously established during development in other parts of the nervous system (Rakic, 1990). Not consistent with this hypothesis is the finding that during the early postnatal period tangential migration along the SEL occurs in the absence of chain organization and glial tubes. In general, migration is orthogonal to the still existing radial glia, thus suggesting that glial substrates are not essential for cell displacement into and through the SEL. A comparative approach extended to the adult rabbit forebrain shows a pattern of cell proliferation and migration very similar to that previously described in rodents, but occurring within a different astrocytic organization—one that is devoid of well-formed glial tubes. In the rabbit, the olfactory ventricles do not close at birth, thus leaving a ventricular cavity in the area corresponding to the 'rostral extension' of rodents that is characterized by the glial tubes. By contrast, the olfactory ventricles of the adult rabbit are surrounded by a poorly defined SEL wherein astrocytes are densely packed but not organized to form channels. However, some chains of cells immunoreactive for the polysialylated form of the neural cell adhesion molecule (PSA-NCAM) can be observed. In rodents, this is a characteristic feature of the long-distance,

tangential cell migration occurring along the glial tubes of the SEL. Thus, the results obtained in the rabbit SEL seem to confirm that, even in an adult mammalian brain, specific structures such as the glial tubes are not required to facilitate cell migration. Ongoing studies in the postnatal rat forebrain show that the assembly of glial tubes in the SEL occurs around the third postnatal week, coincidentally with the progressive maturation of the surrounding brain parenchyma (Peretto *et al.*, 1998). Indeed, the immunocytochemical localization of a variety of glia- and neuron-associated molecules in the SEL of postnatal and adult rodents reveals that both cell types show a certain degree of immaturity. In addition to mature astrocytic markers, cells of the glial tubes also express the intermediate filament protein vimentin, which is abundant in radial glial cells. The migrating neuroblasts retain molecules usually expressed during development, as well as putative regulators of cell migration such as PSA-NCAM, stathmin and the neu-regulin receptor erbB4 (DeMarchis *et al.*, 2000). The shift from a widespread distribution of these molecules during the early postnatal period to their very restricted localization in the SEL occurring at the third postnatal week suggests that glial cells in the SEL, rather than being directly involved in cell migration and guidance, could be implicated in the isolation and compartmentalization of a microenvironment that subserves the persistent neurogenesis which characterizes this region during adulthood. Moreover, the heterogeneous distribution of glial cells in the SEL of postnatal versus adult rodents, as well as in the SEL of different mammalian species, leads us to the conclusion that multiple types of cell migration can be found in the brain of different mammals, and suggests that most of them share a behavior that is rather independent of their local glial substrates.

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