IMPACT OF ANGIOGENESIS INHIBITION ON POSTNATAL NEUROGENESIS

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New neurons are continuously added to the olfactory bulb (OB) throughout the life of mammals. Postnatal neurogenesis is a multistep process that includes proliferation, migration, differentiation and integration of neurons into the circuits. Neuronal precursors destined for the OB arise in the subventricular zone and migrate for a long distances along the rostral migratory stream (RMS). In the RMS, neuroblasts move along each other thus forming chains that are surrounded by astrocytes. Moreover, neuronal precursors are able to divide while migrating. Recently, the role of blood vessels in navigation of neuroblasts toward the OB has been shown. In addition to their trophic function, specifically arranged blood vessels serve as a physical support for migrating neuroblasts as well as produce migration promoting cues. We have focused on the examination of an importance of specific vascular arrangement for migration of neuroblasts. The aim of this study was to examine an impact of angiogenesis inhibition on reorganization of the RMS blood vessels to the migratory scaffold as well as on the migration and proliferation of neuroblasts within the pathway. Rats were administered an inhibitor of angiogenesis - endostatin during the first postnatal week and then they survived till postnatal day 14 (P14) or till adulthood. We have found that the inhibition of angiogenesis, during the critical period when the vasculature scaffold in the RMS is establishing, has influenced the blood vessels density in the RMS of P14 rats and adult rats and has prevented blood vessels from a rearrangement to the proper scaffold structure. This resulted in disorganization of neuroblasts migration in the RMS - they migrated untypically, rather individually than in chains. Moreover, in the RMS rostral parts, neuroblasts migrated out of the migratory pathway. In addition to migration, proliferation of neuroblasts was also affected. The quantification of proliferating cells has shown that the inhibition of angiogenesis caused an increase of the number of proliferating cells. We suppose that this increase might be caused by accumulation of proliferating cells in the RMS due to the disorganized RMS vasculature and impaired neuroblasts migration. We can conclude that manipulation with the angiogenesis during the early postnatal development caused the disruption of neurogenic processes in the RMS. By this study we proved that in the RMS, not only the presence of blood vessels itself but their specific arrangement into the vascular scaffold is necessary for proper functioning of postnatal neurogenesis.

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