Dynamics of glial cell proliferation following excitotoxic damage to the adult and aged rat brain

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We have previously shown that excitotoxicity to the aged rat brain induces a delayed neurodegenerative process, but an earlier onset and a more widespread astroglial response compared to the adult brain. Moreover, aged animals display a prevalence of reactive ramified microglial morphologies with fewer round/pseudopodic microglia/macrophages. However, little is known about the proliferation capacity of glial cells in the aged brain.The aim of this study was to characterise the dynamics of cell proliferation in the adult and aged brain after an intra-striatal injection of NMDA. After intraperitoneal injections of bromodeoxyuridine (BrdU), every 2 hours for 10 hours, animals were sacrificed at 12 hours, 1, 3, 5 and 7 days post-lesion (DPL). After fixation, cryostat sections were processed for double labelling for BrdU and glial fibrillary acidic protein and tomato lectin. At both ages, the temporal and spatial dynamics and phenotypes of proliferating cells were similar, although aged animals always showed a significant decrease in the number of BrdU+ cells. In general, increased amounts of BrdU+ cells were observed in the damaged cortex when compared to the directly injured striatum.Proliferating cells were first found at 1 DPL but maximal numbers were seen at day 3. At this timepoint, BrdU+ cells were mainly located in the cortical lesion border where some of them were identified as ameboid microglia/macrophages and endothelial cells. In the adjacent penumbra only BrdU+ astrocytes were found. At longer survival times, the total number of BrdU+ cells diminished, but BrdU+ microglia/macrophages increased at the lesion border. In conclusion, the aged brain has a decreased capacity of proliferation than the adult. At both ages, BrdU+ cells are mainly located in the cortical lesion border where tissue destruction occurs and meninges are being newly formed.

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