Increased Generation of Neuronal Progenitors after Ischemic Injury in Aged Adult Human Forebrain

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The adult human brain retains the capacity to generate new neurons in the hippocampal formation and neuronal progenitor cells (NPCs) in the forebrain, but to what extend it is capable of reacting to injuries, such as ischemia, is not known. We analyzed postmortem tissue from normal and pathological human brain tissue to study the cellular response to ischemic injury in the forebrain. We observed that cells expressing the NPC marker polysialylated neural adhesion cell molecule (PSA-NCAM) are continuously generated in the adult human subventricular zone (SVZ) and migrate along the olfactory tracts. These cells were not organized in migrating chains as in the adult rodent rostral migratory stream, and their number was lower in the olfactory tracts of brains from old compared to young individuals. Moreover, we show that in brains of patients of advanced age, ischemia led to an elevated number of dividing cells in the ipsilateral SVZ without concomitant apoptotic cell death. Additionally, ischemia led to an increased number of PSA-NCAM-positive NPCs close to the lateral ventricular walls, compared to brains of comparable age without obvious neuropathologic changes. These results suggest that the adult human brain retains a capacity to respond to ischemic injuries and that this capacity is maintained even in old age.