The aging brain: fewer neurons could be better

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Increased production of free radicals and accumulation of nuclear (n) DNA damage are known to be central events in the aging process. Furthermore and in contrast to an old dogma, it has recently become clear that only specific types of neurons show cell loss during aging. We hypothesized that age-related accumulation of unrepaired nDNA damage and age-related loss of neurons interrelate inversely, meaning that certain types of neurons show an accumulation of nDNA damage as they are not reduced in number during aging, whereas other types of neurons do not show an accumulation of nDNA damage but are reduced in number. To test this hypothesis, we investigated changes in the amount of unrepaired nDNA damage (single strand breaks) and in total numbers of neurons of distinct types of neuron in the aging mouse brain *in situ*. The numbers of hippocampal pyramidal and granule cells as well as of cerebellar Purkinje and granule cells were analyzed with stereological techniques in aged mice and were compared to those in adult mice. Furthermore, the amount of unrepaired nDNA damage of the same types of neurons was investigated with In Situ Nick Translation and autoradiography. Indeed we found the hypothesized inverse relation between accumulation of nDNA damage and reduction in number during aging for these types of neurons. These data show that for certain types of neurons (here: Purkinje cells) age-related accumulation of unrepaired nDNA damage might be prevented by neuron loss. Supposed that a lack of accumulation of unrepaired nDNA damage in a certain cell type could be of benefit for the aging brain, our results could serve as a starting point to further investigate cell-type-specific differences in the response to age-related nDNA damage and to develop novel strategies for intervention.
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