Age-related alteration of activity and gene expression of endothelial nitric oxide synthase in different parts of the brain in rats

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Nitric oxide (NO) plays important roles in aging and neurodegeneration. Our previous results indicated that aging differently affects NOS isoforms. Expression of nNOS mRNA was lower while iNOS was absent at any age. However, total NO synthesis increased in aged cerebral cortex and cerebellum as a consequence of changes of nNOS phosphorylation state. The question arise how aging influences activity and expression of eNOS in different parts of adult and aged brain. The levels of eNOS mRNA, protein and activity were measured using RT-PCR, immuno- and radiochemical methods, respectively. Our studies indicated that after inhibition of nNOS with 7-nitroindazole (7-NI) NO synthesis is lower in all parts of aged brain comparing to adults. However, eNOS activity significantly decreases only in cerebellum. The expression of eNOS determined on mRNA level was enhanced in all investigated aged brain parts to 140-190% of adult value and the data were statistically significant for cerebral cortex and cerebellum. The higher level of mRNA is probably the adaptive response to lower NOS activity. However, the Western-blot signal of eNOS protein was unchanged in aged brain parts comparing to adults suggesting age-related disturbances of protein synthesis and its function. It is also possible that a post-translational modification of the enzyme occurs in the aged rat brain. The lower eNOS activity in aged brain may significantly affects the signal transduction processes on the pathway NO/cGMP/PKG.

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