Effetct of healthy aging on blood-brain barrier morphology and function. Does it have any impact on the memory and the protein expression? A comparative study in aged and young rats.

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Objective Severeal articles are published about increased permeability and altered morphology of the blood-brain barrier (BBB) with advanced age. Our study aimed to compare the structure of brain microvessels and function of P-glycoprotein (P-gp) at the BBB and its behavioral consequences in young and aged Wistar rats.

Methods Male Wistar rats 2-3 months (young) and 14-16 months (middle aged) were studied. Dual and triple-probe microdialysis techniques were used to compare BBB permeability for quinidine (QND) in young and aged rats in presence and absence of a specific P-gp inhibitor (PSC-833). Concentrations of QND were analyzed by LCMS-MS. Comparative MR imaging of the brains was performed to study anatomical changes, and also single photon emission computed tomography (SPECT) imaging was applied for comparison P-gp functionality. For ultrastructural analysis, electronmicroscopy was performed. The efflux transporter expression at the BBB was studied at RNA and protein levels. For behavioral analysis Morris-Water maze, New Object Recognition and Pot Jumping tests were used.

Results The control level of QND in absence of PSC-833 was higher in aged than in young rats. In presence of PSC-833, the brain levels increased less in aged than in young animals suggesting lower expression level or impaired functionality of P-gp in old subjects. In MR imaging the extension of cerebral ventricles increased significantly and there were also characteristic ultrastructural changes at the BBB with aging by electronmicroscopy. The P-gp expression seems to be decreased both at protein and at RNA levels in aged rats. However, there was no significant cognitive impairement observed with healthy aging in the behavioral tests.

Conclusions Our results indicate many differences between young adult and aged rats in the structure and function of the BBB. These findings suggest a lower expression and/or reduced P-gp function with aging but, on the other hand, there was no memory and learning deficit observed in the applied behavioral assays in aged subjects. In summary, it can be concluded that healthy aging is a risk factor for increased permeability of BBB, which results in a higher CNS exposure to dangerous xenobiotics and bacterial components in old subjects.