UDK 616.8

ISSN 1331-5196

Neurologia Croatica

SINCE 1953

SAŽETCI
ABSTRACTS

SUPLEMENT

3. – 6. listopada 2018.

Novigrad, Hrvatska

Hrvatski kongres o Alzheimerovoj bolesti (CROCAD-18)

s međunarodnim sudjelovanjem

SUPPLEMENT

October 3 – 6, 2018

Novigrad, Croatia

Croatian Congress on Alzheimer's Disease (CROCAD-18)

with International Participation

NEUROL. CROAT. 2018 67 (Suppl. 3): 1-96

UDK 616.8

ISSN 1331-5196

Neurologia Croatica

SINCE 1953

SAŽETCI / ABSTRACTS

SUPLEMENT

3. – 6. listopada 2018.

Novigrad, Hrvatska

Hrvatski kongres o Alzheimerovoj bolesti
(CROCAD-18)
s međunarodnim sudjelovanjem

SUPPLEMENT

October 3 – 6, 2018

Novigrad, Croatia

Croatian Congress on Alzheimer's Disease
(CROCAD-18)
with International Participation

Urednici suplementa / Supplement Editors:
Goran Šimić, Ninoslav Mimica

Urednik-koordinator / Coordinating Editor:
Damir Petravić

Temeljna istraživanja i neuropatologija u AB / Basic research and neuropathology of AD

THE IMPORTANCE OF BLOOD-BRAIN BARRIER CHANGES FOR ALZHEIMER'S DISEASE

ŠIMIĆ G

Department of Neuroscience, Croatian Institute for Brain Research, University of Zagreb Medical School, Zagreb, Croatia

goransimic@hiim.hr

The blood-brain barrier (BBB) consists of a monolayer of capillary endothelial cells surrounded by pericytes and astrocytic endfeet separated from the endothelium by the basal lamina. The endothelial cells are non-fenestrated due to their interconnection by tight junctions that prevent interstitial exchange. Thus, BBB is largely impermeable to hydrophilic substances, with the exception of rare substances such as glucose, which crosses the BBB by specific sodium dependent and sodium independent glucose transporters that transport glucose against its concentration gradient. Together with other specific membrane transporters expressed by the endothelial cells, this protects brain against waste products, environmental toxins and other potentially harmful molecules and makes brain capillaries almost 100 times less permeable for ions and metabolites than are peripheral microvessels. At the same time, dysregulation or disruption of BBB harbors potential to contribute to development of neurodegenerative diseases. It is therefore possible that the increasing permeability of BBB may be the main reason why the incidence of AD increases with age, as both Aβ and tau proteins can cross BBB. This holds true even for the largest isoform of tau protein of 441 amino acids, which has a molecular weight of 64 kDa. The most recent studies have confirmed the leakage of tau protein to and from the brain through BBB, including phosphorylated or otherwise post-translationally modified tau isoforms. For example, in the blood of asymptomatic individuals 18 to 66 years of age, there were 35 unique clones of circulating memory lymphocytes B and 52 different antibodies found. From those 52 antibodies, 41 were against a proline-rich C-terminus of the tau protein (26 of these were antibodies fully dependent on the phosphorylation of the epitope), and 13 of them showed inhibitory activity in in vitro aggregation assay in lysates of spinal cord of transgenic *MAPT* P301L mice. That circulation of both amyloid and tau molecules, as well as immunocompetent cells, is extremely important is further supported by the finding that passive tau immunization inhibits not only tau but also Aβ pathology in 3xTg AD mice. The best known index of damage to BBB is the measurement of the serum concentration of protein S100β, because damage of BBB causes release of this protein from perivascular astrocytes into the blood. Therefore, it is not surprising that the concentration of S100β in serum correlates well with small vessel disease and cerebral microbleeds, as well as with the degree of cognitive decline in healthy adults. In experimental animals BBB can be opened for about ten minutes by the intraperitoneal administration of mannitol (which is easy to check by administration of Evan's blue dye that diffuses into the brain and spinal cord). Alternatively, BBB can be opened by using the local application of ultrasound. The latter method reduces the build-up of amyloid deposition without causing significant inflammation and increase in the number of activated microglial cells. The method of choice for studying BBB disruption in humans in vivo is dynamic contrast-enhanced MRI (DCE-MRI). However, the method is relatively young and further research is required in order to establish consensus-based recommendations for data acquisition and analysis. In conclusion, despite all of the aforementioned findings and methods, whether breakdown of BBB and tau pathology-dependent remodeling of cerebral arteries occur already before disease onset remains controversial. Latest artificial intelligence deep-learning systems support strong relationship between gut microbiota, where iNOS levels positively correlate with NO production and bacterial killing, and its systemic effect, where released NO may contribute to BBB dysruption, neuroinflammation, and neurodegeneration.

Keywords: Alzheimer's disease, blood-brain barrier, gut microbiota, pathogenesis