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MEETING ABSTRACT

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Chronic treatment with five vascular risk factors causes cerebral amyloid angiopathy but no Alzheimer pathology in C57BL/6 mice

Bettina M. FOIDL and Christian HUMPEL*

Laboratory of Psychiatry and Experimental Alzheimer's Research, Medical University of Innsbruck, Austria

Background: Alzheimer's disease (AD) is the most common form of dementia in the elderly. It is characterized mainly due to the deposition of extracellular amyloid beta (Aβ) plaques and the formation of intracellular neurofibrillary tangles (NFT). However, in more than 80% of all cases also a comorbid deposition of Aβ within the vessel walls, known as cerebral amyloid angiopathy (CAA) is seen. Only a small percentage of both diseases is genetically determined, the much more common forms arise sporadically in the course of aging, affected by different life-style (vascular) risk factors. However, the problem in the currently offered experimental mouse models arises, that these models only represent the genetic and not the sporadic form of the diseases.

Methods: The aim of the present study was therefore, to create and characterize a new mouse model of sporadic CAA and/or AD. We treated young C57BL/6 mice with different vascular risk factors for 35 or 56 weeks, which were lipopolysaccharide, social stress, streptozotozin, high cholesterol diet and copper in the drinking water. Furthermore, four behavioral tests were used to control cognitive changes (black-white box, classical maze, cheeseboard maze and plus-maze discriminative avoidance task).

Results: The treated animals showed impaired learning, memory and executive functions as well as anxiety with increased age. Moreover, they showed increased plasma levels of cortisol, insulin, Interleukin-1β, glucose and cholesterol. Confocal microscopy analysis revealed severe vessel damage already after 35 weeks of treatment. IgG-positive staining points to a drastic blood–brain barrier (BBB) disruption and furthermore, cerebral bleedings were observed in a much higher amount in the treatment group. Interestingly, inclusions of beta-amyloid in the vessels indicated the development of CAA, but no deposition of beta-amyloid plaques and tau pathology in the brains were seen.

Discussion: In summary, this study offers the first mouse model of sporadic cerebral amyloid angiopathy, delineated to an Alzheimer's disease pathology. Therefore, new therapeutic strategies can be tested already in a very early stage of the disease.

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Keywords: Alzheimer's disease – cerebral amyloid angiopathy, sporadic – transgenic mice – vascular pathology – vascular risk factors – behavior

*Corresponding author e-mail: *christian.humpel@i-med.ac.at*