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Defective immune responses against microorganisms in the brain of patients with Alzheimer's disease: Relation with neurodegenerative mechanisms

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Introduction: Alzheimer's disease (AD) is a heterogeneous progressive degenerative dementia usually with a senile onset that affects specific areas of the brain. Senile plaques, neurofibrillary tangles, synapsis loss, neuronal atrophy, cortical neurodegeneration and inflammation are neuro-pathological hallmarks of the disease. The aetiology of the disease is still unclear and the pathogenesis is likely to be multi-factorial with genetic, metabolic and environmental factors interacting with aging. Environmental risk factors, are still largely unrevealed in AD, however they may play a relevant pathogenic role in the disease. Recently, we showed that single nucleotide polymorphisms in genes involved in antiviral responses and located upstream of interferon- λ 3/interleukin-28 (IFN- λ 3/IL-28B), mediator complex-23 (Med23) and interferon regulatory factor-7 (IRF7) were associated with an increased risk of cognitive deterioration and AD. These findings suggested that infections may be a risk factor for AD in the brain of genetically susceptible subjects. Here we show data regarding the mRNA expression level of IFN- λ 3/IL-28B, Med23, IRF7 and IFN-alpha genes in the hippocampus of controls and patients with AD.

Aim: To study the defective immune responses against microorganisms in the brain of patients with Alzheimer's disease; relation with neurodegenerative mechanisms.

Methods: To reinforce the notion of an individual defective immune response against microorganism in AD, the expression of IFN- λ 3/IL-28B, Med23, IRF7 and IFN-alpha genes involved in anti-pathogen defense in hippocampus of 30 patients with neurological defined diagnosis of AD and non-demented controls was investigated.

Results: The majority of AD patients showed a significantly decreased expression levels of IFN- λ 3/IL-28B, Med23, IRF7 and IFN-alpha mRNAs that varied from 0.21 to 0.51 times of the expression levels observed in hippocampus from control brain. Patients with the APOE 4 epsilon allele showed the lowest mRNA levels of IFN- λ 3/IL-28B and IFN-alpha.

Conclusions: These findings support the notion that a defective brain response in antimicrobial defensive mechanisms is a risk factor for developing clinical AD. In fact, subjects with a low mRNA level of IFN- λ 3/IL-28B, Med23, IRF7 and IFN-alpha genes in the hippocampus were more represented among patients with AD. Virus and bacterial infections appear to play an etiological role in neuro-inflammation and in subjects with defective brain defense they induce neurodegeneration and neuron loss leading to AD. These findings suggest new therapy approaches based upon reinforcement of individual immune response, along with the identification of sub clinical viral and bacterial infections and their specific treatment.

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