

NEUROINFLAMMATION SUPPRESSION AND IMPROVED COGNITIVE FUNCTION BY THE ACETYLCHOLINESTERASE INHIBITOR RIVASTIGMINE**E. Nizri¹, M. Irony-Tur-Sinai¹, E. Lavi², W. Marta¹, T. Brenner¹***¹Hadassah-Hebrew University Medical Center, Jerusalem, Israel, ²Weill Medical College, Cornell University, New York, United States*

In this study we sought to determine the influence of the acetylcholinesterase inhibitor rivastigmine on central nervous system (CNS) inflammation in experimental autoimmune encephalomyelitis (EAE), the experimental model for multiple sclerosis (MS). EAE mice were treated with rivastigmine (0.75 mg/kg/day) s.c. or via sustained release minipumps and monitored for clinical severity, the presence of neuropathological markers of inflammation and damage, and T-cell reactivity *ex vivo*. Treatment with selective antagonists of nAChR was used to determine the subtype of receptor through which rivastigmine induced its effect. In addition, spatial memory was assessed in the Morris water maze (MWM) test. Rivastigmine markedly ameliorated clinical symptoms of EAE and the spatial memory deficits induced by EAE. It also reduced demyelination, microglia activation and preserved axons in comparison with the control group, probably due to its anti-inflammatory effect. Rivastigmine decreased the reactivity of encephalitogenic T-cells and the production of pro-inflammatory cytokines (TNF- α , IFN- γ and IL-17) without affecting the production of IL-10. The effects of rivastigmine on T-cells were abolished by $\alpha 7$ nAChR antagonists. Antigen presentation was also affected by this treatment. Thus, rivastigmine showed a multi-level activity on various stages of the immune response in EAE, affecting Th1 and Th17 lineages and antigen presentation, culminating in ameliorated clinical score and cognitive function.