VDR NUCLEAR RECEPTOR IS KEY TO RECOVERY OF COGNITIVE DYSFUNCTION

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During DMM 2006 we reported that chronic inflammatory disease, including much 'autoimmune' disease, was caused by an intraphagocytic biofilm-like microbiota. Recovery followed activation of the VDR with Olmesartan, and long-term administration of subinhibitory antibiotics. Surprisingly, as the inflammatory disease disappeared from the subjects in that cohort, manifestations of comorbid neurological disease also receded. Memory and cognition returned as the inflammation waned, while suicidal ideation, depression, bipolar disorder, peripheral neuropathies and even obsessive compulsive disorder, receded. Additionally, we found that the neurological symptoms fluctuated with the level of Immunopathology during the healing process, presenting special problems with cohort management. The VDR is at the heart of the innate immune system, responsible for expression of a majority of the body's antimicrobial peptides [1]. Changes in lifestyle and medicine during the 20th century have created an environment favorable to the proliferation of pathogens which evade the immune system by suppressing activation of the VDR [2]. Kandel identified that short term memory involves activation of PKA [3]. We have determined that activation of PKA is regulated by the process of VDR homeostasis in chronic immune disease, pointing towards a putative mechanism whereby immune dysfunction can directly suppress short-term memory. However the above subjects not only reported the return of short term memory, but also of mid-term and long-term memory. The molecular mechanisms linking immune dysfunction and cognitive dysfunction are clearly profound. We propose that studies of linked dysfunction will provide more insight than studies of neurological manifestations alone.

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