Neuroinflammation and Alzheimer's Disease

WALKER, Douglas Gordon

Molecular Neuroscience Research Center, Shiga University of Medical Science, Seta, Otsu, JAPAN

email: (walker@belle.shiga-med.ac.jp)

Background

Inflammation has been considered as a pathological mechanism for Alzheimer's disease (AD) for more than 30 years, initially based on the pathological observations of activated microglia identified in postmortem human brains. In recent years, modern gene expression profiling techniques and single nucleotide polymorphism screening have been applied to identify different inflammation associated changes and new proteins involved. There have been discrepancies in the two approaches that need to be considered. Ultimately, the goals of all of these studies are to identify inflammation associated therapeutic targets for AD, but there is still incomplete understanding of how inflammation affects AD and the best way to modulate it. One approach is address the question '**what are microglia in AD brains *actually* doing**".

Methods

Comparison will be made between results from publicly available gene databases of AD and control human brain tissue, and immunohistochemical approaches using human brain tissues to phenotype microglial expression of key target proteins.

Results

Gene expression databases from human materials provide a wealth of information about inflammatory changes in AD brains with results conflicting with established concepts. To address the fundamental question about the extent and localization of activated microglia, we will consider the distribution of microglia expressing the purinergic receptor P2RY12 in relation to AD pathological structures. P2RY12 is considered a marker for non-activated microglia. In addition, genetic studies have linked triggering receptor expressed by myeloid cells-2 (TREM-2), CD33 and progranulin with inflammatory mechanisms of neurodegeneration. The expression of these proteins by microglia and their known biological functions will be considered in the context of AD inflammatory mechanisms.

Conclusions

To understand and develop treatments for AD, an accurate picture of what is happening in human disease affected tissues is needed. This is needed to ensure that animal models used for testing therapies accurately reflect the human disease.

Keywords

Microglia, immunohistochemistry, gene expression, phenotypes, neurodegeneration