Abstract 509

UNDERSTANDING MICROGLIAL RESPONSES IN THE FRONTAL CORTEX OF ALZHEIMER´S DISEASE PATIENTS

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Aims

Microglial cells, the immune cells of the brain, and the neuroinflammatory process associated, have been postulated as a critical factor in AD pathogenesis, since the identification of genetic risk factors related to microglial function. However, the microglial role in the development/progression of AD has not been determined yet. In this sense, we have previously reported a limited activation and microglial degeneration in the hippocampus of AD patients in contrast to the proinflammatory view based on findings in amyloidogenic models. Here, we have further analyzed the functional/phenotypic profile displayed by microglial cells in other vulnerable brain region of AD patients, the frontal cortex.

Methods

Immunohistochemistry and image analysis approaches were performed in the frontal cortex of post mortem samples from controls (Braak 0-II) and AD patients (Braak V-VI) including familial cases.

Results

Microglia of Braak V-VI individuals were observed forming clusters and showed, both plaque ($Iba1^+/TMEM119^+/P2ry12^-/CD45^{high}/Trem2^+$) and inter-plaque ($Iba1^+/TMEM119^+/P2ry12^-/CD45^{high}/Trem2^-$) microglial activation, similar that observed in amyloidogenic mice. By contrast, homeostatic and ramified microglial cells of non-demented Braak II cases presented $Iba1^+/P2ry12^+/TMEM119^+/CD45^{low}/Trem2^-$ profile. Furthermore, different microglial responses were observed between sporadic and familial AD cases.

Conclusions

These different microglial phenotypes associated with AD pathology show the heterogeneity and complexity of the microglial phenotypes and suggest different functional states of these glial cells in a region-specific manner. These data need to be considered for better understand the immunological mechanisms underlying AD progression. Modulating brain inflammatory responses might be a promising avenue to prevent cognitive dysfunction in AD patients. ISCiii:PI18/01557(AG)-PI18/01556(JV);Junta Andalucia:UMA18-FEDERJA211(AG). All cofinanced by FEDER funds (European-Union).

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