Apolipoprotein E epsilon 4 is associated with an increased vulnerability to cell death in Alzheimer's disease

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The presumption to suffer from Alzheimer's disease (AD) accelerates with aging. One important risk factor seems to be the isoform epsilon 4 of the apolipoprotein E gene (Apo epsilon 4), which increases the risk to develop AD at an earlier age. Furthermore, convincing evidence is provided that apoptotic cell death mechanisms play an important role in neuronal cell death in AD. In the present study, we investigated whether abnormalities in apoptosis and caspase-3 activity can be found at the level of lymphocytes and a T cell subtype, CD4 T cells, from AD patients compared to aged sex- and ApoE genotype-matched non-demented controls. Under different experimental conditions (at baseline or after in vitro incubation in the presence of proapoptotic stimuli) increased levels of apoptosis and enhanced caspase-3 activity were detected in lymphocytes from AD patients. This difference was most pronounced in the CD4(+) T cell subtype. Notably, we found a significant increase of apoptotic cells and caspase-3 activity in lymphocytes from AD patients bearing one or two alleles of the ApoE4 compared to non-E4 carriers. Again, these effects were strongest in CD4(+) T cells. Circulating amyloid-beta (A beta) levels did not differ between AD patients bearing ApoE4 and non-ApoE4 and age-matched controls. Therefore, it is likely that circulating A beta is not responsible for the observed effects, which might rather reflect an ongoing systemic response in AD, e.g. an increase in CD95 expression.

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