TAU OR A-BETA IMMUNOTHERAPY IN AD?

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The principal events in the AD process are related to a pathologic cleavage of amyloid precursor protein (APP) and tau protein misfolding leading to intracellular neurofibrillary tangles (NFT) formation. The strongest argument in favour of a pivotal role of A-beta in AD pathology is the effect of the numerous mutations of APP-related genes; however, new evidence both in animal models and in patients suggests an effect of A-beta oligomers on the earliest clinical expression of the disease and the strategy of an early therapeutic intervention.
There is also evidence showing that A-beta and tau pathology are correlated but the debate is open with regard to the determining factor for AD pathogenesis. Some studies in transgenic mice overproducing A-beta suggest that the effect of A-beta may depend on the tau molecule while other emphasizes the role of either A-beta or tau alone.
Which is a better target for AD immunotherapy?
Immunotherapy has focused so far on A-beta clearance showing some therapeutic potential not devoid of vascular risk. Clinical data show that this therapeutic effect may be partially or totally independent of an effect of immunotherapy on tau. On the contrary, other studies performed on transgenic mice overproducing A-beta suggests that the early deleterious effect of this peptide or its oligomers may depend on the tau molecule. However, a role of tau in the synaptic disruption that is caused by A-beta is unknown. Other studies on transgenics, aimed at both tau and A-beta, has shown that modulation of tau levels does not have an effect on the onset or progression of the A-beta pathology.
Only clinical results may give an answer to the question of the relevance of A-beta and tau in AD, once both pathways have been tested by immunotherapy or other treatment.

References

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