Amyloid cascade is not the key biological factor in AD

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The dominant hypothesis of Alzheimer Disease (AD) etiology which has been built around one casual factor only, beta-amyloid, remains unproven. Major evidence which invalidates this hypothesis is: The presence of amyloid pathology (amyloid plaques) in cognitively intact individuals. Individuals diagnosed as AD patients who do not have a-beta pathology. Non-conclusive evidence that a-beta pathology represents the first biomarker of the disease and the first sign of sporadic AD onset (tau deposition and cholinergic neurons degeneration are valid candidates!). Continuing failure of therapies based on the amyloid hypothesis. Treatments aiming to reduce or to eliminate a-beta formation with either gamma- or beta-secretase inhibitors have proven to be toxic or worsen cognition. Immunization with anti-a-beta antibodies has not yet demonstrated a clinical effect. Conclusion: Identifying a-beta pathology may be useful for predicting risk of conversion from symptomatic to non-symptomatic AD. However, the utility of a-beta pathology alone to predict cognitive decline may be limited. Tau has revealed itself as a much stronger correlate of cognitive function in AD patients.