A STOCHASTIC SIMULATION APPROACH TO DISCOVER THE LINKS BETWEEN Aβ AND TAU IN LATE-ONSET AD

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Introduction: Alzheimer’s disease (AD) is characterised by the presence of amyloid-beta plaques and tau tangles and the loss of neurons in specific regions of the brain. The connection between these events is still unclear. The amyloid hypothesis proposes a linear pathway where the formation of plaques precedes the appearance of tangles which precedes cell death. An alternative hypothesis is a dual pathway where an upstream driver leads independently to the formation of plaques and tangles¹.

Aims: Using stochastic simulation we aim to discover whether the link between Aβ and tau is a linear or dual pathway or whether another hypothesis is required.

Methods: We used the Systems Biology Markup Language to modify and extend our previous model². In order to test the different hypotheses, we investigated the effects of increased Aβ clearance. If increased Aβ clearance leads to a reduction in tau tangles, then our model would support a linear pathway but if it has no effect on tau pathology, then it would support the existence of a dual pathway.

Results: The model predicts that less tau tangles form if Aβ clearance is increased. However, it also predicts that tau tangles can form independently of Aβ indicating that neither a linear or dual pathway can fully explain what is happening.

Conclusions: Based on our model predictions we hypothesise that there are independent pathways leading to tau and Aβ pathology. However, the model suggests that Aβ may also affect the formation of tau tangles via another pathway involving a stress response.

References:
