Longitudinal amyloid and tau PET imaging in Alzheimer's disease: A systematic review of methodologies and factors affecting quantification

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Deposition of amyloid and tau pathology can be quantified in vivo using positron emission tomography (PET). Accurate longitudinal measurements of accumulation from these images are critical for characterizing the start and spread of the disease. However, these measurements are challenging; precision and accuracy can be affected substantially by various sources of errors and variability. This review, supported by a systematic search of the literature, summarizes the current design and methodologies of longitudinal PET studies. Intrinsic, biological causes of variability of the Alzheimer's disease (AD) protein load over time are then detailed. Technical factors contributing to longitudinal PET measurement uncertainty are highlighted, followed by suggestions for mitigating these factors, including possible techniques that leverage shared information between serial scans. Controlling for intrinsic variability and reducing measurement uncertainty in longitudinal PET pipelines will provide more accurate and precise markers of disease evolution, improve clinical trial design, and aid therapy response monitoring.

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