Evaluation of novel data-driven metrics of amyloid β deposition for longitudinal PET studies

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Purpose: Positron emission tomography (PET) provides in vivo quantification of amyloid-β (Aβ) pathology. Established methods for assessing Aβ burden can be affected by physiological and technical factors. Novel, data-driven metrics have been developed to account for these sources of variability. We aimed to evaluate the performance of four data-driven amyloid PET metrics against conventional techniques, using a common set of criteria.

Methods: Three cohorts were used for evaluation: Insight 46 (N=464, [18F]florbetapir), AIBL (N=277, [18F]flutemetamol), and an independent test-retest data (N=10, [18F]flutemetamol). Established metrics of amyloid tracer uptake included the Centiloid (CL) and where dynamic data was available, the non-displaceable binding potential (BPND). The four data driven metrics computed were the amyloid load (Aβ load), the Aβ PET pathology accumulation index (Aβ index), the Centiloid derived from non-negative matrix factorisation (CLNMF), and the amyloid pattern similarity score (AMPSS). These metrics were evaluated using reliability and repeatability in test-retest data, associations with BPND and CL, and sample size estimates to detect a 25% slowing in Aβ accumulation.

Results: All metrics showed good reliability. Aβ load, Aβ index and CLNMF were strong associated with the BPND. The associations with CL suggests that cross-sectional measures of CLNMF, Aβ index and Aβ load are robust across studies. Sample size estimates for secondary prevention trial scenarios were the lowest for CLNMF and Aβ load compared to the CL.

Conclusion: Among the novel data-driven metrics evaluated, the Aβ load, the Aβ index and the CLNMF can provide comparable performance to more established quantification methods of Aβ PET tracer uptake. The CLNMF and Aβ load could offer a more precise alternative to CL, although further studies in larger cohorts should be conducted.

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