

The Amyloid Imaging for the Prevention of Alzheimer's Disease Consortium: A European collaboration with a global impact

Lyduine E. Collij, Gill Farrar, David Valléz García, Ilona Bader, Mahnaz Shekari, Luigi Lorenzini, Hugh Pemberton, Daniele Altomare, Sandra Pla, Mery Loor, Pawel Markiewicz, Maqsood Yaqub, Christopher Buckley, Giovanni B. Frisoni, Agneta Nordberg, Pierre Payoux, Andrew Stephens, Rossella Gismondi, Pieter Jelly Visser, Lisa Ford, Mark Schmidt, Cindy Birck, Jean Georges, Anja Mett, Zuzana Walker, Mercé Boada, Alexander Drzezga, Rik Vandenberghe, Bernard Hanseeuw, Frank Jessen, Michael Schöl, Craig Ritchie, Isadora Lopes Alves, Juan Domingo Gispert and Frederik Barkhof on behalf of the AMYPAD consortium

Background: Amyloid- β (A β) accumulation is considered the earliest pathological change in Alzheimer's disease (AD). The Amyloid Imaging to Prevent Alzheimer's Disease (AMYPAD) consortium is a collaborative European framework across European Federation of Pharmaceutical Industries Associations (EFPIA), academic, and 'Small and Medium-sized enterprises' (SME) partners aiming to provide evidence on the clinical utility and cost-effectiveness of Positron Emission Tomography (PET) imaging in diagnostic work-up of AD and to support clinical trial design by developing optimal quantitative methodology in an early AD population. The AMYPAD studies: In the Diagnostic and Patient Management Study (DPMS), 844 participants from eight centres across three clinical subgroups (245 subjective cognitive decline, 342 mild cognitive impairment, and 258 dementia) were included. The Prognostic and Natural History Study (PNHS) recruited pre-dementia subjects across 11 European parent cohorts (PCs). Approximately 1600 unique subjects with historical and prospective data were collected within this study. PET acquisition with [18F]flutemetamol or [18F]florbetaben radiotracers was performed and quantified using the Centiloid (CL) method.

Results: AMYPAD has significantly contributed to the AD field by furthering our understanding of amyloid deposition in the brain and the optimal methodology to measure this process. Main contributions so far include the validation of the dual-time window acquisition protocol to derive the fully quantitative non-displaceable binding potential (BPND), assess the value of this metric in the context of clinical trials, improve PET-sensitivity to emerging A β burden and utilize its available regional information, establish the quantitative accuracy of the Centiloid method across tracers and support implementation of quantitative amyloid-PET measures in the clinical routine.

Future steps: The AMYPAD consortium has succeeded in recruiting and following a large number of prospective subjects and setting up a collaborative framework to integrate data across European PCs. Efforts are currently ongoing in collaboration with ARIDHIA and ADDI to harmonize, integrate, and curate all available clinical data from the PNHS PCs, which will become openly accessible to the wider scientific community.

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