Publishable Summary

In addition to the ambitious aims of AMYPAD in terms of collecting significant amount of amyloid scans not only cross-sectionally but longitudinally, WP5 has as one of its initial goals the collection of external datasets of amyloid imaging in Alzheimer's Disease. This document outlines the motivation behind such an exercise, the process of obtaining these datasets and the strategy for analyzing this data for the benefits of both AMYPAD as a Consortium, but also the general research community.

As a WP focused on advanced analysis of amyloid imaging and disease modeling, most of WP5 work requires large amounts of data and preferentially with longitudinal assessments. As a first consequence, its analyses on AMYPAD-derived data will not take place within the beginning of the project. As a second consequence, the heterogeneity in the data is inevitable, and requires careful consideration and appropriate consideration. Therefore, it is natural for WP5 to begin by building knowledge and expertise in quantitative analysis of large amyloid PET datasets by closely collaborating with existing initiatives in longitudinal and cross-sectional research of Alzheimer's Disease. The goals of collecting existing datasets are to gain experience and expertise in analyzing 1) heterogeneous amyloid PET datasets, and 2) a wide range of disease stages, providing a better understanding of how reproducible the current and future methods are between different populations.

At the moment, WP5 has collected data from ADNI, AIBL and the Baltimore Longitudinal Study of Aging, and has established successful collaborations with the Washington University. Several other research groups, studies and universities have been contacted and expressed their interest in collaborating with AMYPAD WP5. In order to ensure a consistent and appropriate stewardship of the datasets, an internal agreement was reached with our partners in Barcelona (BBRC) in order to utilize their computing resources for image analysis and storage of their XNAT server. This solution also allows for an optimal and structured organization of the datasets, as well as for a controlled method for providing access to different team members on a project-by-project basis.

The current analysis strategy of WP5 is divided into two streamlines: 1) longitudinal analysis of amyloid imaging; 2) disease modeling. The first predominantly refers to the techniques of analysis of multiple time point amyloid image data while accounting for unbalanced and missing data, and allowing for different structure of the covariance matrix in the case of mixed-effects models. The second is more encompassing and refers to staging of the disease, while incorporating additional imaging, demographics and physiological datasets in the statistical analysis aiming to answer biological and clinical questions. A number of specific analysis plans are outlined in the document and compose the initial methodology to be followed by AMYPAD WP5 in both streamlines.

In addition to the potential contributions to the scientific community that can rise from the results of the planned analysis and collection of data, WP5 initial efforts will help in 1) deciding which subjects to select for follow-up scans in WP4 by supporting the work of the Balancing Committee, 2) understand how patients can be better selected into proof-of-concept trials in EPAD, and 3) producing more robust and generalizable disease models by cross-validating findings using several different datasets.

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