

GADIR: Genomics and Digital Neuropathological Phenotyping of Iberian Brains to Refine the Genetic Architecture of Dementia

Poster #T.120

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INTRODUCTION

Alzheimer's disease (AD) and related dementias are genetically complex and neuropathologically heterogeneous. Although genome-wide association studies (GWAS) have identified numerous risk loci, most rely on clinical diagnoses, limiting biological specificity and obscuring pathology-specific genetic signals. Neuropathological confirmation remains essential to accurately resolve the genetic architecture of distinct and co-occurring brain pathologies. To address this challenge, the GADIR project integrates samples from 16 brain banks across Spain and Portugal into a harmonized cohort of approximately 3,500 neuropathologically characterized brains, creating a deeply phenotyped resource for neuropathology-driven genomic studies (**Figure 1**).

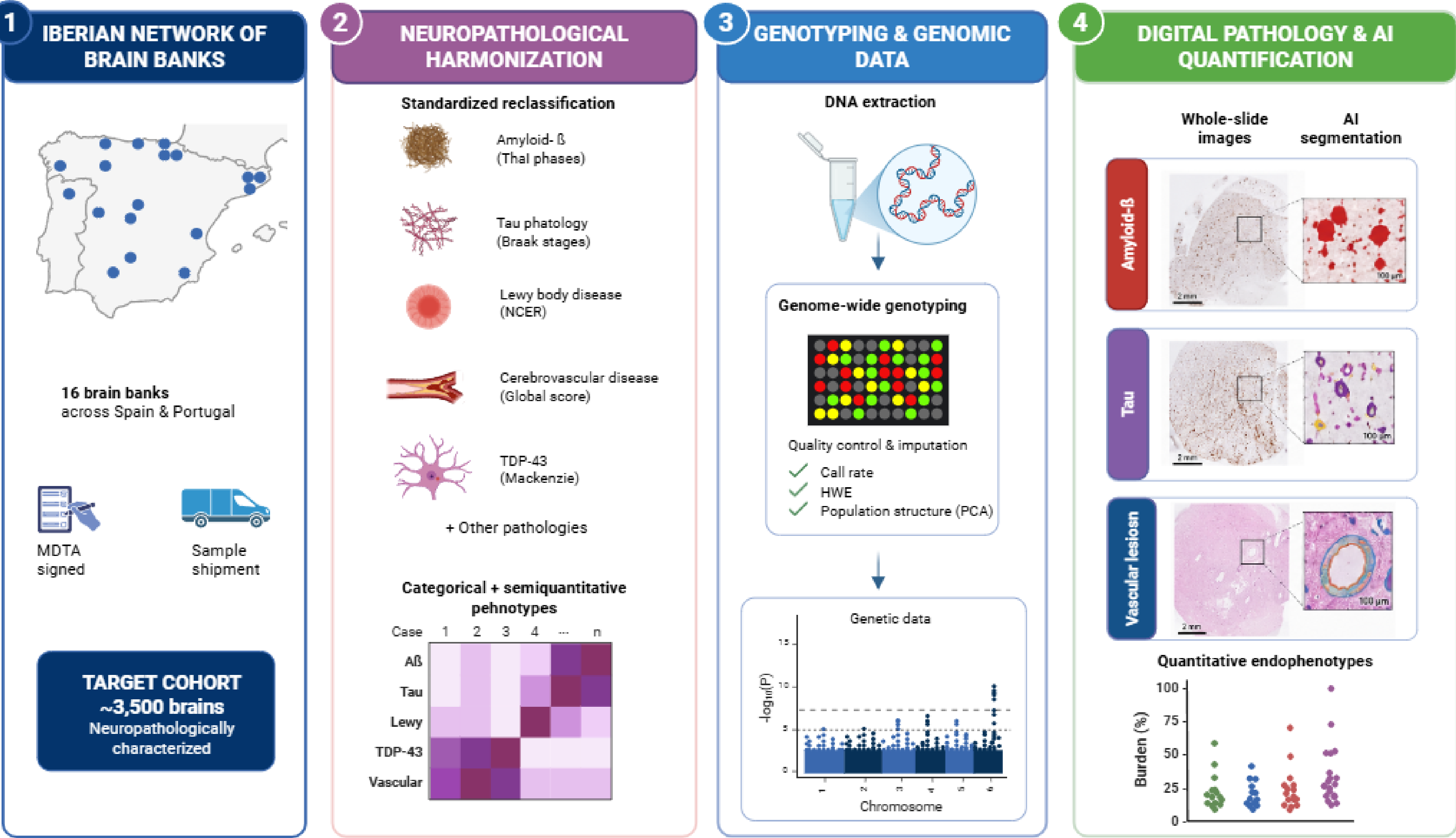


Fig 1. Overview of the GADIR workflow integrating harmonized neuropathology, genomics and AI-based digital pathology.

CURRENT STATUS

Material and Data Transfer Agreements (MDTAs) have been established with participating biobanks. Within the first year, 600 parietal brain samples have initiated workflows for neuropathological standardization (**Figure 2, 3**), DNA extraction, and data processing, demonstrating the feasibility of large-scale integration of multi-center post-mortem data.

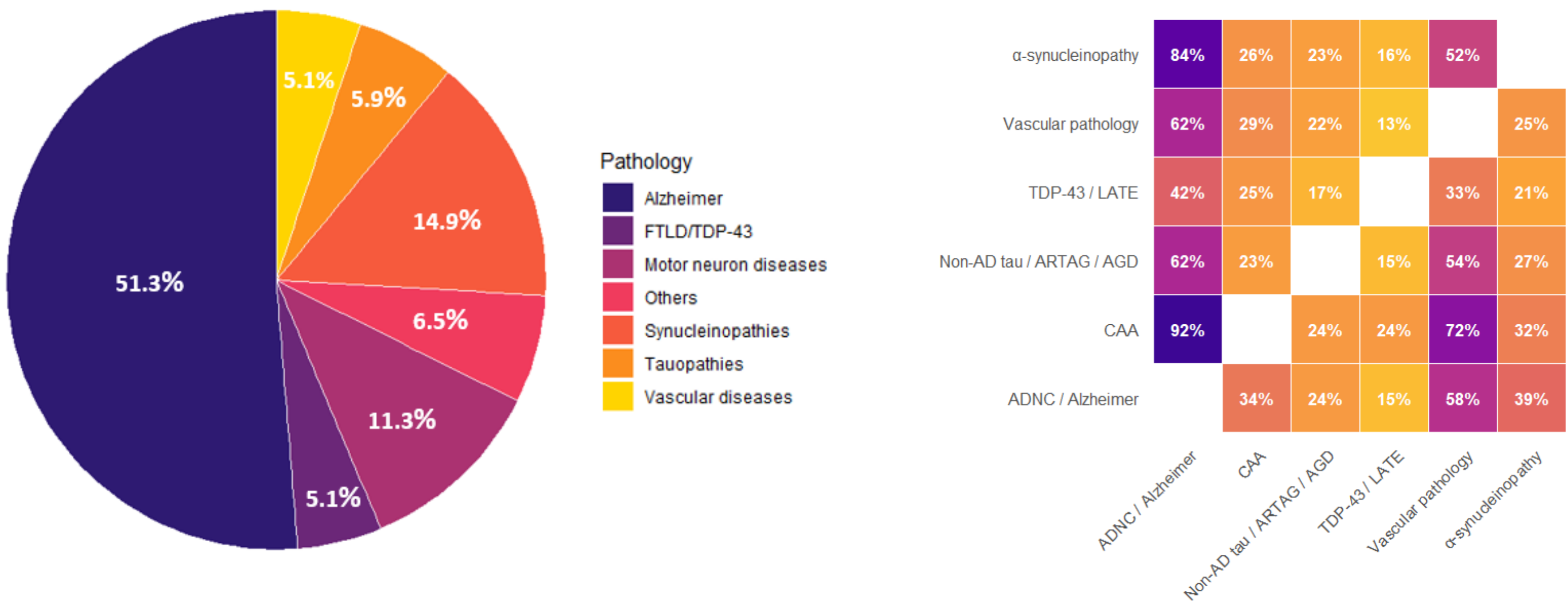


Fig 2. Neuropathological diagnoses among GADIR brain samples available to date.

Fig 3. Co-occurring neuropathological hallmarks in GADIR brain samples available to date.

FUTURE STEPS & CONCLUSIONS

- First genotyping round will start in the fall of 2026
- Additional 600 samples are expected by the end of 2026
- GADIR project is an initiative designed to generate a deeply phenotyped, neuropathology-driven genomic resource
- GADIR is positioned as a foundational effort to catalyze a broader European initiative.

ACKNOWLEDGEMENTS

We are thankful to the families and patients who agreed to donate their brains. This project received funding from the Pasqual Maragall Foundation under the Pasqual Maragall Researchers Programme (PMRP) (Grant Agreement Number 2023-1334).

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