

# GeNED.ar: a Novel Argentine Admixed Cohort to study Brain Aging using MRI-Derived Brain Age

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We present the GeNED.ar cohort, a multimodal resource from the Buenos Aires metropolitan area, Argentina, designed to support the development and validation of region-specific biomarkers.

INTRODUCTION

The generalizability of MRI biomarkers for Alzheimer’s disease to Latin American populations requires further investigation, given differences in genetic ancestry and socioeconomic context. MRI-derived brain age is a promising, widely accessible biomarker of neurodegeneration.

METHODS

Workflow

```
graph TD
    A[GeNED.ar] --> B{500 participants}
    B --> C[Memory Clinic]
    B --> D[Community-based recruitment]
    C --> E{175}
    E --> F[EXCLUDED]
    E --> G[INCLUDED]
    F --> H[Without MRI: 34]
    F --> I[Without T1w: 4]
    F --> J[By Dx: 5]
    F --> K[Incidental finding: 3]
    G --> L[CU: 65]
    G --> M[VD: 6]
    G --> N[AD: 24]
    D --> O{324}
    O --> P[INCLUDED]
    O --> Q[EXCLUDED]
    P --> R[HP<60: 170]
    P --> S[HP≥60: 65]
    Q --> T[Without MRI: 29]
    Q --> U[Without T1w: 20]
    Q --> V[Movement artifact: 5]
    Q --> W[Incidental finding: 29]
    Q --> X[Without Diagnosis: 1]
    R --> Y[HP<60]
    S --> Z[HP≥60]
    L --> AA[MCI]
    M --> AA
    N --> AA
    AA --> AB[34]
    Z --> AC[3]
    Y --> AD[170]
    Z --> AE[65]
    AA --> AF[37]
    AC --> AG[AD]
    AE --> AG
    AF --> AG
    AB --> AG
    AC --> AG
    AE --> AG
    AF --> AG
    AG --> AH[24]
```

RESULTS

1. Sample characteristics

| Group             | HP<60                 | HP≥60                | CU                   | MCI                  | AD                   | p-value |
|-------------------|-----------------------|----------------------|----------------------|----------------------|----------------------|---------|
| N                 | 170                   | 65                   | 65                   | 37                   | 24                   |         |
| Sex (F:M)         | 119:51                | 47:18                | 40:25                | 30:7                 | 40:10                | 0.291   |
| Age (years)       | 38.7 ± 11.6 [18 - 59] | 67.6 ± 5.1 [60 - 85] | 71.4 ± 6.9 [52 - 94] | 71.7 ± 5.9 [63 - 81] | 77.1 ± 7.3 [59 - 90] | <0.001  |
| Schooling (years) | 14.9 ± 2.8 [5 - 21]   | 11.5 ± 4.3 [0 - 20]  | 8.1 ± 3.3 [2 - 17]   | 8.2 ± 4.2 [1 - 18]   | 5.8 ± 4.4 [1 - 20]   | <0.001  |
| Genetics (N)      | 63                    | 39                   | 44                   | 24                   | 16                   |         |
| APOE4 carriers    | 13/64                 | 4/38                 | 15/47                | 8/26                 | 7/18                 | 0.014   |

HP<60, healthy younger than 60 years of age; HP≥60, healthy older than 60 years of age; CU, cognitively unimpaired, MCI, mild cognitive impairment; AD, Alzheimer’s disease.

3. Brain age

MAE = 4.99  
MSE = 39.04  
R2=0.90

4. Ancestry analysis

Populations is an admixture of Native Americans (NAM) and Caucasians (CEU). Cases and controls are >30% NAM.

Significant differences are observed among groups: lower proportion of NAM ancestry in HP group, highest percent in AD and CU.

5. Impact of risk factors on BAG

| Risk factor       | Estimate | SE    | p-value |
|-------------------|----------|-------|---------|
| Schooling         | 0.022    | 0.097 | 0.817   |
| Hypertension      | 0.554    | 0.897 | 0.537   |
| Diabetes          | 1.495    | 0.996 | 0.134   |
| Dyslipidemia      | -0.024   | 0.813 | 0.976   |
| Hyperthyroidism   | 0.904    | 1.026 | 0.379   |
| Family history    | 0.354    | 0.777 | 0.649   |
| Smoking           | -1.938   | 3.071 | 0.529   |
| Stroke            | -1.591   | 8.542 | 0.852   |
| NAM ancestry rate | -2.005   | 2.972 | 0.501   |
| APOE ε4 carriers  | 0.606    | 1.155 | 0.601   |
| BMI               | 0.101    | 0.065 | 0.122   |

SE, standard error; NAM, Native American; BMI, Body Mass Index

CONCLUSIONS

GeNED.ar provides a unique multimodal dataset for studying brain aging and Alzheimer’s disease in an underrepresented Latin American population, enabling the evaluation of neuroimaging biomarkers in a socioeconomically and genetically diverse real-world cohort.

CONTACT

GeNED.ar

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CONICET

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