**1 Participants**

This study included a total of 13,154 participants, among whom 7,550 (57.4%) were female, and the mean age at study baseline was 86.9 (s.d., 11.4) years (Table[1](https://www.nature.com/articles/s43587-022-00180-5#Tab1)). During the follow-up period (mean (s.d.) = 5.7 (3.6) years) from 2008 to 2018, a total of 8,937 (67.94%) deaths were documented. Participants with higher PDI were more likely to be male, better educated and regular exercisers, compared to those with lower PDI.

Three different samples were used to answer these questions: (1) XXX

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Table 1. Overview of samples | | | | |
|  | **CN** | **CN\_validation** | **MCI** |
| ***n* total** | **367** | **59** | **513** |
| Age [avg. years (SD)] | 74.2 (5.68) | 71.7 (4.15) (PET)/  70.4 (4.17) (MRI) | 74.9 (5.77) |
| Sex [%female] | 51 | 59 | 40 |
| CSFAβ1-42 Status  (-/+/NA) | 171/111/85 | NA | 121/270/122 |
| MMSE [avg. score] | 29 (1.24) | 29 (0.85) | 28 (1.77) |
| Education [avg. years (SD)] | 16 (2.72) | 16 (2.70) | 16 (2.70) |

**2 Precision of brain-predicted age**

To compare the potential of FDG-PET SUVR and GMV to predict chronological age, we used a nested five-fold cross-validation approach, yielding one test prediction for (almost) every subject in the ADNI CN sample, and five test predictions for each subject in the CN\_validation and MCI sample. Regional FDG-PET- and MRI-predicted chronological age comparably well (Table 2) with a mean absolute error (MAE) of 1.99 and 1.89 years, respectively. In the ADNI-derived CN test sets, individuals’ brain-predicted age as assessed with FDG-PET and MRI was on average 0.10 and 0.05 years younger than their chronological age, respectively, thus demonstrating high average potential to capture brain aging in a CN cohort. The OASIS-derived CN\_validation sample was used to validate our findings in an external dataset and showed similar MAEs as the ADNI sample, although chronological age was slightly better predicted from FDG-PET as compared to MRI, reflected in a lower MAE across the five models. XXX

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| Table 2. Precision of predicting chronological age from FDG-PET and MRI scans. For CN\_validation and MCI, results of the first model and metrics over all five models are shown. | | | | | | |
|  | **CN** | | **CN\_validation** | | **MCI** | |
|  | **FDG** | **MRI** | **FDG** | **MRI** | **FDG** | **MRI** |
| ***n* total** | 345⁺ | 345⁺ | 59 | 59 | 513 | 513 |
| **MAE** | 1.99 | 1.89 | 1.83 | 2.43 | 1.96 | 2.68 |
| MAE before bias correction | 4.04 | 3.97 |  |  |  |  |
| Mean (SD) over 5 models | - | - | 2.04 (0.30) | 2.45 (0.19) | 2.18 (0.43) | 2.50 (0.12) |
| **Mean difference** | -0.10 | -0.05 | -0.80 | -0.80 | 0.78 | 1.75 |
| Mean (SD) over 5 models | - | - | -0.66 (0.41) | -0.92 (0.16) | 0.77 (0.26) | 1.57 (0.16) |
| *Notes.* +After outlier exclusion using CN train set (IQR > 6) | | | | | | |

**3 BPAD in CN**

**3.1 BPAD and Cognitive Performance**

**3.2 BPAD and AD Neuropathology**

**4 BPAD in MCI**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Table 3. Correlation strength (rho or r) between BPAD and neuropathology/cognitive function across five different models** | | | | |
|  | **FDG-PET** | | **MRI** | |
|  | **Zero-order** | **Partial** | **Zero-order** | **Partial** |
| **CSF ABETA** | **-0.222  [-0.237; -0.172]** | **-0.186  [-0.224; -0.135]** | **-0.316  [-0.319; 0.305]** | **-0.269  [-0.279; -0.266]** |
| **AV45 (global SUVR)** | **0.137  [0.113; 0.154]** | **--** | **0.197  [0.176; 0.217]** | **0.173  [0.163; 0.202]** |
| **CSF Tau** | **--** | **--** | **0.127  [0.121; 0.138]** | **0.124  [0.114; 0.138]** |
| **CSF PTau** | **--** | **--** | **0.146  [0.141; 0.157]** | **0.139**  **[0.131; 0.153]** |
| **ADNI-MEM** | **-0.279 [-0.321; -0.234]** | **-0.250  [-0.257; -0.234]** | **-0.455  [-0.459; -0.443]** | **-0.409  [-0.420; -0.397]** |
| **ADNI-EF** | **-0.272 [-0.323; -0.241]\*** | **-0.255  [-0.258; -0.219]\*** | **-0.325  [-0.339; -0.307]\*** | **-0.290  [-0.301; -0.286]\*** |
| ***Notes.* Median [range] of correlation coefficients are displayed when significant (p<0.05) correlation existed in brain-predicted age according to all five models. Coefficients are Spearman Rho unless marked by an asterisk (\*: Pearson’s r coefficient).** | | | | |