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Association of the Frailty Index with structural brain volumes in The Irish Longitudinal Study on Ageing (TILDA)

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Background and aims: Frailty is a recognised state of vulnerability in older adults. The Frailty Index (FI) measures frailty according to 32 deficits across multiple domains (Table 1) that accumulate with age and could have an impact in brain health. Our aim was to study brain volume signatures of a FI in The Irish Longitudinal Study on Ageing (TILDA).

Methods: We included TILDA wave 3 participants aged 65+ years who took part in a 3T MRI sub-study. Using Freesurfer we measured total cortical grey matter (GM) volume and regional GM volumes according to the Desikan-Killiany atlas. We performed partial correlation analyses with FI and Desikan GM regions volumes adjusted by age, sex and total brain volume; and performed a partial correlation tests to compare total cortical GM volume with each FI item adjusted by age and sex.

Results: In 407 participants, the volumes of regions related with prefrontal cortex and temporal cortex were negatively correlated with the FI and positive correlated with left precuneus (Figure 1). Only FI deficits related with functional impairments, osteoporosis and polypharmacy were associated with total cortex volume (Table 1).

Table 1. Differences in global cortex volume for each item within FI.

| FI Item | R   | p    | FI Item | R   | p    |
|---------|-----|------|---------|-----|------|
| Difficulty walking 100 m | -0.11 | 0.020 | Cataracts | -0.088 | 0.079 |
| Poor self rated physical health | -0.098 | 0.050 | Arthritis | -0.014 | 0.785 |
| Poor self rated vision | -0.110 | 0.028 | Osteoporosis | -0.015 | 0.764 |
| Poor self rated hearing | -0.107 | 0.031 | Cancer | -0.003 | 0.946 |
| Daytime sleepiness | -0.068 | 0.170 | Varicose ulcer | -0.007 | 0.855 |
| Polypharmacy | -0.209 | 0.038 | Difficulty climbing one flight of stairs | -0.029 | 0.562 |
| Knee pain | -0.114 | 0.022 | Glaucoma/Age related macular degeneration | -0.057 | 0.256 |
| Urinary incontinence | 0.020 | 0.696 | Self rated day-to-day memory | -0.006 | 0.911 |
| Hypertension | 0.008 | 0.865 | Difficulty following a conversation with four people | -0.109 | 0.028 |
| Angina | 0.014 | 0.775 | Difficulty stooping, kneeling or crouching | -0.075 | 0.131 |
| Heart attack | - | - | Difficulty reaching above shoulder height | -0.088 | 0.078 |
| Difficulty rising from a chair | -0.062 | 0.664 | Difficulty pushing/pulling large objects | -0.052 | 0.301 |
| Diabetes | -0.085 | 0.087 | Difficulty lifting/carrying weights >10lbs | -0.042 | 0.405 |
| High cholesterol | 0.032 | 0.518 | Difficulty picking up coin from table | -0.007 | 0.887 |
| Irregular heart rhythm | 0.035 | 0.479 | Feeling lonely | 0.026 | 0.605 |
| Other CVD | -0.043 | 0.393 | Stroke or TIA | - | - |

Figure 1. Significant partial correlation coefficient for brain volume by region and FI, adjusted by age, sex and total brain volume.

Conclusion: From a volumetric perspective, results suggest that frailty as captured by a FI may primarily involve the visual-executive-planification coordination systems. Further studies are necessary to replicate this finding with other FIs; compare associations with other frailty measurement tools; complement analyses with connectivity studies. A better understanding of the neuro correlates underlying frailty in older adults is needed for better prevention and treatment of age-related disability.

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