

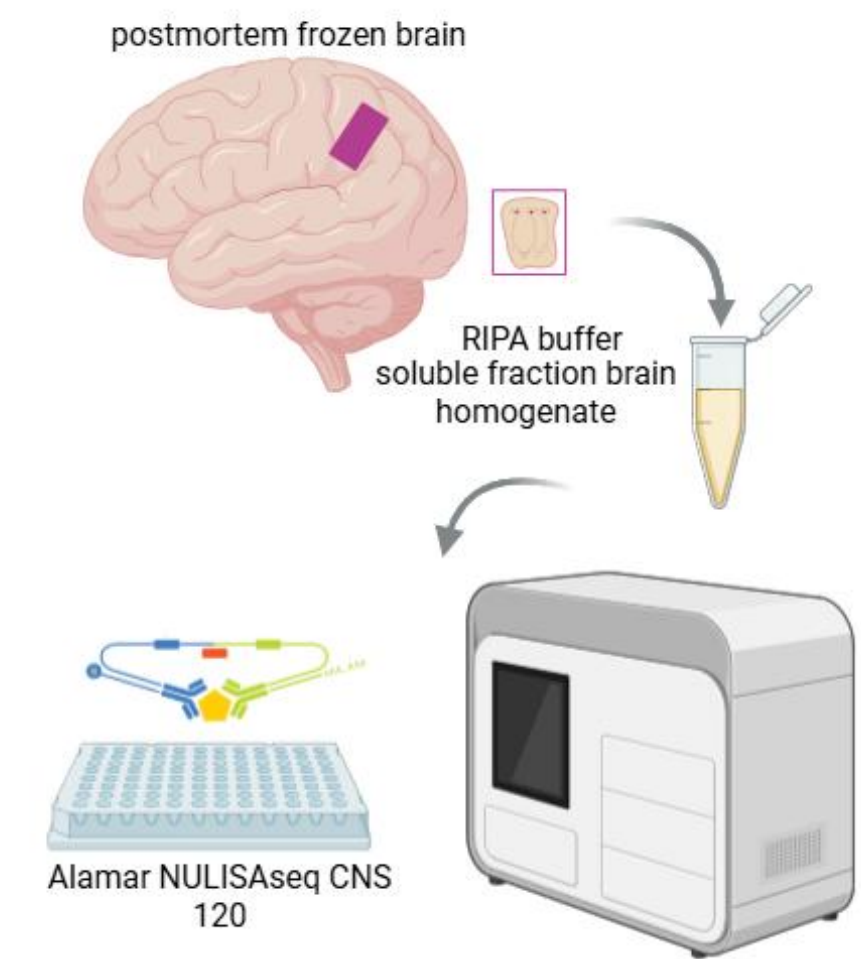


<sup>1</sup>Department of Neuroscience, Mayo Clinic Jacksonville, Florida USA, <sup>2</sup>Department of Quantitative Health Sciences, Mayo Clinic Jacksonville, Florida USA, <sup>3</sup>Department of Neurology, Mayo Clinic Jacksonville, Florida USA, <sup>4</sup>Department of Laboratory Medicine and Pathology, Mayo Clinic Rochester, Minnesota USA, <sup>5</sup>Department of Neurology, Mayo Clinic Rochester, Minnesota USA, <sup>6</sup>Department of Laboratory Medicine and Pathology, Mayo Clinic Jacksonville, Florida USA

## OBJECTIVES

- ## METHODS

| Demographics and Clinical                                                                                                                                                     |                  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|
| Female Sex                                                                                                                                                                    | 5/13 (38%)       |
| APOE ɛ4 (%)                                                                                                                                                                   | 10/13 (77%)      |
| Age at Onset, y                                                                                                                                                               | 63 (56,74)       |
| Age at death, y                                                                                                                                                               | 74 (62,82)       |
| Non-amnesic (%)                                                                                                                                                               | 6/13 (46%)       |
| Neuropathology                                                                                                                                                                |                  |
| Braak stage                                                                                                                                                                   | VI (V, VI)       |
| Thal phase                                                                                                                                                                    | 5 (3,5)          |
| Brain weight (g)                                                                                                                                                              | 1200 (1127,1328) |
| CLix score                                                                                                                                                                    | 13 (6.7,25)      |
| Note: Data of continuous variables reported as median (interquartile range) for all neuropathologically diagnosed AD cases studied. Abbreviations: CLix= corticolimbic index. |                  |



## RESULTS

| Protein Target                  | Estimate (95% CI) | Lower CLix | Higher CLix |
|---------------------------------|-------------------|------------|-------------|
| <b>Amyloid &amp; Tau</b>        |                   |            |             |
| Aβ40                            | -0.84 (-9.9,8.2)  |            |             |
| BD t-Tau                        | 8.5 (2.4,15)*     |            |             |
| BD pTau-181                     | -7.9 (-14,-1.3)*  |            |             |
| pTau-181                        | -1.7 (-14,-0.48)* |            |             |
| BD pTau-217                     | -5.8 (-13.2,1.6)  |            |             |
| pTau-217                        | -3.5 (-12.4,5)    |            |             |
| BD pTau-231                     | -8.3 (-15,-2.0)*  |            |             |
| pTau-231                        | -7.8 (-14,0.31)   |            |             |
| CD63                            | 2.26 (-6.0,10)    |            |             |
| KLK6                            | -0.68 (-9.0,7.7)* |            |             |
| t-Tau                           | 7.5 (0.7,14)*     |            |             |
| PSEN1                           | 5.2 (-2.5,13)     |            |             |
| SFRP1                           | -2.6 (-11,5.6)    |            |             |
| <b>Neurodegeneration</b>        |                   |            |             |
| ANXA5                           | -0.65 (-9.0,7.7)  |            |             |
| CALB2                           | 1.2 (-7.1,9.6)    |            |             |
| CNTN2                           | -2.1 (-10.6,1)    |            |             |
| ENO2                            | -0.02 (-8.4,8.4)  |            |             |
| FGF2                            | -3.3 (-11.6,1)    |            |             |
| GDI1                            | 2.6 (-5.5,10.8)   |            |             |
| GOT1                            | 6.9 (-0.11,14)    |            |             |
| NEFH                            | -4.9 (-13.2,8)    |            |             |
| NEFL                            | -3.5 (-12.4,5)    |            |             |
| NPTX1                           | 5.9 (-1.5,13)     |            |             |
| NPTX2                           | 10 (5.1,15)***    |            |             |
| NPTXR                           | 5.4 (-2.2,13)     |            |             |
| NPY                             | -6.2 (-14,1.1)    |            |             |
| NRGN                            | 5.6 (-2.0,13)     |            |             |
| PDLIM5                          | 0.71 (-7.6,9.1)   |            |             |
| REST                            | -0.72 (-9.1,7.6)  |            |             |
| SMOC1                           | -4.4 (-12.3,4)    |            |             |
| SNAP25                          | 2.3 (-5.9,10)     |            |             |
| p62                             | -7.8 (-14,-1.2)** |            |             |
| UBB                             | -9.0 (-15,-3.1)** |            |             |
| YWHAG                           | -0.44 (-8.8,7.9)  |            |             |
| YWHAZ                           | -5.8 (-13,1.6)    |            |             |
| <b>Synuclein &amp; Synaptic</b> |                   |            |             |
| ARSA                            | -1.8 (-10.6,5)    |            |             |
| FABP3                           | 4.9 (-2.9, 13)    |            |             |
| HTT                             | -0.45 (-8.8,7.9)* |            |             |
| MDH1                            | 7.0 (0.05,14)*    |            |             |
| NGF                             | -0.48 (-8.8,7.9)  |            |             |
| Oligo-SNCA                      | 2.9 (-5.3,11)     |            |             |
| PARK7                           | 4.6 (-3.2,12)     |            |             |
| pSMCA-129                       | -0.40 (-8.8,8.0)  |            |             |
| SNCA                            | 3.0 (-5.1,11)     |            |             |
| SNCB                            | 5.3 (-2.4,13)     |            |             |
| SOD1                            | 4.4 (-3.5,12)     |            |             |
| TARDBP                          | -4.9 (-13,2.9)    |            |             |
| UCHL1                           | -2.9 (-11,5.2)    |            |             |
| VSNL1                           | 5.6 (-1.9,13)     |            |             |

**Funding Support:** *National Institute on Aging* (R01 AG075802, R01 AG073282, P30 AG062677, RF1 AG069052, U01 AG057195, P50 AG047266,), *Rainwater Charitable Foundation, Alzheimer's Association Florida Gulf Chapter. Thank you to our brain donors and families who make this work possible.*