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Cross-sectional amyloid and tau PET in cognitively normal older adults enrolled in the U.S. POINTER lifestyle intervention trial

Theresa M. Harrison[1] | Prashanthi Vemuri[2] | Robert A. Koeppe[3] | Samuel N. Lockhart[4] | Youngkyoo Jung[5] | Bret J. Borowski[2] | Alice Murphy[6] | Tyler Ward[6] | Leslie Gordineer[4] | Nancy Woolard[4] | Mark A. Espeland[4] | Danielle J. Harvey[5] | William J. Jagust[6,7] | Laura Lovato[4] | Arthur W. Toga[8] | Joseph C. Masdeu[9] | Hwamee Oh[10] | Darren R. Gitelman[11] | Neelum T. Aggarwal[12] | Maria C. Carrillo[13] | Heather M. Snyder[13] | Rachel A. Whitmer[14] | Laura D. Baker[4] | Charles S. DeCarli[15] | Susan M. Landau[6] | the U.S. POINTER Study Group

[1] Helen Wills Neuroscience Institute, University of California Berkeley, Berkeley, CA, USA

[2] Mayo Clinic, Rochester, MN, USA

[3] University of Michigan, Ann Arbor, MI, USA

[4] Wake Forest School of Medicine, Winston-Salem, NC, USA

[5] University of California Davis, Davis, CA, USA

[6] University of California Berkeley, Berkeley, CA, USA

[7] Lawrence Berkeley National Laboratory, Berkeley, CA, USA

[8] University of Southern California, Los Angeles, CA, USA

[9] Houston Methodist Neurological Institute, Houston, TX, USA

[10] Alpert Medical School of Brown University, Providence, RI, USA

[11] Advocate Aurora Health, Chicago, IL, USA

[12] Rush University Medical Center, Chicago, IL, USA

[13] Alzheimer's Association, Chicago, IL, USA

[14] University of California, Davis, Davis, CA, USA

[15] University of California, Davis School of Medicine, Sacramento, CA, USA

Correspondence
Theresa M. Harrison, Helen Wills Neuroscience Institute, University of California Berkeley, Berkeley, CA, USA.
Email: theresamaria@gmail.com

Abstract

Background: The U.S. Study to Protect Brain Health Through Lifestyle Intervention to Reduce Risk (U.S. POINTER) is a 2-year randomized controlled trial to evaluate the effect of lifestyle interventions in older adults (60-79 years) who are cognitively unimpaired but at increased risk for cognitive decline/dementia due to factors such as cardiovascular disease and family history. The POINTER Imaging ancillary study is collecting PET and MRI data to evaluate neuroimaging biomarkers of AD and cerebrovascular pathophysiology in this at-risk sample.

Method: POINTER Imaging is actively enrolling 1250 participants, 23% from underrepresented racial/ethnic groups (URG), recruited from five U.S. POINTER clinical sites. Participants have undergone PET imaging with [^{18}F]Florbetaben (FBB) to measure Aβ and [^{18}F]MK-6240 to measure tau burden, as well as MRI to measure brain morphometry, white matter hyperintensities and cerebral blood flow. FBB and MK-6240 data were quality checked, pre-processed, and quantified using previously validated methods. PET images were coregistered to a structural MRI, which was also used to create FreeSurfer-defined reference regions and regions of interest. We examined PET imaging measures (global Aβ, regional tau) and basic demographic (age, sex, race/ethnicity) characteristics of the sample.

Result: 96 participants (mean age 69.3±5.0) have been enrolled in POINTER Imaging. Of these, 59 (61%) are women and 22 (23%) are URG, which is similar to rates of women (75%) and URG (22%) in the main trial. This dataset is <10% of targeted enrollment, was predominantly recruited from 2/5 clinical sites and may not represent the final imaging cohort. FBB quantification (N=20) revealed a mean cortical summary SUVR of 1.09±0.12 (19.6±18.4 centiloids) (whole cerebellum normalization; previously validated positivity threshold=1.08), and 8/20 (40%) of these participants were Aβ+ (Fig.

1A). MK-6240 quantification (N=23) showed predominantly no/minimal binding with a few exceptions in medial and lateral temporal lobes (Fig. 1B&C).

Conclusion: The POINTER imaging study is meeting the target URG enrollment and representative of the main U.S. POINTER trial. Higher frequency of Aβ positivity than published in population cohorts coupled with greater cardiovascular risk factors among POINTER participants highlights our success in recruiting individuals at increased risk of cognitive decline.

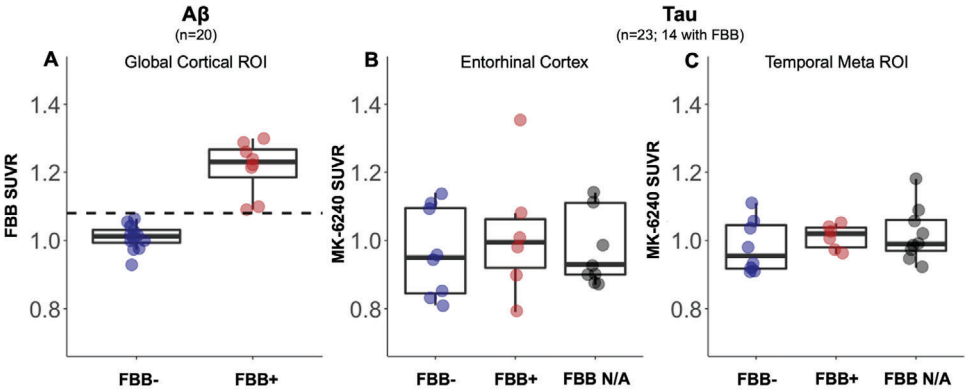

Figure 1. Initial Aβ (with [^{18}F] florbetaben) and tau (with [^{18}F] MK-6240) PET data from POINTER Imaging were processed using previously-validated (in ADNI) methods and show an Aβ+ rate of 40% and variable tau burden in regions that are frequently elevated early in AD. The FBB threshold for positivity (SUVR >1.08) was derived from ADNI FBB data and is denoted with a dashed line in panel A. N/A=not available

FIGURE 1