A New Frontier in ADRD Research in Low-Income Countries

Dried Plasma Spots (DPS) for Dementia Biomarkers in Aging Surveys

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DPS for Detection of Alzheimer's Pathology


nature medicine

Article

A minimally invasive dried blood spot biomarker test for the detection of Alzheimer's disease pathology

- **Minimally invasive data collection:** Finger-prick DPS samples (337 participants, 7 European centers)
- **Strong agreement with venous plasma:** DPS EDTA correlation for p-tau ($r = 0.74$)
- **Accurate detection of AD pathology:** Predicts CSF biomarker positivity (AUC = 0.864)

- **Robust performance across biomarkers:** DPS EDTA correlation for GFAP ($r \approx 0.77$), DPS EDTA correlation for NfL ($r \approx 0.83$)
- **Clinically meaningful differences:** p-Tau217 $\sim$198% higher in AD biomarker-positive individuals
- **Feasible for remote/self-collection:** High concordance; scalable for population studies, but never implemented outside of well controlled clinical environment; not yet clinical-ready; requires further standardization

MLSFH Research Goal: investigate feasibility in a remote low-income context

https://www.MLSFHresearch.org

- 14 rounds of data
- ≈3,500 participants above age 45, ≈10,000 ever-surveyed individuals
- 2024: DBS collected for epigenetic and genetic analyses (N ≈ 3,531)
- 2025: HCAP cognitive assessment (N ≈ 3,531)
- Rare record of 25 years of demographic, socioeconomic, and health data in one of the poorest countries

DPS Sample Selection

Eligibility DPS Collection

- 60+ years old, living in Balaka District
- 2022 Cognitive assessment
- 2024 DBS for genetics/epigenetics
- # of eligible respondents = 142
- Target: $\approx$ 100 DPS samples

EDTA Collection

- Target: 10 Respondents with successful DPS collection

Notes: Data collection completed Oct 26–Nov 1, 2025

DPS Collection & Analysis

p-Tau217 (early and accurate AD blood biomarker)

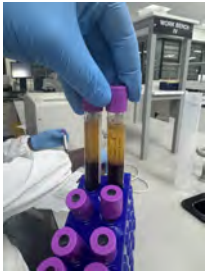
- **Collection:** Capitainer SEP10 Dried Plasma Card
- **Assay:** Janssen Advantage PLUS (formerly known as p-Tau217+)
- **Approach:** Resuspended in 170 µL of custom extraction buffer

NfL (marker for axonal degener. across neurodegenerative diseases)

GFAP (marker for neuroinflammation)

- **Collection:** Capitainer B50 Dried Whole Blood Card
- **Assay:** Neurology 2-Plex B
- **Approach:** Resuspended in 300 µL of custom extraction buffer

EDTA Collection For Validation



- Whole blood samples collected in EDTA tubes for 10 respondents (2 EDTA tubes per respondent)
- Transported in coolers with ice blocks, and air-conditioned cars to the lab at KUHeS in Blantyre (about a 3-hour drive from the field site)
- Processed using ADNI protocol, aliquoted into 2 mL cryovials, and frozen at -80°C
- Cryovials shipped on dry ice to Ashton's lab in Arizona maintaining -80°C
- Each plate was shaken at 37°C (30 min, 500 rpm), then centrifuged 15 min at 2,500 $\times g$. The supernatant was measured on the HD-X platform without dilution (limiting interpretation to relative measurements).

Sample Characteristics: DPS vs. EDTA

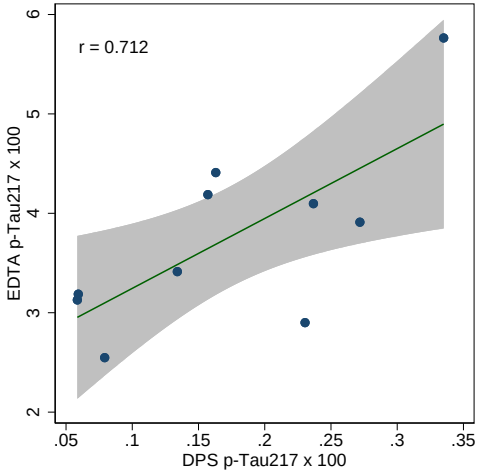
	Panel A: DPS Total Sample			Panel B: EDTA Subsample		
	Women	Men	Total	Women	Men	Total
# of observations	67	38	105	8	2	10
Age	71.0 (8.27)	72.5 (8.44)	71.5 (8.32)	69.6 (9.47)	73.0 (5.66)	70.3 (8.68)
Age group						
60–69	0.48	0.42	0.46	0.62	0.50	0.60
70–79	0.36	0.32	0.34	0.25	0.50	0.30
80+	0.16	0.26	0.20	0.12	0.0	0.10
Schooling						
No formal schooling	0.73	0.29	0.57	0.88	0.50	0.80
Primary	0.27	0.66	0.41	0.12	0.50	0.20
Secondary	0.0	0.053	0.019	0.0	0.0	0.0
Currently married	0.58	0.97	0.72	0.50	1.00	0.60
House has metal/tiled roof	0.76	0.76	0.76	0.75	1.00	0.80
Refusals	1	0	1	1	0	1

Comparison of successful vs. failed p-Tau cards

	DPS Lab Result	
	p-Tau ok	p-Tau fail
# of observations	94	11
Age	71.3	73.0
Schooling (years	1.62	1.09
Currently married	0.71	0.82
Wealth indicator: House has metal/tiled roof	0.76	0.82
Cognition Score (overall)	16.8	18.8
Short Story (Brave Man), delayed recall	5.90	6.55
Long Story (Craft 21), delayed recall	8.52	11.7
Pattern recognition: correct shapes:	16.2	16.7
HIV positive	0.076	0.091
Grip strength (average both hands)	18.8	18.8
Female	0.66	0.45
Time (hours) stored in car	3.25	2.30
Time (hours) stored in fridge	33.3	29.1

Note: None of the differences are statistically significant

DPS and EDTA Biomarkers Correlations



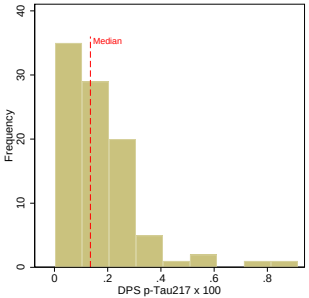
DPS EDTA Correlations

p-Tau: r = .71

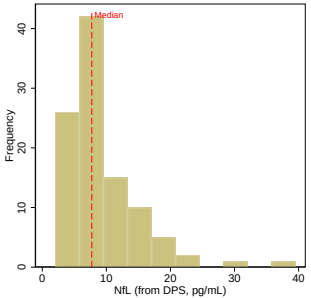
NfL: r = .67

GFAP: r = .98

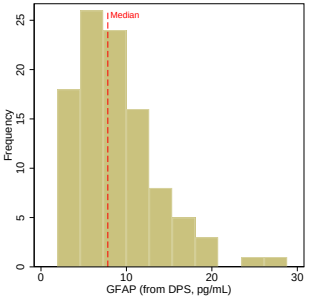
Distribution of Biomarkers (DPS)



p-Tau



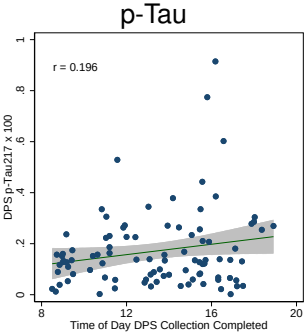
NfL

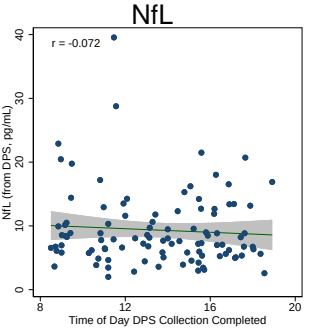


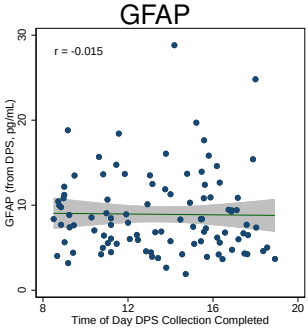
GFAP

Correlations	p-Tau	NfL
NfL	0.09	
GFAP	0.33	0.13

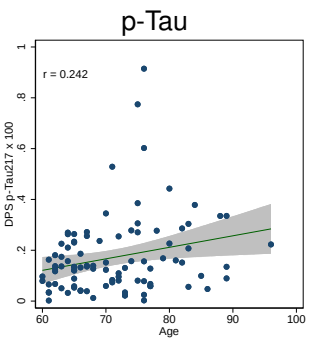
Data Collection Considerations

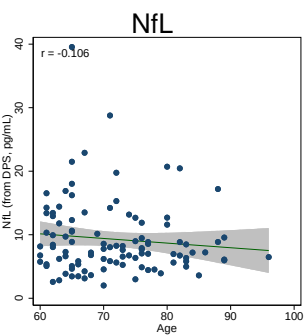


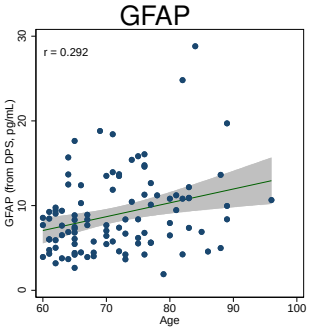




Age Gradient of DPS Biomarkers







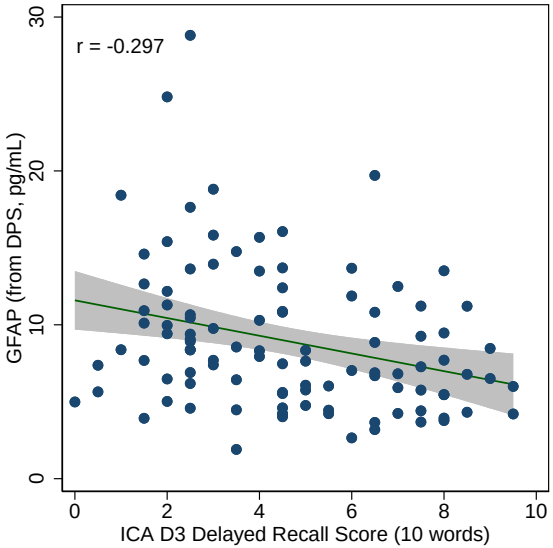
Life-Course Predictors of DPS Biomarkers

	p-Tau	NfL	GFAP
Age	+++		+++
Sex			
Schooling (any)	+		
Curr. married	++	+	
Early-life famine/hunger	+		
Grip strength	−−		−−
BMI		+	−
HIV positive	−−		
Subjective health (1, ..., 5)	−−	−−	
Econ situation: 1 improved, ..., 5 worsened		++	++
Social participation score	−−		−−−
Recent illness		+++	+

+, ++, +++ positive assoc, −, −−, −−− negative assoc, significant at 10%, 5% or 1%

Based on regression analyses additionally controlling for age and sex

DPS Biomarkers & Cognitive Outcomes



DPS Biomarkers & Cognitive Outcomes

	Total Cogn. Score	10 words recall immed.	10 words recall delayed	Pattern recogn.	Story recall delayed
Regression coef., controlling for age and sex					
(reference cat. is none or one)					
p-Tau					
NfL		—	— —	— —	
GFAP			— —	— —	— —

$+, ++, +++$ positive assoc, $-, --, ---$ negative assoc, significant at 10%, 5% or 1%

Based on regression analyses additionally controlling for age and sex, robust SE

DPS Biomarkers & Cognitive Outcomes

	Total Cogn. Score	10 words recall immed.	10 words recall delayed	Pattern recogn.	Story recall delayed
Biomarker top quartile (reference cat. is none or one; N = 72)					
p-tau + NfL (N = 5)		− − −			
p-tau + GFAP (N = 7)		− − −		−	
NfL + GFAP (N = 4)			− − −		
p-tau + NfL + GFAP (N = 3)	− − −	− − −	− − −		−

+, ++, + + + positive assoc, −, −−, − − − negative assoc, significant at 10%, 5% or 1%

Based on regression analyses additionally controlling for age and sex, robust SE

Emerging Evidence from DBS Pilot Study

- DPS approach is feasible outside of clinical, well controlled environments, providing consistent biomarker evidence with prior studies
- Evidence for multiple pathways underlying poor cognition in a low-income context:
  - individuals with all 3 biomarkers elevated are likely Alzheimer's disease AD) cases
  - individuals with intermediate biomarker profiles suggest heterogeneous, non-AD pathways to poor cognition

Pilot study is funded by the NIA Research Centers Collaborative Network (RCCN)
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