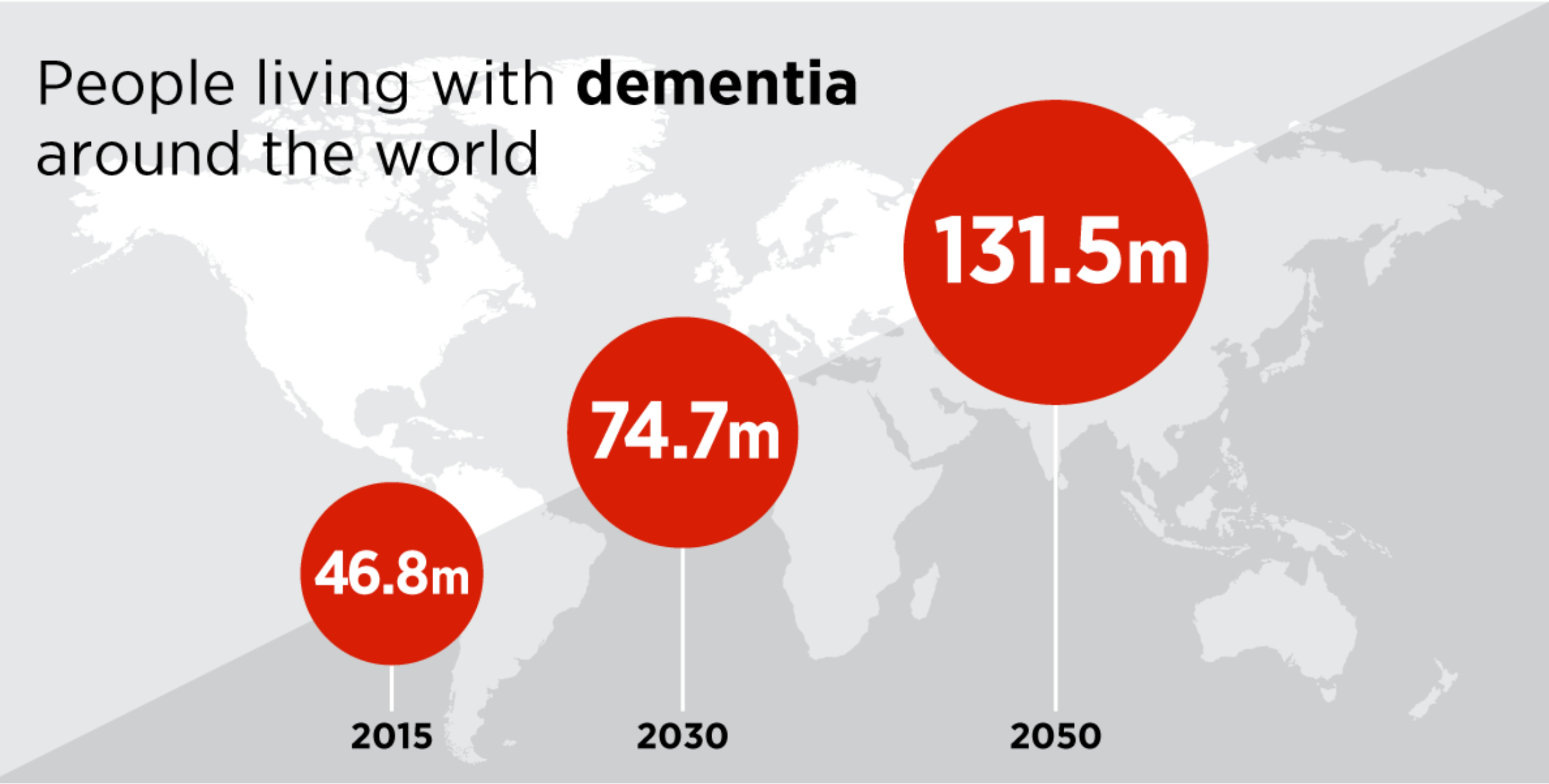
Passive Visuospatial Memory Testing on Mobile Devices

We're putting the eye in AI


People living with **dementia** around the world
46.8m
74.7m
131.5m
2015
2030
2050

The Problem


MONTREAL COGNITIVE ASSESSMENT (MOCA)
NAME :
Education :
Date of birth :
MEMORY
FACE
1st trial
2nd trial
LANGUAGE
ABSTRACTION
DELAYED RECALL
Has to recall words WITH NO CUE
FACE
VELVET
Optional
Category cue
Multiple choice cue
ORIENTATION
[ ] Date
[ ] Month
[ ] Year
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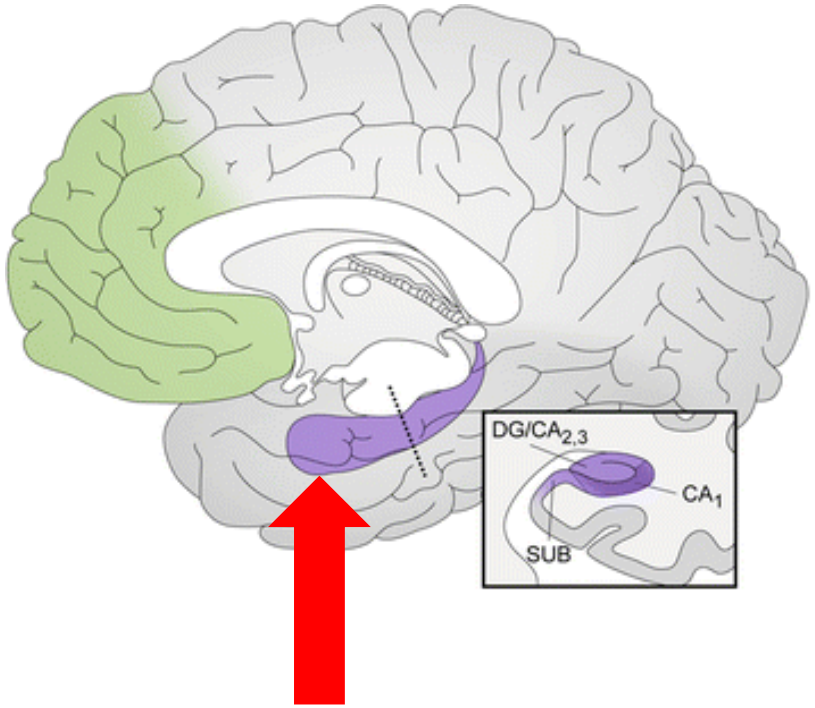
www.mocatest.org
Administered by:

Solution: Visuospatial Memory



Visuospatial Memory is sensitive to the earliest AD pathology

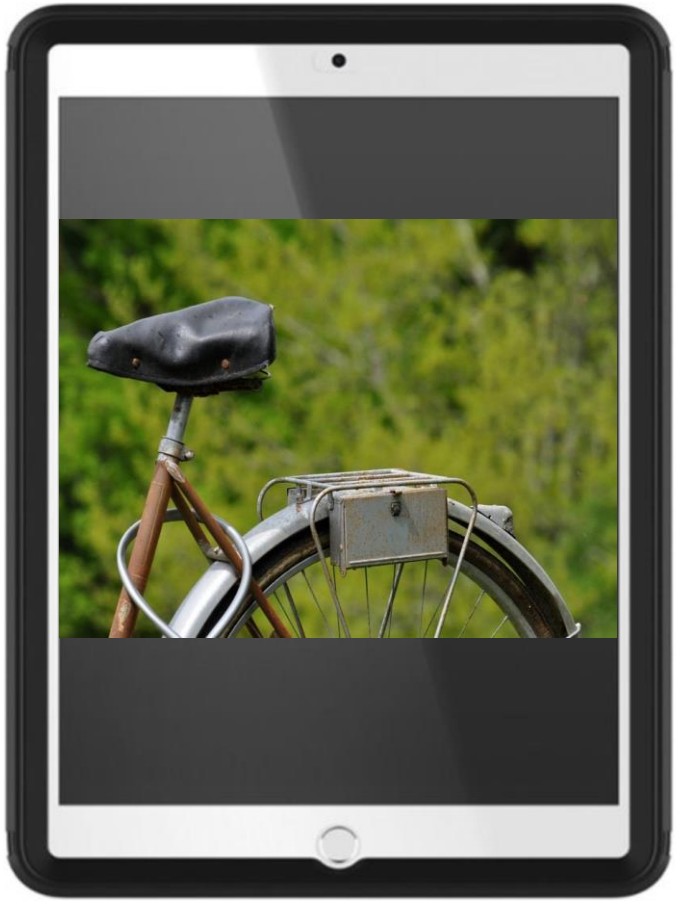
- Visual pattern separation is sensitive to early pathological changes in AD
- Shown to be sensitive to 10% hippocampal lesions in non-human primates

VisMET

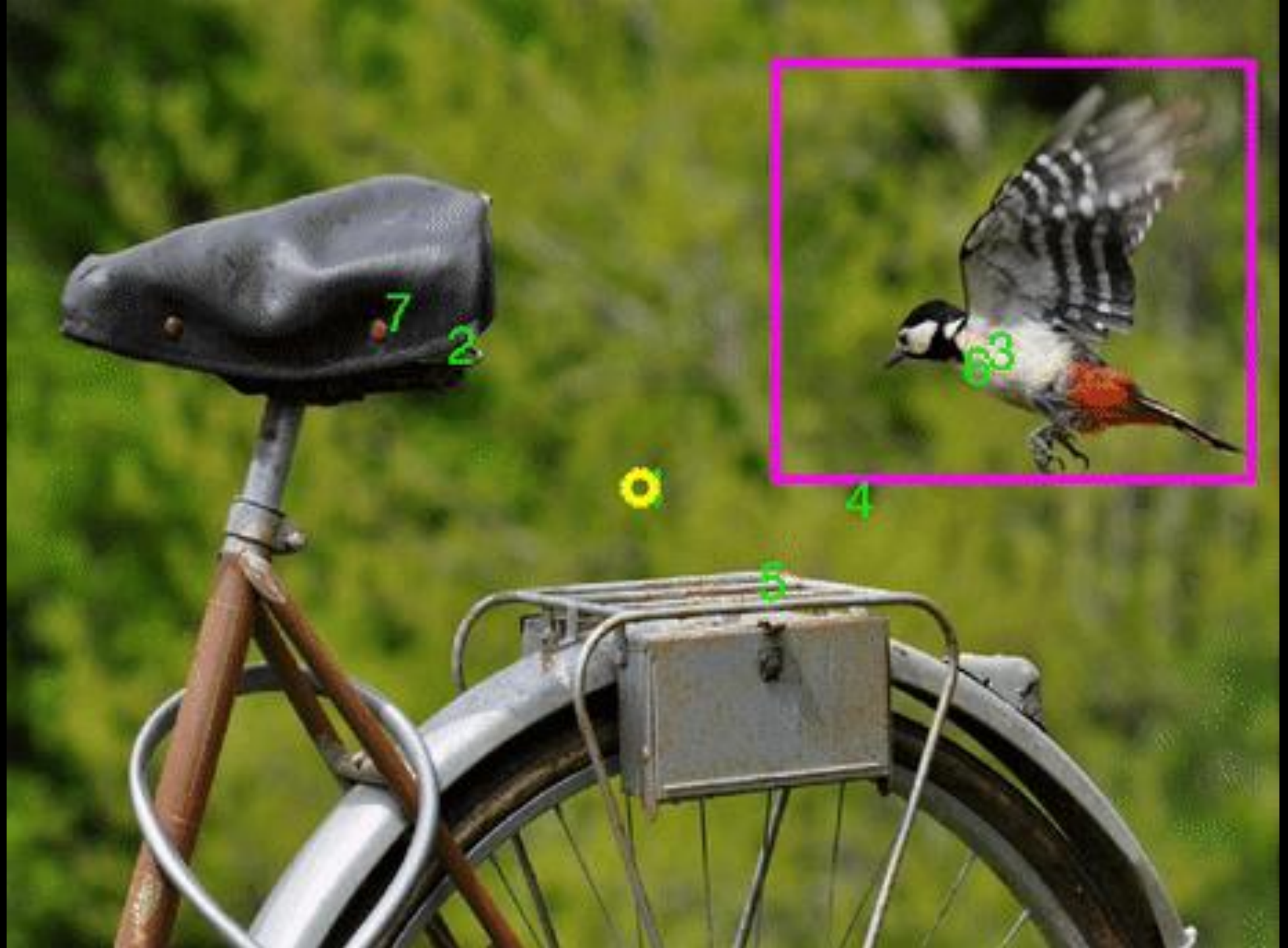
Brief – Passive – Objective – Language-Independent

Encoding Phase
(Images 1-10)

…2 minutes later

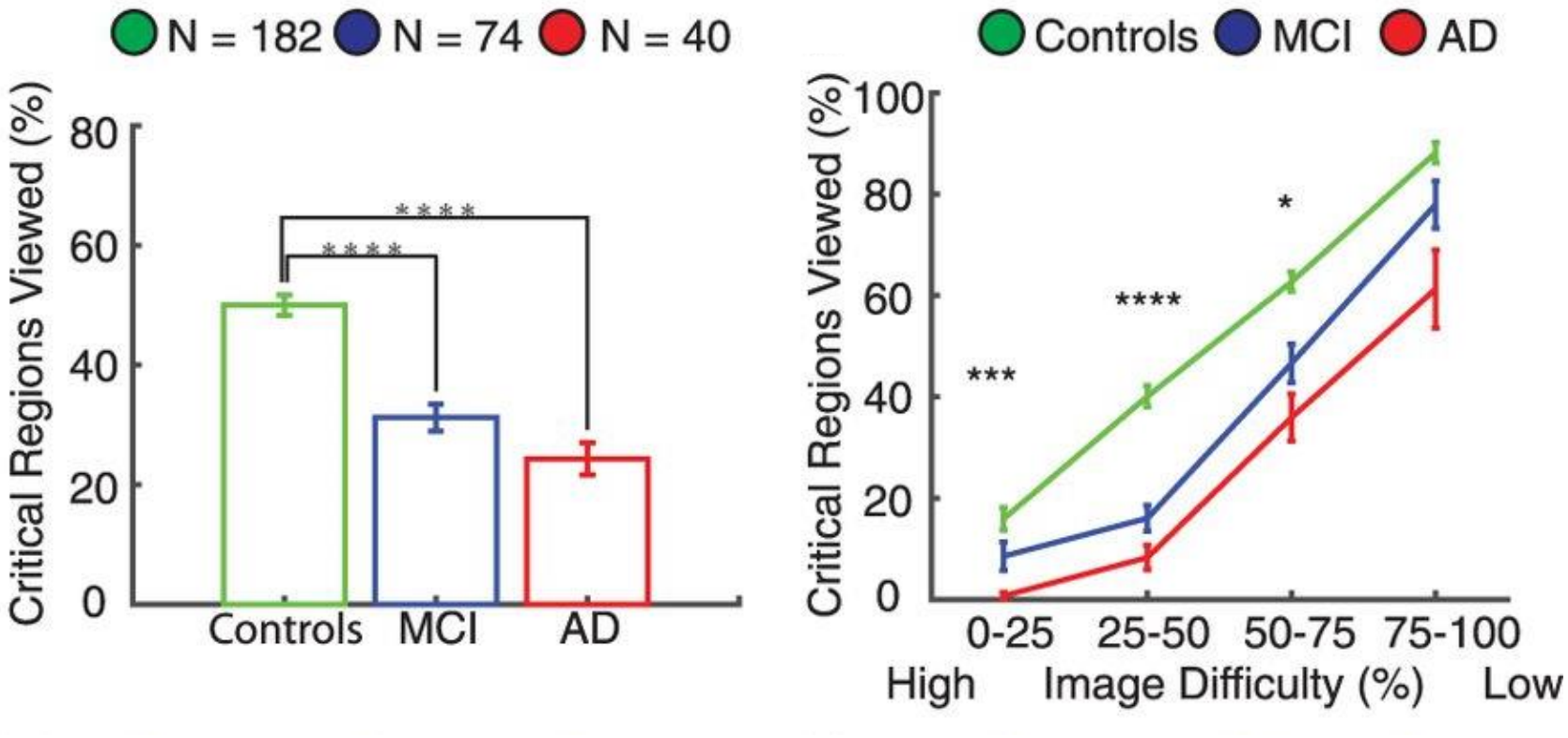


Recognition Phase
(Images 11-20)


7
2
3
4
5

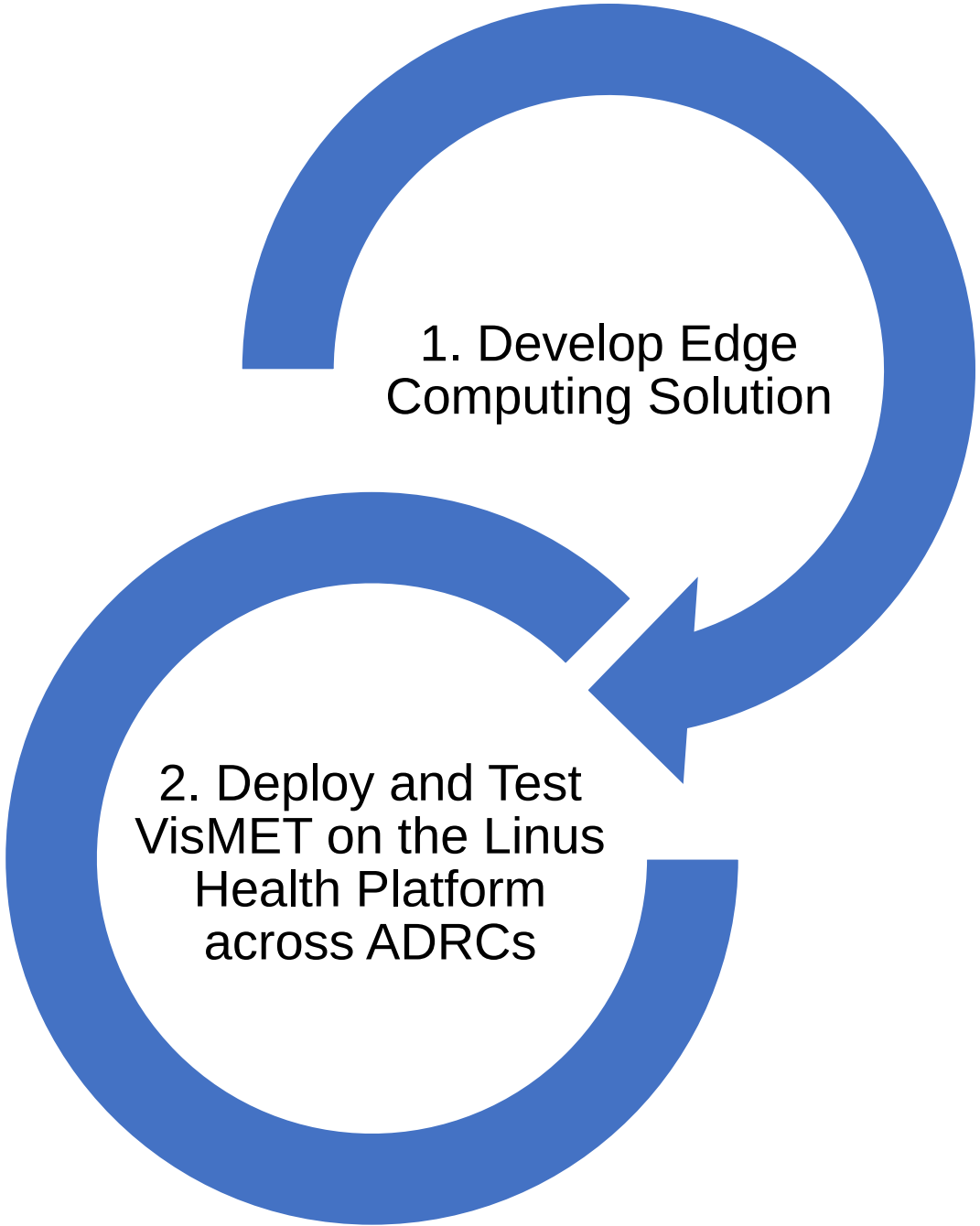
VisMET

Effective Predictor of Cognitive Impairment (AUC= .76-.78)



Haque et al., 2019; Haque et al., 2021; Jiang et al., 2022; Jiang et al., 2023

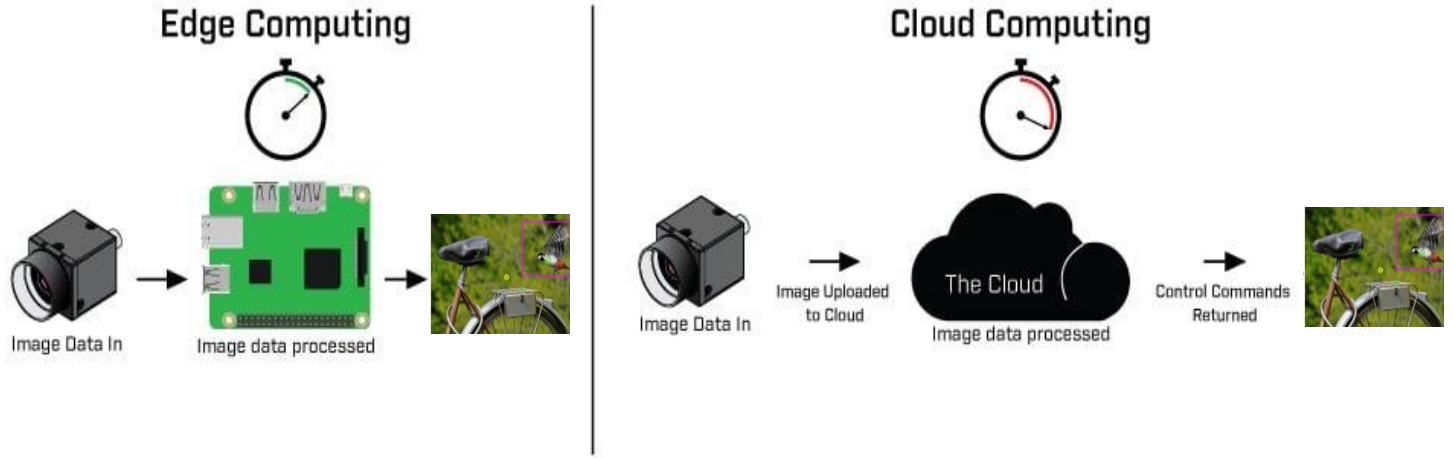
Current Project



1. Develop Edge Computing Solution

2. Dep VisMET on the Linus Health Platform across ADRCs

2. Deploy and Test VisMET on the Linus Health Platform across ADRCs



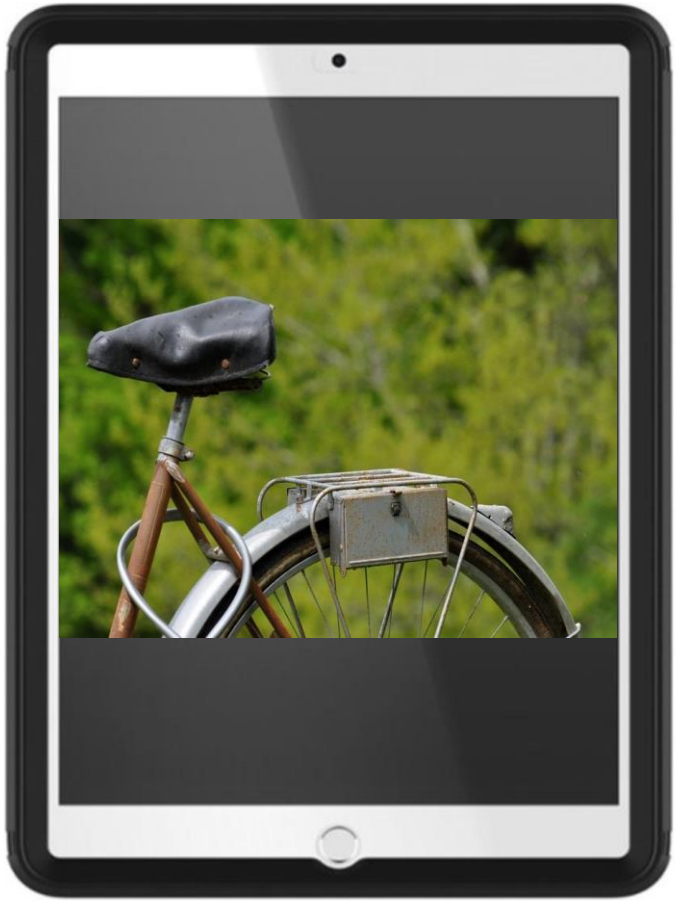
Benefits:

1. Improves patient privacy
2. Reduces burden and cost
3. Enhances data sharing

1. Develop Edge Computing Solution

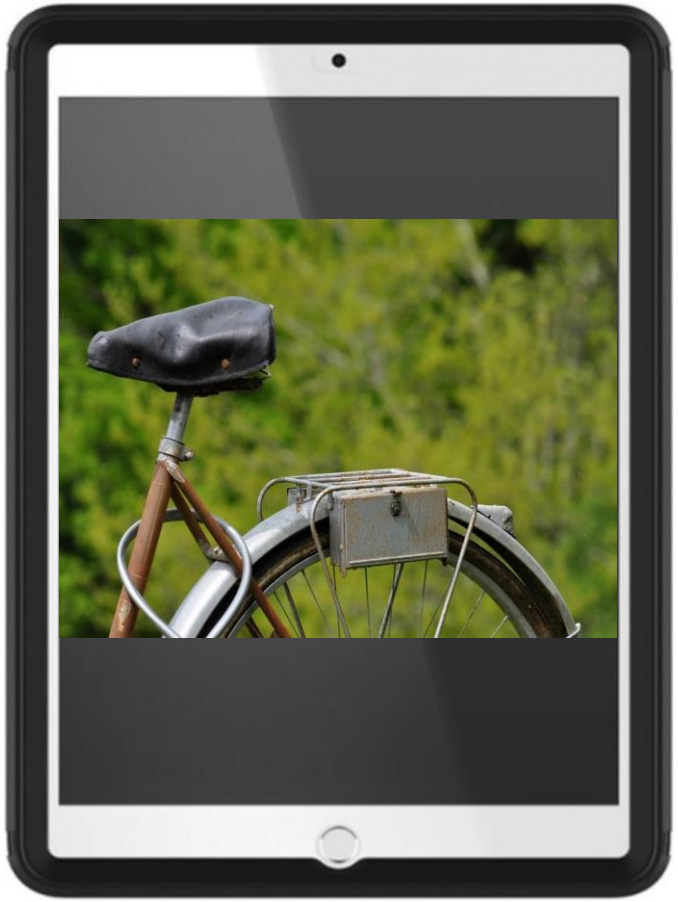
2. Deploy and Test VisMET on the Linus Health Platform across ADRCs

VisMET



- Novel Digital Tool
- Low Burden
- Rich and Objective Data
- Equitable
- Scalable

VisMET



- Scale Nationally
- Create Infrastructure for Global Scaling and Remote Administration

Project Team

EMORY UNIVERSITY
Goizueta Alzheimer's Disease Research Center

EMORY UNIVERSITY SCHOOL OF MEDICINE
Department of Biomedical Informatics

LINUS HEALTH

Cognitive Function and ADRD

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Allan Levey, MD, PhD
Cecelia Manzanares



Healthcare Data Informatics and AI

Gari Clifford, PhD
Salman Seyedi, PhD


Scaling and Commercialization

Sean Tobyne, PhD
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Partnering ADRCs

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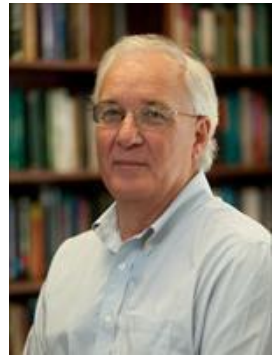

Douglas Galasko, MD
David Salmon, PhD

Q & A

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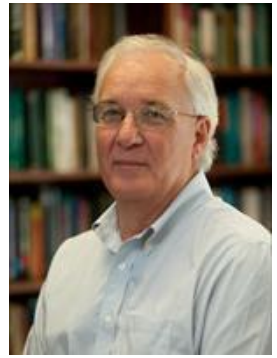

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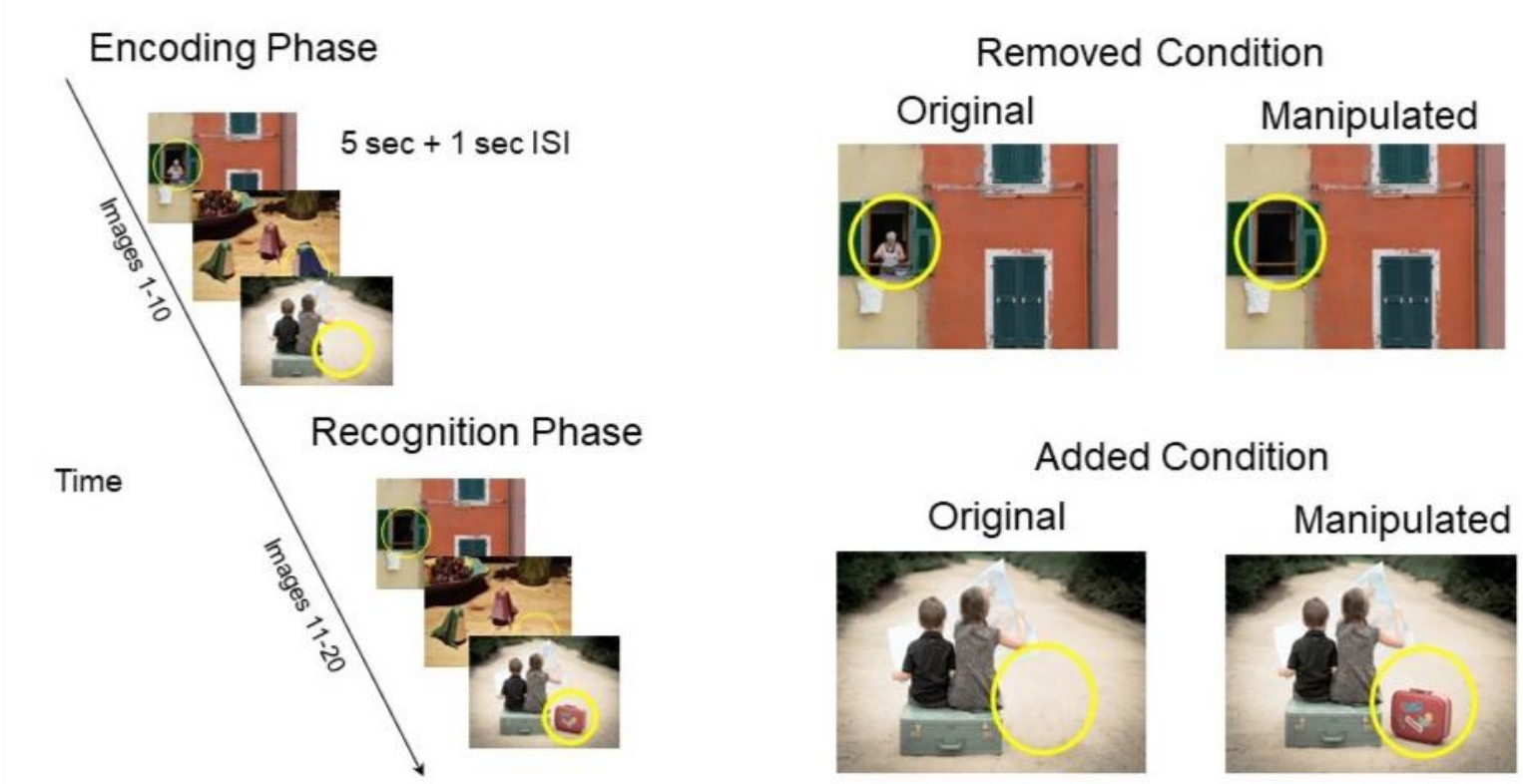
The Visuospatial Memory Eye-Tracking Test (VisMET)



Why Visuospatial Memory?

- VS Memory tasks have been shown to activate the entorhinal-hippocampal circuit and may be promising indicators of early hippocampal changes inherent in AD. (Johnson et al., 2009; Zola et al., 2013; Urgolites et al., 2018)
  - Eye tracking can increase sensitivity to subtle decline in memory retrieval
- VisMET is based upon Visual Paired Comparison (VPC) task paradigm which assess declarative memory by comparing time viewing images that are familiar versus novel. (Urgolites et al, 2018, Zola et al., 2013, Bott et al. 2017, Crutcher et al., 2009)
  - 30-min VPC task reliably predicted the onset of Mild Cognitive Impairment (MCI) or AD within 3-6 years. (Crutcher et al., 2009)
  - Moreover, studies of VPC tasks in non-human primates have shown that VPC plus eye-tracking tasks can detect subtle memory decline in primates who have small hippocampal lesions, even with 70-80% of the structure unaffected. (Zola et al., 2000).

The Visuospatial memory Eye-Tracking Test (VisMET)

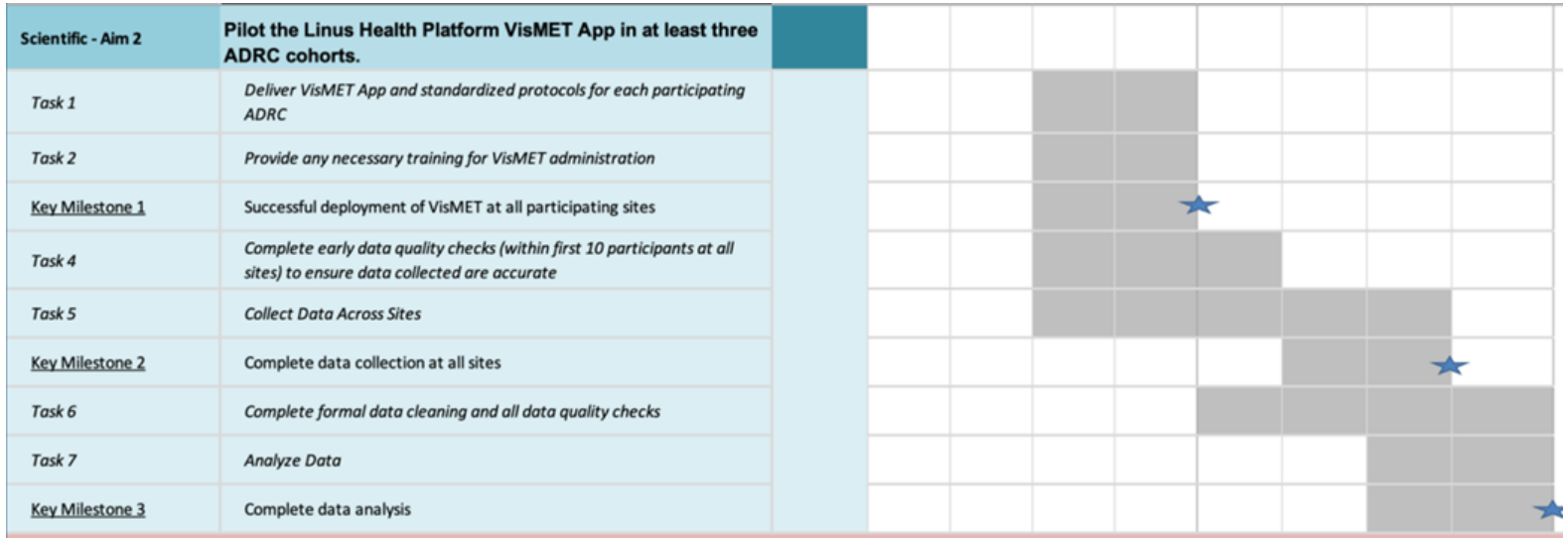
Appears less reliant on demographic factors than traditional measures

	Black/AA Pt (n=38)	nH-White Pt (n=38)
Age (Mean)	74.9 years (SD = 7.8)	74.6 years (SD = 8.2)
Sex	31.6% Male 68.4% Female	31.6% Male 68.4% Female
Education (Mean)	16.6 years (1.9)	16.8 years (1.9)

- **Age** was the only significant demographic predictor of VisMET performance (b=0.00, t=-2.5, p=.01).
- **Sex, race, and education** were not significant.

Aim 2. Pilot the Linus Health Platform VisMET App in at least three ADRC cohorts.

- Key Components of this Aim:
  - Evaluate VisMET performance in at least 300 participants enrolled across the Goizueta ADRC and at external ADRC sites, including UCSD and BU
- Milestones:
  - delivery of study materials to participating sites
  - completed data collection
  - completed data analysis



Scientific - Aim 2	Pilot the Linus Health Platform VisMET App in at least three ADRC cohorts.
Task 1	*Deliver VisMET App and standardized protocols for each participating ADRC*
Task 2	*Provide any necessary training for VisMET administration*
Key Milestone 1	Successful deployment of VisMET at all participating sites
Task 4	*Complete early data quality checks (within first 10 participants at all sites) to ensure data collected are accurate*
Task 5	*Collect Data Across Sites*
Key Milestone 2	Complete data collection at all sites
Task 6	*Complete formal data cleaning and all data quality checks*
Task 7	*Analyze Data*
Key Milestone 3	Complete data analysis

Aim 2. Pilot the Linus Health Platform VisMET App in at least three ADRC cohorts.

- Utilizing existing recruitment mechanisms, we will work with partnering sites to recruit at least 300 participants with a range of cognitive function to complete VisMET alongside their standard UDS-3 testing.
- Hypotheses
  - **2A.** VisMET performance will demonstrate adequate AUC (> .80) for detecting cognitive impairment based on MoCA performance, and that performance will not significantly differ between sites.
  - **2B.** VisMET performance will demonstrate moderate to strong correlations with established measures of verbal and visual memory included in the UDS-3[6].
  - **2C.** VisMET's ability to detect cognitive status in diverse cohorts will not differ by race, sex, or education.

Relationship to other clinically relevant measures

- **Cognitive Measures** (n=98 from Emory Cognitive Clinic + GADRC)
  - Global function (MoCA; r=.28, p< .01)
  - Delayed Memory (Benson Figure Delay: r= .36, p< .01; CERAD Word List Delay: r= .29, p< .01)

- **CSF Biomarker Concentrations** (n=131 from EHBS and ADRC studies)
  - 69.5% control, 19.1% MCI, 6.1% AD, 3% Non-AD Dementia; 51.9% Biomarker Positive
  - Aß42/pTau18 ratio: r= -.31, p< .01
  - In binary logistic regression analyses, VisMET performance significantly predicted CSF biomarker status, $\chi^2(1)= 5.66$, p= .017.

Additional Metrics

- Facial emotions expressed during VisMET significantly differed in participants with cognitive impairment.
- We have also found individuals with cognitive impairment transition less between ROIs, do so in a more unpredictable manner, and with different semantic grouping than those who are cognitively normal, which are features that improve AUC.

TABLE II: **Classification performance of cognitive impairment.** The term *all* represents performance using all images (including those that were modified), and *og* indicates the use of only the original unmodified images.

Feature type	AUROC-all	F1-all	AUROC-og	F1-og
1. Oculomotor features	0.64	0.60	0.58	0.54
2. Spatial distribution (spatial)	0.68	0.63	0.62	0.57
3. HMM transition matrix (temporal)	0.64	0.69	0.59	0.65
4. All HMM features (spatiotemporal)	0.69	0.70	0.64	0.65
5. Semantic viewing time (semantics)	**0.73**	**0.74**	0.65	0.61
6. Modification viewing time (memory) [23]	0.73	0.72	NA	NA
7. Combined (all: 2+4+5)	**0.78**	**0.76**	NA	NA

Jiang et al., 2022, Jiang et al., 2023