The Brain Health Registry: Use of web-based technology for detecting and monitoring changes in cognition and AD risk

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DISCLOSURES

- Funding sources
  - NIA (1K01AG055692, RF1 AG059009, 5U19AG024904)
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BACKGROUND

- A critical need in the field is development of scalable, efficient tools to identify & assess older adults at risk for and with dementia/AD
  - ***recruitment & screening for clinical trials***
  - ***to aid diagnosis in various healthcare settings***
  - ***to identify those who may benefit from new treatments***
- Remote data collection, for example using online registries, presents a unique opportunity
  - ***Emerging evidence for feasibility and construct validity*** *Weiner 2018, Mackin 2018, Nosheny 2018, Langbaum 2019*
  - ***Validity of data compared to in-clinic measures is unknown***
  - ***Other challenges of online approach:*** ***data integrity, selection biases, effectiveness at getting people into in-clinic studies***

BRAIN HEALTH REGISTRY (BHR)

- Internet-based registry with **> 69,000** participants
- Longitudinal cognitive and health data using
  - self- report questionnaires
  - cognitive tests
- **> 6000** participants have an enrolled study partner, with linked data
- **> 550** have APOE using remote saliva collection

Weiner *et al* 2018

HOW IT WORKS

Register, consent online

1 **Sign up**

Self-reported health, cognition, everyday functioning, and lifestyle

2 **Tell us about yourself**

Online cognitive tests

3 **Take some tests**

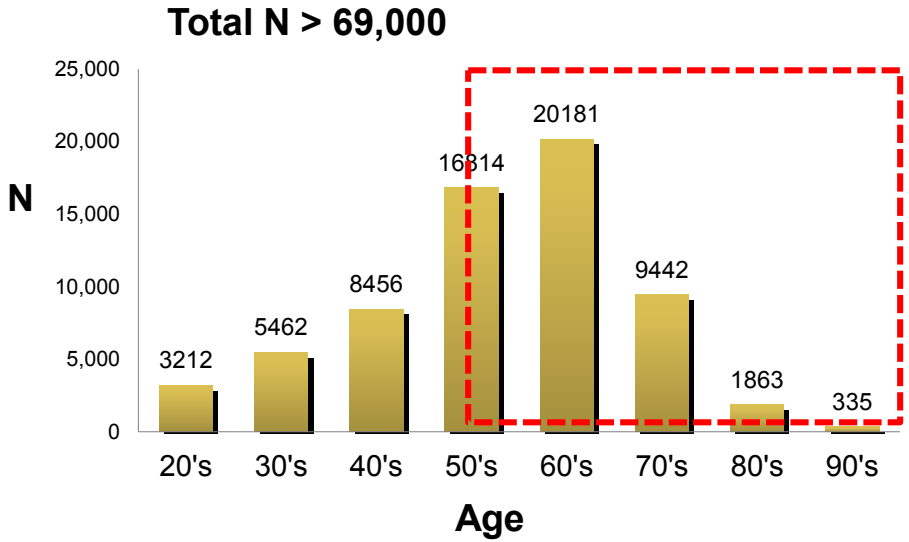
Can separately register, consent, and answer questions about participant and self

4 **Invite a study partner**

Participants and study partners return every 6 months to complete follow-up tasks

5 **Come back…and come back again**

OVERVIEW OF BHR PARTICIPANTS



Age 55+, N = 40,718

	%	N
Female	71%	29,163
Caucasian	86%	35,067
Latino	3.4%	1380
Has enrolled study partner	11%	4672
Memory concern	42%	17,103
Family History of AD	27%	11,068
Self-report MCI	3.6%	1452
Self-report dementia/AD	0.5%	200
Longitudinal data (questionnaires)	43%	15,268
Longitudinal data (Cog. tests)	30%	10,875

Higher retention assoc. with:
--older
--more subjective memory concerns
-- White, non-Latino, more education
Ashford et al 2019 CTAD

CO-ENROLLMENT: ENROLLED IN BOTH AN IN-CLINIC STUDY AND BHR. DATA LINKAGE.

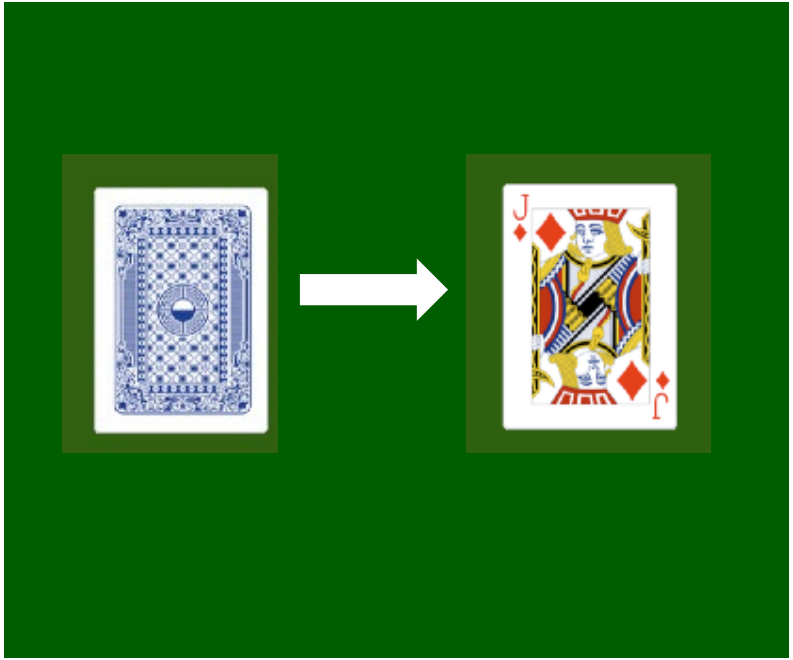
Parent Study	N	Diagnostic Groups	Study Focus	In-clinic data available
ADNI	111	CU, SMC, MCI, AD	Alzheimer's disease	Aβ PET&CSF, clinical diagnosis, neuropsych. testing, ApoE, multiple imaging modalities, CSF, blood-based biomarkers, GWAS
IDEAS	910	MCI, AD, other dementia	Alzheimer's disease and other dementias	Aβ PET, clinical diagnosis, MoCA, MMSE, comorbidities
NVP	1000	CU, MCI	Cognitive aging	Aβ *, neuropsych. testing, ApoE
POCD	24	CU, MCI	Post-operative cognitive decline in older adults	Aβ PET, neuropsych. testing, cormorbid medical diagnoses
Hillblom Healthy Aging	89	CU, MCI	Healthy aging	research diagnosis, Aβ PET, self reported questionnaire data, informant interview data, and neuropsych. evaluations
GenePool Study	550	CU, MCI	Genetic risk	ApoE
Total	**2684**			

CU=Cognitively Unimpaired; SMC= Subjective Memory Complaint; MCI=Mild Cognitive Impairment; AD =Alzheimer's Disease

USING BHR TO IDENTIFY OLDER ADULTS AT RISK FOR DECLINE, MCI, DEMENTIA

- Online cognitive testing
- Subjective measures (decline, concerns)
- Evidence for validity of online data versus in-clinic measures
- β-Amyloid prediction models
- Novel approaches under development

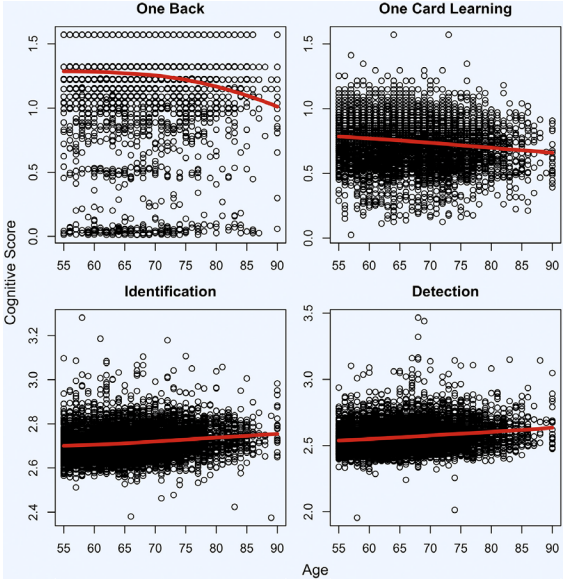
ONLINE COGNITIVE TESTS: COGSTATE BRIEF BATTERY

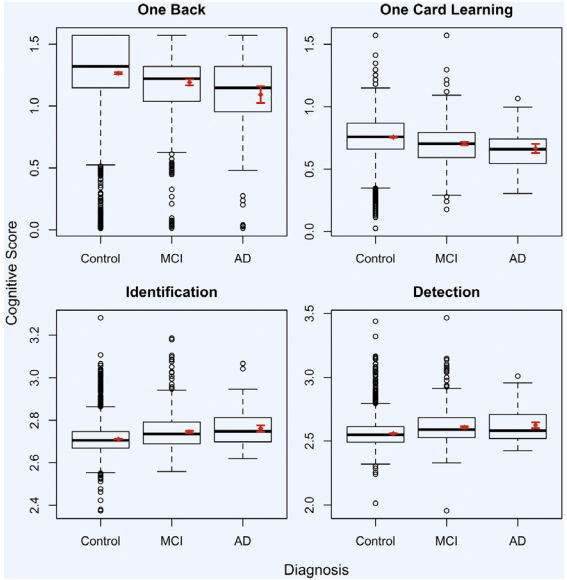


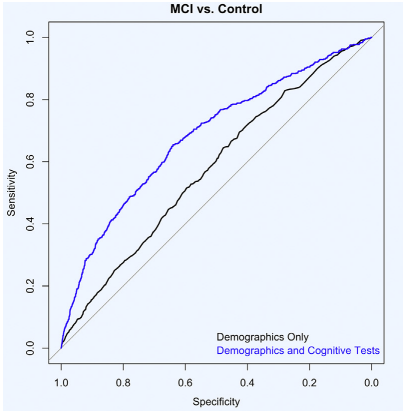
Chen et al, 2010; Lim et al, 2012, 2013; Darby et al, 2011, 2012, 2014

- Four card tests measuring cognitive function across various domains
- Supervised version has clinical validity, reliability and sensitivity to age effects
- Longitudinal decline associated with Aβ+
- Emerging evidence for validity of unsupervised version *Mackin 2018 (BHR), Albala 2018 (ADNI), Mielke (Mayo Clinic Study on Aging)*

UNSUPERVISED BHR COGSTATE RESULTS SUPPORT CONVERGENT VALIDITY. N=6463.







AUC=0.58
AUC=0.68

- Cogstate performance associated with age
- Cogstate performance associated with self-report diagnosis
- Cogstate performance helps identify MCI

Mackin et al 2018

LONGITUDINAL COGSTATE IN BHR

# of test sessions	*N*	*Percent*	*Cumulative N*
1	13849	49%	13,849
2	5178	18%	19,027
3	3045	11%	22,072
4	2136	7.5%	24,208
5	1500	5.3%	25,708
6	1114	3.9%	26,822
7	795	2.8%	27,617
8	422	1.5%	28,039
9	322	1.1%	28,361
10	5	0.02%	28,366

SUBJECTIVE MEASURES IN BHR

- Changes in cognition & everyday functioning, reported by a participant or study partner, are useful for identifying dementia/AD risk in clinic
  - **Associated with objective measures of cognition** *Marshall 2014, Amariglio 2015, Rueda 2015*
  - **Some evidence of associations with AD biomarkers** *Marshall 2011, Gifford 2015*
  - **In some cases, study partner report is more accurate than self report** *Farias 2005, Rueda 2015, Scherling 2016*
  - **Independent predictive power versus objective measures of cognition and other risk factors** *Nosheny 2019*

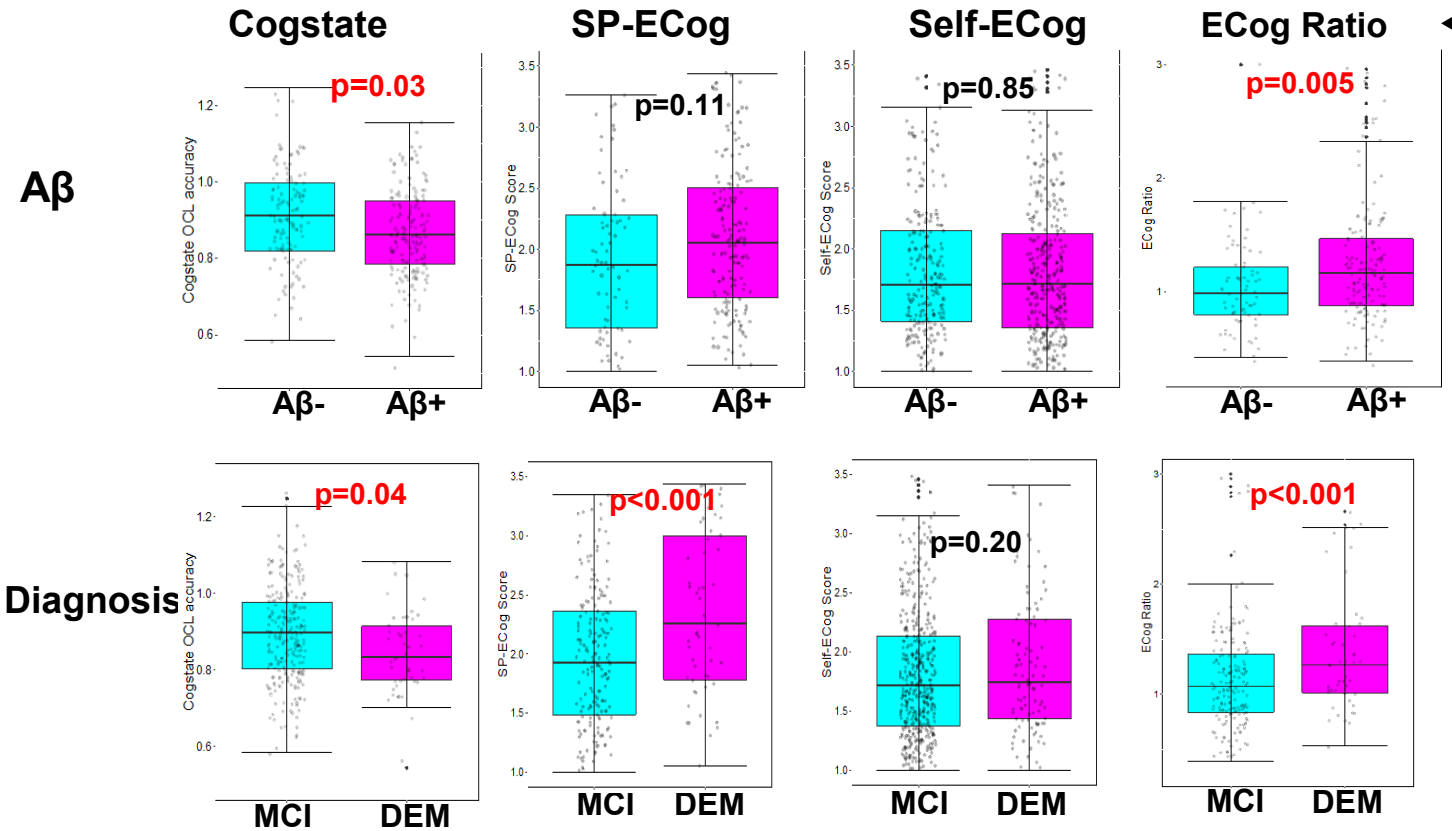
- Subjective measures we collect in BHR
  - **Everyday Cognition (ECog):** self and partner; IADLS that map to 6 cog. domains *Farias 2005*
  - **Functional Activities Questionnaire (FAQ)**: partner; basic ADLs *Brown 2011*
  - **Memory Concerns:** self and partner
  - **Mild Behavioral Impairment-Checklist (MBI-C):** partner; psychiatric/behavioral symptoms *Ismail 2017*

BHR+IDEAS STUDY: USE OF CO-ENROLLMENT TO ADDRESS VALIDITY OF ONLINE DATA

- Participants enrolled in the Imaging Dementia-Evidence for Amyloid Scanning (**IDEAS**) study were recruited to join BHR
  - **Multisite, longitudinal, observational study; participants recruited by dementia specialists from their clinical practice; Aβ PET** *Rabinovici 2019*
  - **N=770 (600 MCI, 170 dementia; diagnosis by dementia specialists in IDEAS) joined BHR with data linkage between in-clinic and online**
  - ***Logistic regression:***

OUTCOMES (IDEAS clinical data)	~	**PREDICTORS** (BHR online data)	+	**CO-VARIATES** (BHR online data)
Aβ PET visual read		Study Partner-report ECog		Age
Diagnosis of MCI v. dementia		Self-report ECog		Gender
		Cogstate		Education

BHR-IDEAS: EVIDENCE FOR VALIDITY OF ONLINE APPROACH



← A measure of discrepancy between SP and self report; Greater values = SP reporting more decline than participant

Nosheny et al 2019 AAIC; under review Alz&Dem

BHR + IN CLINIC NEUROPSYCH: USE OF CO-ENROLLMENT TO ADDRESS VALIDITY OF ONLINE DATA

- N=1000, Age 55+, enrolled in BHR from general public; no self-report MCI or dementia
- Brought into clinic for neuropsych. testing and APOE genotyping

OUTCOMES (in clinical data)	~	**PREDICTORS** (BHR online data)	+	**CO-VARIATES** (BHR online data)
Neuropsych. test scores		Study Partner-report ECog		Age
Memory impairment (+ or -) derived from in-clinic Logical Memory scores		Self-report ECog		Gender
		Cogstate		Education
		APOE		

BHR + IN CLINIC NEUROPSYCH: EVIDENCE FOR VALIDITY OF ONLINE APPROACH

AMYLOID PREDICTION USING BHR

Cognition	0.71-0.80				

NOVEL APPROACHES TO REMOTELY MEASURING COGNITION/FUNCTION/RISK

- Development of electronic versions of the Clinical Dementia Rating and Financial Capacity Instrument
  - **4 year validation study beginning early 2020; N=580**
  - **R. Peterson (Mayo), J. Morris (WashU), D. Marson, E. Roberson (UAB Birmingham)**
- Expansion of APOE genotyping, and addition of polygenic risk scores and plasma biomarkers in a subset of BHR participants
  - **APOE and stored DNA on n=3000 over next 5 years**
  - **Participants sent to a local clinic for blood draw**
- Improved recruitment, engagement, and retention techniques
  - ***Especially those targeting racial/ethnic minority and other underrepresented groups***

SUMMARY

- Online BHR data is associated with in-clinic data, supporting validity
  - in-clinic neuropsych. test performance
  - brain Aβ load
  - clinically-confirmed diagnosis
- Combinations of remote/online measures can help identify those at risk
  - Significant memory impairment
  - Aβ +
- ***Taken together, the results support the feasibility and validity of the online approach to identifying older adults at risk, and provide the rationale for development of novel online/remote methods***

THANK YOU!

BrainHealth REGISTRY
participants & study partners

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University of California San Francisco

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Keith Fargo, Alz. Assoc.
Paul Maruff, Cogstate

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