Detection of Cognitive Impairment from Cognitive Instrument Metadata Using Machine Learning

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Disclosure

- Dr. Doug Scharre sits on the BrainTest® Scientific Advisory Board

Background

- Cognitive impairment (CI) and dementia (DM) including neurodegenerative disorders like Alzheimer's disease (AD) affect millions of people worldwide [1].
  - It is estimated that in 2022, 6.5 million Americans ages 65 or older lived with AD, and 5 million among the same population had mild cognitive impairment (MCI).
  - It is projected that by 2025, the number of AD cases will reach 7.2 million.
  - By 2050, the number of people age 65 and older with Alzheimer's dementia is projected to reach 12.7 million.
- The costs of long-term healthcare for individuals with AD or other dementias are substantial [1].
  - The total payments in 2022 for all individuals with AD or other dementias were estimated to be $321 billion.
  - By 2050, the annual payments for AD healthcare will total almost $1 trillion.
- Unfortunately, there are currently no cures.

Background

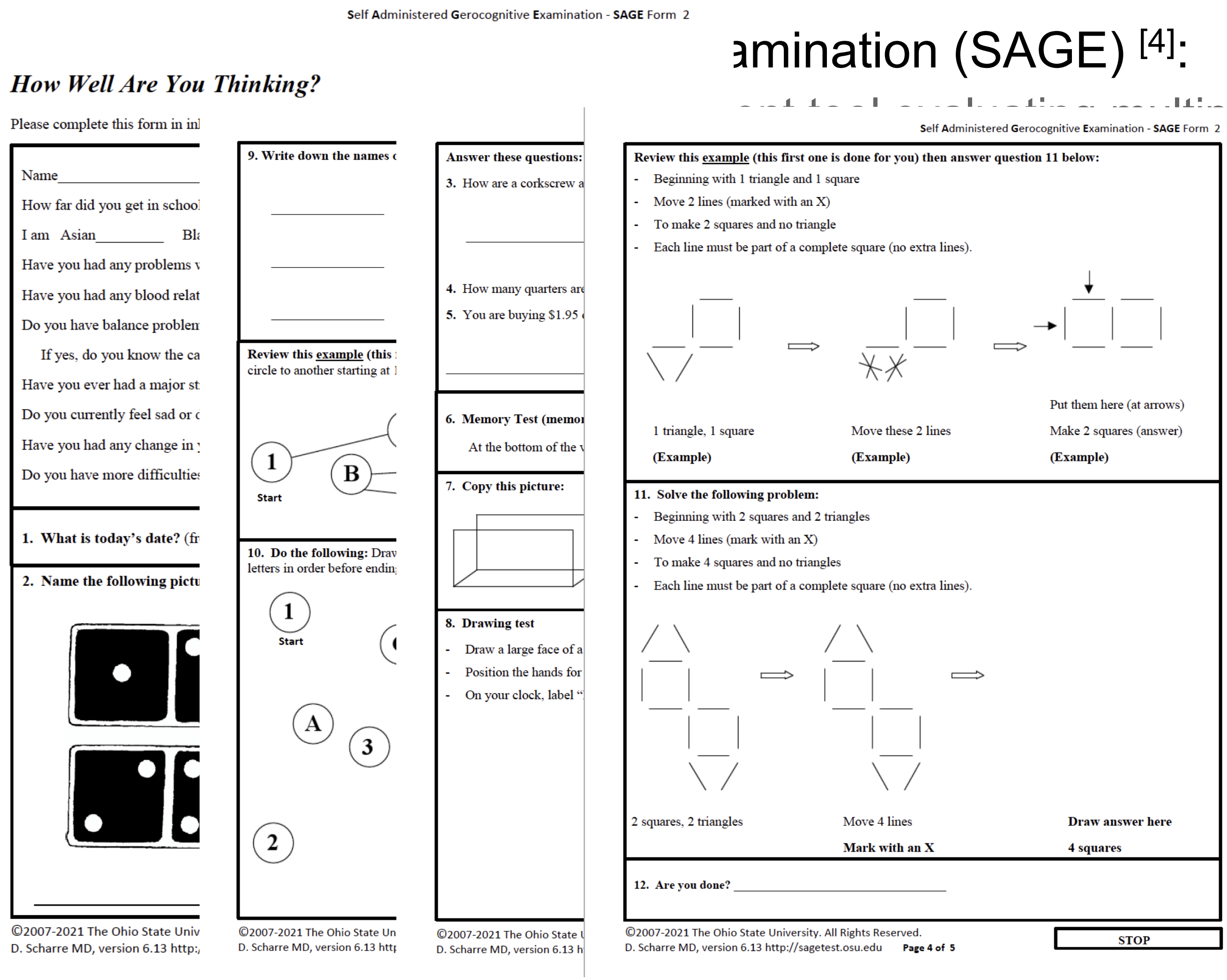
- Identification of cognitive impairment in the MCI stage is critical [1].
  - A treatment that slows the progression of MCI to dementia would have a significant impact on quality of life, caregiver burden, and cost of care.
  - Early diagnosis of AD during the MCI stage could save the US as much as $7 trillion in health and long-term care expenditures.
- There are significant disparities in the prevalence of AD and access to healthcare.
  - Black and Hispanic individuals are disproportionately more likely than White individuals to have AD [2].
  - Socioeconomic disadvantages impede the early detection of MCI or AD [3].

Research Objective

Leverage the electronic Self-Administered Gerocognitive Examination (eSAGE) [4], a variety of metadata collected during eSAGE testing, and machine learning (ML) techniques to facilitate early MCI detection [5]

Self-Administered Gerocognitive Examination

- S… …amination (SAGE) [4]:
  - …ent tool evaluating multiple …
  - …ecutive …
  - …personnel …
  - …ently



Self Administered Gerocognitive Examination - SAGE Form 2

How Well Are You Thinking?

Please complete this form in in…

Name______________

How far did you get in school…

I am Asian_______ Bl…

Have you had any problems v…

Have you had any blood relat…

Do you have balance problem…

If yes, do you know the ca…

Have you ever had a major st…

Do you currently feel sad or d…

Have you had any change in y…

Do you have more difficulties…

1. What is today's date? (fr…

2. Name the following pictu…

9. Write down the names o…

Review this example (this … circle to another starting at 1…

1 Start B

10. Do the following: Draw … letters in order before endin…

1 Start A 3 2

Answer these questions:

3. How are a corkscrew a…

4. How many quarters are…

5. You are buying $1.95 …

6. Memory Test (memo…

At the bottom of the v…

7. Copy this picture:

8. Drawing test

- Draw a large face of a…
- Position the hands for…
- On your clock, label "…

Self Administered Gerocognitive Examination - SAGE Form 2

Review this example (this first one is done for you) then answer question 11 below:

- Beginning with 1 triangle and 1 square
- Move 2 lines (marked with an X)
- To make 2 squares and no triangle
- Each line must be part of a complete square (no extra lines).

1 triangle, 1 square (Example) | Move these 2 lines (Example) | Put them here (at arrows) Make 2 squares (answer) (Example)

11. Solve the following problem:

- Beginning with 2 squares and 2 triangles
- Move 4 lines (mark with an X)
- To make 4 squares and no triangles
- Each line must be part of a complete square (no extra lines).

2 squares, 2 triangles | Move 4 lines **Mark with an X** | **Draw answer here** **4 squares**

12. Are you done? ____________________

STOP

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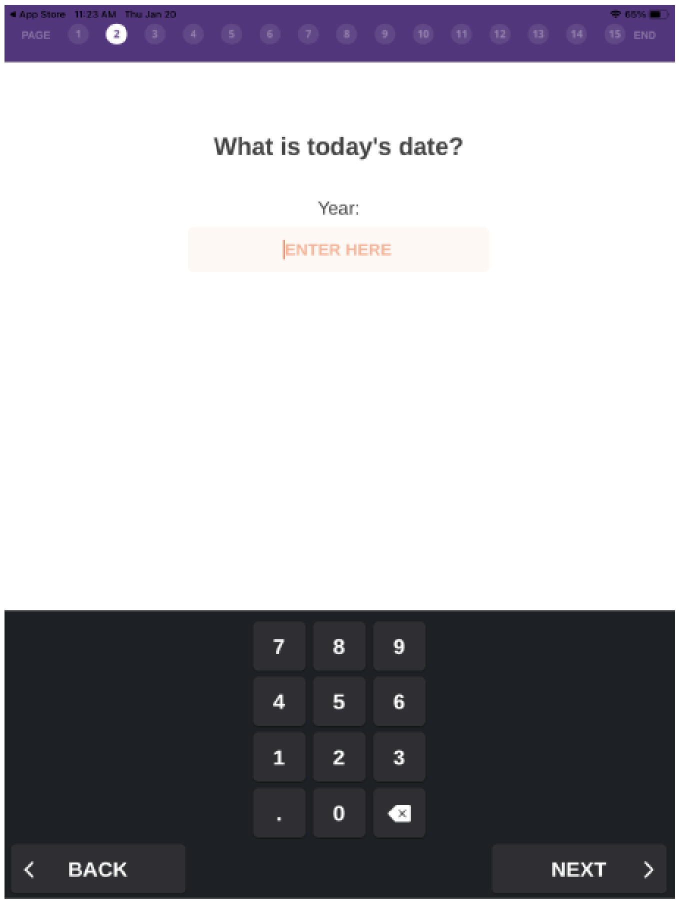
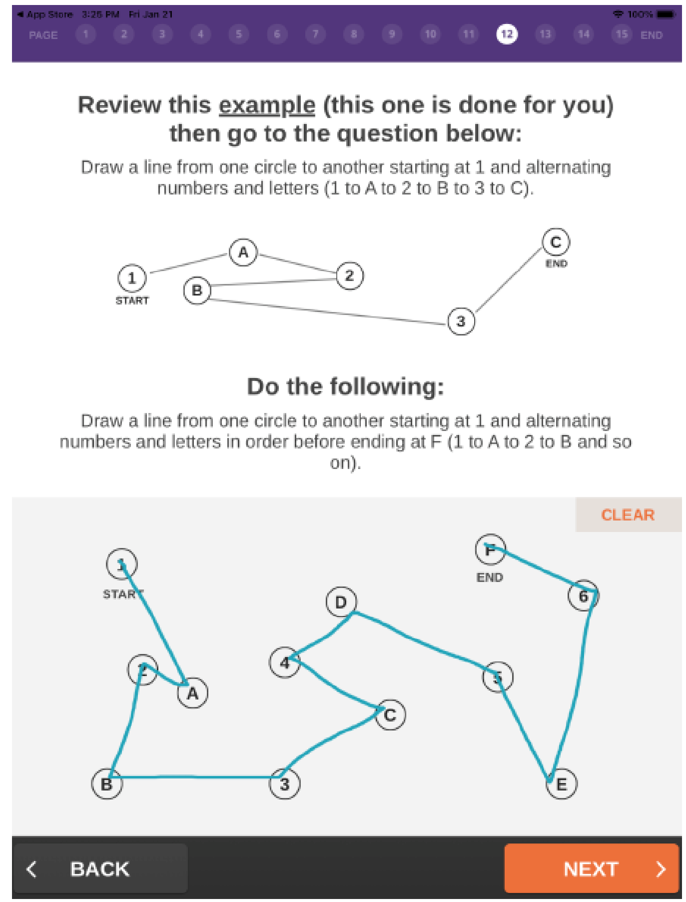
eSAGE

- eSAGE: a digital version of SAGE [6]



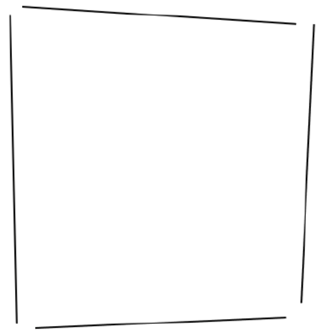


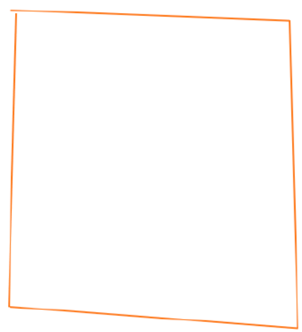
eSAGE Metadata + Machine Learning

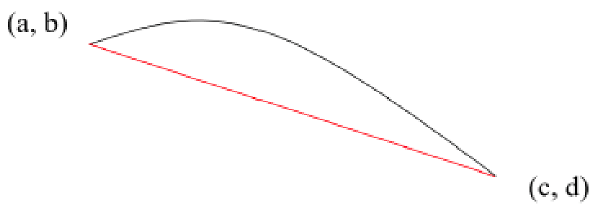
- eSAGE measures
  - Cognitive function in the domains of
    - Orientation (date: 4 points), language (picture naming: 2 points and verbal uency: 2 points), memory (2 points), executive function (modified Trails B: 2 points and problem solving task: 2 points), abstraction (2 points), calculations (2 points), and visuospatial abilities (copying 3-dimentional constructions: 2 points and clock drawing: 2 points).
  - Non-scored items include
    - Demographic information (birthdate, educational achievement, ethnicity, and sex), and questions regarding the individual's past history of strokes and head trauma, family history of cognitive impairment, and current symptoms of memory, balance, mood, personality changes, and impairments of activities of daily living.
- Goal of this study:
  - Investigate ML techniques to predict an individual's cognitive impairment (CI) stage from eSAGE scores and metadata
  - Evaluate behavioral features (metadata) during eSAGE tests as novel biomarkers

eSAGE Metadata and Feature Engineering

- Behavioral features
  - Timing-based features
  - Backtracking-based features
  - Drawing-based features







- eSAGE scores
- In total, 102 features

eSAGE Metadata and Feature Engineering

Feature Name	Description
X Time	The time spent on question X.
X Pages Back	The number of times the subject went back X pages.
X Total Strokes	The total number of strokes used to answer drawing problem X.
X Total Length	The total length of the drawing for drawing problem X.
X Average Stroke Length	The average length per stroke for drawing problem X.
X Average Stroke Speed	The average speed per stroke for drawing problem X.
X Stroke Straightness	The average straightness per stroke for drawing problem X, where straightness is the straight-line distance between the endpoints of a given stroke divided by the stroke length.
X Convex Hull Area	The area of the convex hull around the response for drawing problem X.
X Convex Hull Perimeter	The perimeter of the convex hull around the response for drawing problem X.

Machine Learning from eSAGE Features

- Logistic regression (LR):
  - Binary classifiers that output the probability of the input data being part of the “positive" class (as opposed to the “negative" class), where the probability is calculated via a logistic function.
  - Elasticnet regularization (i.e., both l_1 -norm and l_2 -norm regularization) can be utilized to penalize larger weight parameters so as to prevent overfitting to the training data and conduct feature selection.
- Gradient Boosting Tree Classifier (GBC):
  - An ensemble of decision trees.
  - Begin with a constant model and to iteratively add decision trees to the model. These new decision trees are fit to the residual errors in the model at that step, in order to learn parts of the problem that the model hasn’t figured out yet.

Machine Learning from eSAGE Features

- Classification tasks:
  - (Task 1) CI vs. NC
  - (Task 2) MCI vs. NC
  - (Task 3) DM vs. NC
  - (Task 4) DM vs. MCI
  - (Task 5) DM vs. nDM

Diagnosis	NC	MCI	DM
Number of Subjects	21	24	21

- eSAGE features:
  - F-b: Behavioral features only
  - F-s: scoring features only
  - F-bs: both behavioral and scoring features
- Evaluation metrics:
  - accuracy (acc), precision (prec), recall (rec), F1, AUC

Overall Performance

Task	Classes	Features	Acc	Prec	Rec	F1	AUC
1	CI vs. NC	F-b	0.6824	0.7005	0.9422	0.8001	0.7343
		F-s	0.7846	0.8378	0.8622	0.8434	0.8888
		F-bs	0.7945	0.8393	0.8756	0.8507	**0.8951**
2	MCI vs. NC	F-b	0.5889	0.6046	0.7500	0.6530	0.7050
		F-s	0.7045	0.7702	0.6810	0.6927	0.8310
		F-bs	0.7111	0.7793	0.6780	0.6997	**0.8400**
3	DM vs. NC	F-b	0.7575	0.8269	0.6680	0.7037	0.8183
		F-s	0.9570	0.9960	0.9190	0.9518	0.9684
		F-bs	0.9410	0.9920	0.8910	0.9316	**0.9812**
4	DM vs. MCI	F-b	0.6400	0.6518	0.4440	0.5019	0.7060
		F-s	0.7845	0.8248	0.7170	0.7463	0.8930
		F-bs	0.7800	0.8139	0.7290	0.7469	0.8900
5	DM vs. nDM	F-b	0.7007	0.4723	0.2170	0.2785	0.7666
		F-s	0.8429	0.8090	0.6790	0.7199	0.9182
		F-bs	0.8545	0.8167	0.7080	0.7397	**0.9223**

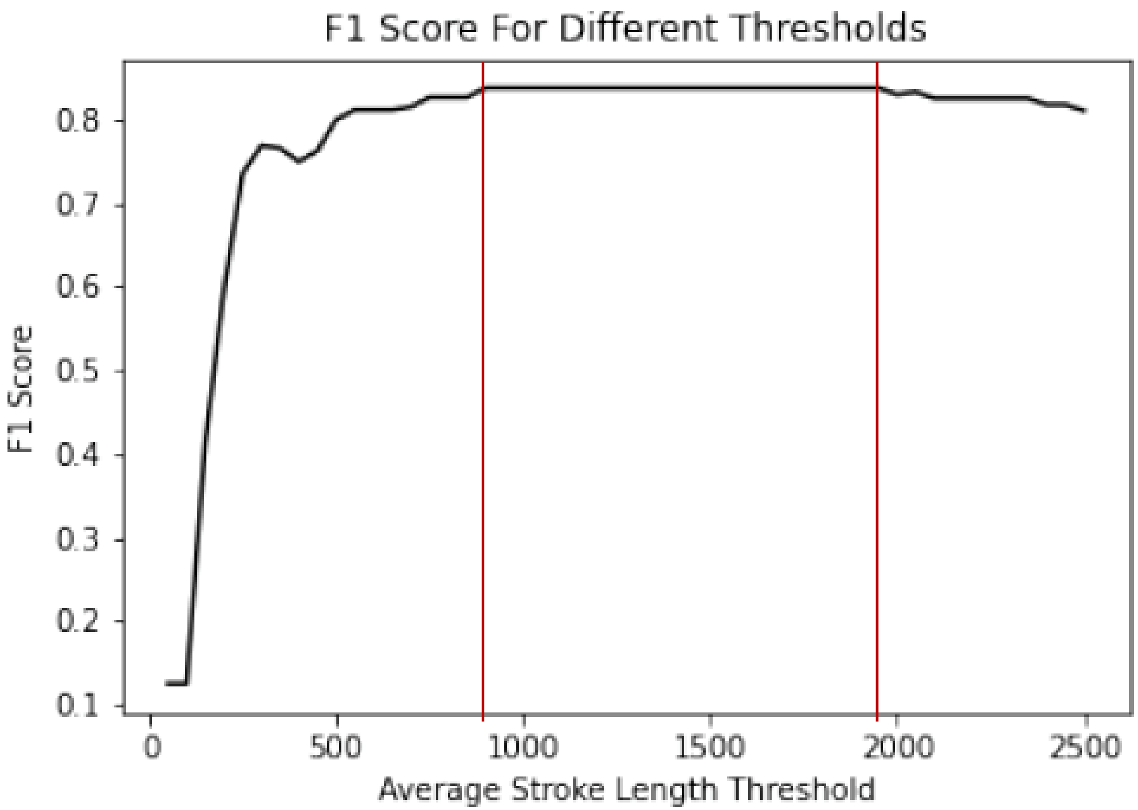
Important Features (behavioral + scores)

Task	Classes	Important Features in F-b			Important features in F-bs		
		Model	Feature	Weight	Model	Feature	Weight
1	CI vs. NC	LR (l1, l2)	Executive Modified Trails B Task Average Stroke Length	0.6396	LR (l2)	Verbal Fluency Score	-0.7862
			Date Question Time	0.4764		Executive Modified Trails B Task Score	-0.7644
			Orientation Questions Time	0.4511		Memory Question Score	-0.7465
			Language Questions Time	0.4009		Executive Modified Trails B Task Average Stroke Length	-0.5380
			Verbal Fluency Question Time	0.3818		Language Questions Score	-0.5167
2	MCI vs. NC	LR (l1, l2)	Executive Modified Trails B Task Average Stroke Length	-1.0601	LR (l2)	Verbal Fluency Score	-1.0734
			Date Question Time	1.0049		Executive Modified Trails B Task Average Stroke Length	-0.7724
			Language Questions Time	0.6159		Visuospatial Construction Copy Task Score	-0.7561
			Verbal Fluency Question Time	0.5365		Executive Modified Trails B Task Score	-0.7248
			Picture Naming Question 1 Time	0.3681		Language Questions Score	-0.6245
3	DM vs. NC	LR (l1, l2)	Month Question Time	1.2820	LR (l1, l2)	Memory Question Score	-1.6942
			Executive Modified Trails B Task Stroke Straightness	-1.2468		Executive Modified Trails B Task Score	-1.1135
			4 Pages Back Count	1.1878		Date Question Score	-0.9361
			Visuospatial Construction Copy Task Time	1.1300		Picture Naming Question 1 score	-0.8951
			Executive Modified Trails B Task Average Stroke Length	-0.9523		Verbal Fluency Question Score	-0.8796

Important Features (behavioral + scores)

Task	Classes	Important Features in F-b			Important features in F-bs		
		Model	Feature	Weight	Model	Feature	Weight
4	DM vs. MCI	LR (l2)	Executive Modified Trails B Task Stroke Straightness	-1.4562	LR (l1, l2)	Calculation Question 2 score	-1.0417
			Visuospatial Construction Copy Task Time	1.1103		Visuospatial Clock Drawing Task Score	-0.6179
			Race Question Time	-0.9712		Date Question Score	-0.5509
			Education Question Time	0.8656		Similarity Question Score	-0.5126
			4 Pages Back Count	0.8229		Orientation Questions Score	-0.4448
5	DM vs. nDM	LR (l2)	Executive Modified Trails B Task Stroke Straightness	-1.1585	LR (l2)	Calculation Question 2 score	-1.0730
			Visuospatial Construction Copy Task Time	0.8232		Memory Question Score	-0.9127
			Month Question Time	0.7795		Similarity Question Score	-0.7243
			4 Pages Back Count	0.7818		Visuospatial Clock Drawing Task Score	-0.7234
			Memory Problems Question Time	-0.5987		4 Pages Back Count	0.8229

Potential New Markers in eSAGE



Top Most Important Features

Task	Classes	Features	Acc	Prec	Rec	F1	AUC
1	CI vs. NC	F-s	0.7846	0.8378	0.8622	0.8434	0.8888
		F-bs	0.7945	0.8393	0.8756	0.8507	0.8951
		top-5	0.8023	0.8661	0.8511	0.8520	**0.9182**
2	MCI vs. NC	F-s	0.7045	0.7702	0.6810	0.6927	0.8310
		F-bs	0.7111	0.7793	0.6780	0.6997	0.8400
		top-5	0.7533	0.8111	0.7260	0.7405	**0.8895**
3	DM vs. NC	F-s	0.9570	0.9960	0.9190	0.9518	0.9684
		F-bs	0.9410	0.9920	0.8910	0.9316	**0.9812**
		top-5	0.9455	0.9490	0.9540	0.9465	0.9721
4	DM vs. MCI	F-s	0.7845	0.8248	0.7170	0.7463	0.8930
		F-bs	0.7800	0.8139	0.7290	0.7469	0.8900
		top-5	0.7867	0.8574	0.6960	0.7290	**0.8950**
5	DM vs. nDM	F-s	0.8429	0.8090	0.6790	0.7199	0.9182
		F-bs	0.8545	0.8167	0.7080	0.7397	0.9223
		top-5	0.8698	0.8609	0.7120	0.7504	**0.9466**

Conclusions

- Behavioral features in eSAGE can be used to better detect cognitive impairment.
- There is the potential to identify additional behavioral features to improve the predictive ability to identify different stages of cognitive impairment.
- The utility of those identified as important behavioral features, would need further validation in clinical settings.
- New versions of eSAGE with such features and underlying predictive analysis could benefit the general public in the early and accurate detection of cognitive decline.

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Thank You!
Questions?

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