

# Assessment of iADL functioning in individuals with subjective cognitive decline using the Virtual Reality Functional Capacity Assessment Tool (VRFCAT)

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## METHODOLOGICAL ISSUE

There is widespread agreement regarding the need for improved functional assessment in AD prevention trials. We address this issue by examining the relationship between performance-based measures of functioning and cognition in individuals with self-reported cognitive complaints and with age-matched controls.

## INTRODUCTION

- Assessment of functioning relies heavily on informant-reported measures that require identification of a reliable informant; these measures often lack sensitivity to subtle functional declines in preclinical and prodromal MCI/AD
- Increasing interest in clinical trials for prevention and early intervention highlights the need for tools that are performance-based and sensitive to subtle deficits in instrumental activities in daily living (iADL) in healthier, non-demented individuals
- The Virtual Reality Functional Capacity Assessment Tool (VRFCAT) is a performance-based assessment of iADL functioning that assesses a participant's ability to complete instrumental activities (called objectives) associated with a shopping trip. In previous studies, the VRFCAT has demonstrated high test-retest reliability and has shown strong relationships to cognition, sensitivity to declines in healthy aging adults, and sensitivity to pronounced functional deficits in schizophrenia (Atkins et al., 2015; Keefe et al., 2016)
- We present findings from an ongoing study to collect census-matched normative data in 650 healthy individuals and 60 individuals with subjective cognitive complaints. We describe preliminary findings comparing performance of healthy older adults (≥55 years) and older adults with subjective cognitive complaints



Figure 1. Virtual Reality Functional Capacity Assessment Tool (VRFCAT)

## METHODS

- Data currently includes 499 participants, including 229 healthy young adults (YA, <55 years), 227 healthy older adults (hOA, ≥55 years), and 43 older adults with subjective cognitive complaints.
- Older adults with cognitive complaints were classified as such based on total scores of ≥ 4 on the self-reported Mail-In Cognitive Function Screening Instrument and MCFSI
- In addition to the VRFCAT, all participants completed the UCSD Performance-based Skills Assessment (UPSA VIM) as well as several standard cognitive assessments, including the Montreal Cognitive Assessment (MoCA), the Brief Assessment of Cognition (BAC App), Trail Making Part B, and Logical Memory subtests of the Wechsler Memory Scale
- Participants ≥ 55 years of age completed the MCFSI. Those with cognitive complaints were asked to provide an informant to complete the ADCS Activities of Daily Living-Prevention Instrument (ADCS-ADL-PI)
- The VRFCAT provides automatic scoring and data management in compliance with 21 CFR Part 11 requirements. Key outcome measures for the VRFCAT include total time to complete all 12 objectives (Adjusted Total Time) as well as individual objective times and error rates (9 VRFCAT Errors)

## METHODS (cont.)

### Participant Characteristics

AGE AND EDUCATION			
		AGE	EDU YEARS
Young Adults	Mean	38.74	14.45
	SD	10.18	2.11
Healthy Older Adults	Mean	68.41	15.33
	SD	8.01	2.78
Cognitive Complaints	Mean	71.00	14.46
	SD	9.61	2.21

SEX			
	FEMALE	MALE	TOTAL
Young Adults	129	100	229
Healthy Older Adults	140	87	227
Cognitive Complaints	34	9	43
TOTAL	303	196	499

Figure 2. Sample age, education and sex

## RESULTS

### Group difference in cognitive performance

Participants with subjective cognitive complaints performed significantly lower than hOAs without subjective decline on most standard neurocognitive measures, indicating subjective decline was associated with objective deficits

	hOA		Cognitive Complaints		Cohen's d	p value
	Mean	SD	Mean	SD		
MoCA	26.82	1.85	24.88	3.23	0.66	<.001
BAC Verbal Memory	41.32	8.48	36.48	8.88	0.42	<.001
BAC Delayed Free Recall	8.07	3.33	6.10	4.07	0.41	<.001
BAC Digit Sequencing	20.44	3.77	19.12	3.70	0.26	<.05
BAC Token Motor	59.72	23.38	54.59	23.51	0.29	ns
BAC Semantic Fluency	21.23	5.64	18.98	5.32	0.30	<.05
BAC Letter Fluency	31.76	9.07	28.79	8.30	0.24	<.05
BAC Symbol Coding	34.64	10.29	29.35	10.14	0.38	<.01
BAC Tower of London	16.04	2.99	15.47	3.54	0.14	ns
BAC Visuo-spatial WM	14.48	5.49	11.90	4.83	0.35	<.01

Figure 3. Reduced cognitive performance in participants with subjective complaints

### VRFCAT Sensitivity to Cognitive Complaints

VRFCAT total completion time, error rate and number of forced progressions all demonstrated strong sensitivity to differences between groups ( $p \leq .001$  for all omnibus and pairwise comparisons)

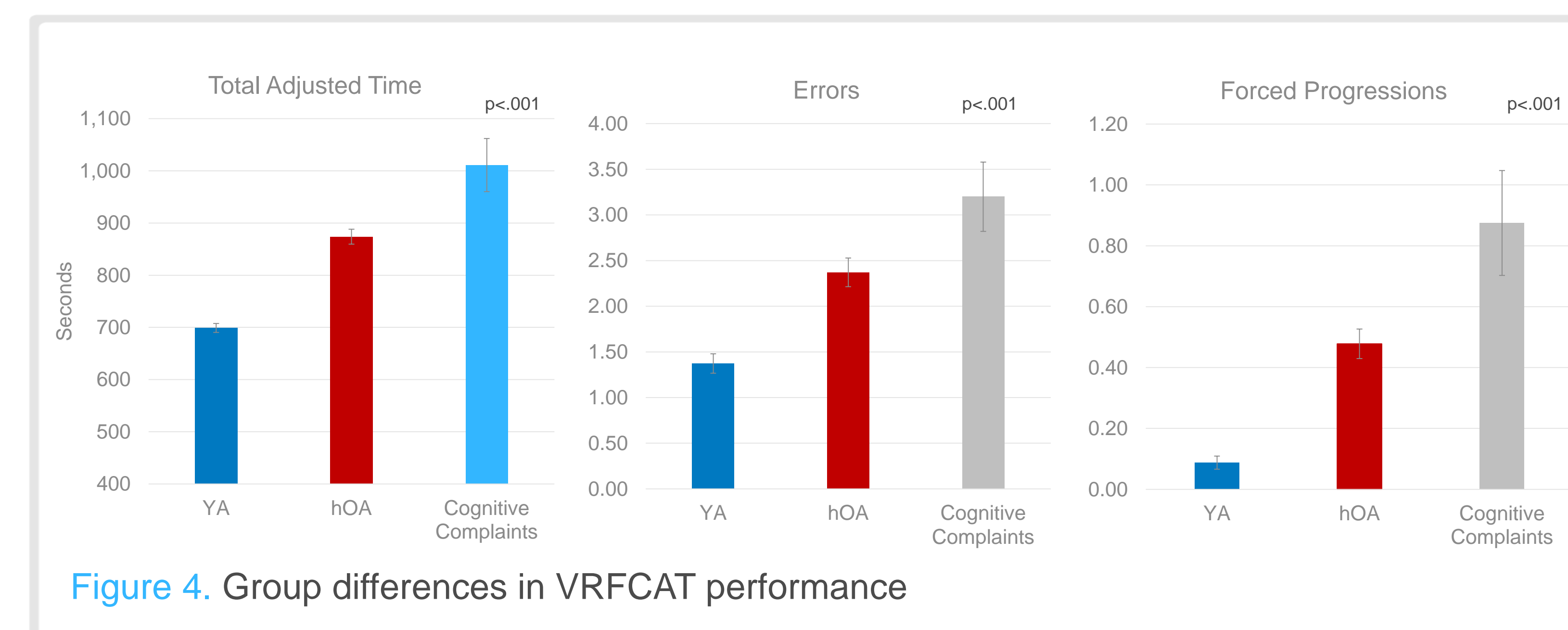


Figure 4. Group differences in VRFCAT performance

## CONCLUSIONS

- Results indicate that the VRFCAT is sensitive to differences between healthy OAs and those with subjective cognitive complaints, and demonstrate convergence between VRFCAT findings, objective cognitive testing, and informant reports of declining function.
- Findings support further development and customization of the VRFCAT as a performance-based measure of functioning for prevention and early MCI/AD trials.

## DISCLOSURES AND SUPPORT

AS Atkins is a full-time employee of NeuroCog Trials, Durham, NC, USA, and has received support from National Institute of Mental Health and National Institute on Aging; A Khan is a full-time employee of NeuroCog Trials, Durham, NC, USA, and has received support from National Institute of Mental Health, Janssen, Celgene, Teva Pharmaceuticals, and Stanley Medical Research Foundation. A Vaughn and D Balentin are full-time employees of NeuroCog Trials, Durham, NC, USA. RSE Keefe currently or in the past 3 years has received investigator-initiated research funding support from the Department of Veteran's Affairs, Feinstein Institute for Medical Research, GlaxoSmithKline, National Institute of Mental Health, National Institute on Aging, Novartis, Psychogenics, Research Foundation for Mental Hygiene, Inc., and the Singapore National Medical Research Council. He currently or in the past 3 years has received honoraria, served as a consultant, or advisory board member for AbbVie, Akebia, Amgen, Asubio, AviNeuro/ChemRx, BiolineRx, Biogen Idec, Biomarin, Boehringer-Ingelheim, Eli Lilly, EnVivo/FORUM, GW Pharmaceuticals, Janssen, Lundbeck, Merck, Minerva Neurosciences, Inc., Mitsubishi, Novartis, NY State Office of Mental Health, Otsuka, Pfizer, Reviva, Roche, Sanofi/Aventis, Shire, Sunovion, Takeda, Targacept, and the University of Texas South West Medical Center. Dr. Keefe receives royalties from the BACS testing battery, the MATRICS Battery (BACS Symbol Coding) and the Virtual Reality Functional Capacity Assessment Tool (VRFCAT). He is also a shareholder in NeuroCog Trials and Sengenix.

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## RESULTS

### VRFCAT relationship to informant-reported iADL function and UPSA performance in individuals with cognitive complaints

VRFCAT performance was correlated with relevant aspects of informant-reported iADL function on the ADCS-ADL PI

- VRFCAT completion time was positively correlated with informant reported difficulties in shopping,  $r = .456$ ,  $p < .001$
- VRFCAT errors were positively correlated with informant reported difficulties in completing complex activities,  $p = .38$ ,  $p < .05$

Strong correlation between VRFCAT completion time and performance-based function UPSA-VIM,  $r = .53$ ,  $p < .001$

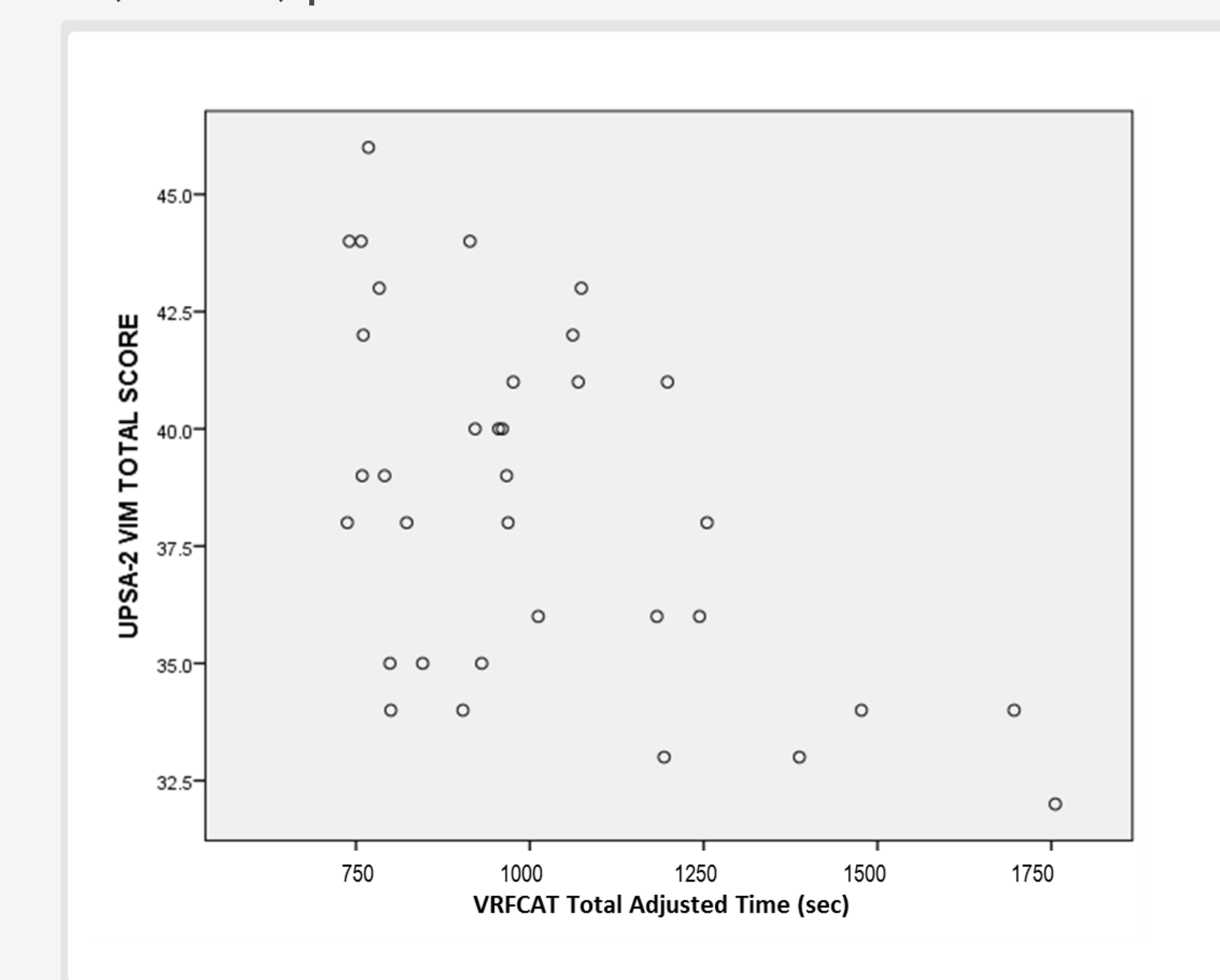


Figure 5. Correlation between VRFCAT total time and UPSA-VIM Total in participants with cognitive complaints,  $r = .53$ ,  $p < .001$

### Relationship to cognitive measures

VRFCAT performance demonstrated strong correlations with standard cognitive measures assessed

- MoCA:  $r = -.51$ ,  $p < .001$
- BAC Verbal memory:  $r = -.50$ ,  $p < .001$
- BAC Delayed free recall:  $r = -.40$ ,  $p < .05$
- TMT-B:  $r = .60$ ,  $p < .001$
- BAC Semantic fluency:  $r = -.41$ ,  $p < .01$
- BAC Symbol coding:  $r = -.55$ ,  $p < .001$
- BAC Tower of London:  $r = -.46$ ,  $p < .001$
- BAC Visuo-spatial working memory:  $r = -.58$ ,  $p < .001$

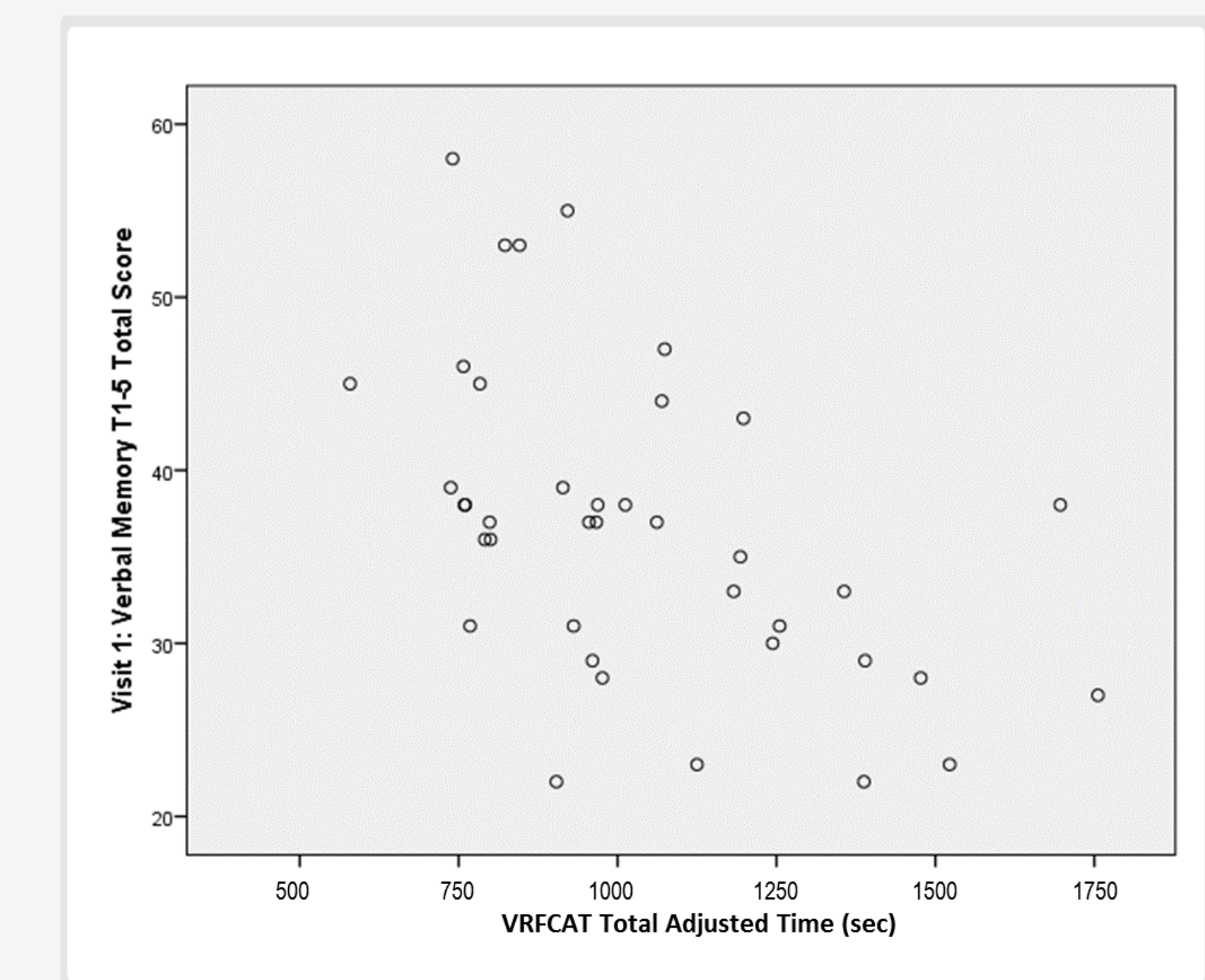


Figure 6. Correlation between VRFCAT total time and BAC verbal memory in participants with cognitive complaints,  $r = .50$ ,  $p < .001$ .