The Virtual Reality Functional Capacity Assessment Tool (VRFCAT): A New Co-Primary Cognitive Measure for Schizophrenia Drug Trials

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Background

- Representatives from FDA have repeatedly stated that improvement on traditional measures of cognition will not be sufficient for approval of a new drug for cognitive enhancement.
- In addition to showing improvement on traditional cognitive measures, patients must also demonstrate improvement on a measure of "functional capacity" meant to approximate competence in activities of daily living.
- Currently, no co-primary measure has been universally endorsed and the method to achieve this end lacks definition.
- The Virtual Reality Functional Capacity Assessment Tool (VRFCAT) is designed to create a realistic, simulated environment using state-of-the-art gaming software to assess patients' proficiency for navigating everyday life.

Methods

- The authors worked closely with Applied Research Associates to create a realistic environment approximating everyday life.
- The environment consists of three settings: a kitchen; a bus stop; and a supermarket
- The subject was tasked with checking the kitchen for ingredients needed to fulfill a recipe; using the correct change and taking the correct bus to the supermarket based on a bus schedule; purchasing the correct quantity of groceries; counting exact change to pay the grocery bill; and taking the bus back to the apartment.
- Six versions of the task have been created with modifications to the details that minimize practice effects and increase utilization for clinical trials.
- A shorter tutorial version was used to minimize any ancillary effects due to subject differences in computer experience.
- Sixty-eight healthy controls were recruited through random telephone sampling and classified advertisements.
- Each participant was tested and then re-tested 7 to 14 days later with a different version.

Results

- Descriptive statistics for each version revealed that Version 4 contained significantly outlying data, thus the Factor Analysis conducted to determine the VRFCAT factor structure excluded data from Version 4.
- The total sample size for the Factor Analysis was n=46, since any subject having received Version 4 at either visit was not included in this analysis.
- The Factor Analysis explained 91% of variance and revealed three factors, which the authors have labeled Reasoning and Problem Solving; Speed of Processing; and Working Memory.
- The domains were combined into a composite, which yielded an ICC of .61 between testing visits.

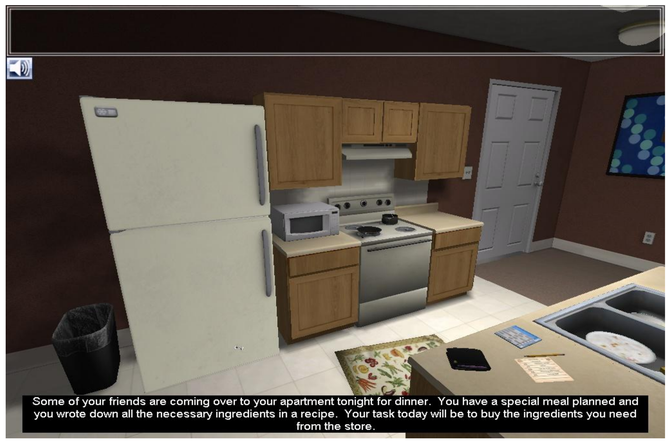
Table 1. Demographics and Total Score by Visit

	All Subjects (N=68)
Age	39.7 (SD=13.3)
Gender	Male 22 (32%); Female 46 (68%)
Race	White 41 (6%) African American 26 (38%) Other 1 (2%)
VRFCAT T-Score – Visit 1	Mean 45.7(SD=8.4) N = 59
VRFCAT T-Score – Visit 2	Mean 50.0 (SD=6.4) N = 55

Table 2. Results of Factor Analysis

Objective	Factors		
	1 (Reasoning / Problem Solving)	2 (Speed of Processing)	3 (Working Memory)
Time to add bus fare	**0.92**	0.19	0.14
Errors adding bus fare	**0.92**	0.12	0.16
Time to add grocery money	**0.87**	0.16	0.09
Errors adding grocery money	**0.79**	0.13	0.12
No. times bus schedule accessed	**0.50**	0.34	0.25
Errors adding bus fare	**0.48**	0.24	0.08
Time to shop for items	0.29	**0.82**	0.28
Errors shopping for items	0.11	**0.82**	0.21
Time to board bus	0.25	**0.78**	0.01
Time to board bus	0.13	**0.69**	-0.06
Time to cross off items	0.21	0.04	**0.90**
Errors crossing off items	0.31	0.01	**0.86**
No. times recipe accessed	0.00	0.20	**0.68**

VRFCAT Screenshots



Apartment Kitchen

Bus Stop

Supermarket

Figure 1: Relationship between Performance at Visit 1 and Visit 2 by Sex

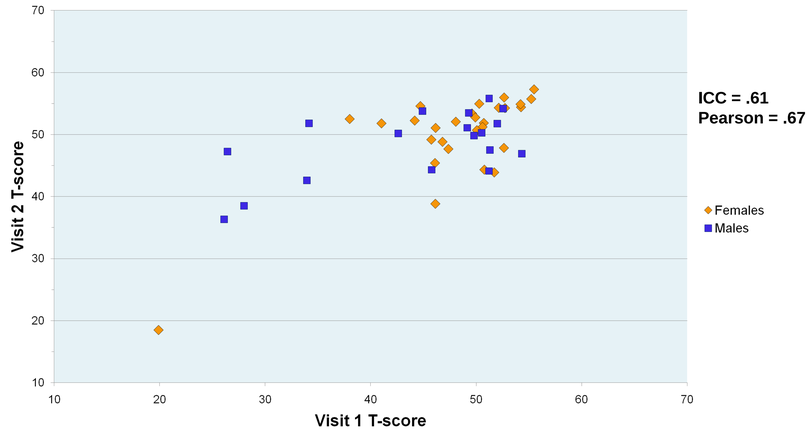
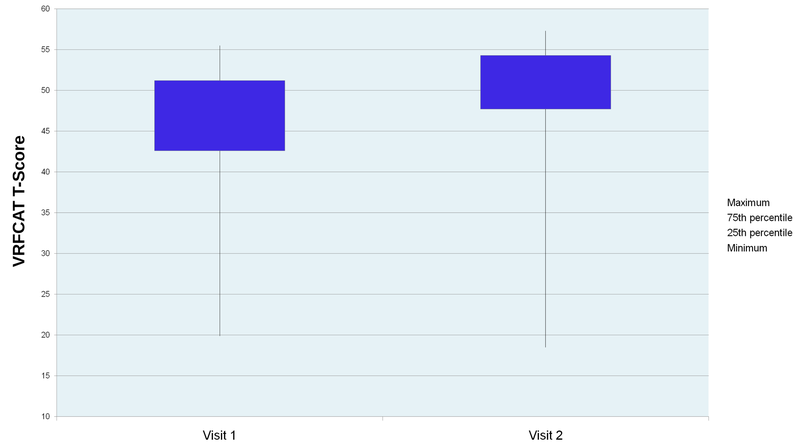


Figure 2: T-score Percentile Distributions by Visit



Discussion

- The VRFCAT was successfully implemented in 68 healthy controls.
- One version of the test was eliminated because of the presence of an unexpected number of outliers due to task difficulty.
- The ICC test-retest value is acceptable but falls short of expectations. However, it is consistent with or better than those for currently used co-primary measures in healthy control samples. We expect that this will increase in schizophrenia samples with greater variability of performance.
- Further testing with a refined measure will be conducted shortly with patients with schizophrenia.

Author Disclosures

KH Fox is a full-time employee of NeuroCog Trials, Inc. S Ruse is a part-time employee of NeuroCog Trials, Inc. VG Davis is a part-time employee of NeuroCog Trials, Inc. PD Harvey currently or in the past 12 months has served as a consultant for Shire, Cypress Bioscience, EnVivo Pharma, BMS, Genentech, Merck and Company, Sunovion Pharma, and has received royalties from the Brief Assessment of Cognition in Schizophrenia (BACS) testing battery. RKR Krishnan has holdings in Orexigen and indirect holdings and consultancy in Cenerx He has consulted for Eisai for the past 12 months. RSE Keefe currently or in the past 2 years has received investigator-initiated research funding support from the National Institute of Mental Health, Allon, Astra-Zeneca, GlaxoSmithKline, Novartis, Department of Veteran's Affairs, and the Singapore National Medical Research Council. He currently or in the past 2 years has received honoraria, served as a consultant, or advisory board member for Abbott, Acadia, Astra-Zeneca, BiolineRx, BrainCells, BMS, CHDI, Cypress Bioscience, Dainippon Sumitomo Pharma, Eli Lilly, EnVivo, Johnson & Johnson, Lundbeck, Merck, Memory, Neurosearch, Orion, Otsuka, Pfizer, Prophase, Roche, Sanofi-Aventis, Shire, Solvay, Takeda, World Wide Clinical Trials, and Wyeth. Dr. Keefe receives royalties from the BACS testing battery and the MATRICS Battery (BACS Symbol Coding). He is also a shareholder in NeuroCog Trials, Inc.