USE OF INTERNET BASED ASSESSMENT FOR TRACKING THE COURSE OF EARLY ALZHEIMER’S DISEASE WITH POTENTIAL FOR DETERMINING RESPONSE TO TREATMENT

31 MARCH 2016
**EXAMPLE: ONE BACK TASK**

<table>
<thead>
<tr>
<th>Task Name</th>
<th>Question</th>
<th>Main Domain Measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection</td>
<td>Has the card turned over?</td>
<td>Psychomotor Function</td>
</tr>
<tr>
<td>Identification</td>
<td>Is the card red?</td>
<td>Attention</td>
</tr>
<tr>
<td>One Card Learning</td>
<td>Have you seen this card before?</td>
<td>Learning</td>
</tr>
<tr>
<td>One Back</td>
<td>Is this card the same as the previous card?</td>
<td>Working Memory</td>
</tr>
</tbody>
</table>

**Objective:** Is it the same as previous?
Have you seen this card before?
COGSTATE:  SUMMARY OF PHASE III STUDIES AND DISEASE AREAS

- 30 phase III studies

- 13 compounds that were approved:
  - Latuda, Opdivo, Latuda, Vyvanse, VESIcare, Tolvaptan, Brintellix, Lyrica, Ketanest S, Topamax, Juxtapid, Vyvanse, Feraheme

- Indications include:
  - Alzheimer’s Disease, Anemia, Cardiovascular, Childhood and Adult Epilepsy, Major Depressive Disorder, Oncology, Overactive Bladder, Parkinson's Disease, Pediatric Bipolar Depression, Pediatric Hyponatremia, Schizophrenia

Clinical trials by Study Phases

Current FDA approved amyloid studies
NEED OPTIMIZATION FOR UNSUPERVISED AND ONLINE ASSESSMENT

MINIMAL DEPENDENCE ON INSTRUCTIONS
Task stimuli and response requirements are trained dynamically

DYNAMIC INTRODUCTION OF TASK RULES
Once individual demonstrates understanding of requirements then rules for task performance are introduced, again dynamically

INCREASE TASK DIFFICULTY
Once simple tasks have been acquired and performed. Introduce the more complex rules for memory and working memory tasks.
VALIDATION OF UNSUPERVISED ASSESSMENT METHOD

The nature and rate of cognitive maturation from late childhood to adulthood

Jason A. Cronen1,2, Adrian J. Schenker1,3, Brian T. Harel1,2,3 and Paul Maruff4,5

1Cognitive Science, University of New Hampshire, Durham, NH, USA
2Cognitive Science, Northeastern University, Boston, MA, USA
3Technology, Optal Neuroscience, Melbourne, VIC, Australia
4School of Medicine, University of Melbourne, Melbourne, VIC, Australia
5Neurological Sciences, Mayo Clinic, Rochester, MN, USA

To better understand the nature and rate of cognitive change across adolescence, the CogState Brief Battery (CBB) was utilized to assess psychomotor function, attention, working memory, and visual learning in individuals aged 10-18 years old. Since all CBB tasks have equivalent perceptual, motor, and linguistic demands as well as being appropriate for both children and adults, the approach allowed direct across-age comparison of multiple cognitive domains. Exponential increases in reaction time and linear increases in accuracy were observed across adolescent development in a cross-sectional sample of 50 individuals and confirmed in a 5789 individual longitudinal sample with 1-year repeat assessments. These results have important implications for the repeated assessment of cognition during development where expected maturation changes in cognition must be accounted for during cognitive testing.

Performance of the CogState computerized battery in the Mayo Clinic Study on Aging

Michelle M. Mielke1,2,9, Mary M. Machulda1,3, Clinton E. Hagen4, Kelly K. Edwards4, Rosebud O. Roberts1,2, V. Shane Pankratz5, David S. Knopman6, Clifford R. Jack, Jr.1,7, Ronald C. Petersen1

1Division of Epidemiology, Department of Health Sciences Research, Mayo Clinic, Rochester, MN, USA
2Department of Neurology, Mayo Clinic, Rochester, MN, USA
3Department of Psychiatry and Psychology, Mayo Clinic, Rochester, MN, USA
4Division of Biomedical Statistics and Informatics, Department of Health Sciences Research, Mayo Clinic, Rochester, MN, USA
5Department of Internal Medicine, University of New Mexico Health Sciences Center, Albuquerque, NM, USA
6Department of Radiology, Mayo Clinic, Rochester, MN, USA

Abstract

Background: The feasibility and validity of brief computerized cognitive batteries at the population-level are unknown.

Methods: Non-demented participants (n = 1660, age 50-97 years in the Mayo Clinic Study on Aging completed the computerized CogState battery and standard neuropsychological battery. The correlation between tests was examined and comparisons of CogState performance on the personal computer (PC) and iPad (n = 331), and in the clinic vs. at home (n = 183) were assessed.

Results: We obtained valid data on greater than 97% of participants on each test. Correlations between CogState and standard neuropsychological measures were significant. CogState scores were significantly lower in the mobile app version compared to the PC version.

Comparison of Cognitive Performance on the Cogstate Brief Battery When Taken In-Clinic, In-Group, and Unsupervised

Jason A. Cronen1,2, Brian T. Harel1,2, Karen Yu1, Jaclyn S. Valadhar2,3, Jack W. Bruniuin2,3, Cameron D. Crawford1, Linda C. Mayes1, and Paul Maruff1,4

1Child Study Center, Yale University, New Haven, CT, USA
2Cognitive Science, Northeastern University, Boston, MA, USA
3Technology, Optal Neuroscience, Melbourne, VIC, Australia
4School of Medicine, University of Melbourne, Melbourne, VIC, Australia

The feasibility of mobile computerized cognitive testing for use in clinical trials

D.M. Rentz1, M. Dekhtyar2, J. Sherman1, S. Burnham1, D. Blacker2, S.L. Aghajanian3, K.V. Papp4, R.E. Amariglio1,6, A. Schembri1, T. Chenhall1, P. Maruff1, P. Aisen5, B.T. Hyman2, R.A. Sperling6

1Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; 2Boston University, Boston, MA, USA; 3University of Chicago, Chicago, IL, USA; 4Commonwealth Scientific and Industrial Research Organizations (CSIRO), eHealth WestGroup, Western Australia; 5Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; 6Department of Neurology, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA; 7CogState, Ltd, Melbourne, Australia; 8University of California at San Diego, San Diego, CA, USA

Corresponding Author: Doreen M. Rentz, MD, Division of Cognitive and Behavioral Neurology, 221 Longwood Avenue, M07, Boston, MA 02115. drentz@partners.org. Telephone: 617-730-8835, Fax: 617-738-9122

© 2015 Cogstate Ltd. All rights reserved.
LEARNINGS FROM STUDY OF ONLINE AD AT-RISK GROUPS

1. Serious study run by serious people
2. Don’t need to see my data
3. Someone will make a decision based on my data and let me know
4. Important medical issue relevant to me
5. “Will do it if my doctor says”
6. Brevity is good but not necessary
EXAMPLE OF ONLINE ASSESSMENT OUTCOMES

Total Subjects 2428
Females 1904,
mean age =61.8, (SD = 6.81)

Usability and acceptability summary

<table>
<thead>
<tr>
<th>Task</th>
<th>Complete</th>
<th>Integrity</th>
<th>Number of Task Attempts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Detection</td>
<td>100%</td>
<td>97.6%</td>
<td>94.4% 5.3% 0.3%</td>
</tr>
<tr>
<td>Identification</td>
<td>100%</td>
<td>99.3%</td>
<td>98.1% 1.4% 0.5%</td>
</tr>
<tr>
<td>OCL</td>
<td>96.9%</td>
<td>99.7%</td>
<td>96.0% 3.2% 0.8%</td>
</tr>
<tr>
<td>One Back</td>
<td>99.9%</td>
<td>99.9%</td>
<td>97.5% 2.1% 0.4%</td>
</tr>
</tbody>
</table>
HIGH ACCEPTABILITY, USABILITY AND VALIDITY IN BHR

ANSWER QUESTIONS & TAKE TESTS

When you complete online brain tests, we get “snapshots” of your health and brain performance. With many snapshots, from you and others, we can make a huge difference.

See How It Works »

It’s safe, easy and free.

JOIN NOW

Already a member? Log in here

Macklin et al CTAD: Philadelphia, PA 2015
Cognitively normal older adults (n=321)
Amyloid status known (high amyloid = SUVr>1.4, n=121):
Three years of annual online assessments
EFFECT OF HIGH AMYLOID IN CN ADULTS – AIBL ONLINE STUDY

Learning/working memory composite

N=200
N=121
WHAT WOULD A TREATMENT EFFECT LOOK LIKE IN THIS MODEL?

[Graph showing learning/working memory composite across different age groups with N=200, N=89, and N=32]
WHAT WOULD A TREATMENT EFFECT LOOK LIKE IN THIS MODEL?

Low $\text{A} \beta$

High $\text{A} \beta$, $\text{APOE e4}$ -

High $\text{A} \beta$, $\text{APOE e4}$ +
SUMMARY

- Simplicity
- Serious
- Important
- Clear question, clear decision pathway.
- Brevity
- Unsupervised Vs online
- Prospective