Developing Digital Assessments for Down-Syndrome Associated AD

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- DSMB Chair: Wall-E (NIA: Jacobs, PI)
Overview

- Measurement burst designs for mobile monitoring of cognition.
- Developing a smartphone application for a global Phase 2/3 prevention trial for Down syndrome-associated Alzheimer’s disease.
- Adapting existing tasks from the Ambulatory Research in Cognition (ARC) smartphone app
- Accessibility and User Experience: Design Considerations for Down syndrome participants
- If time: Advantages and perils of bring your own device (BYOD) study designs
LIMITATIONS OF TRADITIONAL COGNITIVE ASSESSMENTS

ARTIFICIAL
- Assessments very removed from reality.
- Feeling of being “tested” by other person.
- “White-coat” testing effects.
- Effects of daily stressors (fatigue, mood, illness, traveling to sites).

“ONE-SHOT”
- Testing typically completed in one extended session

High Variability = Drastic reductions in statistical power.

**Figure credit to M. Sliwinski**
Ambulatory Research in Cognition (ARC)

The ARC app administers very brief cognitive tests four times per day for one week. Each test session takes less than 3 minutes.

Participants use their personal smartphone, industry term is BYOD (Bring Your Own Device).

The idea behind ARC is simple:

1. Test often and everywhere.
2. Keep it short.
3. Combine the results.

With this simple formula we hope to significantly improve the precision of cognitive testing.
7-day “Burst” Design

**Mon**
- 7 A
- 8 A
- 9 A
- 10 A
- 12 P
- 1 P
- 2 P
- 3 P
- 4 P
- 5 P
- 6 P
- 7 P
- 8 P
- 9 P
- 10 P

**Tues**
- 7
- 8
- 9
- 10
- 12
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10

**Wed**
- 7
- 8
- 9
- 10
- 12
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10

**Thu**
- 7
- 8
- 9
- 10
- 12
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10

**Fri**
- 7
- 8
- 9
- 10
- 12
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10

**Sat**
- 7
- 8
- 9
- 10
- 12
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10

**Sun**
- 7
- 8
- 9
- 10
- 12
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10

**KEY:**
- 🟢 = Grids task
- $ = Prices task
- 🌟 = Symbols task
ARC sensitive to Dominantly Inherited Alzheimer Disease (DIAD). Good correlations between in-clinic cognitive assessments, AD biomarkers, and predicts disease onset. Hassenstab et al., 2020 *Alzheimer’s & Dementia*.

Bring your own device (BYOD): Device-specific response latencies (both tapping and display latencies) vary considerably depending upon programming and quality of devices. Nicosia et al., 2022 *Behavior Research Methods*.

Smartphone-naïve older adults can enroll and successfully use smartphones, with very good adherence. Nicosia et al., 2022 *Frontiers in Digital Health*.

In a sporadic AD population, good correlations with in-clinic tests, AD biomarkers, and excellent retest reliability at 6mos and 1-year (0.90 & 0.97). Nicosia et al., 2022 *Journal of the International Neuropsychological Society*.

Also in sporadic AD, ARC was sensitive to time of day. Worse evening performance, and those with elevated AD biomarkers showed more decline in evening. Wilks et al., 2021 *Journal of Clinical and Experimental Neuropsychology*. 
Can we adapt our tool for global Down syndrome studies?
Considerations

◉ Intellectual disability (ID): Extremely wide range of intellectual abilities in DS Fortea et al, 2021 *Lancet Neurol*

◉ Many individuals with DS struggle with literacy.

◉ Physical considerations: Speech difficulties, low vision are common. Edgin et al., 2010 *Neurodev Disord*

◉ Do older adults with DS actually use smartphones?

◉ What role will study partners have?
**Original Symbols Test (20-40 seconds) Processing Speed**

**SYMBOLS Test**

Participants are asked Which pair below matches one of the pairs on top?

**SYMBOLS Test**

Participants complete 12 trials as quickly as possible. Primary outcome: Number correct and response time.

Nicosia et al. 2022 *JINS*
DS-ARC Shapes Test (60 seconds)
Processing Speed

ARC SYMBOLS Test
• 12 trials
• Matching two abstract shapes
• Written instructions & tutorial

DS-ARC SHAPES Test
• 10 trials
• Matching one abstract shape
• Instructions & tutorial via audio

Nicosia et al. 2022 JINS
ARC Prices Test
• 10 Price-item pairs per session
• At least $1.50 between item pairs
• 3s presentation
• Primary Outcome: Percent Errors
DS-ARC Prices Test (90 seconds)

DS-ARC Prices Test
- 6 Price-item pairs per session
- 2-digit prices
- At least $3 between item pairs
- 6s presentation
- Uses pictures of food items
Original ARC GRIDS Test (30-40 seconds)
Spatial Working Memory

Wilks et al, 2021 JCEN; Nicosia et. 2022 JINS
DS-ARC PETS Test (60 seconds)
Spatial Working Memory
Accessibility Resources for Tech Development

Web Content Accessibility Guidelines (WCAG; w3.org/WAI)

• Applies to any digital content, including smartphone apps, websites, gaming, productivity software, etc.
## Web Accessibility Checklist

A checklist for creating accessible websites and web applications.

### Share:

- [x] Images should have meaningful alternative text
- [x] Links should be visually identifiable
- [x] Use descriptive section headings
- [x] Use correct semantic HTML element structure for your content
- [x] Forms have descriptive labels
- [x] Information should not depend on color, sound, shape, size, or visual location

[webaccessibilitychecklist.com](http://webaccessibilitychecklist.com)
If BYOD, What about device latencies?
WALT Latency Timing Device

Developed by Google/Android engineers to assess smartphone and tablet performance.

“Suggested” Tap Latency Protocol
Enter the TapBOT, AKA Tappy

First Prototype
TAPBOT 2.0
TAPBOT 3.0 “Tappy”
Tappy iOS Tap Latency Results: CPU Load by Power Modes

- Normal Power Mode
- Power Saver Mode

Phone Model:
- iPhone 5s
- iPhone 6
- iPhone 7
- iPhone SE

Tap Delay (seconds)

CPU Load (%)
Latency and Timing Assessment Robot (LaTAR Bot)

- LaTAR Bot Outcomes:
  - Tapping Latency
  - Display Latency
  - Physical Tapping Latency

Optical Sensor (Display Latency)
Solenoid w/Probe (Tap Latency)
Sensor (Variable Capacitance)

Nicosia et al, 2022 Beh Res Meth
LaTAR Bot Configuration

- **Laptop**
  - GUI
  - Server Process

- **Phone**
  - LaTAR mobile application

- **LaTARbot**
  - LaTAR embedded application

Connections:
- Screen brightness commands & capacitive touch timestamps from Laptop to Phone
- Capacitive touch commands & screen brightness timestamps from Laptop to LaTARbot
- Capacitive touch actuator between Phone and LaTARbot
- Screen brightness sensor between Phone and LaTARbot
Display Latencies for 26 Popular Smartphones

(A) Mean Device Display Latencies

Phone Model

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Tap Latencies for 26 Popular Smartphones

(B) Mean Device Tap Latencies
How is this useful for clinical research?
Optimal Response Times (in Theory)

- t0: Application calls draw function (display "callback time")
- t1: App draw function returns (display "action time")
- t2: OS renders the frame (drawing complete)
- t3: Screen begins refresh, photons leaving parts of screen
- t4: Screen completes refresh, photons leaving screen
- t5: Photons reach human eye or LaTAR photodiode
- t6: Visual input received by human brain / LaTAR CPU

- LaTAR display callback latency
  - ~0-1 ms
  - 10s of ms
  - 10s-100s of ms

- LaTAR display action latency
  - <17 ms @ 60 Hz Refresh Rate
  - <1 ms
  - <4 +/- 2 ms

- LaTAR touch callback latency
  - ~17 ms @ 60 Hz Sample Rate

- LaTAR touch action latency
  - ~2-3 ms

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## Guidelines for BYOD Studies

### (A) BYOD Study Design Choice

<table>
<thead>
<tr>
<th>Within-Person</th>
<th>Potential Effect on Response Times</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid-Study Change to Same Device</td>
<td>mild</td>
</tr>
<tr>
<td>Mid-Study Change to Same Manufacturer</td>
<td>moderate</td>
</tr>
<tr>
<td>Mid-Study Change to Different Manufacturer</td>
<td>severe</td>
</tr>
<tr>
<td>Mid-Study OS Software Update</td>
<td>moderate</td>
</tr>
<tr>
<td>Same Device, Same OS</td>
<td>mild</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Between-Person</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Different OS Versions (Same Device)</td>
<td>moderate</td>
</tr>
<tr>
<td>Different Devices (Same Manufacturer)</td>
<td>moderate</td>
</tr>
<tr>
<td>Different Devices (Different OS and/or Manufacturers)</td>
<td>severe</td>
</tr>
</tbody>
</table>

### (B) BYOD Study Design Tradeoffs

<table>
<thead>
<tr>
<th>Response Time Precision</th>
<th>Participant Sampling Pool</th>
<th>Cost</th>
<th>BYOD Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>~105 ms total device variability</td>
<td>Large</td>
<td>$</td>
<td>Full BYOD</td>
</tr>
<tr>
<td>max - min for all devices in the study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>~70 ms total device variability</td>
<td>Moderate</td>
<td>$$</td>
<td>Selective BYOD</td>
</tr>
<tr>
<td>max - min for iOS only devices in the study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>~17 ms total device variability</td>
<td>Small</td>
<td>$$$</td>
<td>Device Provided</td>
</tr>
<tr>
<td>theoretical total latency variability of</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>device with 120 Hz refresh &amp; sampling rate</td>
<td></td>
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