Cognitive Dysfunction in Psychosis: Identification and Intervention

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Public Presentation:
• Bright 16 year old male
• Shy, introverted
• Socially anxious
• Grades dropped from A’s to B’s, then C’s, eventually D’s
• By junior year of high school, he was failing classes
• Few friends, not initiating peer contact
Academic Difficulties

• Concentration
• Initiative
• Organization
• Reading
• Writing
• Memory
• Academic supports put in place
• Discontinued brief psychotherapy
What are reasons for neuropsychological assessment?

- Problems in organization and planning
- Forgetfulness
- Difficulty concentrating and sustaining studying
- First-time evaluation - many adolescents or adults have never received a clear diagnosis.
- Re-evaluation to determine change over time.
- Assessment of treatment effects.
- Request for accommodations in college, exams, etc..
- Understanding of own strengths and weaknesses for self and significant others (e.g., parents, spouse).
A typical neuropsychological evaluation will involve assessment of the following:

- General intellectual functioning
- Higher level executive skills (e.g., sequencing, reasoning, problem solving)
- Attention and concentration
- Learning and memory
- Language
- Visual–spatial skills (e.g., perception)
- Motor and sensory skills
- Mood and personality
- Some abilities may be measured in more detail than others, depending on the needs of the person
Name the color of the word…

Did you have a STROOPs! Effect?

Selective ATTENTION

Healthy persons activate Anterior cingulate when they Detect errors
ABF: Abstraction & Mental Flexibility

EASY

HARD

CATEGORIZATION TASK
SPATIAL: Line Orientation

EASY

HARD
Characteristic profile in schizophrenia: maximal impairment in memory, attention, and executive function; relative preservation of old learning and visual perceptual skills.

Heinrichs & Zakzanis
Neuropsychology 1998
Cognition in Psychosis: Core Feature of the Illness

• Present before onset of clinical symptoms
• Seen in unaffected first-degree relatives
• Relatively stable across clinical state; life span until late adulthood
• Low cross sectional correlations with psychotic symptoms
• Discrepancy between clinical and cognitive effects of antipsychotic medications
Cognitive Functioning in Prodromal Psychosis: A Meta-analysis
Paolo Fusar-Poli, MD, PhD; Giacomo Deste, MD; Renata Smieskova, PhD; Stefano Barlati, MD; Alison R. Yung, MD; Oliver Howes, BM, BCh, MA, MRCPsych, PhD, DM; Rolf-Dieter Stieglitz, PhD; Antonio Vita, MD, PhD; Philip McGuire, BSc, MB, ChB, MD, PhD, FRCPsych; Stefan Borgwardt, MD, PhD

Arch Gen Psychiatry. 2012;69(6):562-571.

Table. Studies of Subjects at HR for Psychosis Included in the Meta-analysis

<table>
<thead>
<tr>
<th>Source (Year)</th>
<th>HR Subjects</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brewer et al(^{23}) (2005)(^{a})</td>
<td>UHR</td>
<td>98</td>
</tr>
<tr>
<td>Silverstein et al(^{24}) (2006)</td>
<td>UHR</td>
<td>70</td>
</tr>
<tr>
<td>Simon et al(^{25}) (2007)</td>
<td>UHR, BS</td>
<td>69</td>
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<tr>
<td>Pflueger et al(^{26}) (2007)(^{b})</td>
<td>UHR</td>
<td>60</td>
</tr>
<tr>
<td>Broome et al(^{27}) (2007)(^{c})</td>
<td>UHR</td>
<td>35</td>
</tr>
<tr>
<td>Addington et al(^{28}) (2008)</td>
<td>UHR</td>
<td>86</td>
</tr>
<tr>
<td>Chung et al(^{29}) (2008)</td>
<td>UHR</td>
<td>33</td>
</tr>
<tr>
<td>Szily and Kéri(^{30}) (2009)</td>
<td>UHR, BS</td>
<td>26</td>
</tr>
<tr>
<td>Korver et al(^{31}) (2010)</td>
<td>UHR, BS</td>
<td>63</td>
</tr>
<tr>
<td>Seidman et al(^{32}) (2010)</td>
<td>UHR</td>
<td>167</td>
</tr>
<tr>
<td>An et al(^{33}) (2010)</td>
<td>UHR</td>
<td>24</td>
</tr>
<tr>
<td>Ilonen et al(^{34}) (2010)</td>
<td>UHR</td>
<td>22</td>
</tr>
<tr>
<td>Woodberry et al(^{35}) (2010)</td>
<td>UHR</td>
<td>73</td>
</tr>
<tr>
<td>Lindgren et al(^{36}) (2010)</td>
<td>UHR</td>
<td>62</td>
</tr>
<tr>
<td>Magaud et al(^{37}) (2010)</td>
<td>UHR</td>
<td>77</td>
</tr>
<tr>
<td>van Rijn et al(^{38}) (2011)</td>
<td>UHR, BS</td>
<td>36</td>
</tr>
<tr>
<td>Green et al(^{39}) (2011)</td>
<td>UHR</td>
<td>50</td>
</tr>
<tr>
<td>Koutsoulas et al(^{40}) (2011)</td>
<td>UHR</td>
<td>48</td>
</tr>
<tr>
<td>Frommann et al(^{41}) (2011)(^{b})</td>
<td>BS</td>
<td>89</td>
</tr>
</tbody>
</table>

Abbreviations: AT, attention; BS, basic symptoms; EF, executive function; GI, general intelligence; HR, clinical high risk; PS, processing speed; SC, social cognition; UHR, ultra high risk; VF, verbal fluency; VIM, visual memory; VM, verbal memory; WM, working memory.

\(^{a}\)Attention reported in Francey et al\(^{42}\).

\(^{b}\)High-risk subjects who later developed psychosis vs HR subjects who did not develop a psychotic disorder reported in Riecher-Rössler et al\(^{43}\); PS reported in Geschwandtner et al\(^{44}\).

\(^{c}\)Verbal fluency, PS, and VIM reported in Broome et al\(^{45}\) and Fusar-Poli et al\(^{46}\).

\(^{d}\)Visual memory and subjects at HR who later developed psychosis vs HR subjects who did not develop a psychotic disorder reported in Becker et al\(^{47}\).

\(^{e}\)Subjects at HR who later developed psychosis vs HR subjects who did not develop a psychotic disorder reported in Pukrop et al\(^{48}\).
Cognitive Alterations Associated with Vulnerability to Psychosis

The largest deficits were seen in: Visual and Verbal Memory

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<table>
<thead>
<tr>
<th>Cognitive Domains</th>
<th>No. of Studies</th>
<th>No. of HR</th>
<th>No. of C</th>
<th>Hedges' g Mean (95% CI)</th>
<th>z Score</th>
<th>P</th>
<th>Test for Heterogeneity</th>
</tr>
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<tbody>
<tr>
<td>GI</td>
<td>11</td>
<td>690</td>
<td>557</td>
<td>-0.224 -0.346 -0.101</td>
<td>-3.585</td>
<td>&lt;.001</td>
<td>11.660 14.280 .308</td>
</tr>
<tr>
<td>EF</td>
<td>9</td>
<td>620</td>
<td>596</td>
<td>-0.218 -0.397 -0.118</td>
<td>-3.616</td>
<td>.005</td>
<td>10.714 25.329 .218</td>
</tr>
<tr>
<td>VF</td>
<td>11</td>
<td>814</td>
<td>568</td>
<td>-0.308 -0.486 -0.130</td>
<td>-3.389</td>
<td>.001</td>
<td>27.926 64.190 .002</td>
</tr>
<tr>
<td>PS</td>
<td>14</td>
<td>892</td>
<td>754</td>
<td>-0.176 -0.176 0.066</td>
<td>-1.143</td>
<td>.109</td>
<td>27.586 52.970 .010</td>
</tr>
<tr>
<td>AT</td>
<td>8</td>
<td>681</td>
<td>469</td>
<td>-0.225 -0.432 -0.218</td>
<td>-2.955</td>
<td>.045</td>
<td>4.059 0.000 .773</td>
</tr>
<tr>
<td>VIM</td>
<td>5</td>
<td>291</td>
<td>198</td>
<td>-0.396 -0.595 -0.196</td>
<td>-3.889</td>
<td>&lt;.001</td>
<td>2.953 0.000 .566</td>
</tr>
<tr>
<td>VM</td>
<td>8</td>
<td>535</td>
<td>375</td>
<td>-0.392 -0.579 -0.206</td>
<td>-4.127</td>
<td>&lt;.001</td>
<td>15.536 54.940 .030</td>
</tr>
<tr>
<td>WM</td>
<td>11</td>
<td>756</td>
<td>715</td>
<td>-0.360 -0.512 -0.209</td>
<td>-4.661</td>
<td>&lt;.001</td>
<td>19.971 49.930 .030</td>
</tr>
<tr>
<td>SC</td>
<td>6</td>
<td>255</td>
<td>235</td>
<td>-0.547 -0.730 -0.363</td>
<td>-5.481</td>
<td>&lt;.001</td>
<td>1.447 0.000 .919</td>
</tr>
</tbody>
</table>
Cognitive functioning in clinical high-risk subjects who later developed psychosis (HR-T) compared with HR subjects who did not develop a psychotic disorder (HR-NT)

Hedges' g scores (mean and 95% CI) across cognitive domains are given (negative values indicate worse performance in HR subjects who later developed psychosis compared with HR subjects who did not develop a psychotic disorder). The dotted red line (Hedges' g = 0) indicates no significant difference between HR-T and HR-NT. AT indicates attention; EF, executive functioning; GI, general intelligence; PS, processing speed; VF, verbal fluency; ViM, visual memory; VM, verbal memory; WM, working memory.

RBANS results at different stages during the course of psychosis.


http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0125784
Neurocognitive Deficits are related to Functional Outcome

- Community Functioning
- Instrumental & Problem Solving Skills
- Psychosocial Rehabilitation Programs

Scores:
- Large
- Medium
- Small
- Verbal Memory
- Immediate Memory
- Executive Functions
- Vigilance
- Summary Scores

All P’s <.0001

Green et al, 2000
Penn Group Studies
The computerized battery: Illustration of test stimuli

Gur et al., Neuropsychology, 2012
Neurocognitive Profile of Psychosis Spectrum (PS, n=1171) Compared to No Psychosis (NP, n=3684) Age 11-21

Calkins et al., WJP 2015
Cognitive deficits in Psychosis

- Speed
- Memory
- Attention
- Reasoning
- Tact/Social cognition
- Synthesis

Cognitive deficits in psychosis are
- Pervasive
- Persistent
- Present early
- Progress early
- Predict functional disability
Person-Centered Approach
Variability in performance can be helpful or hurtful

Think about the first time you rode a bike. At first you wobble, but over time you learn to control the bike. The wobbling in the beginning helped you (and your brain) figure out the best way to ride a bike!
Variability in performance can be helpful or hurtful

Now that you know how to ride a bike you don’t wobble much. But a bumpy road, a flat tire or talking on your cell phone while riding your bike will cause you to wobble more. Too much wobbling from these problems or distractions may cause you to fall!

A similar thing can happen in the brain.
Some people show more inconsistency ("wobble") in their performance on tests of ability.

<table>
<thead>
<tr>
<th>Subject</th>
<th>High IIV</th>
<th>Low IIV</th>
<th>sPCPTnl: High vs Low IIV subject</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

Push the button when see the letter X

How quickly was the button pushed?

<table>
<thead>
<tr>
<th>Time (ms)</th>
<th>Fast</th>
<th>Slow</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>300</td>
<td></td>
<td></td>
</tr>
<tr>
<td>600</td>
<td></td>
<td></td>
</tr>
<tr>
<td>900</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

![Graph showing response times for typical and atypical wobble](image-url)
Inconsistency ("wobble") can get better, stay the same, or get worse over time.

Neuroscientists are working on the best ways to study this brain ‘wobble’. They hope to figure out when it is a good thing and when it is a bad thing.
What are Possible Treatments for Cognitive Dysfunction?
Pharmacological Treatments for Cognition

Enter: cognitive remediation
Key Cognitive Remediation Points

• Brain is remarkably plastic

• Altered neuroplasticity and psychosis

• Plasticity based interventions may remedy cognitive deficits
The power of plasticity

Physical Practice

Mental Practice

Pascual-Leone et al. JNP 1994
London Taxi drivers (A) have larger hippocampi than matched control subjects (B)

McGuire 2009
Cognitive remediation works!

The meta-analysis (2,104 participants) yielded durable effects on global cognition and functioning.
PERC Cognitive Remediation

- 8–Week Program
- Cognitive training, education, support

✓ **Cognitive Remediation**
  - Weekly 2-hour group that meets in Neuropsychiatry Program at HUP
  - Focus on cognitive impairments commonly seen in psychiatric illness such as attention, memory, problem-solving, etc.
  - Computer exercises (BrainHQ), both in group (weekly) with coaching by clinicians and at-home (daily) by the participant
  - In addition, participants learn behavioral compensatory strategies that mesh with computer training

✓ **Group Exercises**
  - Training in utilizing compensatory and organization strategies in real-life
  - Practice in perspective-taking, non-verbal communication, emotional temperature perception, etc.
  - Socialization, cognitive trouble-shooting and dealing with barriers to training/practice

Computer exercises done in group & at-home

Group sessions with exercises and homework
Other approaches: Cognitive adaptation is of value as well (Velligan et al 2006)

**Figure 1**
Use of environmental supports in cognitive adaptation training and generic environmental supports

<table>
<thead>
<tr>
<th></th>
<th>Cognitive adaptation training</th>
<th>Generic environmental supports</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td><img src="image" alt="Bar graph for Overall" /></td>
<td><img src="image" alt="Bar graph for Generic environmental supports" /></td>
</tr>
<tr>
<td>Medication management</td>
<td><img src="image" alt="Bar graph for Medication management" /></td>
<td><img src="image" alt="Bar graph for Generic environmental supports" /></td>
</tr>
<tr>
<td>Orientation</td>
<td><img src="image" alt="Bar graph for Orientation" /></td>
<td><img src="image" alt="Bar graph for Generic environmental supports" /></td>
</tr>
<tr>
<td>Grooming and hygiene</td>
<td><img src="image" alt="Bar graph for Grooming and hygiene" /></td>
<td><img src="image" alt="Bar graph for Generic environmental supports" /></td>
</tr>
</tbody>
</table>
Take home points

• Cognitive deficits (Speed, Memory, Attention, Reasoning, Tact, Synthesis) are related to altered brain plasticity

• Cognitive deficits and the brain changes may be reversible with neuroplasticity based cognitive remediation, have durable real-world benefits

• Cognitive remediation works best when it is Repetitive, Adaptive, Individualized, Strategic and includes a Motivational component.

• Deficits in brain plasticity may set in early. Early intervention may have large positive implications for outcome