Cognitive Dysfunction in Psychosis: Identification and Intervention

Paul J. Moberg, Ph.D. Penn Psychosis Evaluation and Recovery Center (PERC)

Paul

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...



ABF: Abstraction & Mental Flexibility



HARD





CATEGORIZATION TASK

SPATIAL: Line Orientation

EASY



HARD



Cognitive Impairment Magnitude in Schizophrenia

Meta-Analysis; 204 studies, 7420 patients and 5865 controls



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

Healthy Comparison Mean

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.

		HR Subjects			Controls			
Source (Year)	HR Group	No.	% Female	Age, y, Mean (SD)	No.	% Female	Age, y, Mean (SD)	Cognitive Domain
Brewer et al ³⁸ (2005) ^a	UHR	98	48	19.7 (3.9)	37	24	20.7 (4.3)	GI, EF, PS, VIM, VM, VF, WM, A
Silverstein et al ³⁹ (2006)	UHR	70	34	17.4 (3.6)	24	25	20.7 (4.4)	PS
Simon et al 40 (2007)	UHR, BS	69	42	20.5 (5.2)	49	20	21.8 (4.9)	AT, EF, PS, VF, VM, WM
Pflueger et al ⁴¹ (2007) ^b	UHR	60	43	27.2 (8.7)	51	45	23.4 (4.9)	EF, WM, AT, PS
Broome et al ⁴² (2007) ^c	UHR	35	47	24.2 (4.3)	23	40	24.9 (3.0)	GI,WM, VF, VIM, PS
Addington et al ⁴³ (2008)	UHR	86	43	19.2 (2.6)	55	40	21.2 (6.1)	SC
Chung et al44 (2008)	UHR	33	42	20.9 (3.2)	36	44	22.0 (2.5)	GI, EF, VF, WM, VIM, VM, PS, S
Szily and Kéri ⁴⁵ (2009)	UHR, BS	26	58	22.0 (8.7)	50	62	21.1 (6.3)	GI, SC
Korver et al ⁴⁶ (2010) ^d	UHR, BS	63	34	19.6 (3.3)	30	50	19.8 (3.4)	GI, VM, VF, AT, PS, ViM
Seidman et al ⁴⁷ (2010)	UHR	167	36	18.2 (4.9)	109	56	18.8 (4.5)	GI, EF, PS, WM, AT, VF
An et al ⁴⁸ (2010)	UHR	24	42	20.0 (3.9)	39	59	19.7 (3.5)	SC
Ionen et al ⁴⁹ (2010)	UHR	22	91	15.7 (1.8)	187	63	15.5 (1.7)	GI, EF, PS, WM
Noodberry et al ⁵⁰ (2010)	UHR	73	51	16.5 (2.7)	34	47	16.2 (2.5)	GI, AT, VM, WM, VF, EF, PS
_indgren et al ⁵¹ (2010)	UHR	62	79	16.6 (0.9)	72	78	16.4 (1.5)	VF, PS, VM, ViM, WM, AT, EF
Magaud et al ⁵² (2010)	UHR	77	23	21.0 (3.4)	61	24	19.6 (3.3)	VF
ran Rijn et al ⁵³ (2011)	UHR, BS	36	31	15.2 (2.1)	21	43	15.9 (1.4)	GI, SC, EF, PS
Green et al ⁵ (2011)	UHR	50	28	18.3 (3.1)	34	44	19.0 (2.8)	SC
Koutsouleris et al ⁵⁴ (2011)	UHR	48	33	24.7 (5.8)	30	40	26.0 (2.7)	GI, PS, WM, VM, VF
Frommann et al ⁵⁵ (2011) ^e	BS	89	40	25.3 (6.4)	87	44	25.5 (4.4)	GI, VM, WM, PS, VF, AT

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

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.

^aAttention reported in Francey et al.⁵⁶

^b High-risk subjects who later developed psychosis vs HR subjects who did not develop a psychotic disorder reported in Riecher-Rössler et al.⁵⁷; PS reported in Gschwandtner et al.⁵⁸

^cVerbal fluency, PS, and ViM reported in Broome et al⁵⁹ and Fusar-Poli et al.⁶⁰

^dVisual memory and subjects at HR who later developed psychosis vs HR subjects who did not develop a psychotic disorder reported in Becker et al.⁶¹ ^eSubjects at HR who later developed psychosis vs HR subjects who did not develop a psychotic disorder reported in Pukrop et al.⁶²

Cognitive Alterations Associated with Vulnerability to Psychosis



The largest deficits were seen in: Visual and Verbal Memory

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)



Verbal Fluency

Verbal Memory

Visual Memory

Working Memory

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.



Zhang T, Li H, Stone WS, Woodberry KA, Seidman LJ, et al. (2015) Neuropsychological Impairment in Prodromal, First-Episode, and Chronic Psychosis: Assessing RBANS Performance. PLoS ONE 10(5): e0125784. doi:10.1371/journal.pone.0125784 http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0125784

Neurocognitive Deficits are related to Functional Outcome



Green et al, 2000

Penn Group Studies



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 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 you 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



Push the button when see the letter X

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



FIGURE 1. Forest Plot of Global Cognition Among Studies in Cognitive Remediation Therapy"

Löpes Luengo and Vit quet 2005 0.45 (=0.36 to 1.3) Othrich and Muttypy 1990 0.21 (=0.51 to 0.3) Beredick etal. 1994 0.55 (=0.14 to 1.3) uen der Gaag et al. 2002 0.12 (=0.51 to 0.3) Hedalis etal. 1992 0.01 (=0.97 to 0.3) Medalis etal. 1992 0.01 (=0.97 to 0.3) Medalis etal. 1992 0.25 (=0.05 to 2.3) Medalis etal. 1997 0.25 (=0.07 to 0.3) Medalis etal. 2001 0.55 (=0.07 to 0.3) Medalis etal. 2002 0.03 (=0.05 to 0.3) Cavallaro etal. 2003 0.31 (=0.05 to 0.3) Deredick and Harrio 1929 0.32 (=0.05 to 0.3) Barda etal. 2001 0.32 (=0.05 to 0.3) Medalis etal. 2001 0.32 (=0.05 to 0.3) Barda etal. 2001 0.32 (=0.05 to 0.3) Medaloridor, etal. 2001 0.32 (=0.05 to 0.3) </th <th>1.9 2.3 3.5 1.7</th>	1.9 2.3 3.5 1.7
Benedick etal. 1994 0.55 (+0.14 to 1.3) uen der Gaag et al. 2002 0.12 (+0.49 to 0.3) Bedalis etal. 2009 0.29 (+0.25 to 0.3) Medalis etal. 1992 0.29 (+0.25 to 0.3) Field etal. 1997 0.25 (+0.14 to 1.3) Medalis etal. 2001 0.29 (+0.25 to 0.3) Medalis etal. 2001 0.55 (+0.14 to 1.3) Medalis etal. 2001 0.29 (+0.25 to 0.3) Medalis etal. 2001 0.55 (+0.05 to 0.3) Medalis etal. 2000 -0.05 (+0.05 to 0.3) Utland and found 2004 -0.05 (+0.05 to 0.3) Teamley etal. 2009 0.31 (+0.35 to 0.3) Benedick and Harris 1989 0.32 (+0.35 to 0.3) Benedick and Harris 1989 0.57 (+0.25 to 0.3) Benedick and 1994	2.3 2.6 1.4 3.0 0.9 2.4 2.5 1.9 2.3 3.5 1.7
um der Gaag et al. 2002 0.12(-049 to 0.2) Lecardeur et al. 2009 0.02(-027 to 0.2) Medalia et al. 1992 0.22(-025 to 0.2) Field et al. 1997 0.25(-007 to 0.2) Medalia et al. 2000 0.55(-007 to 0.2) Medalia et al. 2000 0.34(-025 to 0.2) Medalia et al. 2000 0.34(-025 to 0.2) Challaro et al. 2000 0.34(-025 to 0.2) Densedid and Harrio 1929 0.35(-007 to 0.2) Benedid and Harrio 1929 0.25(-007 to 0.2) Medalia et al. 2000 0.25(-007 to 0.2) Bardia et al. 2000 0.25(-007 to 0.2) Benedid and Harrio 1929 0.25(-007 to 0.2) Benedid and Harrio 1929 0.29(-003 to 0.2) Bardia et al. 2000 0.29(-003 to 0.2) Bardia et al. 2001 0.29(-003 to 0.2) Hadae-tidar, et al. 2001 0.29(-003 to 0.2) Heidhenbaum and Converso 0.20(-003 to 0.2)	2.6 1.4 3.0 0.9 2.4 2.5 1.9 2.3 3.5 1.7
Lesardeur etal 2009 Heddia etal 2009 Heddia etal 1992 Sield etal 1997 Heddia etal 2001 Heddia etal 2001 Heddia etal 2001 Urland and Bun d2004 Urland and Bun d2004 Challero etal 2009 Beredict and Harris 1989 Beredict and Harris 1989 Beredict and Harris 1989 Hedder etal 2010 Beredict and Harris 1989 Hedder etal 2010 Beredict and Harris 1989 Hedder etal 2001 Hedder etal 2009 Beredict and Harris 1989 Hedder etal 2010 Beredict and Harris 1989 Hedder etal 2001 Hedder etal 2005 Heiden barm and Converso	14 3.0 0.9 24 25 1.9 23 3.5 1.7
Heddia etal. 1992 0.29 (-0.25 to 0.25) Field etal. 1997 0.25 (-0.05 to 2.15) Heddia etal. 2001 0.55 (-0.07 to 1.25) Heddia etal. 2000 -0.05 (-0.07 to 1.25) Using and ton d/2004 -0.05 (-0.07 to 1.25) Teamley etal. 2009 0.29 (-0.25 to 0.25) Challar etal. 2009 0.29 (-0.25 to 0.25) Benedict and Harris 1929 0.29 (-0.25 to 0.25)	3.0 0.9 2.4 2.5 1.9 2.3 3.5 1.7
Field etal. 1997 0.25 (-045 to 27) Heddia etal. 2001 0.55 (-045 to 27) Heddia etal. 2000 -005 (-045 to 27) Usind and tan d/2004 -005 (-045 to 27) Treamley etal. 2009 -0.25 (-025 to 0.25) Crailaro etal. 2009 0.25 (-025 to 0.25) Benedict and Harris 1929 0.25 (-025 to 0.25) Benedict and Harris 1929 0.25 (-025 to 0.25) Barda etal. 2010 0.25 (-025 to 0.25) Barda etal. 2010 0.25 (-025 to 0.25) Barda etal. 2010 0.25 (-025 to 0.25) Barda etal. 2001 0.27 (-025 to 0.25) Hedden etal. 2005 0.25 (-025 to 0.25) Barda etal. 2001 0.27 (-025 to 0.25) Hedden tider, etal. 2001 0.27 (-025 to 0.25) Heiden barm and Conteron -025 (-025 to 0.25)	0.9 24 25 1.9 23 3.5 1.7
Heddin etal, 2001 0.552/007b01.29 Heddin etal, 2000 -0052/007b01.29 Utland and Run d/2004 -0052/007b01.09 Treamley etal, 2002 0.31/(-0.25b01.09) Challaro etal, 2009 0.32/(-0.25b01.09) Benedict and Harris 1929 0.22/(-0.25b0.0.09) Benedict and Harris 1929 0.22/(-0.25b0.0.29) Bunda etal, 2010 0.22/(-0.25b0.0.29) Bunda etal, 2001 0.22/(-0.25b0.0.29) Heddewite etal, 2010 0.22/(-0.25b0.0.29) Bunda etal, 2001 0.22/(-0.25b0.0.29) Heddewite etal, 2001 0.22/(-0.25b0.0.29) Heddewite etal, 2001 0.22/(-0.25b0.0.29) Heidewite etal, 2005 0.22/(-0.25b0.0.29) Heidewite etal, 2005 0.22/(-0.25b0.0.29)	24 25 1.9 23 3.5 1.7
Heddia etal. 2000 -005 (-0.62 to 0.67) Uland and Run d 2004 -0.12 (-0.07 to 0.67) Teamley etal. 2002 0.34 (-0.35 to 1.02) Challero etal. 2009 0.25 (-0.20 to 0.67) Beredi d: and Harris 1929 0.25 (-0.25 to 0.87) Hedge etal. 2010 0.29 (-0.35 to 1.02) Barda etal. 1934 0.57 (0.05 to 1.02) Hedge etal. 2010 0.57 (0.05 to 1.02) Barda etal. 1934 0.57 (0.05 to 1.02) Hedge-tider, etal. 2001 1.27 (1.32 to 2.02) Hedge-tider, etal. 2005 1.27 (1.32 to 2.02) Heidenbarm and Omeron 0.20 (-0.03 to 0.32)	2.5 1.9 2.3 3.5 1.7
Utand and four d 2004 -0.12 (-0.37 to 0.77 Teambey et al. 2002 0.34 (-0.35 to 1.05) Chalbro et al. 2009 0.25 (-0.20 to 0.05) Benedict and Harris 1929 1.57 (0.77 to 243) Hodge et al. 2010 0.29 (-0.35 to 0.28) Burds et al. 2010 0.29 (-0.35 to 0.28) Hodge et al. 2010 0.57 (0.02 to 1.05) Hodge et al. 2001 1.57 (1.72 to 243) Hodge et al. 2005 1.57 (0.72 to 2.05) Heidenbaum and Omeron 0.29 (-0.25 to 0.28)	1.9 2.3 3.5 1.7
Teamby etal. 2002 0.34 (-0.35 to 1.0) Cnalbro etal. 2009 0.25 (-0.20 to 0.0) Benedict and Harris 1929 1.57 (0.71 to 243) Hodge etal. 2010 0.29 (-0.35 to 0.28) Barda etal. 1924 0.57 (0.02 to 1.08) Hadzo-tider, etal. 2001 1.27 (1.52 to 243) Hadzo-tider, etal. 2005 1.27 (1.52 to 243) Heidenbaum and Omeron 0.25 (-0.28 to 0.35)	2.3 3.5 1.7
Canalbaro et al. 2009 0.225 (-0.2016) 0.459 Benedict and Harris 1929 1577 (0.71 lo 243) Hodge et al. 2010 0.29 (-0.3516) 0.459 Burda et al. 1994 0.577 (0.02 lo 1.059 Hadro-Lidor, et al. 2005 1277 (1.52 lo 243) Heiden-Lidor, et al. 2005 1277 (1.52 lo 243) Heiden-Lidor, et al. 2005	3.5 1.7
Beredik and Harris 1929 157 (0.71 lb 203) Hodge et al. 2010 0.29 (-0.35 lb 0.28) Burda et al. 1934 0.57 (0.02 lb 1.08) Hodge et al. 2001 127 (1.32 lb 203) Hodge-tide, et al. 2001 127 (1.32 lb 203) Heiden-tide, et al. 2005 -0.12 (-0.35 lb 0.35) Heiden-baum and Omeron -0.27 (0.02 lb 0.35)	1.7
Hodge et al. 2010 0.29 (-0.35 to 0.28) Barda et al. 1984 0.57 (0.02 to 1.08) Hodge-tide, et al. 2001 1.27 (1.52 to 243) Sherthein et al. 2005 -0.12 (-0.35 to 0.35) Heidenbaum and Omeron 0.29 (-0.35 to 0.35)	
Burda etal. 1994 057 (002 ls 1.09) Hadao-Lidor, etal. 2001 127 (1.52 ls 242) Shertsein et al. 2005	
Hadao-Lidor, etal. 2001 127(1.52 to 243) Shurthin et al. 2005 -0.12(0.02 to 0.55) Heidenbaum and Omeron 0.0000	2.5
dherstein et al. 2005	3.2
Heidenbaum and Omeron	2.9
	2.2
	0.2
Eads +6 al 2009 0.000 (0.07 to 1.13)	3.0
Linden mayer et al. 2002	3.4
Hoganiy etail 2004	4.0
Heidenbaum and Omeron	0.9
Bell & al 2007-2007	3.9
Grég et al. 2007	3.1
Wykwo+t al 2007	2.3
Vaudh +8al. 2005 0.00 (0.32 is 142)	3.0
Belluci et al 2002	2.3
Hemanutz and Getri (h 1991	1.7
Sarbory +8al 2005 0.52(-0.04 to 1.20)	2.6
Nuntz et al. 2007 0.356-0.2580.0.87	2.6
McGark+8al.2005 0.44 (-0.15to 1.49)	2.7
Perader etal. 2005 1.02(0.29to 1.75)	2.2
Wyther+t all 1999 0.20(-0.50)to 0.30	2.3
Fisher etal. 2009 039 (044 to 1.54)	2.9
40/www.et.al. 2005	2.3
pauláng é al 1999 – – – – – – – – – – 0.22(-0.2010.07)	3.6
Dickingon et al. 2010	3.2
wykowski ali 2007	_
Ownall 📥 🚸 045(037 to 039)	3.5

Cognitive remediation works!



Til Wykes et al

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

* Dudies are listed by their Clinical Trial Assessment Measures as res (Table 1) in accending order.

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, problemsolving, 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)



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