

Cognitive Dysfunction in Psychosis: Identification and Intervention

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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...

Blue

Did you have a

Yellow

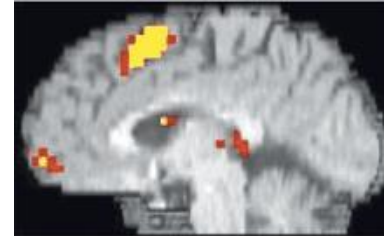
STROOPs! Effect?

Red

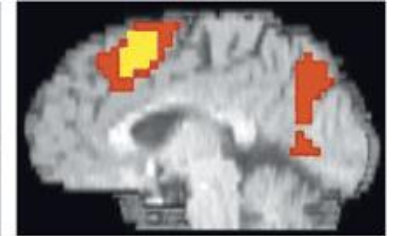
Green

Blue

Green



Conflict



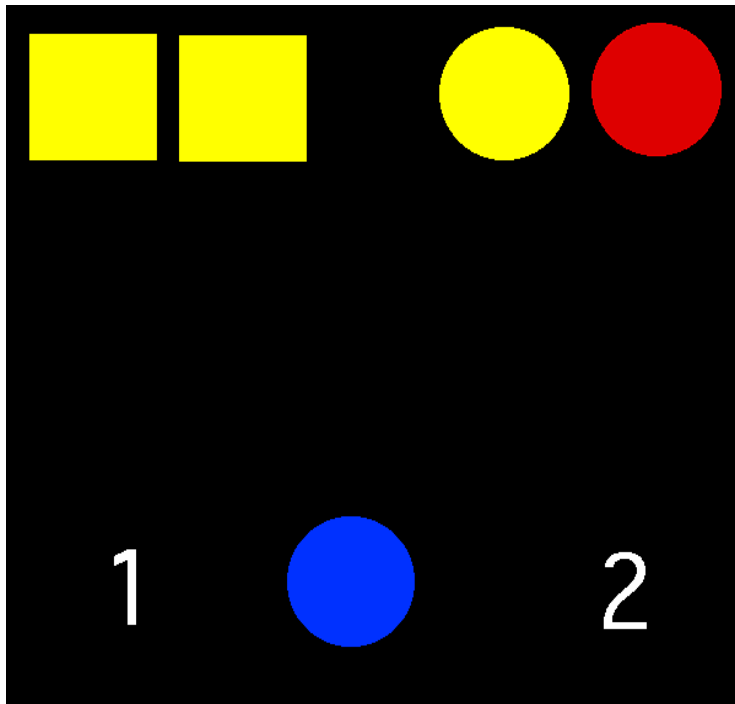
Error

Healthy persons activate
Anterior cingulate when they
Detect errors

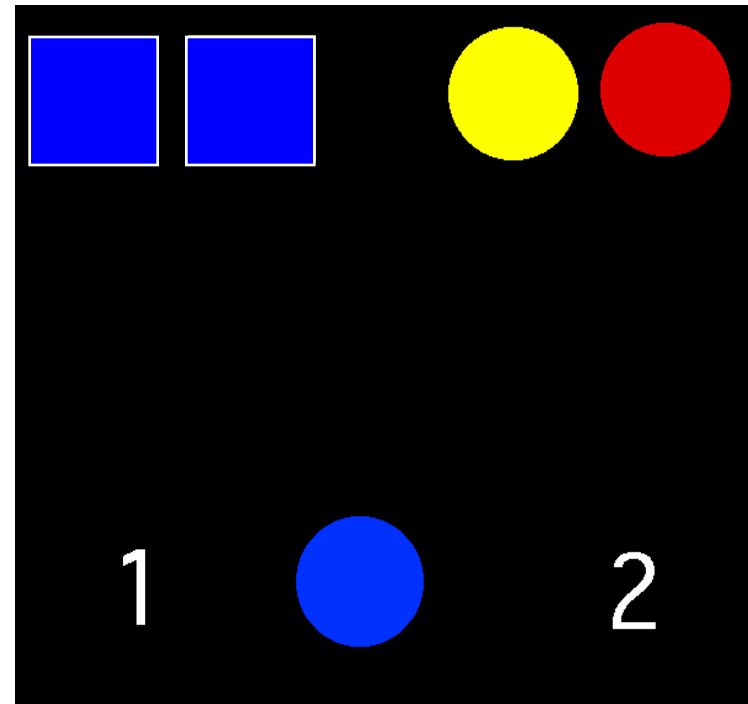
Selective ATTENTION

ABF: Abstraction & Mental Flexibility

EASY



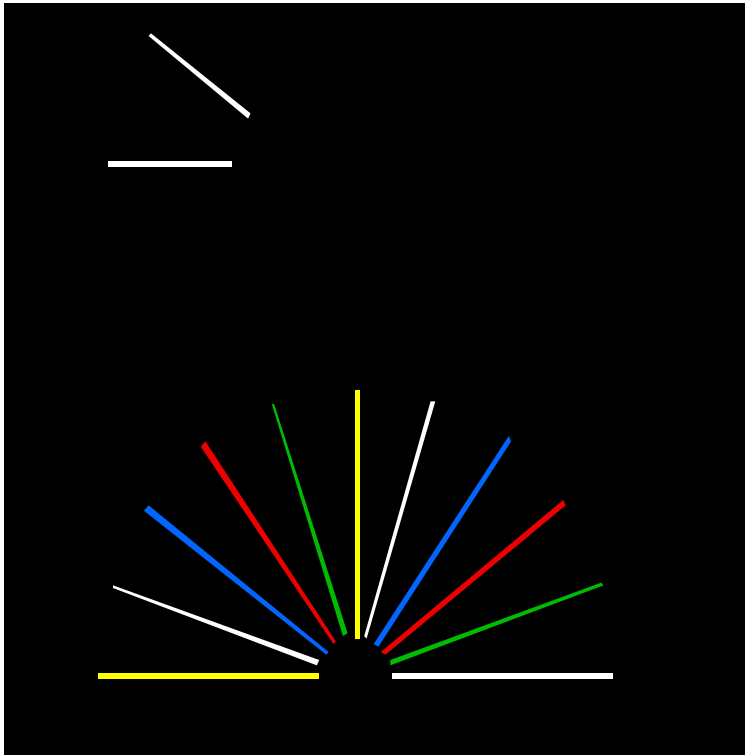
HARD



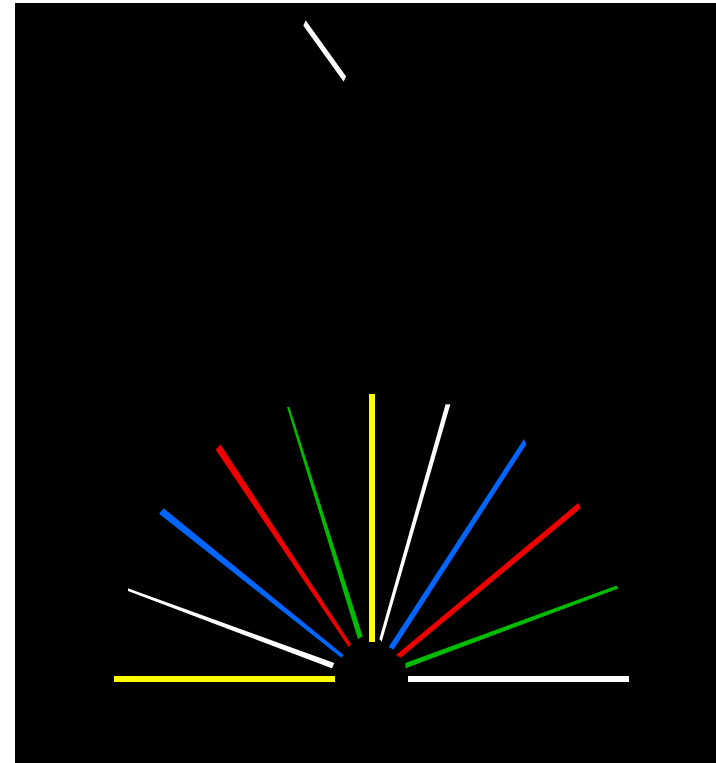
CATEGORIZATION TASK

SPATIAL: Line Orientation

EASY

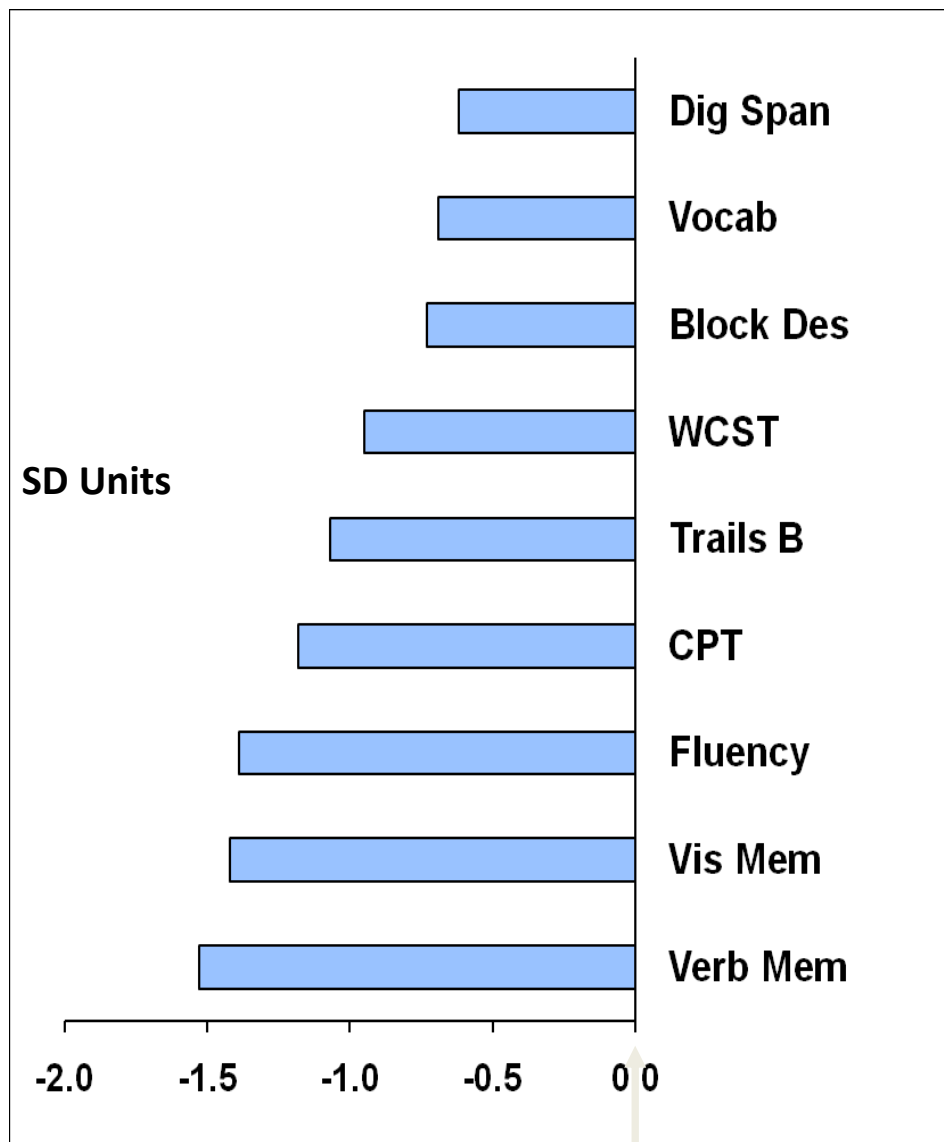


HARD



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

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

Source (Year)	HR Group	HR Subjects			Controls			Cognitive Domain
		No.	% Female	Age, y, Mean (SD)	No.	% Female	Age, y, Mean (SD)	
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, AT
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 al ⁴⁴ (2008)	UHR	33	42	20.9 (3.2)	36	44	22.0 (2.5)	GI, EF, VF, WM, ViM, VM, PS, SC
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
Ilonen et al ⁴⁹ (2010)	UHR	22	91	15.7 (1.8)	187	63	15.5 (1.7)	GI, EF, PS, WM
Woodberry et al ⁵⁰ (2010)	UHR	73	51	16.5 (2.7)	34	47	16.2 (2.5)	GI, AT, VM, WM, VF, EF, PS
Lindgren 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
van 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

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

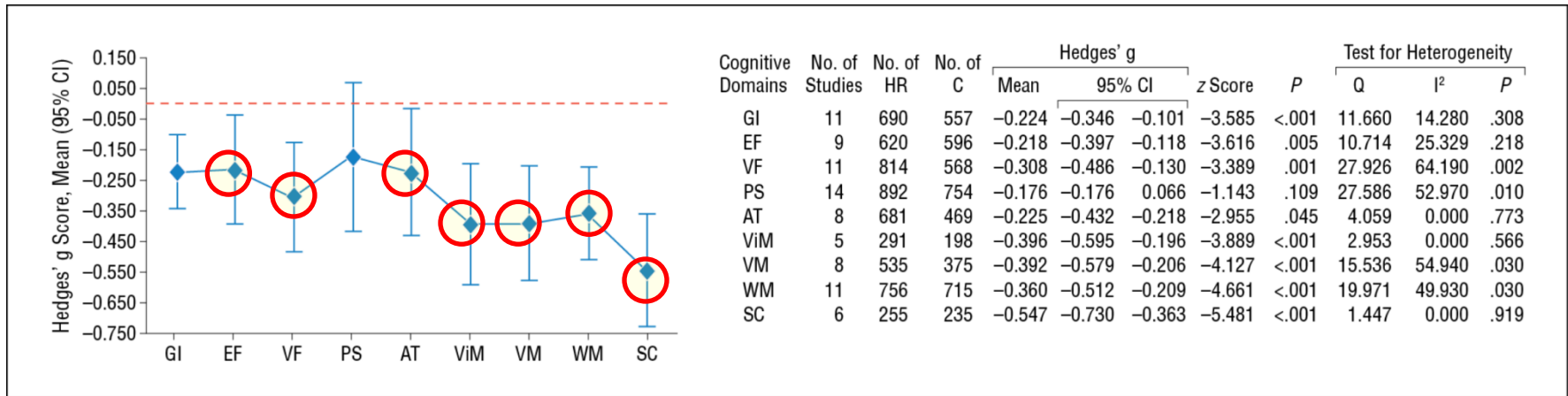
^bHigh-risk subjects who later developed psychosis vs HR subjects who did not develop a psychotic disorder reported in Riecher-Rössler et al⁵⁷; PS reported in Gschwandtner et al.⁵⁸

^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

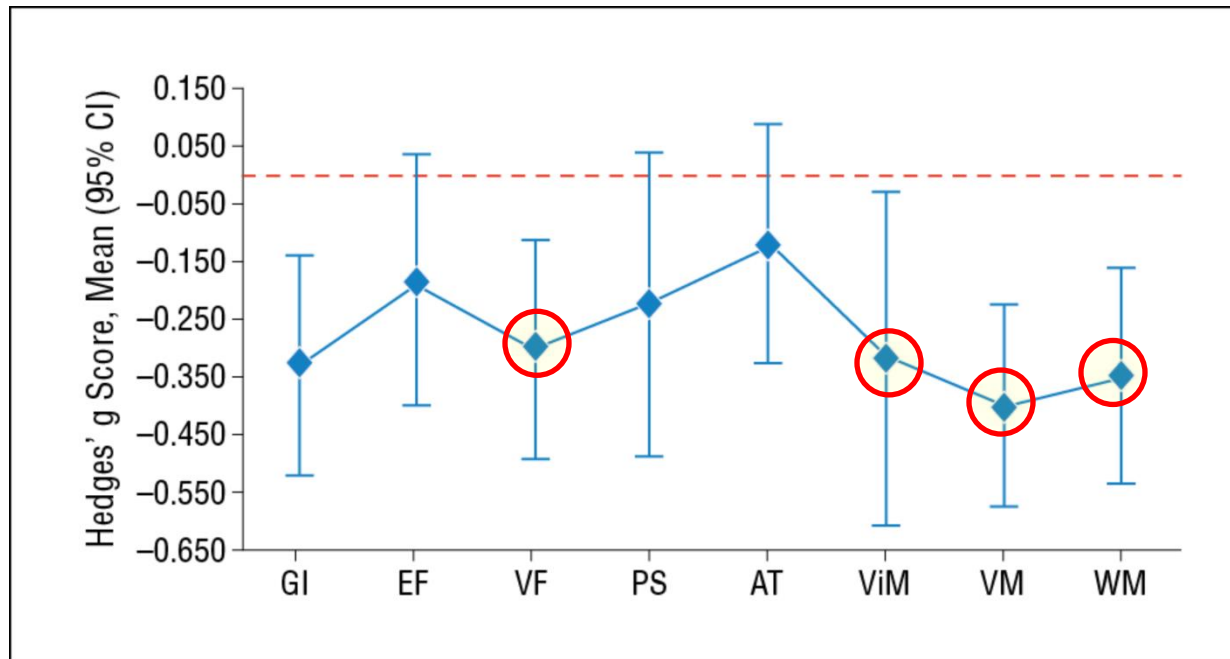
^eSubjects at HR who later developed psychosis vs HR subjects who did not develop a psychotic disorder reported in Pukrop et al.⁶²

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

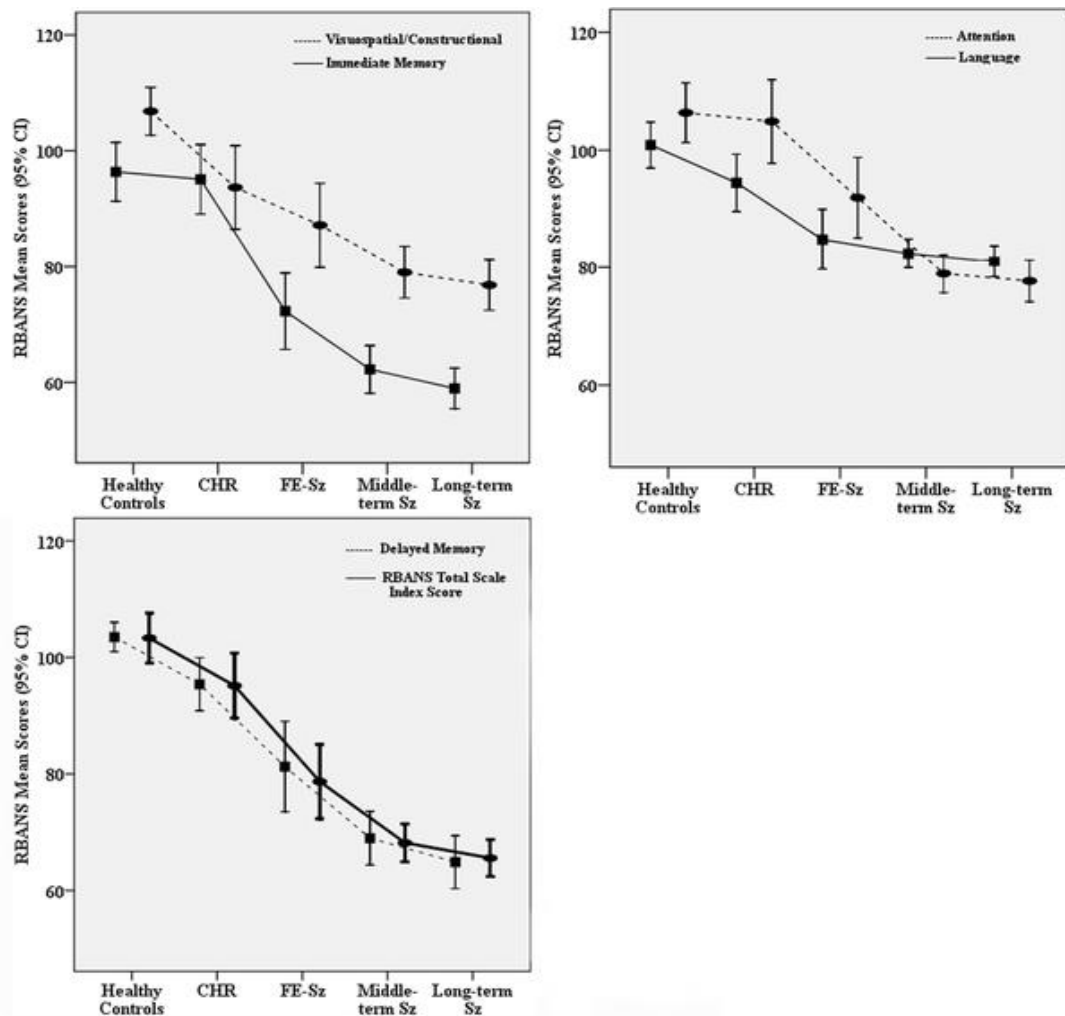
Verbal Memory

Visual Memory

Working Memory

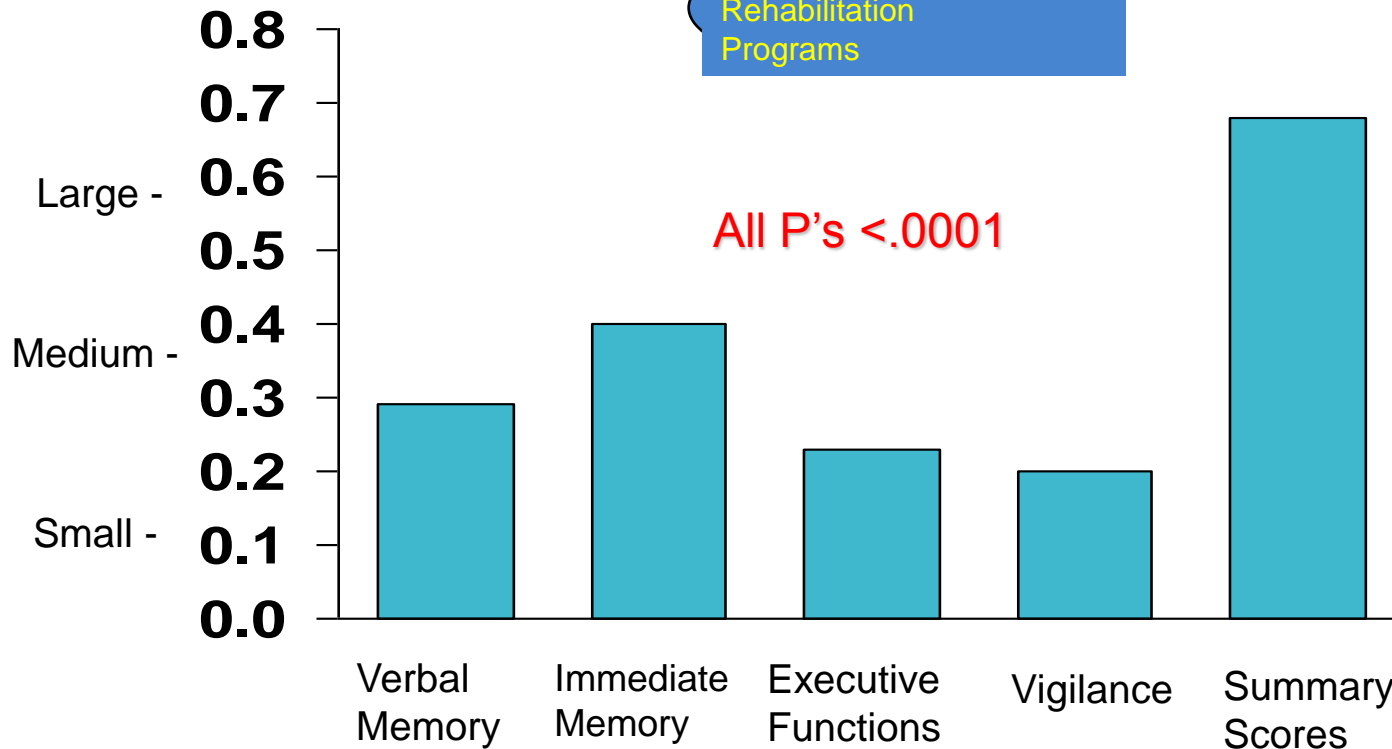
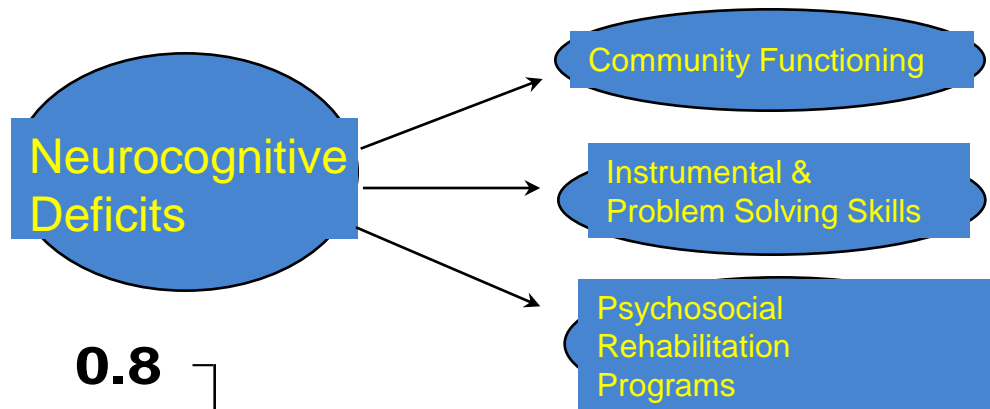
Hedges' g scores (mean and 95% CI) across cognitive domains are given (negative values indicate worse performance in HR subjects who later developed psychosis compared with HR subjects who did not develop a psychotic disorder). The dotted red line (Hedges' g = 0) indicates no significant difference between 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



Penn Group Studies

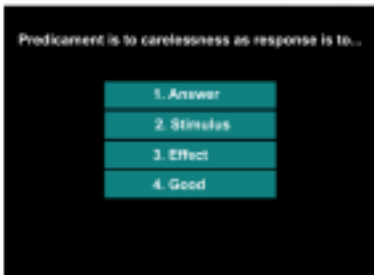
ABSTRACTION & MENTAL FLEXIBILITY (PCET)



WORD MEMORY



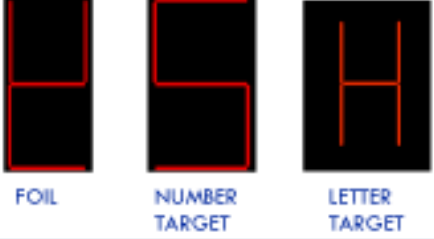
LANGUAGE REASONING (PVRT)



SENSORIMOTOR (MP)



ATTENTION (CPT)



FACE MEMORY



SPATIAL ABILITY (PLOT)



MOTOR SPEED (TAP)



WORKING MEMORY



SPATIAL MEMORY



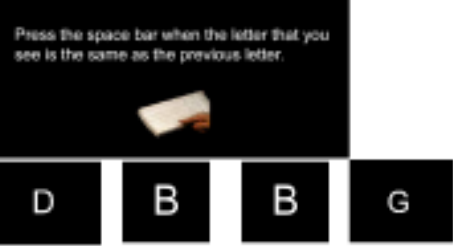
EMOTION (ER40)



EMOTION DISCRIMINATION (MEDF)



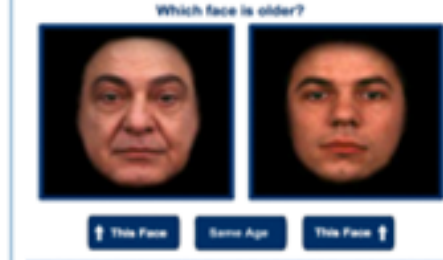
1-BACK



2-BACK

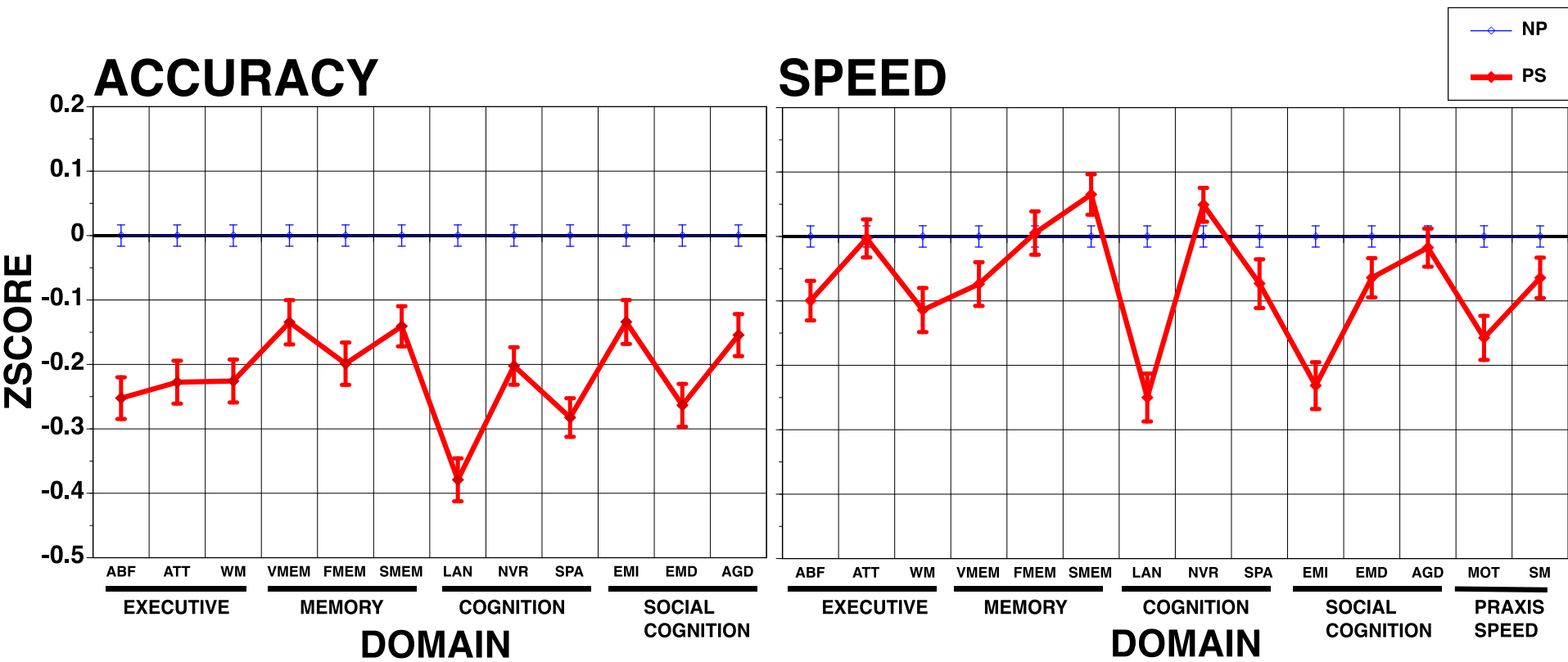


AGE DIFFERENTIATION (ADT)



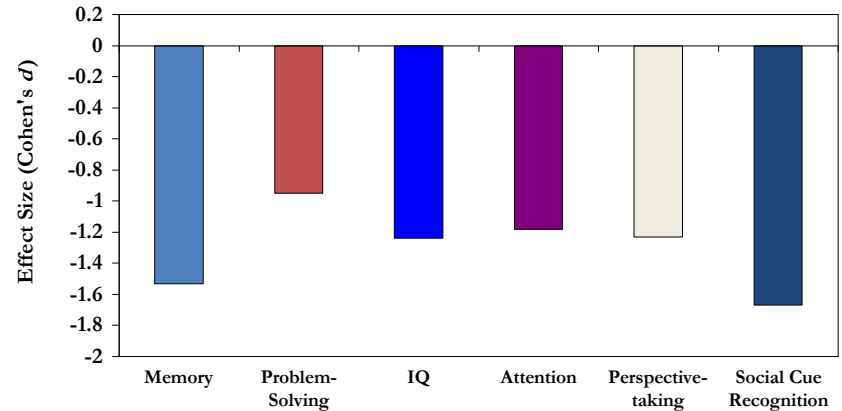
The computerized battery: Illustration of test stimuli

Neurocognitive Profile of Psychosis Spectrum (PS, n=1171) Compared to No Psychosis (NP, n=3684) Age 11-21



Cognitive deficits in Psychosis

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



Cognitive deficits in psychosis are

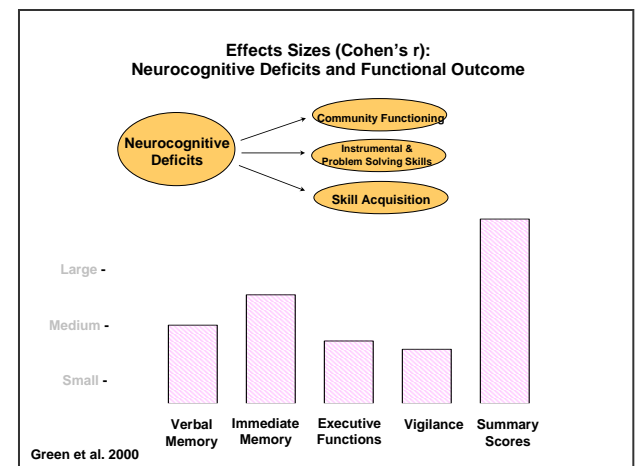
Pervasive

Persistent

Present early

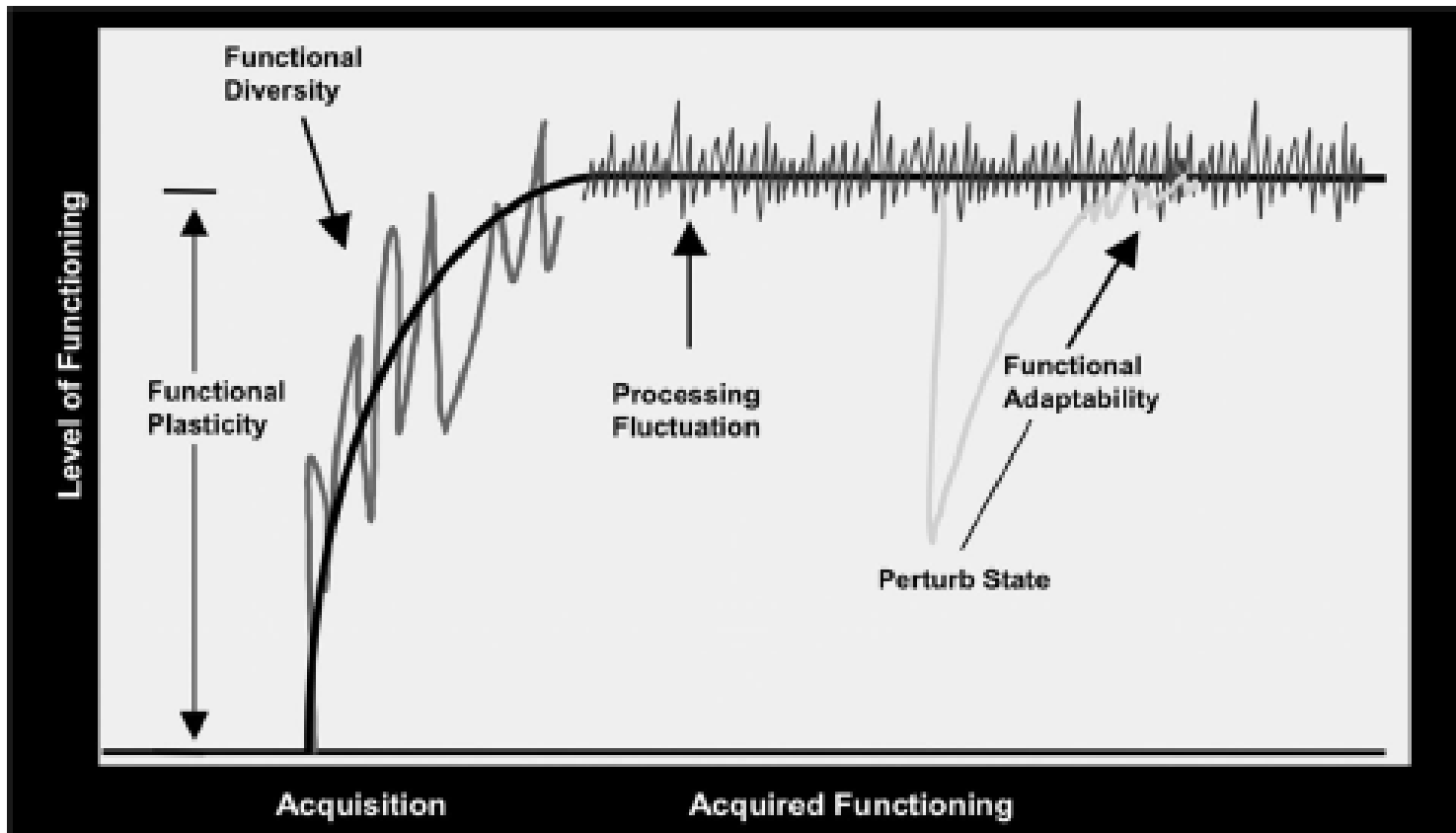
Progress early

Predict functional disability



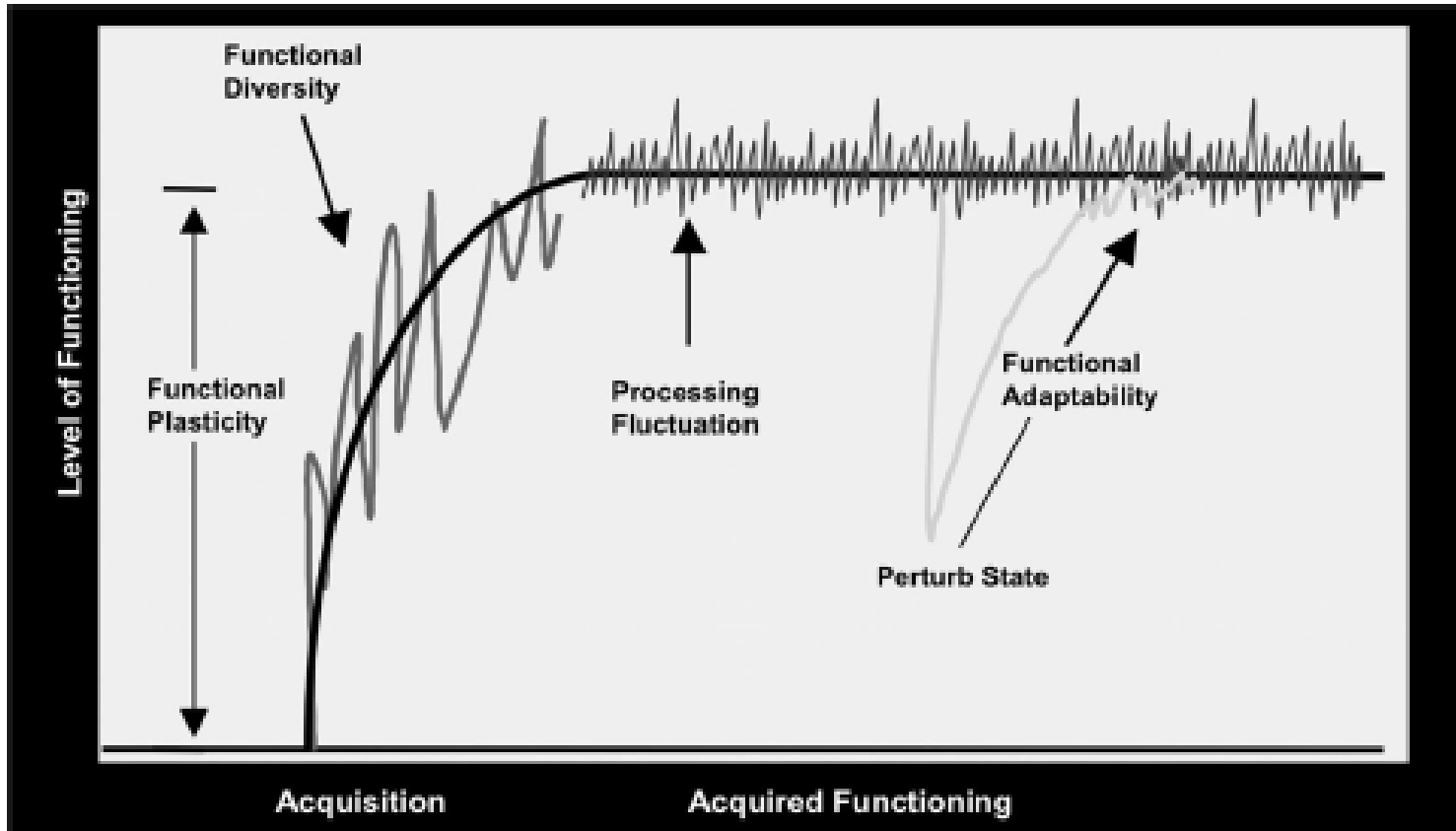
Person-Centered Approach

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



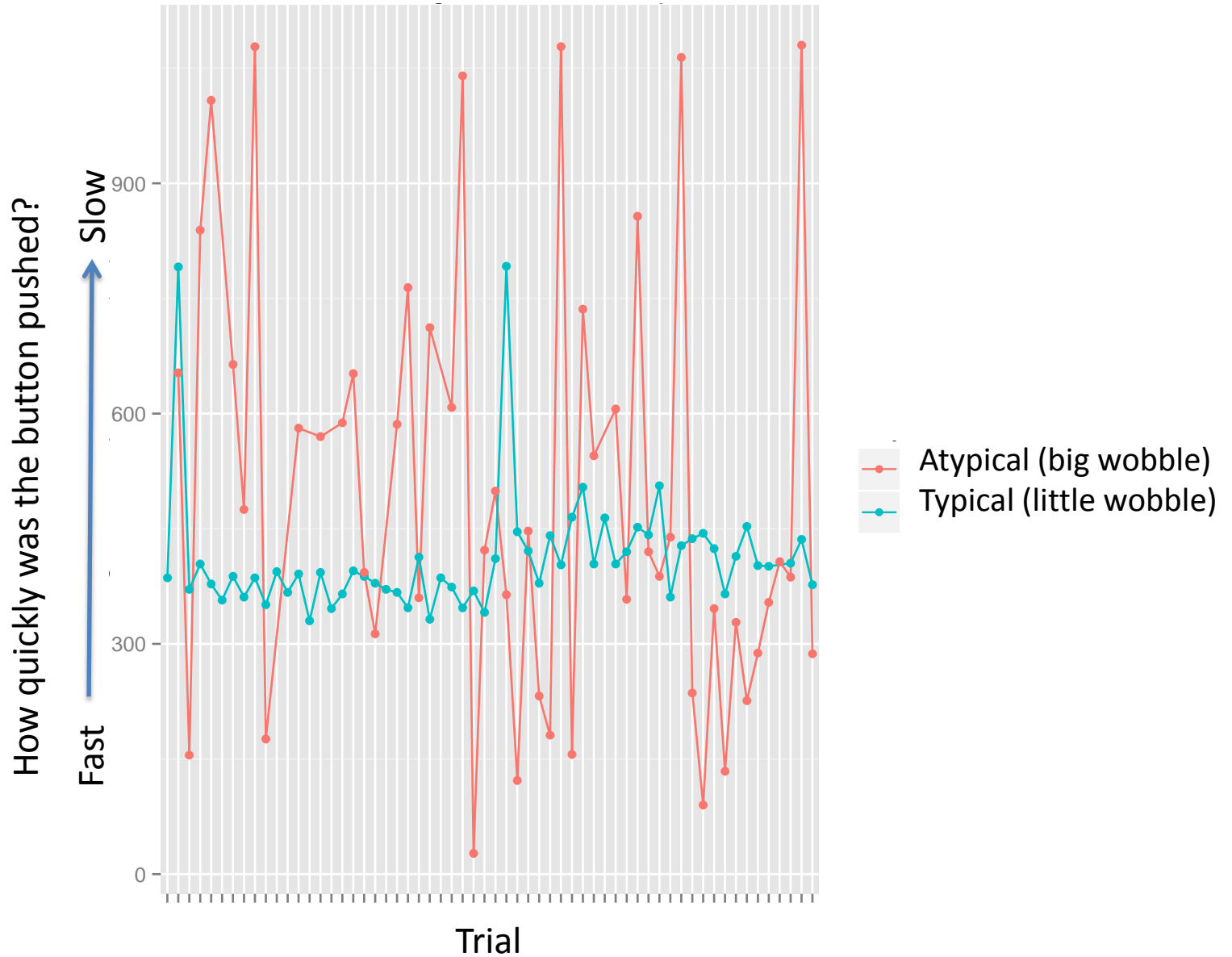
Now that you know how to ride a bike you don't wobble much. But a bumpy road, a flat tire or talking on your cell phone while riding your bike will cause you to wobble more. Too much wobbling from these problems or distractions may cause you to fall!

A similar thing can happen in the brain.

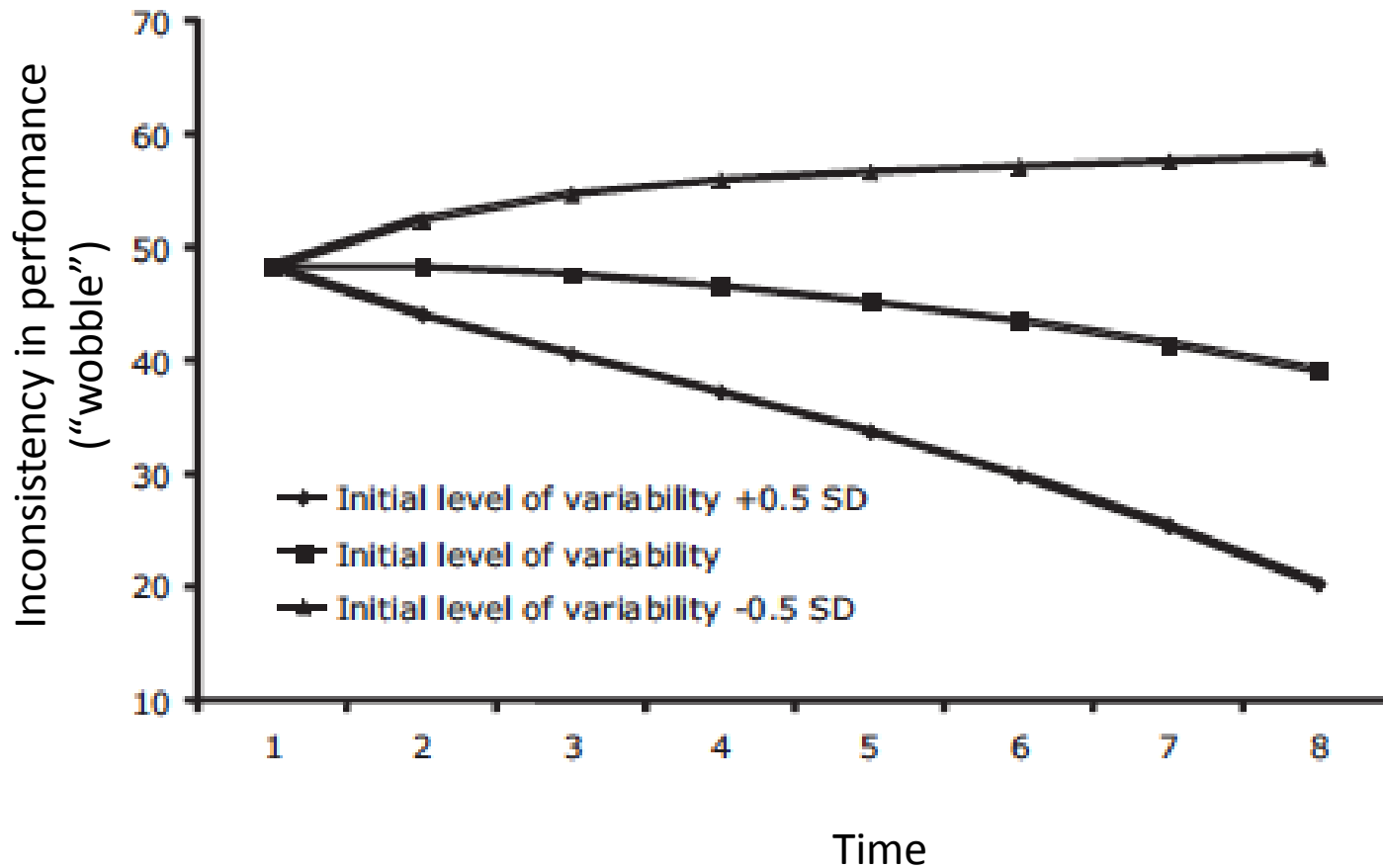


Some people show more inconsistency (“wobble”) in their performance on tests of ability

Push the button when see the letter X



Inconsistency (“wobble”) can get better, stay the same, or get worse over time

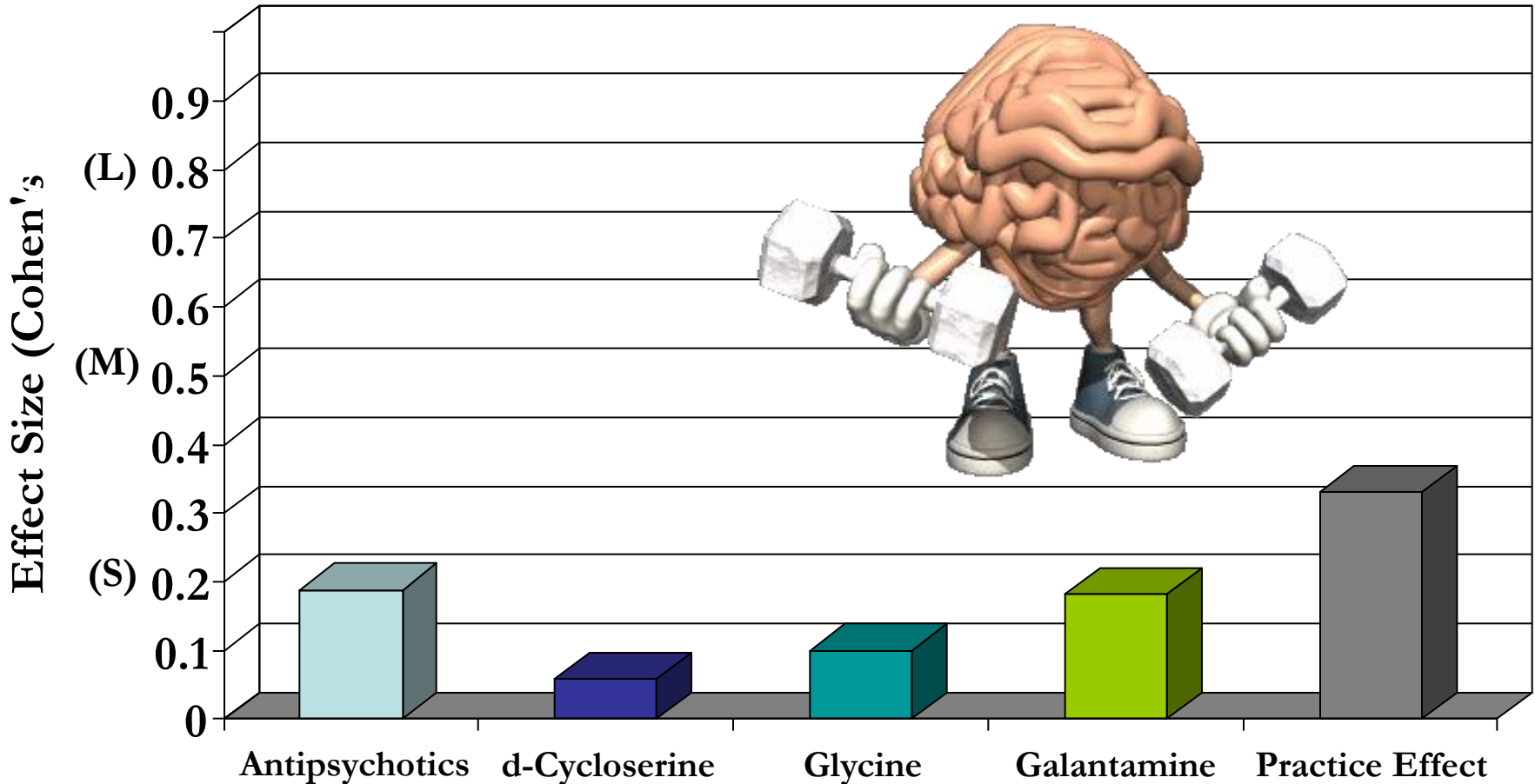


Neuroscientists are working on the best ways to study this brain ‘wobble’. They hope to figure out when it is a good thing and when it is a bad thing.

What are Possible Treatments for
Cognitive Dysfunction?

Pharmacological Treatments for Cognition

Enter: **cognitive remediation**

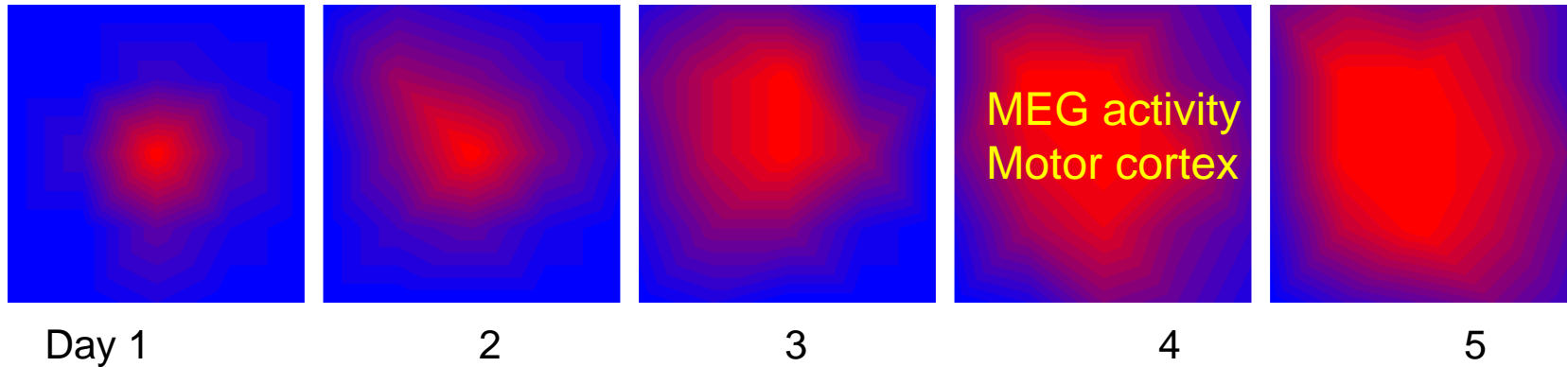


Key Cognitive Remediation Points

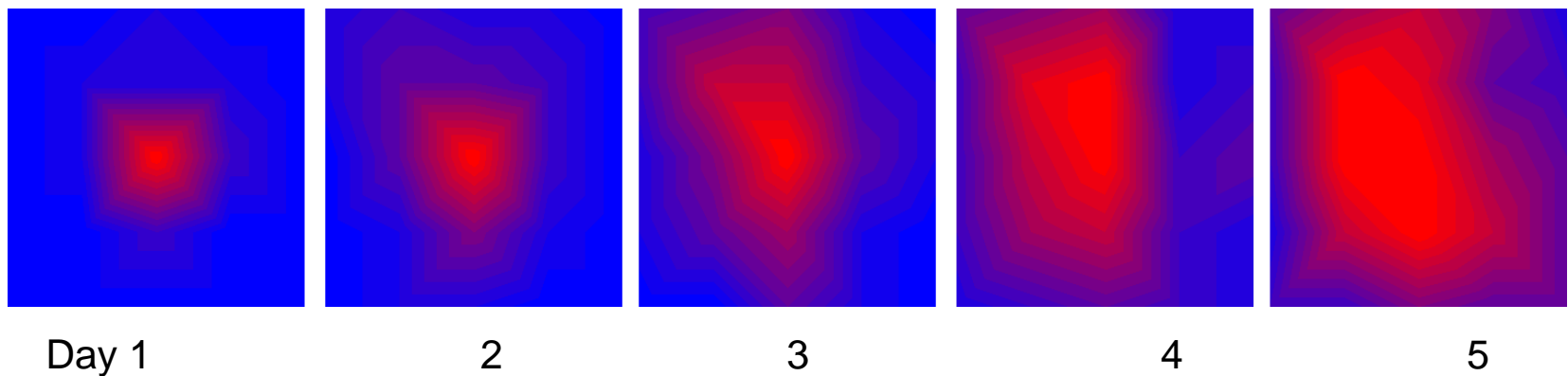
- Brain is remarkably plastic
- Altered neuroplasticity and psychosis
- Plasticity based interventions may remedy cognitive deficits

The power of plasticity

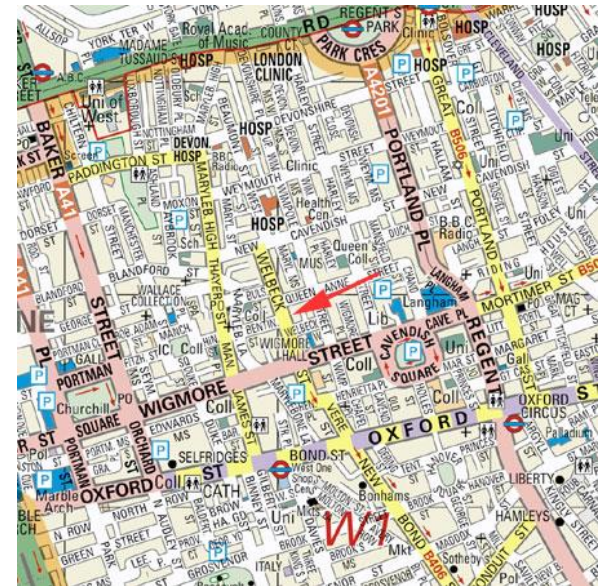
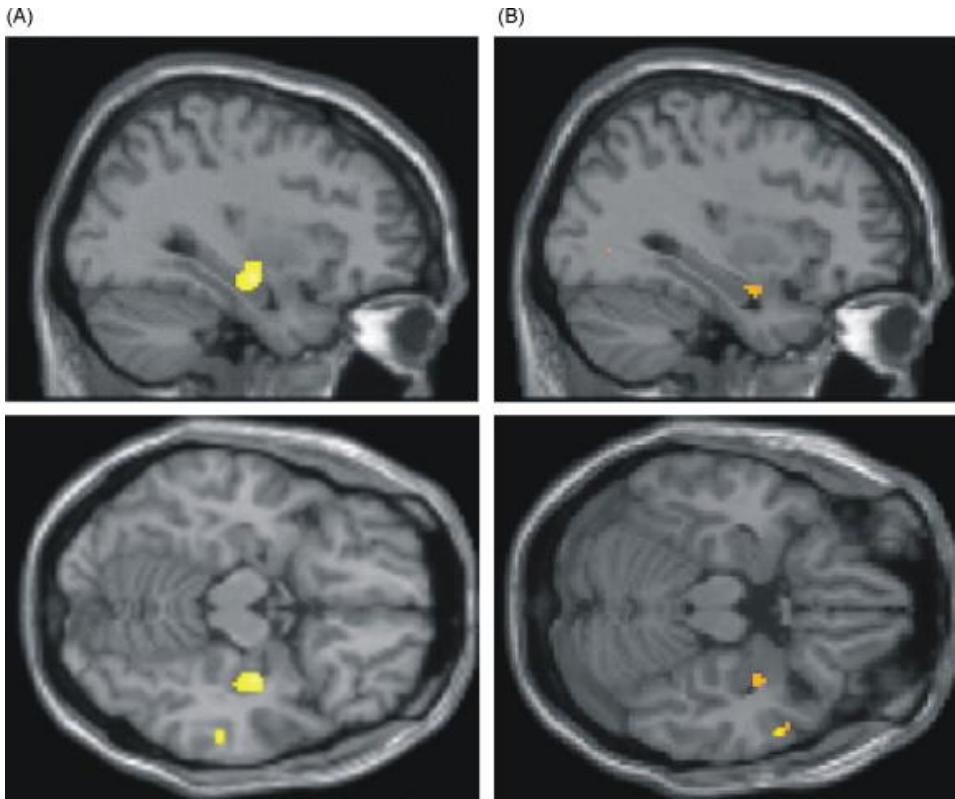
Physical Practice



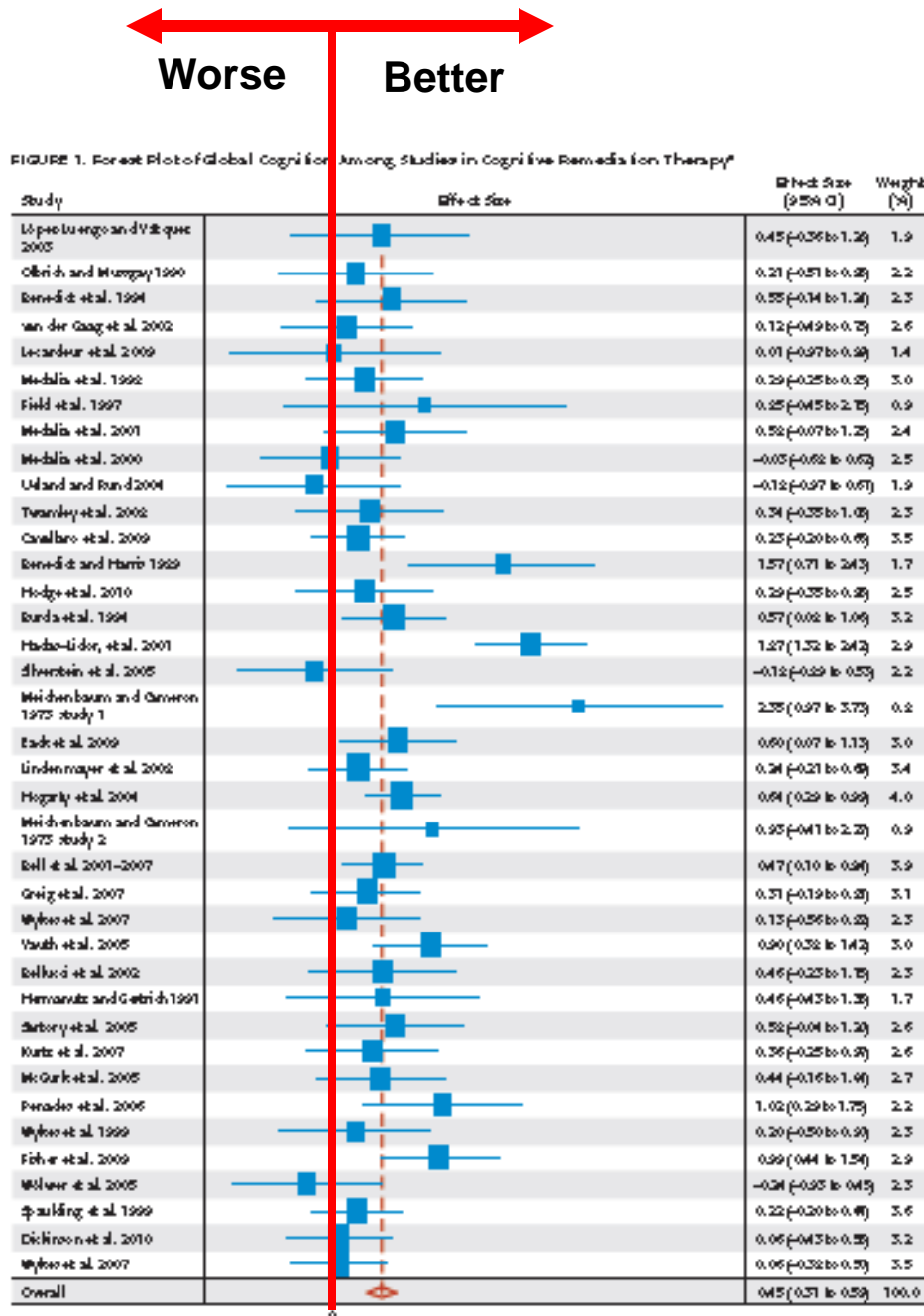
Mental Practice



London Taxi drivers (A) have larger hippocampi than matched control subjects (B)



Cognitive remediation works!



* Studies are listed by their Clinical Trial Registration Number (Table 1) in ascending order.



Til Wykes et al

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

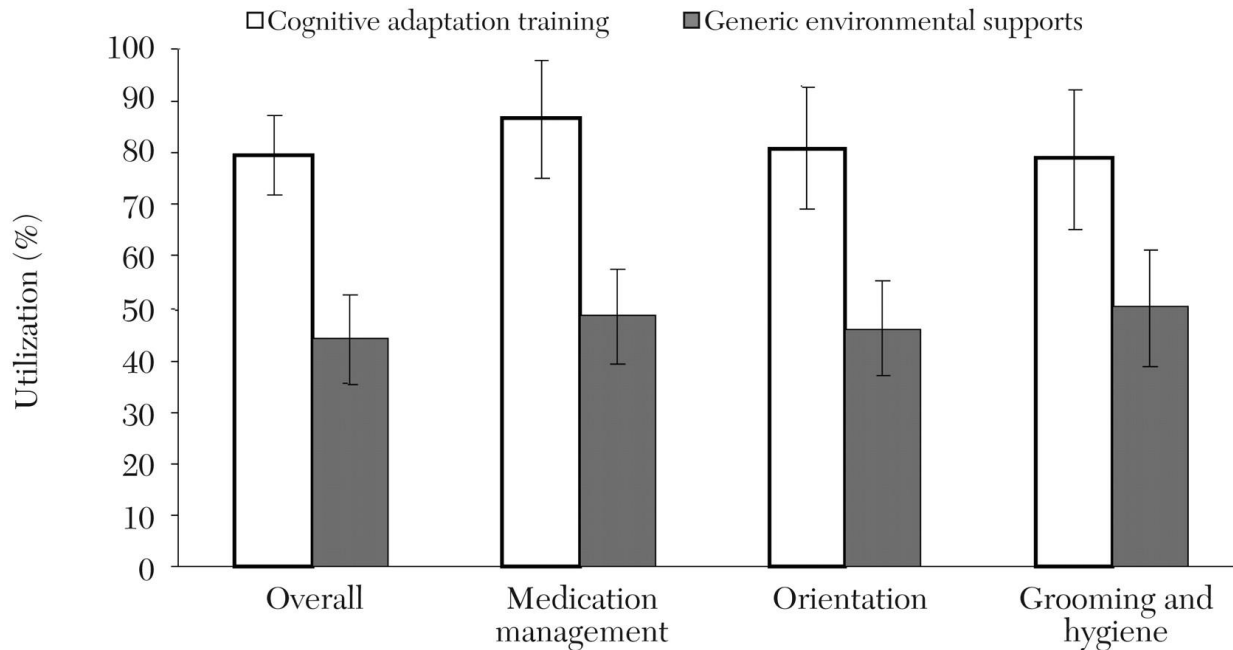


Group sessions with exercises and homework

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



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