

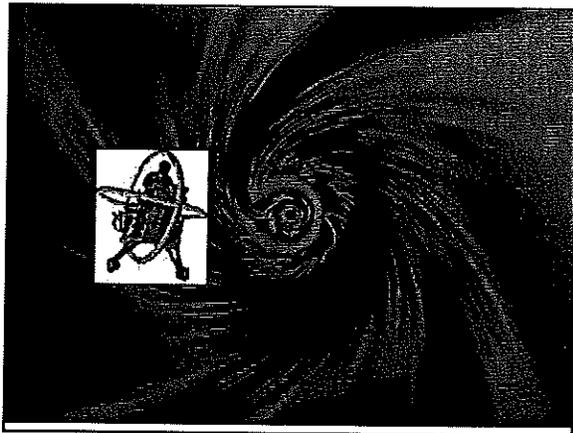
## THE MISSING LINK COGNITIVE DYSFUNCTION IN SCHIZOPHRENIA

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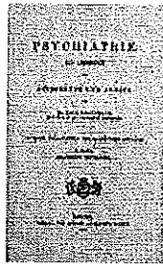


## DISCLOSURE

Dr. Riley and Mr. Borish state that they do not have any relevant financial relationships with any corporate organizations to disclose regarding today's presentation. Neither the course director nor members of the planning committee have any relevant financial relationships with any corporate organizations to disclose regarding today's presentation.



## EMIL KRAEPELIN

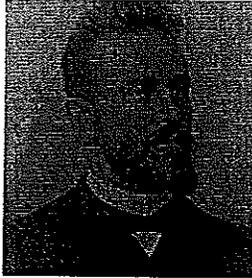


## DEMENTIA PRAECOX



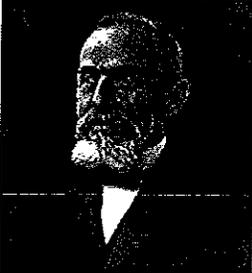
- A progressively deteriorating disease from which no one recovered.
- "Verblodun" (deterioration)
- "Schwachsinn" (mental weakness)
- "Defekt" (defect)

## EUGEN BLEULER



- Spent one year on medical study trips to Jean-Martin Charcot
- Became interested in Sigmund Freud's work, favorably reviewing Josef Breuer and Sigmund Freud's *Studies on Hysteria*.

## SCHIZOPHRENIA



"For the sake of further discussion I wish to emphasize that in Kraepelin's dementia praecox it is neither a question of an essential dementia nor of a necessary precociousness. For this reason, and because from the expression *dementia praecox* one cannot form further adjectives nor substantives, I am taking the liberty of employing the word *schizophrenia* for revising the Kraepelinian concept. In my opinion the breaking up or splitting of psychic functioning is an excellent symptom of the whole group"

## SYMPTOMS VS. COGNITIVE DEFICIT

- **Positive Symptoms**
  - Delusions
  - Conceptual Disorganization
  - Hallucinations
  - Excitement
  - Grandiosity
  - Suspiciousness
  - Hostility
- **Negative Symptoms**
  - Blunted affect
  - Emotional Withdrawal
  - Poor Rapport
  - Difficulty in Abstract Thinking
  - Lack of Spontaneity
  - Stereotyped thinking




## NEGATIVE SYMPTOMS



Symptom	Behavior
Blunted affect	Diminished emotional responsiveness, as reflected by a reduction in facial expression, modulation of feelings and communicative gestures.
Emotional withdrawal	Emotional withdrawal. Lack of interest in, involvement with, and affective commitment to life's events.
Poor rapport	Lack of interpersonal empathy, openness in conversation, and sense of closeness, interest or involvement with the interviewer.
Passive/apathetic social withdrawal	Diminished interest and initiation in social interactions due to passivity, apathy, anergy or avolition.

## NEGATIVE SYMPTOMS



Symptom	Behavior
Lack of spontaneity and flow of conversation	Reduction in the normal flow of communication associated with apathy, avolition, defensiveness or cognitive deficit.
Stereotyped thinking	Decreased fluidity, spontaneity and flexibility of thinking, as evidenced in rigid, repetitious or barren thought content.
Difficulty in abstract thinking	Difficulty in classifications, forming generalizations, and proceeding beyond concrete or egocentric thinking in problem-solving tasks.

## IS THERE A COGNITIVE DEFICIT?



## THERE IS A COGNITIVE DEFICIT

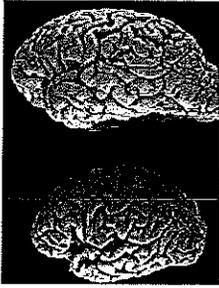
- Maybe 4 clusters of individuals
  - Normal or near-normal functioning
  - Severely impaired functioning
  - Generalized moderate impairment
    - With/without prominent deficits in abstract reasoning
    - With/without motor dysfunction
  - Average to low-average functioning with impaired psychomotor abilities



Seaton, Goldstein & Allen (2001)

### CLINICAL RELATION TO DEFICIT

- When test results indicate severely impaired
  - Slightly older
  - Less well educated
  - A more severe prodrome?
  - Greater sulcal widening



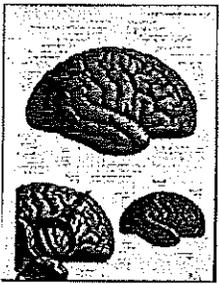

### NO DIFFERENCES IN

- Age of onset
- Substance abuse
- Length of hospitalization
- Antipsychotic medication status
- Undiagnosed neurologic disorder



### PATTERNS OF MEMORY DYSFUNCTION

- **Frontal lobe/subcortical:** impaired immediate recall with less impairment on recognition tests
- **Mesial temporal lobe:** intact immediate recall, but deficits in delayed recall (severe, rapid forgetting)



### WHAT ARE THE COGNITIVE SKILLS INVOLVED?

Skill	Behavior
Attention	The cognitive process of focusing on one aspect of the environment while ignoring others.
Vigilance (sustained attention)	Ability to maintain a readiness to respond to a signal (target stimuli) and not respond to non-targets (noise).
Immediate memory	Ability to acquire and hold information for brief (seconds) periods of time.
Secondary memory	Ability to acquire and store information over periods of several minutes and longer.

Based on Green, et al., (2000)

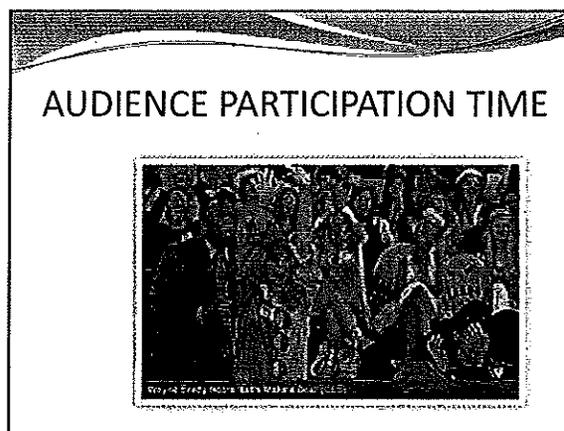
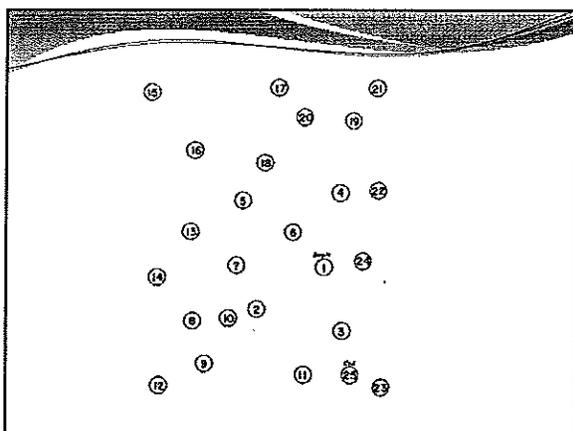
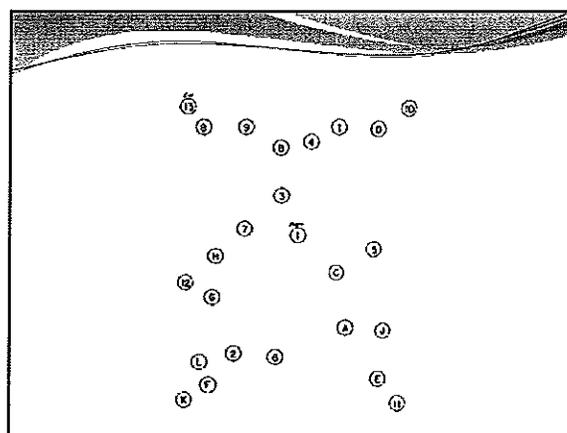
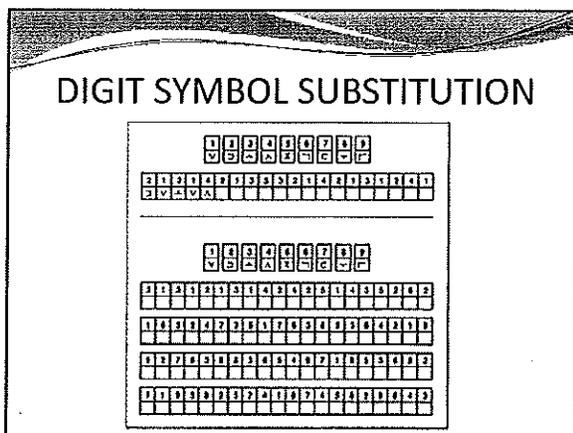
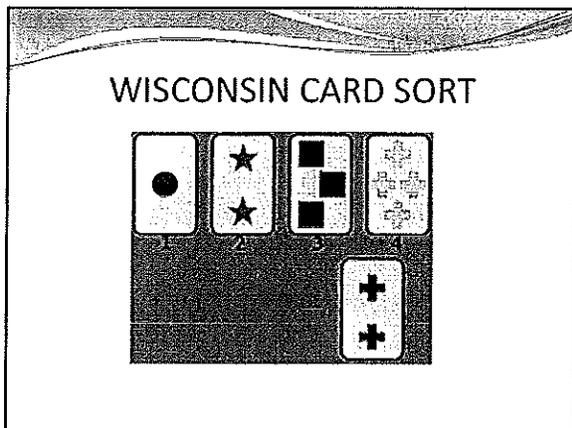
### WHAT ARE THE COGNITIVE SKILLS INVOLVED?

Skill	Behavior
Motor skills	Perform tasks with speed and/or dexterity.
Verbal Fluency	Generate words according to rules/parameters.
Executive Functioning	Volition, planning, purposive action, self-monitoring, ability to attain, maintain and shift cognitive set.

Based on Green, et al., (2000)

### EXECUTIVE FUNCTION

- Wisconsin Card Sorting Test (WCST)
- Digit Substitution Tests
- Hallstead Category Test
- Verbal fluency
- Stroop Color-Word test
- Trailmaking Tests



**Demonstration: Stroop Test**  
State the colors as fast as you can

Row 1    

Row 2    

Row 3    

From John Gosbee, MD, MS, VA National Center for Patient Safety

Now state the colors as fast as you can

Row 1 Red Blue Green

Row 2 Green Blue Red

Row 3 Green Red Blue

From John Gosbee, MD, MS, VA National Center for Patient Safety

Again, state the colors as fast as you can

Row 1 Red Green Yellow

Row 2 Yellow Green Blue Red

Row 3 Red Yellow Blue

From John Gosbee, MD, MS, VA National Center for Patient Safety

**BENTON CONTROLLED WORD FLUENCY TEST**

"Now I want you to name things according to some rules. I want you to name as many words as you can beginning with the letter "F" in one minute. You can use any part of speech but you are not allowed to say: proper names like "Fred" or different forms of the same word. For example, if you were to list names of things beginning with the letter "B" you could say "bend" but then you couldn't say "bends" or "bending." Remember, name as many words as you can think of that begin with the letter "F". Ready? Begin!"

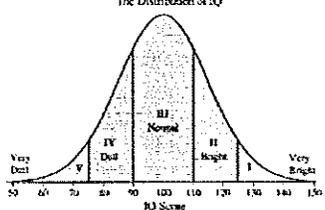
**THE ROLE OF INTELLIGENCE IN NEUROPSYCHOLOGICAL TESTING**



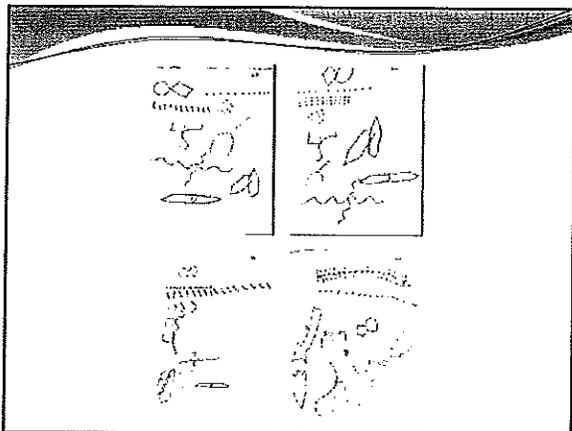
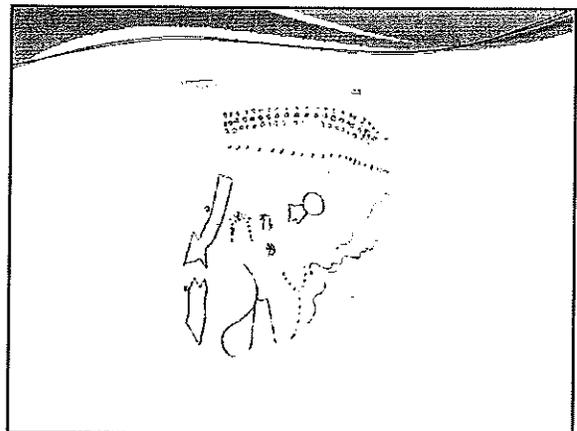
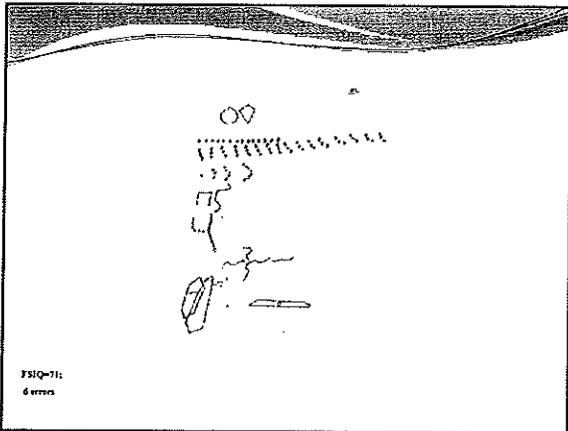
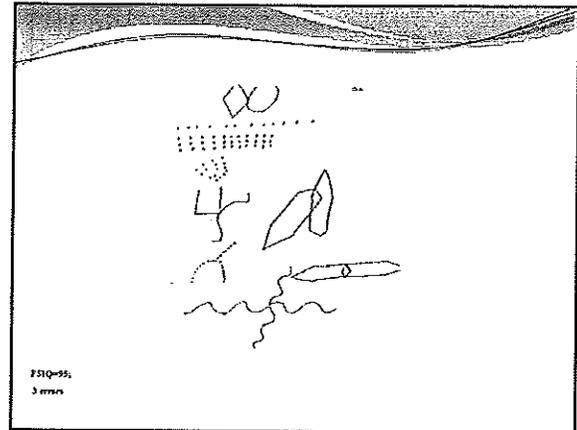
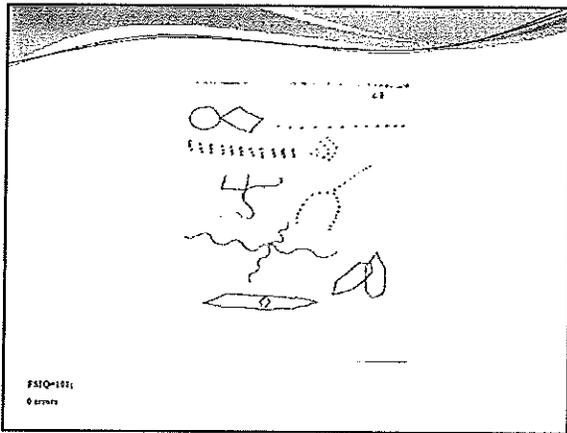
**RANGES OF INTELLIGENCE**

Defining the cognitive classes

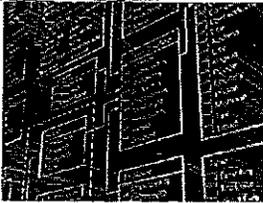
The Distribution of IQ



IQ Score	Cognitive Class
50	Very Dull (V)
70	Dull (IV)
90	Dull (III)
100	Normal (II)
110	Normal (I)
120	Bright (I)
130	Bright (I)
140	Bright (I)
150	Very Bright (V)



## INTELLIGENCE



- Predicts rate of learning
- Informs learning strategies
- Allows clinicians to "step back"
- Dictates intervention strategies
- Allows participant to be understood

### ASSESSMENT OF COGNITIVE FUNCTION

- Where is the person "at"?
- How does compare to where "they should be"?
- Are there exogenous factors effecting cognition (e.g., diabetes)?
- Are effects permanent or transitory?
- Should interventions be modified?

### ETHICAL CONCERNS

- Competency
- Training/Specialization
- Practicing outside professional role
- Involvement of other team members
- Overcompensation/false attributions/narcissism

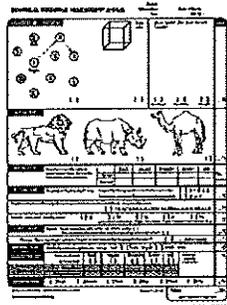
### MONTREAL COGNITIVE ASSESSMENT

- Simple screening measure
- Takes only a few minutes
- May be used, reproduced, and distributed **WITHOUT** permission
- No neuropsychological training required
- Multiple cognitive skills assessed



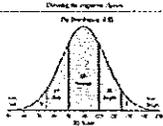
### MONTREAL COGNITIVE ASSESSMENT

- Visuo-spatial capacity
- Executive function
- Naming
- Memory
- Attention
- Language
- Abstraction
- Delayed recall
- Orientation



### PREMORBID INTELLIGENCE

- Estimating "where the person is at"
- Comparing to "where the person is"



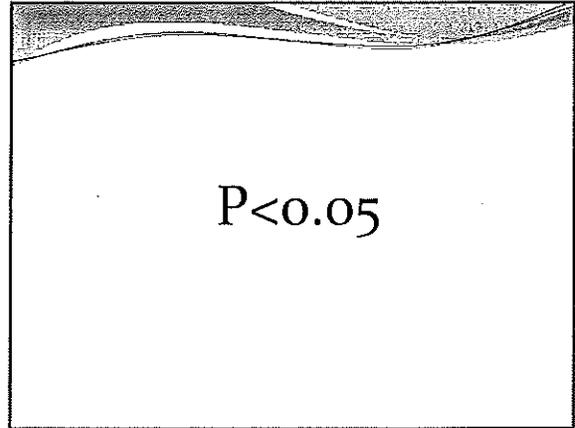
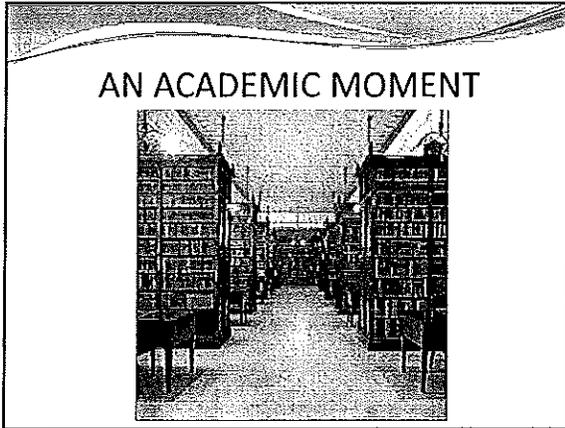
- Methods
  - Standardized intelligence tests
  - Use of regression techniques
  - Reading tests (crystalized intelligence)
    - National Adult reading Test
    - Reading subtest of Wide Range achievement Test

### PREMORBID INTELLIGENCE

- 241 individuals with Schizophrenia
- Age, education and occupation coded
- National Adult Reading Test
  - Accurately pronounce irregular words (e.g., debt)
- Regression equation developed

$$FSIQ = 78.02 + 0.24 \times \text{Age} + 2.14 \times \text{Education} - 1.48 \times \text{Occupation}$$

Dragovic, Waters & Jablensky (2008)



### $P < 0.05$

If the study was repeated with the same measures, the same population and the same sample size, the chances that the results would be obtained by chance are less than 5 in 100.

Small results (e.g., a correlation of 0.1) can be statistically significant if the sample is large (e.g., 1,000)

### EFFECT SIZE

Effect Size	Cohen's <i>d</i>
Small	0.20-0.30
Medium	0.50
Large	0.80

### EFFECT SIZE

- A measure of the strength of relationship between two variables.
- Conveys the estimated magnitude of a relationship without assuming statistical significance (p)
  - E.g. "average weight loss of 30 pounds"

### COGNITION AND FUNCTIONAL OUTCOMES

- Meta-analysis
- 37 studies
- Samples between 188-1002 subjects
- Vigilance
- Card sorting
- Immediate/secondary verbal memory
  - (Green, et al, 2000)

### FUNCTIONAL OUTCOMES

Type	Example
Success in psychosocial skills acquisition	Basic life skills; conversation skills, symptom and medication management, leisure skills
Laboratory assessments of instrumental skills and social problem-solving ability	Analogue measures of social competence or social problem solving (e.g., response to videotapes)
Community outcome/Daily activities	Occupational functioning, social attainment, degree of independent living; ADL's amount or level of work or school; type and quality of social support networks

Green, et l., (2000)

### COGNITION AND FUNCTIONAL OUTCOMES

- In general, 20-60% of variance (effect sizes) in functional outcomes can be explained by neurocognition
- Path analysis: Global measure of cognition:
  - 48% of variance in ADL's (1<sup>st</sup> sample)
  - 42% of variance in ADL's (2<sup>nd</sup> sample)

### META-ANALYSIS OF COGNITION AND FUNCTIONAL OUTCOME

- 37 studies

Domain	Total Sample Size	Effectsize
Secondary Verbal Memory	777	Medium
Immediate Verbal Memory	188	Medium-large
Card Sorting	1,002	Small-medium
Vigilance	682	Small-medium

### COGNITIVE FUNCTION AND FUNCTIONAL SKILLS

- Global measure of cognition accounted for 42-48% of variance in Activities of Daily Living
- Cognitive impairment and not symptoms influences functional outcomes



### COGNITIVE REMEDIATION

- Meta-analysis
- 26 randomized, controlled trials
- 1,151 people
  - Medium effect size (0.41) for cognitive performance
  - Medium effect size (0.36) for psychosocial functioning
  - Small effect size (0.28) for symptoms

### EFFECT ON COGNITIVE PERFORMANCE

Outcome Domain	Effect Size
Social cognition	0.54
Verbal working memory	0.52
Speed of processing	0.48
Reasoning/problem solving	0.47
Global cognition	0.41
Attention/vigilance	0.41
Verbal learning & memory	0.39
Functioning	0.35
Symptoms	0.28
Visual learning & memory	0.09

### EFFECTS ON SYMPTOMS AND FUNCTIONING

- Small effect size (0.28) on symptoms
- Small-to-medium effect size (0.35) on functioning
  - Stronger effect sizes in studies that provided adjunctive psychosocial rehabilitation
  - Programs that use drill and practice plus strategy coaching better than drill and practice only
  - Greater effect for older than younger participants

McGurk, et al, 2007

### THE BOTTOM LINE



"...the effect of cognitive remediation on functioning was moderated by several factors, including provision of adjunctive psychiatric rehabilitation, cognitive training method, and patient age, suggesting potentially important factors for improving the impact of treatment programs."

McGurk, et al, 2007

### RELATIONSHIP TO INSIGHT AND SOCIAL FUNCTIONING

- 94 people with first episode schizophrenia or schizophreniform disorder
- Greater global insight associated with more severe depression
- Poor overall insight associated with:
  - Poor working memory
  - More severe negative and disorganization symptoms
  - Unrealistic self-ratings of ability to function competently and independently on routine activities



### WHO'S LIFE IS IT ANYWAY?

- 52 Japanese people with chronic schizophrenia
- Average illness duration about 13 years
- Psychosocial Quality of life
  - Duration of disorder (+)
  - PANSS depression & anxiety factors (-)
- Motivation/Energy QOL
  - PANSS depression & anxiety factor (+)
- Symptoms/side effects QOL
  - WCS categories achieved score (+)

### WHO'S LIFE IS IT ANYWAY?

- The longer the duration of the disorder, the more opportunity to acclimate to it.
- The lower the executive functioning, the more people become indifferent symptoms and side-effects



### TYPES OF LEARNERS

- Learners: start out with poor performance and improve a requisite amount following instruction.
- Non-learners: start out poorly and do not improve with instruction.
- High Scorers: start out performing well and continue to perform well after instruction.



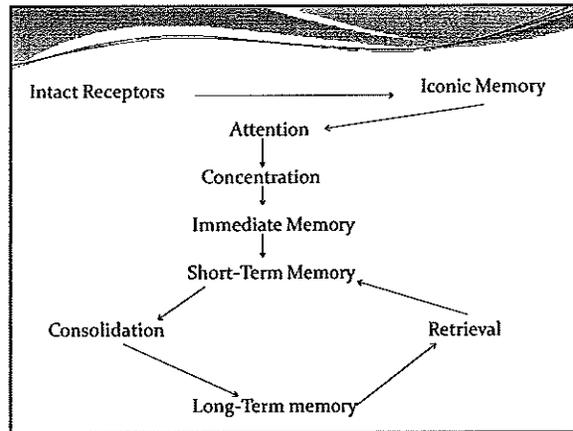
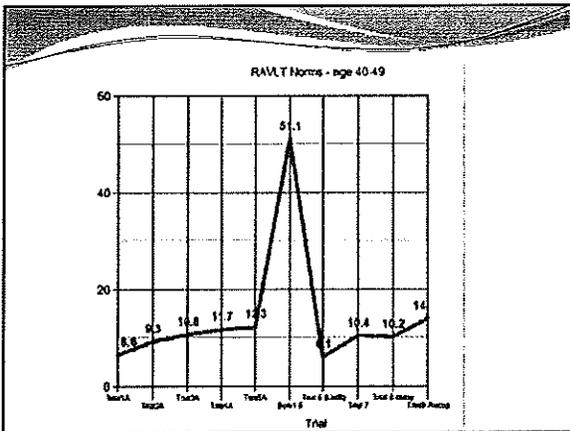
Green, et l., (2000)

### REY AUDITORY VERBAL LEARNING TEST

"I am going to read a list of words. Listen carefully, for when I stop, you are to repeat back as many words as you can remember. It doesn't matter in what order you repeat them. Just try to remember as many words as you can."

### REY AUDITORY VERBAL LEARNING TEST

<b>Drum</b>	<b>Hat</b>
Curtain	Farmer
Bell	Nose
Coffee	Turkey
School	Color
Parent	House
Moon	River
Garden	



### MEMORY ENHANCEMENT STRATEGIES

- The registration process
  - keep distractions (such as noise) to a minimum
  - focus attention only on one task at a time
  - schedule breaks between and within tasks
  - set conditions so that can learn at own pace
  - consider obtaining games, such as "concentration", "Simon", or computer games to exercise attention, concentration and registration of information

### MEMORY ENHANCEMENT STRATEGIES

- The storage process
  - rehearsal of information (like repeating a telephone number)
  - mental pictures, verbal associations or the use of rhymes
  - if verbal or pictorial memory is stronger, attempt to encode information in that modality
  - write down instructions

### MEMORY ENHANCEMENT STRATEGIES

- The retrieval process
  - use cues to enhance recall
  - list/schedule of daily events
  - ask people to give you more time when trying to recall
  - make a joke or glide over a situation once in a while
  - tell people that when you are feeling tense, tired or sick, your memory is not as good as usual

### MEMORY ENHANCEMENT STRATEGIES

- Use of external compensatory aids
  - a watch that can be set to beep at certain times
  - timers for the kitchen
  - daily/grocery lists, memos or daily calendar
  - develop the habit of writing things down
  - obtain pre-printed grocery lists
  - a *memory basket* can be kept in the living room or kitchen to leave items (keys, glasses) in so they do not become lost/misplaced

### COGNITIVE PROSTHETICS

- Lists
- Handouts
- Schedules
- Modifying length of session
- Modifying frequency of sessions

**PERSONAL COGNITIVE STRATEGY PROFILE**

Flowchart: A sequence of boxes labeled 1 through 6, connected by arrows.

Illustrations: A dog, a pig, and a camel.

Category	Score	Interpretation
Attention	12	12-15: Average
Organization	10	10-12: Below Average
Memory	8	8-10: Below Average
Problem Solving	11	11-13: Average
Executive Function	9	9-11: Below Average
Learning	10	10-12: Below Average
Communication	11	11-13: Average
Emotion Regulation	10	10-12: Below Average
Self-Management	11	11-13: Average
Overall	10	10-12: Below Average

### VISUAL-MOTOR ORGANIZATION AND CONSTRUCTION

- Expressive skills are deficient
- Receptive skills are intact
- Sequencing skills are deficient

### SEQUENCING

- Multiple-step processes failing
- Sequencing is deficient
- Cognitive flexibility is impaired

## LANGUAGE



- Naming is intact
- Receptive and expressive skills (repetition) are intact
- Fluency (Executive function) is impaired

<b>LANGUAGE</b>	Repeat: I only know that John is the one to help today. I'll try to change that under the words when they come to the screen. <i>1/1</i>		<i>2/2</i>
	Fluency / Name maximum number of words in one minute that begin with the letter <i>1</i>		<i>0/1</i>

## MEMORY

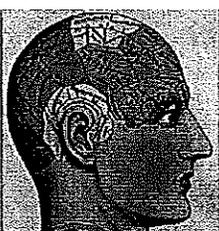
<b>MEMORY</b>	Read list of words. Subject must repeat them. Do 3 trials over 2 1/2 min's maximum. Do a recall after 5 minutes.					
		FACE	VELVET	CORNCH	DASTY	RED
	1st Trial	✓	✓	✓	✓	✓
	2nd Trial	✓	✓	✓	✓	✓

<b>ATTENTION</b>	Read list of digits (0-9) right side. Subject has to repeat them in the forward order. Subject has to repeat them in the backward order.				
	1-7-2-1-8-9-4				<i>2/2</i>
	1-5-7-4-2				

<b>DELETED RECALL</b>	No verbal recall WITH AND CLUE					
		FACE	VELVET	CORNCH	DASTY	RED
		✓	✓	✓	✓	✓

Optional

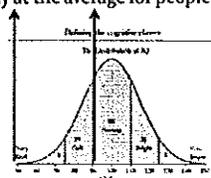
## MEMORY



- Attention intact
- Vigilance intact
- Immediate memory *mildly impaired*
- Short-term memory *grossly impaired*

## NOW AND THEN

- Premorbid IQ (estimated by WRAT) = 90
  - Low average range
- Current performance on MOCA 17/30
  - Essentially at the average for people with Alzheimer's



## OVERVIEW COGNITIVE SKILLS

<p style="text-align: center;">Intact</p> <ul style="list-style-type: none"> <li>• Receptive language</li> <li>• Attention</li> <li>• Vigilance</li> <li>• Immediate memory</li> <li>• Naming</li> <li>• Receptive and expressive skills (repetition)</li> </ul>	<p style="text-align: center;">Impaired</p> <ul style="list-style-type: none"> <li>• Sequencing skills</li> <li>• 2-D construction</li> <li>• Concentration</li> <li>• Multiple-step processes</li> <li>• Sequencing</li> <li>• Cognitive flexibility</li> <li>• Fluency (Executive function)</li> <li>• Verbal abstraction</li> <li>• Delayed recall (memory)</li> </ul>
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## PROGRAMMATIC ADAPTATIONS

- Personal Medicine cards
- Prioritizing tasks
- Session notes/handouts
- Memory board
- Writable calendar
- Chaining behaviors

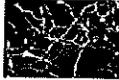


## NEUROGENESIS

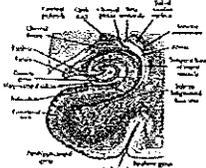
- Previous belief: all brain cells given at birth
- New Data:
  - New cells are generated
    - In Olfactory Bulbs
    - In Dentate Gyrus of hippocampus



## NEUROGENESIS



- Dentate gyrus of hippocampus produces new cells
  - If stimulate, attach and functionally connect
    - "Integrate anatomically into existing neuronal networks"
    - Functionally connect more than existing cells
    - Activate more than existing cells
- If not, "go away"



## THE LOOP COMPLETED`

The programming and interventions that have been developed for people with "Dementia Praecox" may help people who have true dementia



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