Cleveland Clinic

Neuropsychology of Epilepsy

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September 24, 2020

*Slides adapted from Robyn Busch, PhD, ABPP

Disclosures

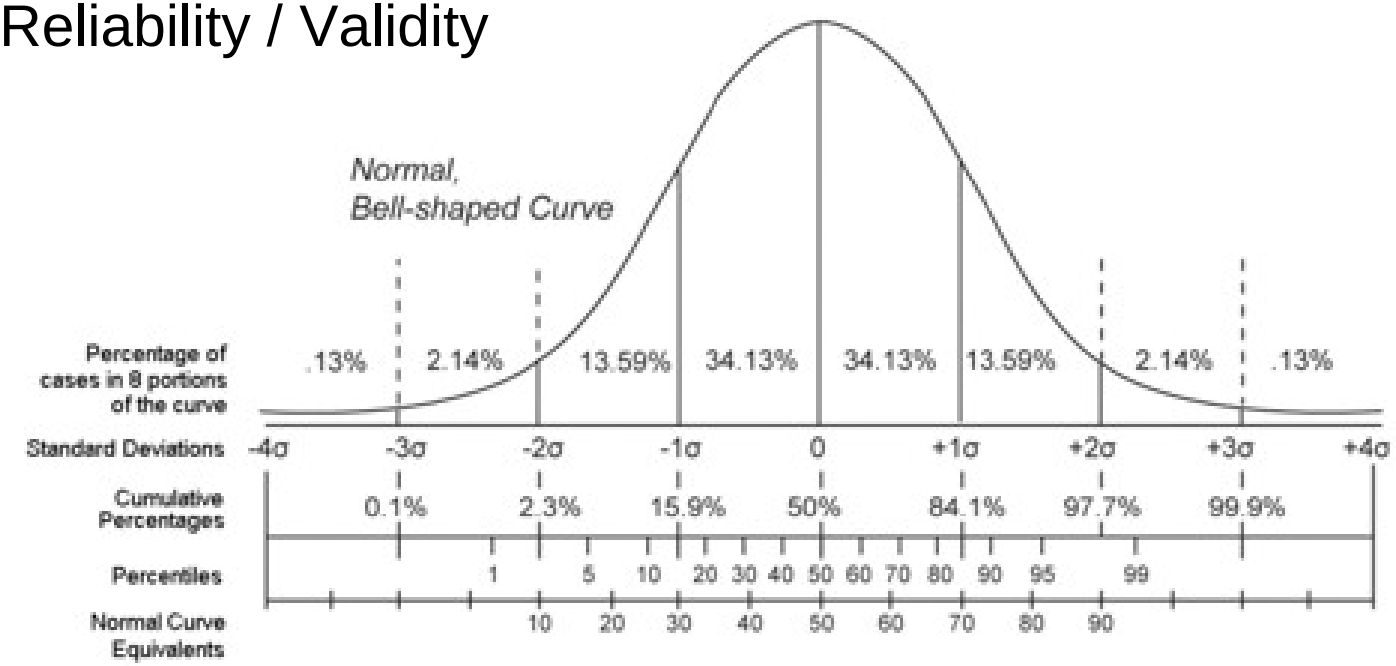
None

Overview

1) Components of a neuropsychological assessment
   - Indications for evaluation in epilepsy
2) Factors that affect cognition in epilepsy
3) Patterns of cognitive performance in focal epilepsies
4) Cognitive change after epilepsy surgery
   - Methods for assessing hemisphere dominance
   - Risk factors for post-surgical cognitive decline

Neuropsychological Assessment

- Systematically measure various aspects of behavior
- Standardized assessment techniques
- Normative data
  - Adjustment for age, education, sex
- Reliability / Validity



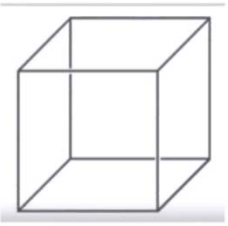
Primary Cognitive Domains

Intelligence (Premorbid Function)

Attention/ Working Memory

Processing Speed

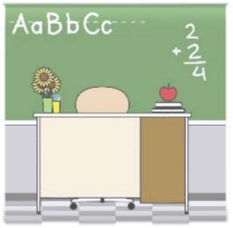
Language



Visuospatial Skills

Executive Function

Learning/ Memory



Academic Skills

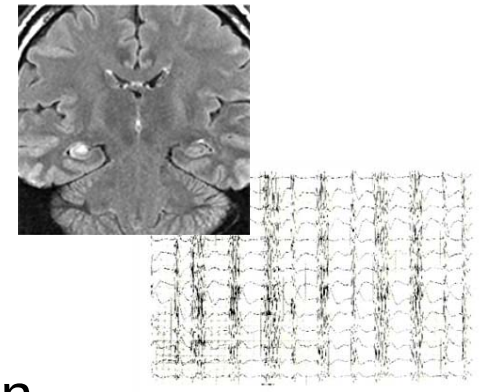
Motor Function

Personality/ Mood

Indications for Cognitive Assessment

- Document cognitive abilities (strengths/weaknesses)
  - Cognitive complaint or change
  - School difficulty / learning problems
  - Work performance
  - Disability
  - Competency
- Impact of seizures on cognitive functioning
  - Lateralization / localized deficits
  - Indications re: typical/atypical dominance
- Establish a baseline to assess change following intervention
  - Medication change
  - Epilepsy surgery
    - Prediction of likelihood of cognitive decline

Factors that Influence Cognition in Epilepsy



- Seizure etiology and type
- Seizure frequency, duration, and severity
- Cerebral lesions
- Age at seizure onset
- Ictal and interictal physiological dysfunction
- Structural damage due to repetitive or prolonged seizures
- Hereditary factors
- Antiepileptic drug effects
- Psychosocial conditions
- Psychiatric comorbidities

Elger (2004)

Psychological Functioning in Epilepsy

- Psychiatric disturbance in 20-40% of epilepsy patients
  - As high as 70% in refractory epilepsy
- Depression most common psychiatric disorder in intractable epilepsy – 20 to 55%
  - Also high rates of other psych disorders (e.g., anxiety, ADHD, ASD)
- High prevalence after surgical intervention, even when seizures well-controlled
- Severity of depression associated with greater cognitive impairment in patients with intractable seizures
- Relationship between poor mood state and impaired memory, especially in left TLE

Tsopelas (2001), Gilliam (2004), Devinsky (2005), Helmstaedter (2004) , Paradiso (2001), Dulay (2004)

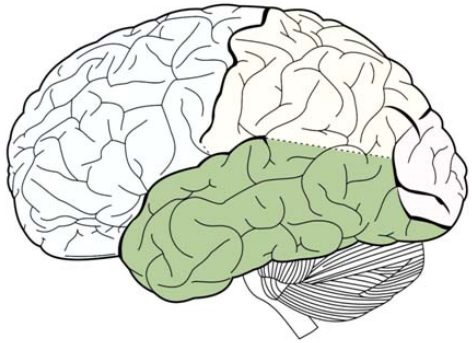
Patterns of Cognitive Performance in Epilepsy

- Cognitive / behavior problems exist even prior to diagnosis and treatment
- Children with new onset epilepsy
  - Mild diffuse cognitive impairment, regardless of syndrome
  - Academic underachievement that predates first seizure
  - Greater behavior difficulties
- Adults with new onset epilepsy
  - Cognitive deficits compared to normal controls across a number of cognitive domains (attention, concentration, motor function, executive functioning, memory, and learning)
- Cognitive impairment in epilepsy not solely due effects of seizures and medications

Hermann (2006); Austin (2002); Taylor (2010); Witt (2012)

Patterns of Cognitive Performance in Epilepsy

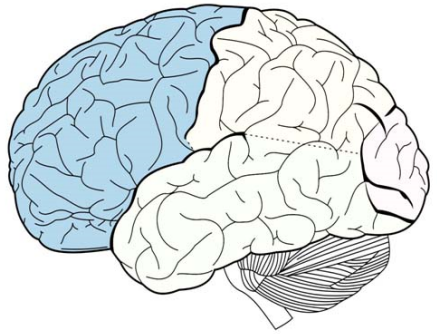
- **Temporal Lobe Epilepsy**
  - Material-specific memory deficits
    - Particularly if dominant side
    - Impaired recall AND recognition
  - Reduced confrontation naming
    - Word-retrieval problems
  - Other cognitive issues in subset
    - Attention difficulties
    - Executive dysfunction



For review and specific references, see Busch (2011) and Elger (2004)

Patterns of Cognitive Performance in Epilepsy

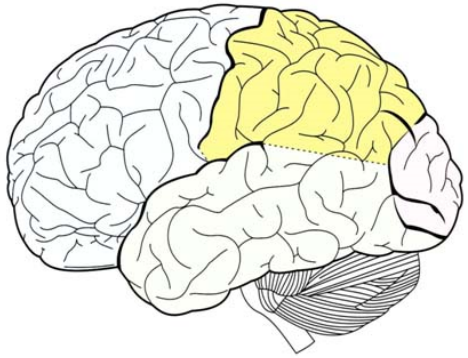
- **Frontal Lobe Epilepsy**
  - Reduced performance on wide range of “frontal” tasks
    - Attention / working memory / slowed psychomotor speed
    - Executive dysfunction
    - Reduced motor coordination and sequencing
  - Other cognitive issues in subset
    - Memory (retrieval) problems
      - Impaired recall, INTACT recognition
    - Effects on social cognition
      - Faux pas, humor appreciation
      - Facial affect recognition

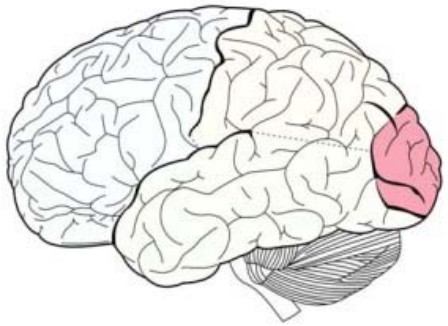


For review and specific references, see Busch (2011) and Elger (2004)

Patterns of Cognitive Performance in Epilepsy

- **Parietal Lobe Epilepsy**
  - Variable deficits depending on seizure side and location
  - Most common deficits
    - Agnosia / Apraxia
    - Visuospatial difficulties
    - Left-right confusion
    - Hemineglect
  - Other potential deficits
    - Linguistic
    - Problem-solving
- **Occipital Lobe Epilepsy**
  - Very limited research





For review and specific references, see Busch (2011)

Subjective Memory Ability

- Poor correlation between subjective and objective memory abilities
- Subjective memory complaints are often more related to depression than to actual memory ability
- Self-reported cognitive declines are uncommon after epilepsy surgery (9%)
- Self-reported gains were more frequent (18%) and ironically often observed in the domains where objective cognitive declines occurred

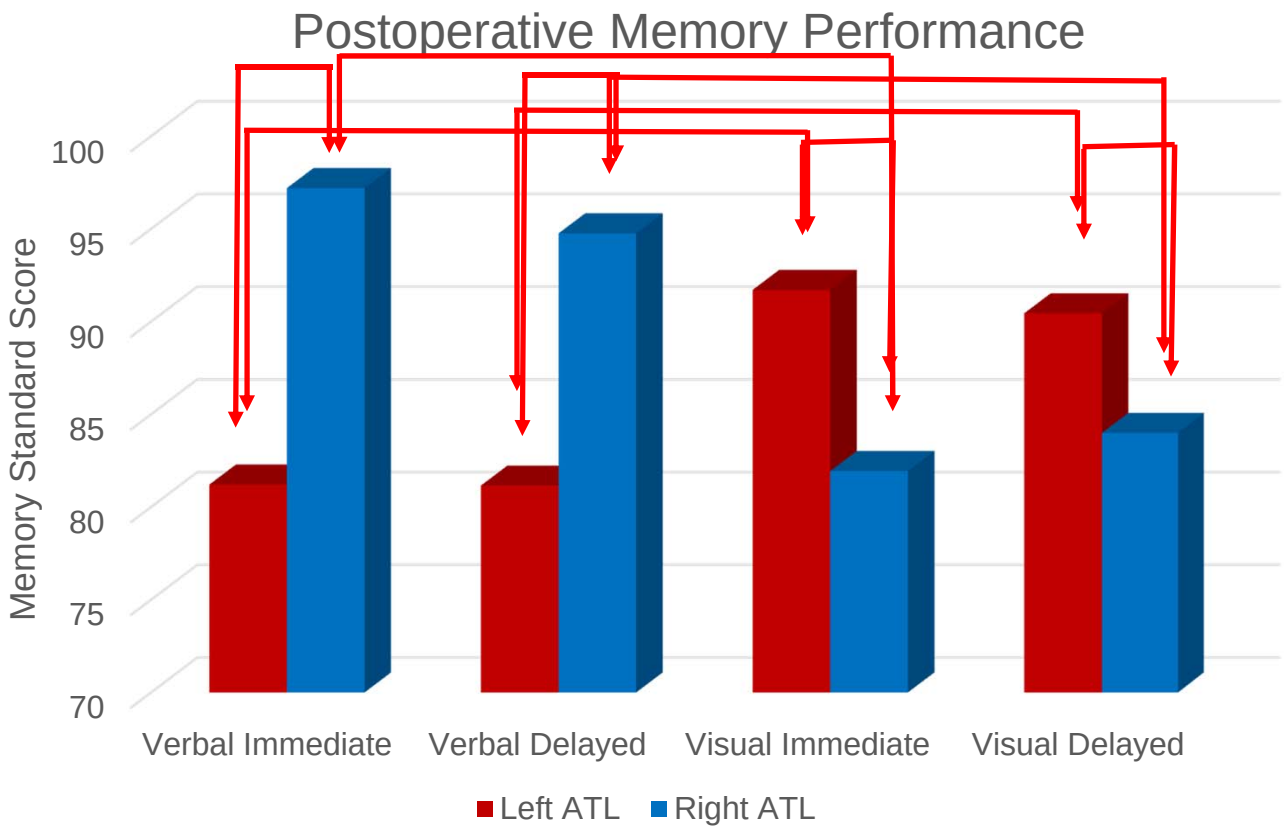
Rayner (2010), Sherman (2011)

Cognitive Change After Epilepsy Surgery

- Temporal lobectomy most comprehensively studied
  - Left ATL
    - 44% verbal memory decline; 7% improve
    - 39% naming decline; 4% improve
    - 10% verbal fluency decline; 27% improve
  - Right ATL
    - 23% show visual memory decline; 10% improve
  - Few declines in IQ, executive functioning, or attention
- Variation in surgical technique had no large effect on cognitive outcome, except naming

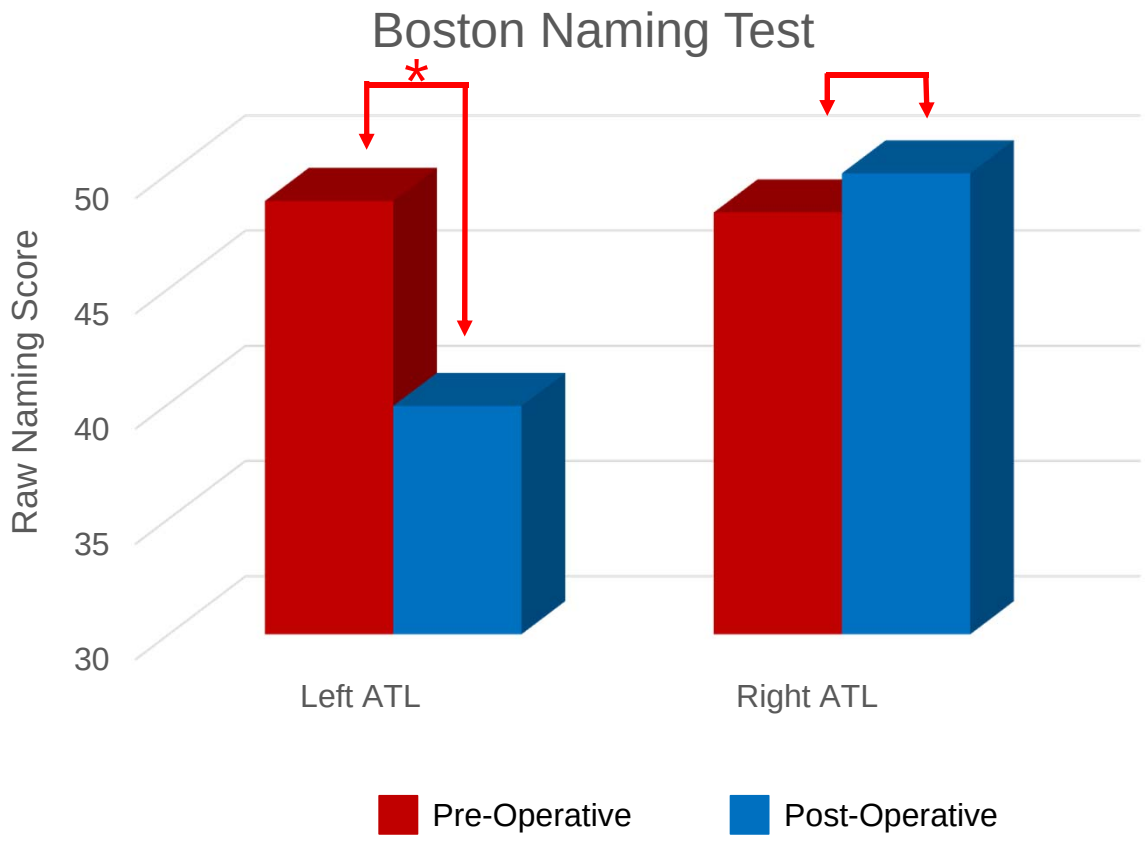
Sherman (2011)

Cognitive Change After Epilepsy Surgery



Doss (2004)

Cognitive Change After Epilepsy Surgery



Sabsevitz (2003)

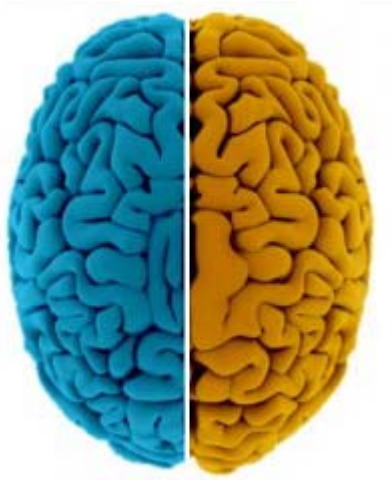
Language Dominance & Handedness

	Left Dominant	Bilateral Symmetric	Right Dominant
Right-Handed			
Neurologically Normal	94%	0%	6%
Epilepsy	78%	16%	6%
Left-Handed / Ambidex			
Neurologically Normal	78%	14%	8%
Epilepsy	46%	9%	45%

Springer (1999), Szaflarski (2002), Sabbah (2003)

Neuropsychology – Lateralization and Risk

- Laterality
  - Is cognitive pattern consistent with suspected side and site of seizure onset?
  - Anything to suggest atypical dominance?



- Cognitive risk
  - Most research in temporal lobe epilepsy
    - Higher presurgical scores (memory, naming) associated with greater risk for declines
    - Low verbal-nonverbal memory discrepancy scores associated with greater risk for memory decline

Chelune (1991)

Neuropsychology – Advantages / Limitations

- Advantages
  - Uses standardized tests that are validated/reliable
  - Noninvasive and easily repeatable
  - Methods to control for practice effects
  - Not subject to time constraints
  - Useful in identifying lateralized dysfunction
  - Provides baseline to evaluate postoperative change
  - Identifies risk for postoperative cognitive decline
- Limitations
  - Relationship between nondominant temporal function and performance on visual memory measures is variable
  - Poor localization abilities for specific memory functions
  - Unable to identify *essential* areas

Wada Test – Lateralization and Risk

- Lateralization
  - Temporary “inactivation” of ipsilateral cerebral hemisphere to allow independent testing of contralateral hemisphere

- Cognitive risk
  - Memory decline associated with
    - **poor** memory after **ipsilateral** injection (limited reserve)
    - **good** memory after **contralateral** injection (intact adequacy)

Wada & Rasmussen (1960); Milner (1962)

Wada Test – Advantages / Limitations

- Advantages
  - Temporary inactivation technique
  - Simulates effects of actual surgical ablation
  - Is predictive of postoperative cognitive outcome
- Limitations
  - Invasive
  - No uniform testing procedure across centers
  - Clinical effects (confusion, agitation, somnolence)
  - Not readily repeatable
  - Aphasia following dominant injection
  - Insufficient time for detailed testing
  - Limited in distinguishing material-specific deficits
  - Crossflow issues
  - Poor spatial resolution – hippocampal function?

fMRI – Lateralization and Risk

- Lateralization
  - Activation technique to assess brain activity during cognitive processes
  - Evidence for utility in language and memory lateralization
  - High concordance with Wada results
  - Requires control or baseline task to differentiate functions
- Cognitive risk
  - Both language dominance and mesial temporal activation during word encoding are predictive of memory outcome after ATL
  - fMRI language laterality index has incremental validity in predicting memory outcome after left ATL
  - ***Ipsilateral*** activation of MTL during memory tasks is associated with postsurgical naming and memory declines; ***Contralateral*** activation of MTL during memory tasks is associated with postsurgical memory improvements

For review and specific references, see Binder (2011)

fMRI - Advantages and Limitations

- Advantages
  - Noninvasive and easily repeatable
  - Good spatial and temporal resolution
  - Permits study of multiple brain functions
  - No strict time limitations
  - Can be used sequentially
  - Can identify mesial temporal activations during memory encoding
- Limitations
  - Disruption of neurovascular coupling
  - Relatively gross temporal resolution
  - Head motion can cause artifact
  - Susceptibility artifact
  - Difficult to identify *essential* areas
  - Thinking/problem-solving during rest state?
  - Surgical planning issues

Risk Factors for Memory Decline

- Left (dominant) temporal surgery
- Average or better presurgical memory
- Small verbal-visual memory discrepancy
- Anterior hippocampal activation on fMRI
- Good memory after contralateral Wada injection
- Limited asymmetry in hippocampal volume
- Absence of MTS or limited hippocampal neuron loss
- Later age at seizure onset
- Older age at time of surgery

Risk Factors for Naming Decline

- Left (dominant) temporal surgery
- Older age at seizure onset
- Older age at time of surgery
- fMRI language activation ipsilateral>contralateral
- Nonlesional or mild HS

Summary

- Neuropsychological evaluation involves assessment of wide range of cognitive abilities
- Patterns of performance can provide clues re: language dominance and seizure lateralization/localization
- Useful to document cognitive strengths/weaknesses and establish baseline functioning prior to treatment
- Important to predict cognitive outcome and to objectively measure cognitive change following surgery
- Wada and fMRI are other methods useful in establishing dominance and predicting cognitive outcome
- A host of factors can influence cognition and relate to cognitive outcome

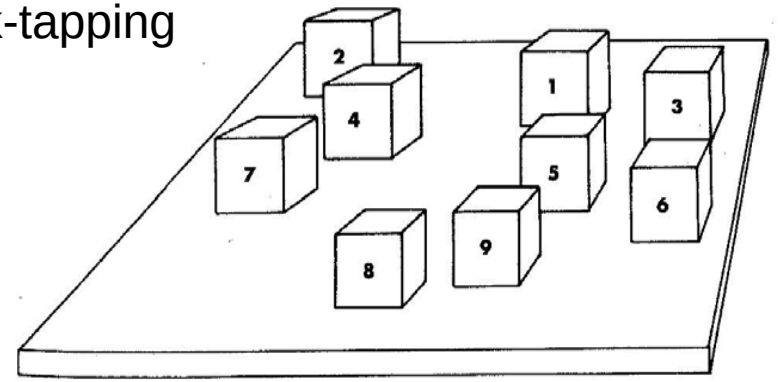
Intellectual Functioning

- Wechsler Scales
  - Wechsler Preschool and Primary Scale of Intelligence (WPPSI)
  - Wechsler Intelligence Scale for Children (WISC)
  - Wechsler Adult Intelligence Scale (WAIS)

- Scores Produced
  - Full Scale IQ
    - Verbal Comprehension
    - Perceptual Organization / Perceptual Reasoning
    - Working Memory
    - Processing Speed
  - Subtest scaled scores

Attention Measures

- Attentional Capacity / Attention Span
  - Digit Span - Forward (5-9-7-3-4-6 ⟶ 5-9-7-3-4-6)
  - Spatial Span / Corsi Block-tapping



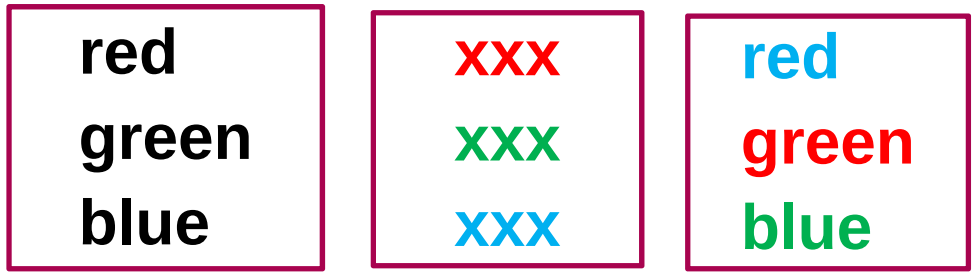
Milner (1971)

- Working Memory / Mental Tracking
  - Digit Span – Backward (5-9-7-3-4-6 ⟶ 6-4-3-7-9-5)
  - Spatial Span – Backward
  - Letter-Number Sequencing (6-F-2-B-5-Q ⟶ 2-5-6-B-F-Q)
  - Arithmetic

Attention Measures

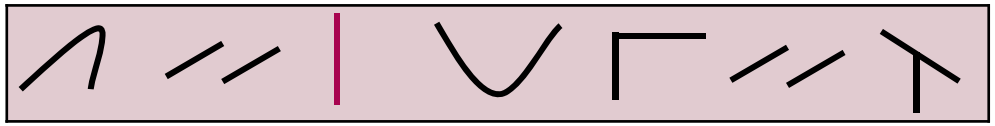
- Concentration / Sustained or Focused Attention
  - Continuous Performance Test

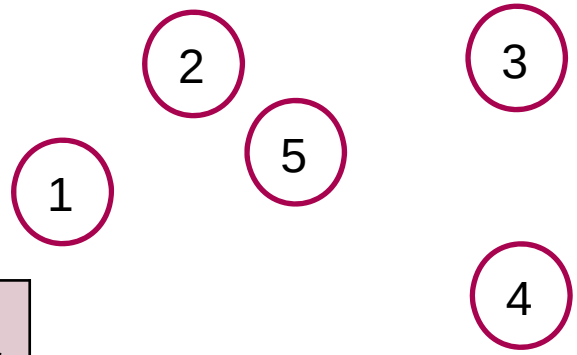
  - Stroop Tests



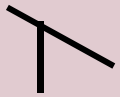
Processing Speed

- Visuomotor Processing Speed
  - Trail Making Test – Part A
  - Symbol Search





  - Digit Symbol Test / Coding
  - Symbol Digit Modalities Test

1	2	3	4	5
				

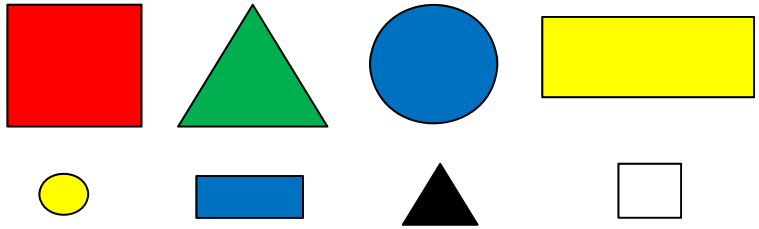
2	1	3	5	4

Language

- Naming
  - Boston Naming Test
  - Visual Naming Test
  - Auditory Description Naming
  - Expressive One-Word Picture Vocabulary Test

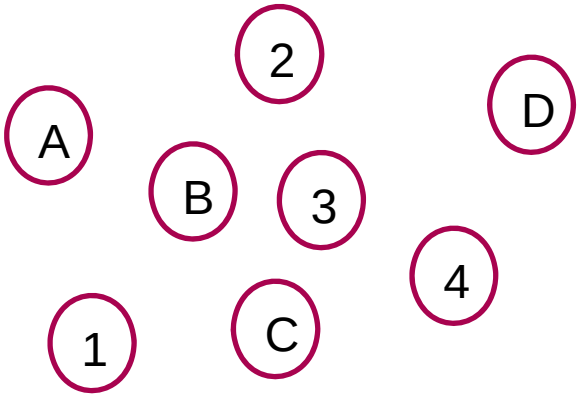
Instrument with black and white keys.
Animal with a very long neck.

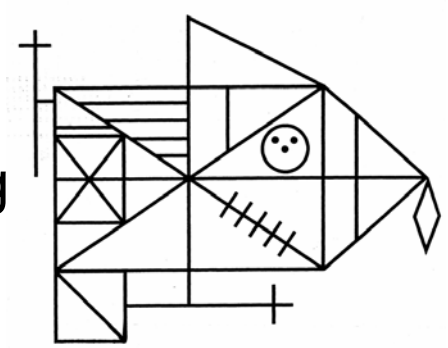
- Fluency
  - Phonemic (letter)
  - Semantic (category)
- Repetition
- Verbal Comprehension
  - Token Test

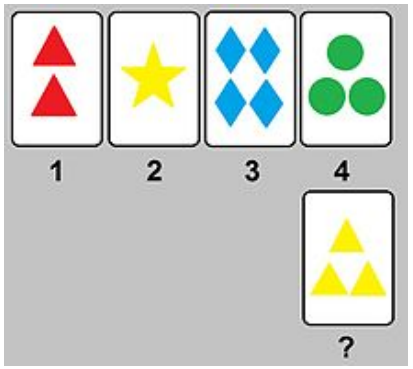


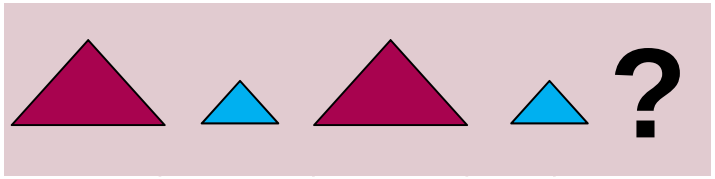
Executive Functioning

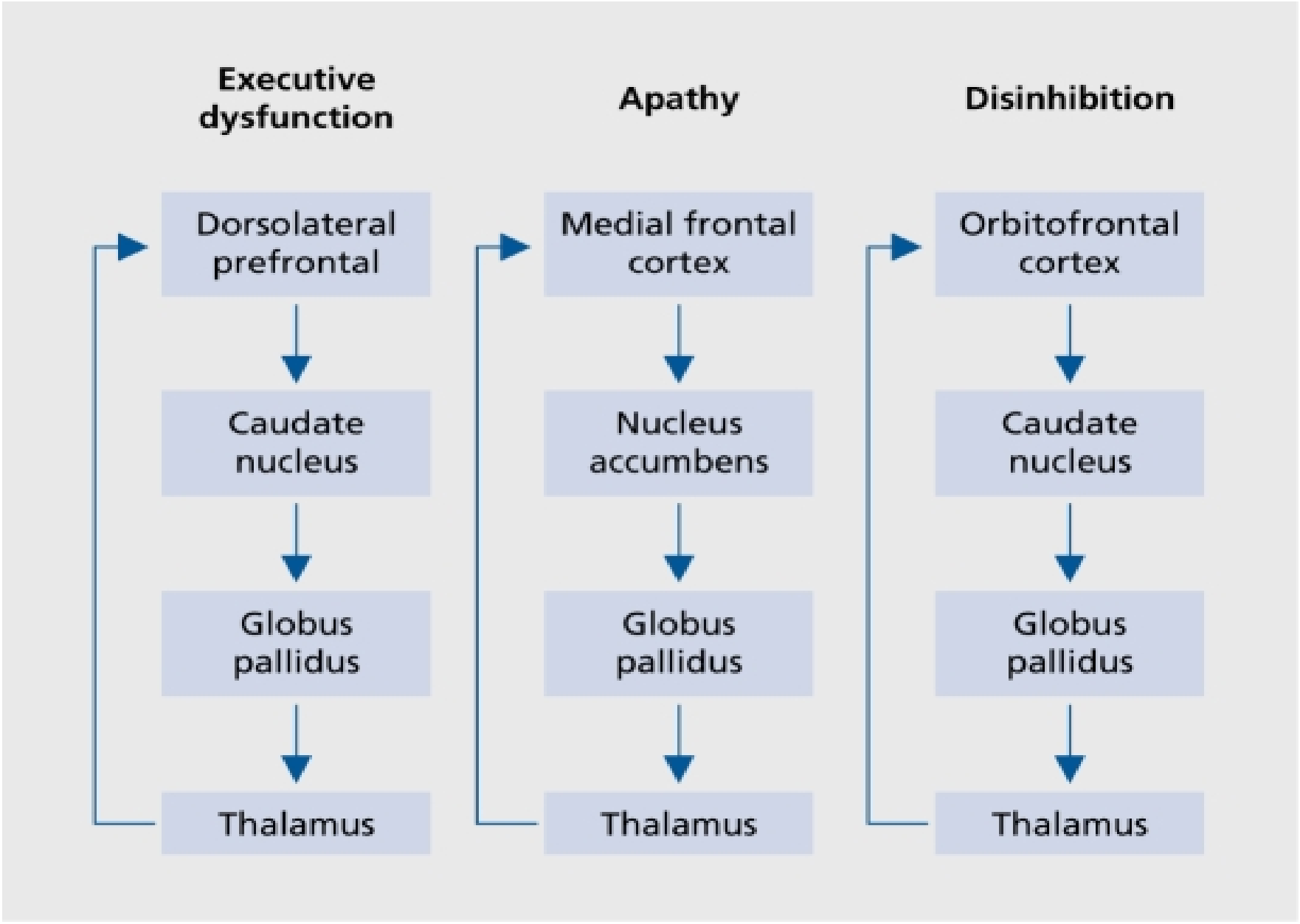
- Set Shifting / Mental Flexibility
  - Trail Making Test – Part B
- Organization / Approach
- Abstract Reasoning
  - Similarities
  - Matrix Reasoning
- Planning & Problem Solving
  - Wisconsin Card Sorting Test
- Decision Making
- Family Report







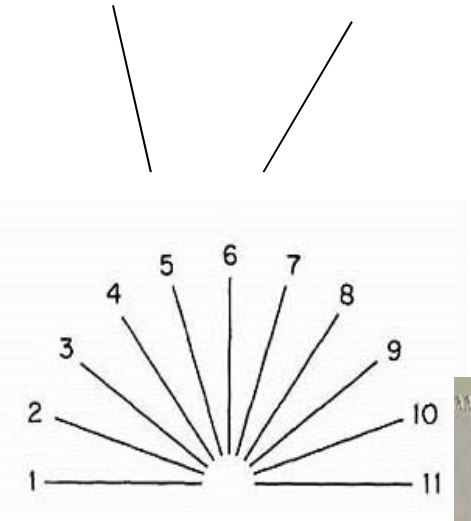


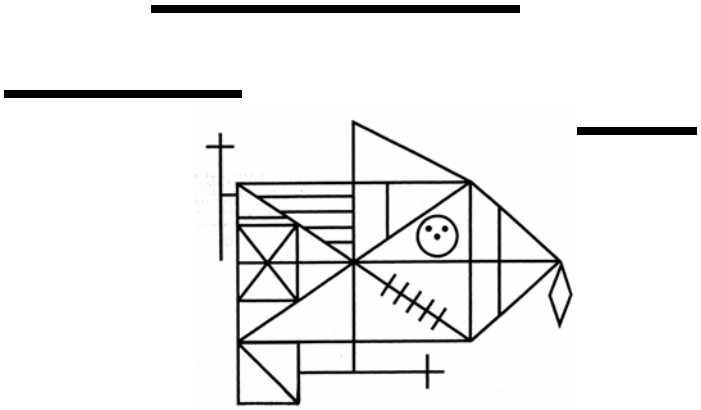


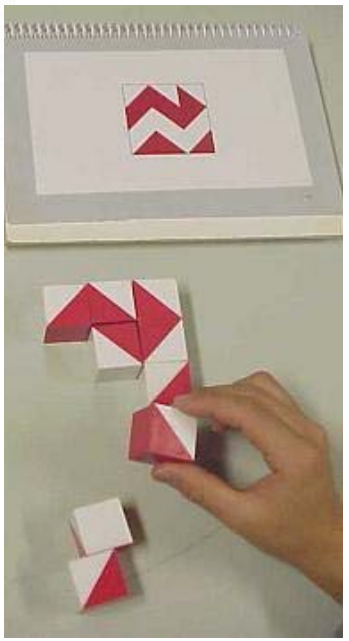
Bonelli & Cummings (2007)

Visuospatial Skills

- Perception
  - Judgment of Line Orientation
  - Line Bisection
  - Test of Visual Perceptual Skills
- Construction
  - Block Design
  - Rey-Osterrieth Complex Figure







Memory

- Verbal Memory
  - Stories / Paragraphs
  - Word Pairs
  - Word List Learning (e.g., Rey AVLT, California AVLT)
- Visual Memory
  - Designs
  - Faces
  - Scenes

- Immediate Memory
- Delayed Memory
- Recognition Memory

Academic Achievement

- Woodcock Johnson Tests of Achievement
  - Reading
  - Written Language
  - Mathematics
  - Listening Comprehension

- Wide Range Achievement Test
  - Reading
  - Spelling
  - Math Computation

Motor Skills

- Grip Strength
  - Dynamometer
- Motor Speed
  - Finger Tapping
- Manual Dexterity
  - Grooved Pegboard
  - Purdue Pegboard
- Lateralization of Motor Skills

Photos: Lafayette Instrument - www.lafayetteevaluation.com

Emotional Functioning

- Self Report Questionnaires
  - Anxiety
    - Beck Anxiety Inventory
    - State-Trait Anxiety Inventory
    - Revised Children's Manifest Anxiety Scale
  - Depression
    - Beck Depression Inventory
    - Center for Epidemiological Studies Depression Inventory
    - Neurological Disorders Depression Inventory for Epilepsy
    - Children's Depression Inventory
- Personality Style
  - Minnesota Multiphasic Personality Inventory
  - Personality Assessment Inventory
- Family Report

Behavioral Observations

- Eye Contact
- Interpersonal Style
- Disinhibition
- Impulsivity
- Fatigue
- Frustration Tolerance
- Hyperactivity
- Motor function
- Effort (e.g., SVTs)
- Family Report

Cognitive Effects of Antiepileptic Drugs

- Dependent on host of factors
  - Type of drug
  - Dosage
  - Serum level
  - Drug interactions
  - Duration of treatment
  - Individual characteristics
- In general…
  - Older AEDs
    - PB and PRM: poorest cognitive profiles
    - CBZ: motor speed and attention difficulties
    - PHT: usually restricted to visually guided motor functions
  - Newer AEDs
    - TPM: greatest risk for cognitive impairment
    - ZNS: little data, but appears worse than other new agents
    - GBP, LTG, LEV: more positive cognitive profiles
  - Polytherapy not adequately addressed
  - Most studies based on adults (not children or elderly)

For summary and specific references, see Jokeit (2011) and Eddy (2011)

Evaluating Cognitive Change Over Time

- Reliable Change Indices
  - Identify distribution of test-retest change scores in absence of any real underlying change
  - Establish confidence intervals
  - Test-retest scores outside of CI reflect degree of change is rare and unlikely due to chance score fluctuations
- Standardized Regression-Based Change Scores
  - Account for test-retest reliability and practice
  - Control for bias of demographic and epilepsy factors
  - More accurate prediction of retest performance using these variables as predictors into linear regression
  - Consideration of individual patient's preoperative test performance to control for regression to the mean

Jacobson & Truax (1991), Chelune (1993), McSweeny (1993)