Acknowledgements

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Disclosures

None

Overview

• Components of a neuropsychological assessment
• Factors that affect cognition in epilepsy
• Patterns of cognitive performance in various epilepsies
• Cognitive change after epilepsy surgery
• Methods for assessing language and memory dominance
• Risk factors for cognitive decline following epilepsy surgery
Neuropsychological Assessment

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

Primary Cognitive Domains

- Intelligence (Current and Premorbid)
- Speech / Language
- Visuospatial Abilities
- Processing Speed
- Attention / Working Memory
- Executive Functioning
- Learning / Memory
- Academic Skills
- Motor Functioning
- Emotional Functioning

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
- Psychosocial conditions
- Psychiatric comorbidities
- Antiepileptic drug effects
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); W.B. (2012)

Patterns of Cognitive Performance in Epilepsy

• Temporal Lobe Epilepsy
  – Material-specific memory (encoding) 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 range of “frontal” tasks
    – Attention / working memory / Executive dysfunction
    – Slowed psychomotor speed
    – Reduced motor coordination and sequencing
  – Other cognitive issues in subset
    – Memory (retrieval) problems
    – Impaired recall, INTACT recognition
    – Effects on social cognition
    – Faux pas, Humor
    – Facial affect recognition

For review and specific references, see Busch (2011) and Elger (2004)
Patterns of Cognitive Performance in Epilepsy

• Parietal Lobe Epilepsy
  – Variable depending on seizure side and location
  – Most common deficits
    – Agnosia / Apraxia
    – Visuospatial difficulties
    – Left-right confusion
    – Hemineglect
  – Other (Linguistic, Problem solving)

• Occipital Lobe Epilepsy
  – Very limited research

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%) and self-reported gains were more frequent (18%) in the domains where objective cognitive declines occurred

Cognitive Change After Epilepsy Surgery

• Temporal lobectomy most comprehensively studied
  – Left ATL
    – 44% verbal memory decline; 7% improve
    – 34% naming decline; 4% improve
    – 27% verbal fluency improvement; 10% decline
  – Right ATL
    – 20% show visual memory decline
  – Few declines in IQ, executive functioning, or attention
• Variation in surgical technique had no large effect on cognitive outcome, except naming
• Too little data on extratemporal surgeries or surgeries in children
**Postsurgical Memory Performance**

![Graph showing memory performance](image)

- **Verbal Immediate**
- **Verbal Delayed**
- **Visual Immediate**
- **Visual Delayed**

Doss et al. (2004)

**Language Dominance & Handedness**

<table>
<thead>
<tr>
<th></th>
<th>Left Dominant</th>
<th>Bilateral Symmetric</th>
<th>Right Dominant</th>
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<tr>
<td><strong>Right-Handed</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>94%</td>
<td>0%</td>
<td>6%</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>78%</td>
<td>16%</td>
<td>6%</td>
</tr>
<tr>
<td><strong>Left-Handed / Ambdx</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>78%</td>
<td>14%</td>
<td>8%</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>46%</td>
<td>9%</td>
<td>45%</td>
</tr>
</tbody>
</table>


**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
  - Those with highest presurgical scores (memory, naming) at greatest risk for postsurgical decline
  - Those with lowest verbal-nonverbal discrepancy scores are at greatest risk for postsurgical 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
  – Identifies risk for postoperative cognitive decline
  – Provides baseline to evaluate postoperative change

• 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
  – Initially used for speech lateralization
  – First applied to memory function in epilepsy by Milner

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

Wada & Rasmussen (1968); 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
  – Vascular structure - Crossflow issues, spatial resolution?
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
  – fMRI language laterality index has incremental validity in predicting memory outcome after left ATL
  – **Contralateral** MTL activation during memory = postsurgical naming and memory declines

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
  – Artifact (Head motion, susceptibility)
  – Difficult to identify essential areas
  – Thinking/problem-solving during rest state?
  – Surgical planning issues

Risk Factors for Memory Decline

• Dominant temporal surgery
• Average or better presurgical memory
• No MRI evidence for MTS/cell Loss/atrophy
• Small verbal-visual memory discrepancy
• Good memory after contralateral Wada injection
• Late age at seizure onset
• Short epilepsy duration
• Relatively low seizure frequency
• Partial seizures with no hx of GTC or status epilepticus
• Older age at time of surgery
• Male
• Comorbid depression
Summary

- Neuropsychological evaluation involves assessment of wide range of cognitive abilities
- Patterns of performance can provide clues re: language dominance and seizure lateralization/localization
- 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
- Host of factors, including demographic and epilepsy variables, are related 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

Normal Score Distribution

Wechsler Nomenclature

<table>
<thead>
<tr>
<th>Standard Score</th>
<th>Scaled Score</th>
<th>Interpretive Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥130</td>
<td>≥ 16</td>
<td>Very Superior</td>
</tr>
<tr>
<td>120-129</td>
<td>14-15</td>
<td>Superior</td>
</tr>
<tr>
<td>110-119</td>
<td>12-13</td>
<td>High Average</td>
</tr>
<tr>
<td>90-109</td>
<td>8-11</td>
<td>Average</td>
</tr>
<tr>
<td>80-89</td>
<td>6-7</td>
<td>Low Average</td>
</tr>
<tr>
<td>70-79</td>
<td>4-5</td>
<td>Borderline</td>
</tr>
<tr>
<td>≤69</td>
<td>1-3</td>
<td>Extremely Low</td>
</tr>
</tbody>
</table>
**Language**

- **Naming**
  - Boston Naming Test
  - Visual Naming Test
  - Auditory Description Naming

- **Fluency**
  - Phonemic (letter)
  - Semantic (category)

- **Repetition**

- **Verbal Comprehension**
  - Token Test

**Visuospatial Skills**

- **Perception**
  - Judgment of Line Orientation
  - Line Bisection

- **Construction**
  - Block Design
  - Rey-Osterrieth Complex Figure

**Processing Speed**

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

  - Digit Symbol / Coding
  - Symbol Digit Modalities Test
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

- 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

Executive Function Measures

- Concentration / Sustained or Focused Attention
  - Continuous Performance Test
  - Stroop Tests
  - Organization
  - Problem Solving
  - Most tests index Dorsolateral/superior medial prefrontal function

Memory

- Verbal Memory
  - Stories / Prose Passage / Logical Memory
  - Word Pairs
  - Word List Learning (California Verbal Learning Test)

- Visual Memory
  - Design Recall / Visual Reproduction / Brief Visual Memory Test
  - Face Recognition
  - Scenes / Family Pictures

- 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

**Emotional Functioning**

- Self Report Questionnaires
  - Anxiety
    - Beck Anxiety Inventory
    - State-Trait Anxiety Inventory
  - Depression
    - Beck Depression Inventory
    - Center for Epidemiological Studies Depression Inventory
    - Neurological Disorders Depression Inventory for Epilepsy
- Personality Style
  - Minnesota Multiphasic Personality Inventory
  - Personality Assessment Inventory
- Family Report
More on the MMPI

- Validity scales
  - L - Lie
  - F - Infrequency
  - K - Defensiveness
- Clinical scales
  - Hypochondriasis (Hs)
  - Depression (D)
  - Hysteria (Hy)
  - Psychopathic deviate (Pd)
  - Masculinity/Femininity (Mf)
- Content and Supplemental Scales
  - Conversion “V” (high Hs, low D, high Hy)


Evaluating Cognitive Change Over Time

- Compare differences in mean test scores from baseline to retest among patient groups and controls
- Examine individual change using difference scores
- Factors that can affect Time 2 performance independent of any intervention:
  - normal test score variability and measurement error
  - practice effects
  - regression toward the mean
  - demographic variables (e.g., age, education)
  - seizure variables (e.g., age at onset, duration of epilepsy)
- To accurately assess “true” cognitive change, extraneous factors must be controlled
  - Reliable Change Indices and Standardized Regression Based Change Scores.


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
RCIs vs. SRBs

- Predictive accuracy similar for both measures
- RCIs are simpler to use in clinical practice because they only require calculation of basic test-retest differences, which are directly compared to established cut-off scores
- Some epilepsy researchers prefer the SRB approach
  - Takes presurgical test performance into account
  - Does not assume equal practice effects for each individual
  - Provides a common metric allowing direct comparison of change across many cognitive measures in a battery


Indications for Cognitive Assessment

- Document cognitive abilities (strengths/weaknesses)
  - Cognitive complaint or change
  - School / work performance
  - Disability
  - Competency
- Impact of seizures on cognitive functioning
  - Lateralization / localized deficits
  - Indications re: language dominance
- Establish a baseline to assess change following intervention
  - Medication change
  - Epilepsy surgery

Cognitive Effects of Antiepileptic Drugs

- Dependent on host of factors
  - Type of drug — Serum level — Duration of treatment
  - Dosage — Drug interactions — 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)
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