Evaluation of the Person with Epilepsy: Neuropsychological Evaluation

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Learning Objectives:
At the end of the epilepsy fellowship the fellow will understand the importance of incorporating neuropsychological evaluation into the care of children with epilepsy by meeting the following objectives:

1. Know the purpose of neuropsychological evaluation in order to pose appropriate referral questions.
2. Recognize the components of a neuropsychological evaluation in order to be able to extract information most relevant to epilepsy treatment planning.
3. Develop a working knowledge of the literature for neuropsychological outcomes by seizure type in order to anticipate as early as possible comorbid neuropsychological problems.
4. Recognize the role of neuropsychologist in mapping cognition through different techniques.

What is a neuropsychological evaluation?

Neuropsychology is the study of learning and behavior in relationship to the brain. It is a framework that draws from neurology, neuroanatomy, cognitive sciences, and clinical, social, developmental, and biological psychology. A neuropsychologist has earned a PhD in clinical psychology and completed 2 years of specialized postdoctoral training. As with other disciplines, it is critical that with pediatric evaluation, the brain is understood in the context of developmental change.

Purpose of a neuropsychological evaluation:

There are several reasons people with epilepsy might undergo neuropsychological evaluation:

- Obtain a profile of neurocognitive strengths and weaknesses
    - Measure presence and degree of behavioral and cognitive difficulties
    - Identify strengths to inform treatment planning
- Determine if there is evidence for lateralization of localization of dysfunction/function
- Measure the cognitive or behavioral impact/risk of rehabilitation, pharmacological, surgical or therapeutic interventions
    - Establish baseline of functioning for systematic comparisons across time
- Increase patient preparedness and inform items selection/protocol adjustments on an individual basis for cognitive mapping procedures: Intracarotid Amytal Test (IAT)/WADA, functional MRI (fMRI), Electro Cortical Stimulation (ECS)
- Help formulate appropriate treatment plans (educational/vocational and medical)
- Predict individual's ability to achieve success in particular settings

Components of a neuropsychological evaluation:

There are several components to an evaluation: 1) History, 2) Testing and Behavioral observations, 3) Impressions/diagnosis, 4) Recommendations. In general, there is an examination of external behavior to make inferences about brain function and structure. This is information is integrated and interpreted in the context of the patient's history to determine if any psychiatric diagnoses are present and offer recommendations.

- The history is similar to other providers where information is systematically gathered through interview with the patient and their caregivers/spouses, and record review.
- Formal testing of abilities and behavioral observations are conducted over the course of one or more office visits or, less ideally, on an inpatient basis. There are numerous neuropsychological measures available. Formal testing refers to a standardized method of administration and scoring of responses. A profile of strengths and weaknesses is derived by comparing a person's test scores to a normative population of a similar age across domains. Domains of functioning include:
    - General cognitive functioning/Intelligence Quotient (IQ)
    - Language
    - Memory & Learning
    - Attention
    - Executive-regulatory function-Processing Speed

  - Visual/Spatial/Nonverbal processing
  - Motor
  - Academic Achievement
  - Adaptive Functioning
  - Social/emotional
  - Personality

- Impressions are the summary of the profile of strengths and weaknesses and if diagnostic criteria are met based on criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) published by the American Psychiatric Association (APA). Impressions also often outline risks to the patient given their profile.
- Recommendations are offered based on the diagnoses and risks and may include further evaluation by other specialties, environmental/behavioral supports for school or the workplace, resources including websites, apps, or books, and treatment including pharmacological consultation or therapy.

Neuropsychological outcomes in epilepsy: General Themes

The literature on neuropsychological outcomes is extensive and expanding. This overview represents a summary and general conclusions, and is by no means exhaustive.

- It is long recognized that persons with epilepsy have greater incidence of cognitive and psychiatric comorbidities (Gowers 1881).
- Consistent with the heterogeneity of seizure disorders, but even often within a single type of epilepsy, no single cognitive profile exists for epilepsy.
- Seizures (focal or generalized) may impact functioning across any or all domains.
- Focal epilepsy does not necessarily equate to focal deficits. Although there are some findings that focal epilepsy is associated with focal deficits, this is true for adults more than children likely due to the plasticity of children's brains. Therefore, children do not follow adult profiles. Moreover, even though focal epilepsy may result in a deficit related to the location of the epilepsy, this is often not the only deficit that the person is contending with. For example, a person with left temporal lobe epilepsy may have verbal memory difficulties, but also has inattention and slow processing speed.
- Cognitive difficulties may predate and/or persist beyond onset, which may indicate that cognitive difficulties may share a common underlying neuroanatomic substrate with what is generating the seizures.

- Progressive deterioration of cognitive skills is observed in a minority of individuals. As such, a plateau and/or regression of skills is a strong impetus for surgery; in particular for hemispherectomy, but any other resection as well.

Neuropsychological outcomes in epilepsy: By Domain

Intelligence

Approximately 1/3 of people with epilepsy have IQ scores below 70, which falls in the Intellectually Deficient (ID—formally MR) range. The majority (≈2/3) of people with epilepsy have average range (or higher) intelligence. Nonetheless, even taking this cohort—excluding the 1/3 with IQ<70)—there is a downward shift of IQ with a Mean IQ (≈90) which falls in the Low Average range compared to the normal population where Mean IQ=100.

Language

Along with memory, language is one of the most studied domains in people with epilepsy given that focal epilepsy is most often in the temporal, followed by frontal lobes.

- Language representation: there is a higher incidence (25-30%) of atypical dominance (right or bilateral) than the normal right-handed population (5%).
- Atypical language dominance is more likely with large, early in development insults (e.g. perinatal stroke), with earlier onset, and with left-handedness.
- If language remains ipsilateral to focus, a left hemispheric focus may have impact on language functions (speeded naming)
- Strengths include appropriate simple, single word knowledge, untimed language skills
- Adults with Temporal Lobe Epilepsy (TLE) frequently have word finding problems, which is revealed by confrontation naming tasks (e.g. Boston Naming Test), which may be related to the hippocampal role in word retrieval.
- Progressive language impairment is associated with Rasmussen's encephalitis and Landau-Kleffner Syndrome; both of which have a period of normal language development.

Memory

Similar to language findings, memory difficulties are commonly associated with TLE.

- Presence of mesial temporal pathology and degree of hippocampal atrophy is associated with greater impairment
- "Material specificity" of memory problems is true more so in adults such that left TLE is associated with verbal memory problems. Similarly, right TLE is associated (but not as strongly) with visual memory problems. This finding is the basis of the utility of presurgical evaluation by providing evidence for location of seizure focus and determining the risk of post-surgical cognitive deficits. Paired associate learning paradigms tend to be the most predictive of hippocampal dysfunction.
- Unlike for other areas of functioning, there is evidence for progressive loss with continued seizures which is consistent with the changes seen on MRI
- One hypothesis of why memory deficits are not specific to TLE is that memory performance may also be disrupted due to other skills such as poor organization or attention that rely on frontal lobe functions.

Attention/Executive Functions

Beyond the effects of IQ, attention problems are commonly observed.

- Prevalence of ADHD is 20-40%
- ADHD Inattentive Presentation is more common and boys and girls are equally represented, which is different from general developmental ADHD populations
- There may be higher rates of attention problems with FLE and CAE.
- Associated issues like nocturnal seizures or medication side effects may be primary cause of inattention
- Myth buster: Stimulants used for ADHD symptoms will lower seizure threshold. Many studies have shown this to be untrue. Thus, epilepsy is not a contraindication to treating ADHD symptoms.
- Executive functioning (EF), a set of skills that are necessary for efficient and goal-directed behavior is a common difficulty. Aspects of EF that are shown to be impaired in people with epilepsy include shifting, cognitive flexibility, working memory, organization.

Visual/Spatial

Findings are less consistent for visuospatial skills such as object recognition, drawing objects, visual closure, etc. While some studies have found these to be lower in right-hemispheric seizure foci, others have noted that language dominance may be an important factor. If language function has reorganized to the right related to a left hemispheric focus, a deficit in visuospatial processing may develop because the transfer of language to the right hemisphere is displacing visuospatial function to preserve language. This is referred to as the "crowding hypothesis."

Psychomotor/Reaction Time

Slowed processing speed is a common finding in people with epilepsy and may be due to neuroanatomic anomalies or treatment effects.

- Processing speed deficits are the most common side effect of AEDs. Slower speed is associated with polytherapy (defined by load or toxicity as well as number) and type of AED (topiramate; phenobarbital; GABA-ergic inhibition)
- Seizure type has been implicated, particularly FLE and Benign Rolandic Epilepsy

Academic Functioning/Vocation

Poor academic achievement is associated with all epilepsy types. Outcome is moderated by psychosocial variables. As with other cognitive skills, problems may predate seizure onset; however, should seizure control disrupt school attendance, there may be a larger gap following seizure onset.

- More recent long-term outcome studies show that seizure control is the most important predictor of outcome such that ongoing seizure activity is associated with worse outcome

Psychosocial

There are increased rates of mood disorders (anxiety/depression) with a lifetime prevalence risk of 35%.

- Limbic/temporal seizures have greater risk, which may be an evidence of shared neurophysiology
- Less clear evidence of increased rates of aggression or psychosis
- Evidence for both environmental causes (stigma, missed school/work, unpredictability/lifestyle changes) and shared neurophysiology (higher rates than other medical disorders)

Impact of specific epilepsy characteristics:

There are multiple factors that combine to determine neuropsychological outcome. Those that are often studied include: Age of onset, Seizure type/Seizure location, Seizure frequency, Underlying pathology, Neuronal discharges (ictal and interictal), Episodes of status, Antiepileptic drugs (AEDs) (number and type).

In addition to epilepsy characteristics, there is the impact of psychosocial, socioeconomic status, and genetic factors. The challenge has been to unravel this complex picture given the lack of quality studies and challenges (e.g., suitable controls, complex interactions; sensitivity of neuropsychological test; small sample sizes/lots of tests; validity). With that caveat, some risk factors for worse outcome include:

- Generalized seizures have worse outcome than focal, and tonic-clonic seizures have worse than absence
- Earlier onset is associated with more difficulties
- Severe volumetric abnormalities
- Frequent seizures, more episodes of status epilepticus
- Polytherapy
- Comorbid diagnoses (e.g. autism)

Neuropsychologist role in mapping cognition:

Neuropsychologists often work in tandem with neurologist and the rest of the medical team to map cognition. The purpose is to localize function so as to avoid morbidity of surgical procedure.

- Techniques used to map language, memory, and motor functions are changing with available technology.
- Prior gold standard method was to pharmacologically inactivate ipsilateral anterior and middle cerebral arteries for several minutes. This procedure is referred to many ways including the intracarotid amobarbital test (IAT)/Wada or etomidate speech and memory test (eSAM), and has no standard protocol. The aims are to: 1) lateralize function (language and memory) and 2) demonstrate capacity of contralateral hemisphere to sustain function.
    - Use of IAT/Wada on the decline due to drug availability and clinical validity of fMRI

  - Consists of presenting language and memory items during a brief window (1-2 min) of drug effect; eSAM protocol allows for continuous infusion which is a distinct advantage but not widely used
  - Based on each hemisphere and in context of baseline functioning, count errors or aphasia to get an asymmetric index of functioning for language and memory
  - Disadvantages are that it is invasive, site specific methods, feasibility relies on institution
  - Advantage is that it is still best-established method for memory functioning (at this point) and is probably more widely used in adult centers for that reason

- Functional MRI (fMRI) involves having the patient do language or motor tasks while in an MRI. The Blood Oxygen Level Dependent (BOLD) signal is extracted and analyzed. There is increasing availability of fMRI packages on standard clinical systems. There is an advantage of localization and lateralization of function noninvasively; however, mapping of memory functioning is still fraught with practical and technical challenges. Disadvantage is that movement may render a study uninterpretable; however, technological advances are making progress to combat this.
- Electrocortical stimulation (ECS) mapping is either intraoperative or bedside mapping (grids) of function for motor or language functions. Grids for seizure localization purposes are not discussed here. Again, no standardized protocol exists; however, in general, language responses must be brief enough to occur during the stimulation timeframe, so they may be limited to single words. The patient must also be able to answer questions immediately (without long pauses) at baseline to ensure accurate interpretation of pauses in responding related to stimulation.

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