The Impact of Pediatric Epilepsy Surgery on Cognition

Mary Lou Smith, PhD

UNIVERSITY OF TORONTO MISSISSAUGA

SickKids

Every child deserves a healthy start, a strong mind and a bright future

SickKids | Centre for Brain & Mental Health

Quality of Life in Pediatric Epilepsy

(Arunkumar et al., 2000)

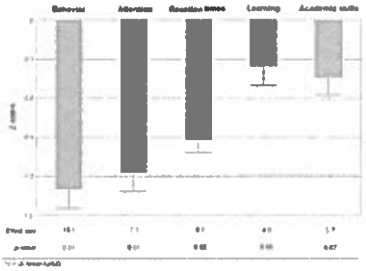
Parents	Children
• AED side effects	• Social problems
➢ *Cognitive effects*	➢ *Cognitive effects*
• Future	• Driving
• Injury	• Sports restrictions
• Independence	• AED side effects
• Brain damage	• School
• Dependence	• Dependence
• + others	• + others

Epilepsy: Prevalence of Cognitive Comorbidities

- Intelligence
  - Intellectual disability – 25-40 %
  - Mild or subtle intellectual deficits - 30%
- Learning disabilities / Academic problems
  - 70 % – low achievement
  - 40 % – underachievement
- Attention
  - 30% ADHD
- Executive functions
  - 30%

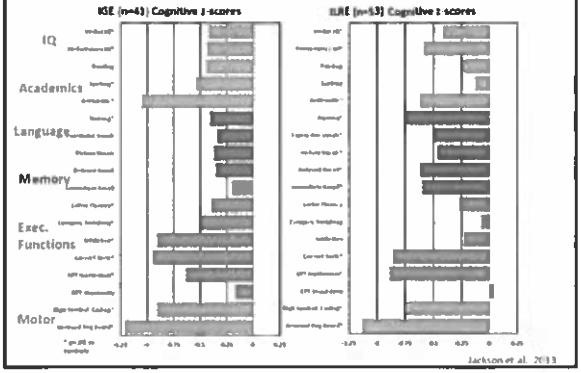
Can we put all the blame on seizures?

New Onset Idiopathic Epilepsy: Prior to Medication Treatment



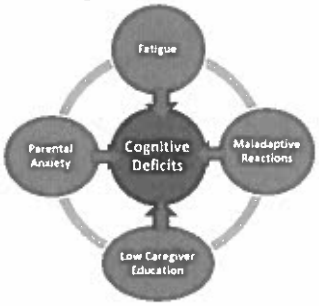
Oostrum et al., 2003

Cognitive Performance by Epilepsy Syndrome



Jackson et al., 2013

Other Factors Contributing to Cognitive Deficits



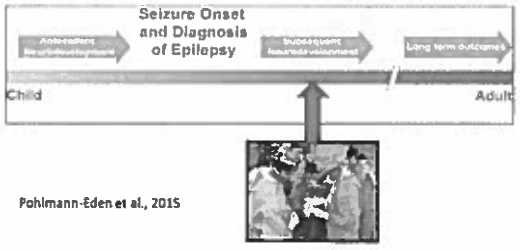
Does a treatment intended to eliminate seizures result in improved cognition?

- Epilepsy Surgery

  30% of people with epilepsy are medically intractable

  Of these, approximately 1/3 are surgical candidates

Disentangling the contributing epilepsy factors from preexisting and ongoing neurodevelopmental processes



Pohlmann-Eden et al., 2015

Arguments for early surgery

- The cognitive and psychosocial sequelae of epilepsy may not be as entrenched in childhood as they would be later in life, and earlier intervention is a form of prevention.
- Seizures interfere with brain functioning and their elimination will increase the likelihood of achieving optimal cognitive and psychological attainments.
- The capacity for plasticity in the young brain will allow for restitution or reorganization to support further development.
- Change in cognition after epilepsy surgery in children ??

Possible outcomes of epilepsy surgery with respect to cognition

Improvement in performance
- Elimination/reduction of seizures
- Ongoing development

No change

Decline in performance
- Removal of functional brain tissue
- Ongoing development

Evaluating the outcome of surgery

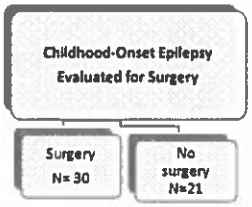
- Has surgery altered the course of development as it would have unfolded had the child continued to have seizures?
- Importance of comparison groups

Impact of Epilepsy Surgery:

- Comorbidities studied in our research program
  - Cognitive
  - Emotional
  - Behavioural
  - Social
  - Quality of Life

Pediatric surgical patients – prospective, longitudinal study

- Surgery < 18 years
- Comparison group evaluated for surgery < 18 years
- Follow-up at 1 and 2 years



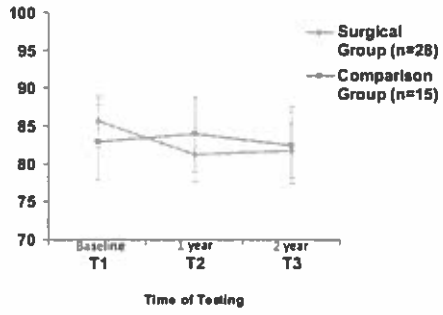
Longitudinal Study: Cognitive Measures Outcomes 1 & 2 years after surgery

- Intelligence
- Verbal Memory
  - Stories
  - Word Lists
- Visual Memory
  - Faces
  - Design
- Academic Skills
  - Reading
  - Reading Comprehension
  - Spelling
  - Arithmetic
- Sustained Visual Attention
  - Without
  - With distraction

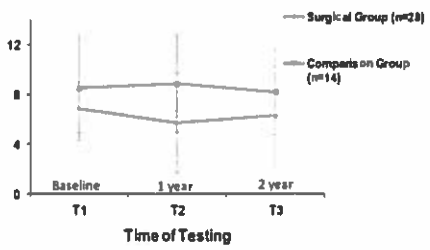
Analyses and Results

- ANOVAs were conducted with the following independent variables
  - Group (Surgical, Non-surgical)
  - Time (Baseline, 1 and 2 years later)
- Most common finding was a Time Effect
- No Group x Time Interactions to suggest a specific effect within the surgical group
- 3 major patterns in the data

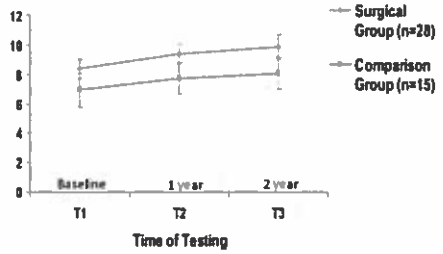
Intelligence over Time



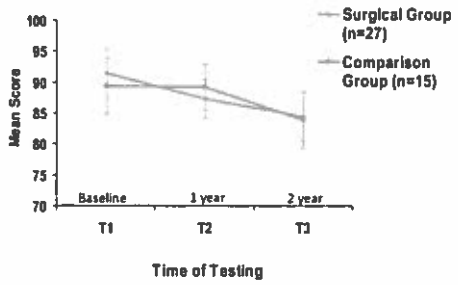
Story Recall over Time



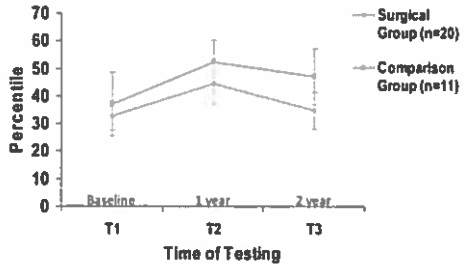
Face Recognition over Time



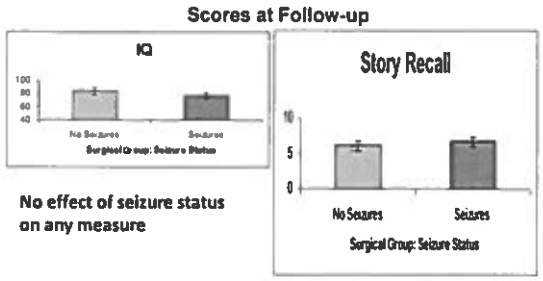
Reading Comprehension over Time



Sustained Visual Attention Over Time



Does Seizure Outcome Make a Difference?

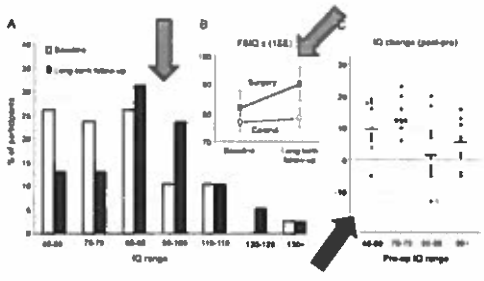


No effect of seizure status on any measure

Summary

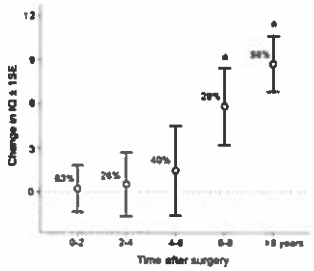
- No impact of seizure cessation
- Other factors that may contribute to cognitive comorbidities are not changed by surgery
- Co-morbidities are present at baseline
- Role of the underlying abnormal neural substrate
- BUT: Do we need more time?
  Later rather than sooner?

Temporal Lobectomy - Changes in Intelligence



Skirrow et al., 2011

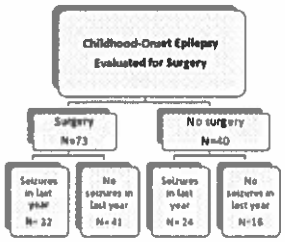
Profile of IQ Change Over Time



Skirrow et al., 2011

Pediatric surgical patients – long-term follow-up

- Surgery < 18 years
- Comparison group evaluated for surgery < 18 years
- Follow-up of 4-11 years
- Surgical and control Ss had baseline data
  - longitudinal analyses



Surgical and Non-Surgical Groups

Heterogenous - Site of Surgical Resection - Pathology

- Age (baseline, follow-up)
- Age at seizure onset
- Sex
- Laterality of focus
- Cognition at baseline
- Focality of seizures
- # AEDs at follow-up (related to seizure outcome)

No differences | Differences

Participants

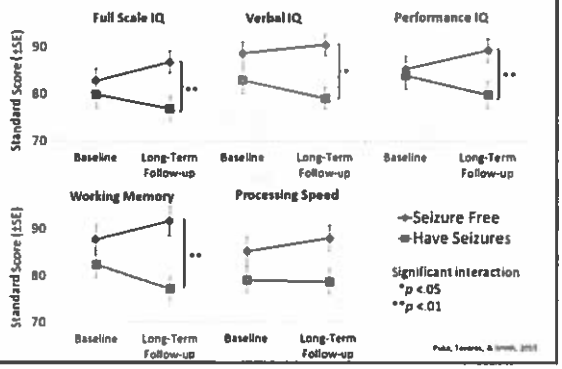
	Surgicals	Controls	*P* value
N	73	40	
Sex (Male, %)	41.09	32.50	0.37
Age at baseline (SD)	12.13 (4.31)	12.82 (3.23)	0.34
Age at follow-up (SD)	19.87 (4.46)	20.31 (4.01)	0.60
Duration of follow-up (SD)	7.67 (2.35)	7.35 (2.25)	0.48
Seizure free (%)	56.16	40	0.10
Temporal lobe (%)	43.84	30	0.15

Long-Term Follow Up

Intelligence and Memory

No effect of surgical status

Intelligence



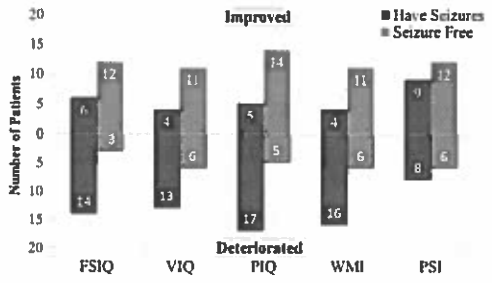
Predictors of Change

Lower scores at baseline → improvements in all indices

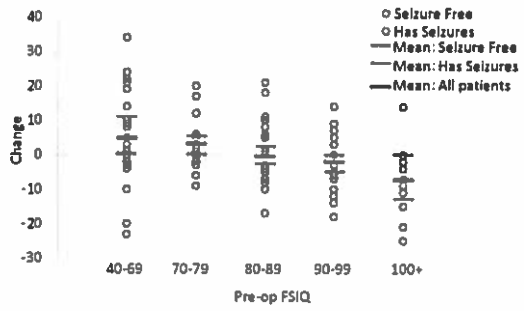
Temporal lobe resections → improvement in Processing Speed

Older age at follow-up → improvement in Performance IQ

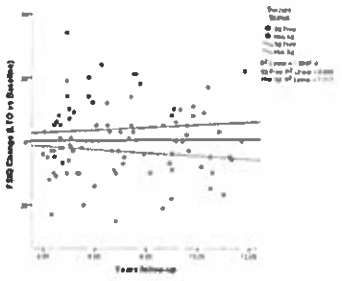
Meaningful Change in IQ Score



FSIQ: Change vs. Pre-op Score



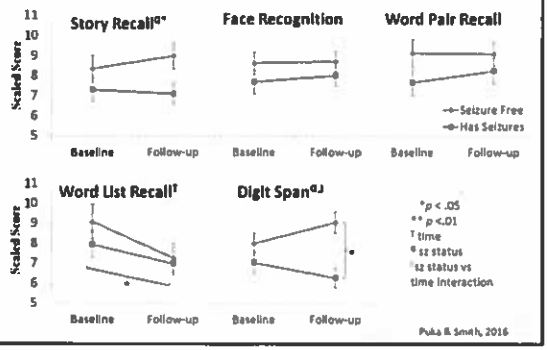
FSIQ: No Relation of Change and Length of Follow-Up



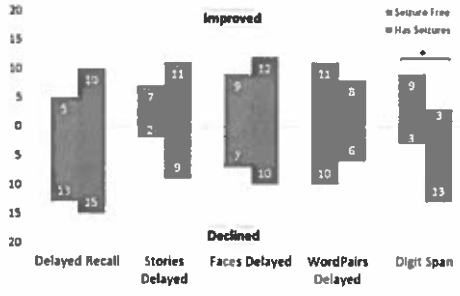
Memory

- Story Recall
- Word List Learning / Recall
- Paired Associate Learning / Recall
- Face Recognition
- Digit Span

Change over Time



Meaningful Change

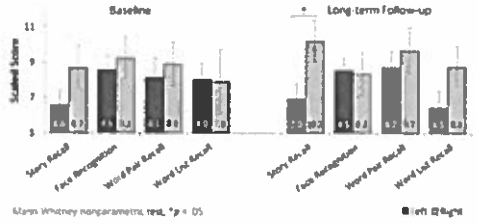


Predictors of Change

Lower baseline scores → greater improvement on all tasks

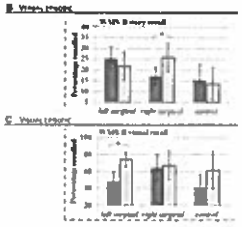
Older age at surgery → greater improvement in story recall

Long-term Outcome After Epilepsy Surgery Temporal Lobe Resections



Puka & Smith, 2016

Long-term outcome of memory after temporal lobectomy



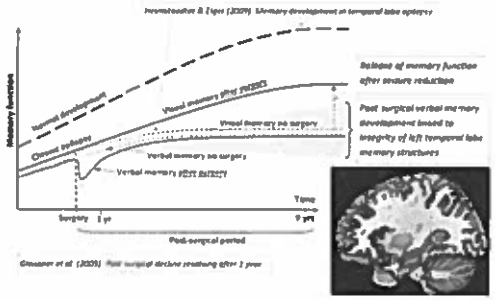
Verbal: Improved in right-sided cases

Visual: Improved in left-sided cases

Barrow C et al. Brain 2015;138:80-93

BRAIN

A diagrammatic overview of memory change before and after left temporal lobe surgery in children



Barrow C et al. Brain 2015;138:80-93

BRAIN

Summary

- No effects of surgery
- Minimal number of effects related to seizure outcome
- Require closer examination of brain structure
- There may be subgroups of children who show improvements - site, laterality

Disentangling the contributing epilepsy factors from preexisting and ongoing neurodevelopmental processes