Autism Spectrum Disorders and Epilepsy

Roberto Tuchman, M.D.
Director, Brain Development Network
Miami Children’s Hospital Dan Marino Center
Department of Neurology and Psychiatry & Behavioral Health
Herbert Wertheim College of Medicine, FIU

Autism Spectrum and Epilepsy Clinical Overlap

Prevalence study using the nationwide Norwegian Patient Register (n=731,318)
All diagnoses in this study were confirmed by specialists
11.2% of children with ASD had Epilepsy
6.1% of children with Epilepsy had a co-existing diagnosis of ASD


Epilepsy in Autism Spectrum Disorders

In a meta-analysis of 24 reports on autism and epilepsy published from 1963 to 2006: Pooled prevalence of epilepsy

- 21.4% in 1485 individuals with autism and intellectual disability (IQ < 70)
- 8% in 627 persons with autism without intellectual disability (IQ >70)


Increased morbidity & mortality when Epilepsy and ASD co-exist

Pickett, J., et al. (2011). "Mortality in Individuals with Autism, with and without Epilepsy." J Child Neurol

Cumulative risk 67% by age 10 in ASD + severe ID & CP
Cumulative risk 27% by age 10 in children with ASD + severe ID
Cumulative risk 6% by age 10 ASD No ID
8% in the language impaired non-ASD


McVicar, K. A., et al. (2005). “Epileptic encephalopathy: a condition in which the epileptiform abnormalities themselves are believed to contribute to the progressive disturbance in cerebral function”


Epileptic encephalopathy

"a condition in which the epileptiform abnormalities themselves are believed to contribute to the progressive disturbance in cerebral function"


Epilepsy in 22% of individuals; mean age of seizure onset was 13.3 years, the majority was post age 10 years

Epilepsy more common in those with intellectual disability, low levels of language, and in females

Presence of epilepsy in the proband was a significant predictor of a relative having the broader autism phenotype


Cross-sectional study using four samples of ASD children: Total n=5,815

average prevalence of epilepsy was 15% and reached 28% by adolescence

multivariate regression model: only age and cognitive ability were independently associated with epilepsy

Children age 10 or older had 2.35 times the odds of being diagnosed with epilepsy (p<.001) and for a one standard deviation increase in IQ, the odds of having epilepsy decreased by 47% (p<.001)


N=577 11% with epilepsy (n=64)

Cluster 1: epilepsy: 11%—most developmentally impaired (global developmental disorder)

Cluster 2: epilepsy 29%

earliest age of ASD recognition

greatest rate of repetitive object use and unusual sensory interests

late onset of first words

high frequency of gross motor coordination problems

Cluster 3: epilepsy: 11%----- language regression

Clusters 4 and 5: epilepsy: 8%----- least cognitive impairment
Research Questions Epilepsy in ASD

Early identification of children with ASD at risk to develop Epilepsy?

ASD is not an Epileptic Encephalopathy (EE) however why does ASD frequently travel along with EE?

What is the contribution, added effect, of epilepsy or Interictal Epileptiform Discharges (IEDs) on the development of ASD?


Epilepsy in ASD: How often do Autism Spectrum Disorders occur in Epilepsy?

32% of 97 children with epilepsy screened positive for ASD

15% of 519 patients with epilepsy had ASD

37% of 65 children, average age 2.5 years, screened positive for ASD

21% of 85 children with active epilepsy had ASD

Autism Spectrum Disorder (ASD) in Epilepsy

Prospective Community Based Study (n=555)
(Connecticut Epilepsy Cohort)

5% met criteria for ASD
10% of those whose seizures start in the first 2 years met criteria for ASD
13.8% in those with IQ less than 80 met criteria for ASD
2.2% with normal cognitive abilities met criteria for ASD
West syndrome (Infantile Spasms) 30% with ASD, intellectual impairment, male sex independently associated with ASD
Younger age (of seizures) at onset did not contribute independently to ASD


First Epilepsy than Autism Spectrum Disorder (ASD)
(Epilepsy in first year of life)

7% of 84 children with seizures in the first year of life diagnosed with ASD all with intellectual disability
35% (n=6) of 17 children with Infantile Spasms* diagnosed with ASD
5 other etiologies (symptomatic) and 4 with severe intellectual disability


Autism Spectrum Disorders in Epilepsy

Nationally representative population-based study (n=7,403)

ASD in population of individuals with epilepsy 16 years and older was 8.1%.

After adjusting for verbal IQ, an individual with epilepsy had a sevenfold increase in the odds of having an autism spectrum disorder


Research Questions ASD in Epilepsy

Early identification of children with Epilepsy at risk for ASD?

What is the contribution, added effect, of ASD on children with Epilepsy?

Why do children some children with Epilepsy and ID or with an Epileptic Encephalopathy not develop ASD

Identification of protective factors.

What we need to understand

Does epileptic activity contribute to worse outcomes above and beyond what would be expected from the underlying etiology?

Pathophysiology (Risk Process)

- Intellectual Disability
- Sociogenesis

Epilepsies
- Altered neuronal networks (structural and molecular connectivity)
- Altered neuronal excitation/inhibition


SHARED MECHANISMS

Interventions:
- Behavioral (EIBI)
- Pharmacological/AEDs/
  Immune modulators/
  Molecular treatments:
  - MTor
  - AMPA Receptor
  - NMDA Receptor
  - Shank 3 mutations
  - FMRP
  - MECP2

Lippman-Row, J. E., et al. (2013). “AMPA receptor antagonist NMDA receptor-selective late-life epileptic seizures and autistic-like social deficits following neonatal seizures.” Epilepsy