Autism & Epilepsy: Which Comes First?

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No Disclosures
Learning Objectives

Autism and Epilepsy

- Shifting Perspectives & Common Mechanisms
- Which comes first Autism or Epilepsy
- Clinical and Research Synergies
Autism and Epilepsy: Shifting Perspectives

Neurodevelopmental Disorders

Happe, F., et al. (2006). "Time to give up on a single explanation for autism." Nat Neurosci

Epilepsy, like autism, is increasingly being described as a spectrum disorder


multiple etiologies
variable clinical symptoms
variable outcomes
Epilepsy and Autism Commonly Co-exist

Mouridsen, S. E., et al. (2011). "A longitudinal study of epilepsy and other central nervous system diseases in individuals with and without a history of infantile autism." Brain Dev


Increased morbidity and mortality


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

Common Mechanisms: Common Number Variants (CNVs)

Common recurrent microdeletions associated with generalized epilepsy seen at a frequency of 1% at 15q13.3, 16p13.11, and 15q11.2.

These three regions have been tied to multiple neurobehavioral phenotypes including epilepsy, autism, intellectual disability, and schizophrenia.

Intellectual Disability

Epilepsy

Autism Spectrum Disorders

**SHARED MECHANISMS**

Risk Factors: risk genes
Risk Process: (Epileptogenesis-Sociogenesis)
Altered neuronal excitation/inhibition (interneuron)
Altered neuronal networks
Altered pattern of interaction between child and environment

**INTERVENTION**

mTOR pathway

**Behavioral**

specific synaptic or other molecular pathways
Which comes first
Definitions: Autism Deconstructed

- RRBIs
- Motor
- Language
- Intellectual Disability
- Social Interaction
- Social
Which comes first: Joint Attention

capacity of individuals to coordinate attention with a social partner in relation to some object or event

begins to emerge by 6 months of age

eyearly and critical foundation
language & social cognition
After 6 months......

ASD group shows a rapid decline in

eye contact
social smiling
examiner-rated social responsiveness

By 12 months.....

Not Responding to Name by 8 to 12 months

Pointing or Gestures by 12 months

Responding to Joint Attention by 12 to 18 months

Repetitive Actions

Unusual Sensory Responses


Epilepsy in Children with ASD
Pediatrics

AGE AT TIME OF SEIZURE (Years)

0  5  10  15  20  25  30

0  0.2  0.4  0.6  0.8  1.0

Infantile Spasms
Epileptic Encephalopathy
ongoing neurological process
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 versus
8% in 627 persons with autism without intellectual disability

Amiet, C. et al., Epilepsy in autism is associated with intellectual disability and gender: evidence from a meta-analysis. Biol Psychiatry 2008
Autism spectrum disorders in children with seizures in the first year of life - a population-based study. Epilepsia

7% with ASD all with intellectual disability

Risk of autism spectrum disorders after infantile spasms: a population-based study nested in a cohort with seizures in the first year of life. Epilepsia

Overall 14% with ASD
ASD in 46% of those with Infantile Spasms
ASD in 69% of those whose seizures were associated with brain insults

Saemundsen, E., P. Ludvigsson, et al. (2007)

- 5% met criteria for ASD
- 10% of those whose seizures start in the first 2 years of life 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
Clinical and Research Synergies

ILAE-AS Task Force
Key Points

- Identify infants with seizures at risk for autism and those with autism at risk for epilepsy
- Identify genetic and environmental risk factors common to epilepsy-autism
- Explore the underlying mechanisms of convergence between autism and epilepsy
Key Points

- Coordinate tissue and brain banking efforts in epilepsy-autism

- Develop treatment models behavioral and pharmacological in infants with epilepsy-autism (or at risk for autism)
The NINDS, in conjunction with Autism Speaks and CURE, will host a workshop in the spring of 2012

**Research Agenda**

Coordination of Resources

Common Mechanisms

Treatment approaches