2014 IACC Workshop on Under-Recognized Co-Occurring Conditions

Epilepsy and ASD

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objectives

Who are we talking about?

What are the clinical and biological relationships between ASD and epilepsy?

How do we address research and treatment in this population?

VIEWS & REVIEWS

NINDS epilepsy and autism spectrum disorders workshop report

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ABSTRACT

The association of epilepsy and autism spectrum disorders (ASD), although well-recognized, is poorly understood. The purpose of this report is to summarize the discussion of a workshop sponsored by the National Institute of Neurological Disorders and Stroke, with support from the National Institute of Child Health and Human Development, Autism Speaks, and Citizens United for Research in Epilepsy, that took place in Bethesda, Maryland, on May 29 and 30, 2012. The goals of this workshop were to highlight the clinical and biological relationships between ASD and epilepsy, to determine both short- and long-term goals that address research and treatment conundrums in individuals with both ASD and epilepsy, and to identify resources that can further both clinical and basic research. Topics discussed included epidemiology, genetics, environmental factors, common mechanisms, neuroimaging, neuropathology, neurophysiology, treatment, and research gaps and challenges in this unique population. *Neurology*® 2013;81:1630–1636

Individuals with both ASD & epilepsy

These are common disorders with extensive overlap

Prevalence of epilepsy in ASD is affected by ID and age

21.5% if ID is present, 8% if IQ> 70 *(Amiet et al Biol Psych, 2008)*

Increase in epilepsy in adolescence *(Woolfenden et al,* Dev Med Child Neurol, *2012)*

Highest risk in people with ID

Prevalence of ASD in epilepsy

Pediatric population: 4- 5% (Geerts et al. Epilepsia 2011, Berg et al, J Child Neurology 2011)

Sevenfold increase in odds of having ASD if you have epilepsy (Rai et al, Epilepsia, 2012)

Highest risk in people with ID

What causes them to occur together?

Early Neurodevelopment

High rates of synaptogenesis

Rapid maturation of synaptic plasticity mechanisms

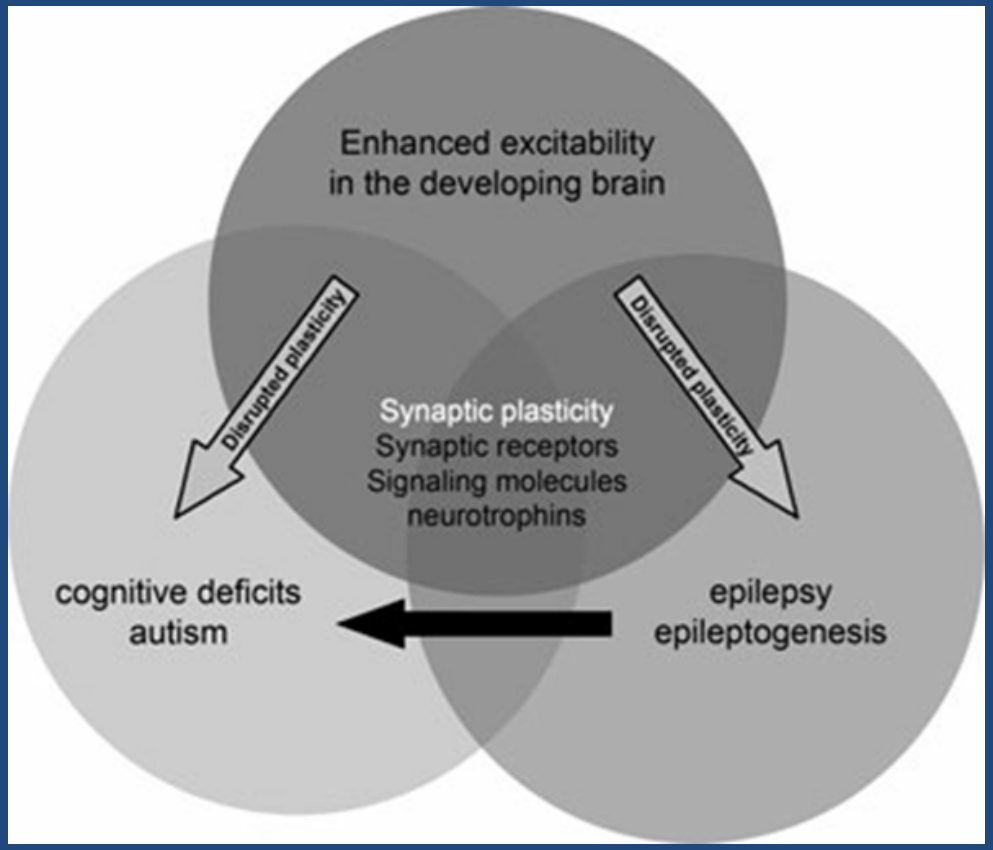
Excitatory mechanisms>>inhibitory *(Rakhade & Jensen et al, 2009)*

ASD, Epilepsy *PLUS* Intellectual Disability

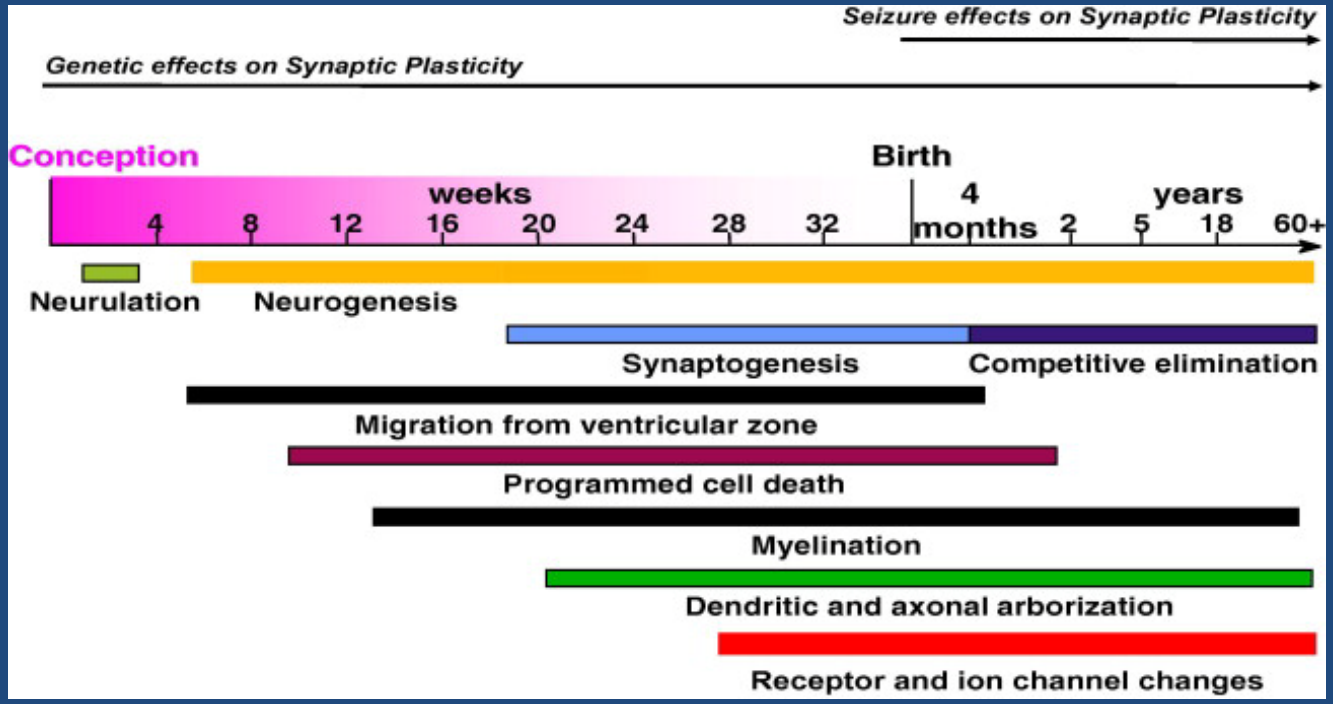
- When in same person may represent a primary disruption (genetic, early insult) in synaptogenesis causing both ASD and seizures
- Seizures themselves may be the primary disruption resulting in both cognitive impairment and ASD
- Seizures may further exacerbate cognitive impairment in ASD

Autism Spectrum Disorders and Epilepsy

The association between epilepsy and autism spectrum disorders is both well recognized and not well understood



Epilepsia ILAE



Amy Brooks-Kayal

Epilepsy and autism spectrum disorders: Are there common developmental mechanisms?

Brain and Development, Volume 32, Issue 9, 2010, 731 - 738

http://dx.doi.org/10.1016/j.braindev.2010.04.010

What Can Research on Syndromes tell us?

Single gene disorders with high occurrence of ASD and epilepsy

TSC

FXS

RTT

Through various pathways, the end common result may be a marked imbalance in the excitatory/inhibitory brain circuits in the developing brain predisposing to ASD, epilepsy *and* ID (Fu et al, Stafstrom , 2012, Mcleod 2013)

Summary
What We Know

Both ASD and Epilepsy are spectrum disorders

Both may be conceptualized as disorders of neural connectivity resulting from dysregulation of synaptic plasticity

Comorbidity with ID increases the risk of having the other

Summary
What we want to know more about

Better characterization of the seizure patterns in ASD

What is the role of ID in outcomes in ASD, in epilepsy and in ASD-epilepsy phenotypes?

Is there a critical window for intervention that can arrest or reverse the dysfunction in neural circuitry?

Summary
What we need or next steps

Put newly identified ASD genes in context with what is known about molecular pathways and brain circuitry

Better animal models

Effective collaborations across labs

Models to identify and correct neural dysfunction in populations with both ASD/epilepsy and include people with ID