Autism Spectrum and Epilepsy

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co-occurrence of epilepsy and autism

- Autism and epilepsy often co-occur.
- Seventy-four studies reporting on 283,549 patients were included in this systematic review. The median overall period **prevalence of epilepsy in people with autism was 12.1%** while the median overall period **prevalence of autism in people with epilepsy was 9.0%** when including all population types

The co-occurrence of epilepsy and autism: A systematic review/ Epilepsy & Behavior, Volume 98, SEP, 01, 2019

- These findings highlight the **importance of screening** for autism in people who have epilepsy and epilepsy in people who have autism

The co-occurrence of epilepsy and autism: A systematic review/ Epilepsy & Behavior, Volume 98, SEP, 01, 2019

- **All seizure types** occur in ASD
- **Bimodal distribution of age of onset**, with peaks occurring at younger than 5 years and during adolescence
- The **prevalence** of epilepsy was 21.5% in subjects with ASD and ID compared with 8% in those with ASD and no ID
- The presence of **CP or focal motor findings** also increases risk

- In this systematic review authors asked a number of questions. They include the following.
- Does epilepsy **cause autism**?
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- Are there **underlying brain mechanisms** that predispose to both conditions?
- What is the role of **genetics**?
- What is the importance of **environmental factors**?
- Do any of the proposed **relationships** between autism and epilepsy provide insight into useful management or treatment?
- Is the **prognosis** of either autism or epilepsy different when the other condition is present?
- What is the role of additional **comorbidities**, such as ID or ADHD?

- **Many of the issues reflected in these questions remain controversial.**

Epilepsy in patients with autism: links, risks and treatment challenges Frank MC Besag. Neuropsychiatr Dis Treat. 2018

- **Male:female ratio** of autism in those with epilepsy was close to **2:1**, compared to a ratio of 3.5:1 in those without epilepsy.
- This analysis established very clearly that **ID greatly increases** the risk of epilepsy in people with autism.

Does epilepsy cause autism?

- In certain circumstances, for example, **NCSE** and **LKS,** epilepsy may cause features that have a strong resemblance to autism.
- Autism is a pervasive developmental disorder that persists over time. If either NCSE or LKS is treated effectively, the features of autism may decrease or even resolve.

- **While on one hand**, it is important to treat the epilepsy early and effectively if it is suspected as being the cause of the autistic features, **on the other hand**, the epilepsy in most children will not be the cause of any autistic features.

Are specific epilepsy syndromes associated with autism?

- Attention should be drawn to at least two syndromes, **LKS** and **West syndrome** (infantile spasms, hypsarrhythmia and loss of skills). There is a high rate of autism in children who have West syndrome as a result of the genetic disorder, tuberous sclerosis.

Can autism cause epilepsy?

- There is **no plausible argument** for suggesting that autism could cause epilepsy. It seems that the weight of evidence now favors **a common underlying cause** for both conditions. Broadly speaking, such underlying causes could be divided into **genetic** and **environmental**.

What is the role of genetics in determining conditions that underlie both epilepsy and autism?

- With regard to autism, advances are epitomized in the title of the paper by Betancur, "**Etiological heterogeneity in autism spectrum disorders: more than 100 genetic and genomic disorders and still counting"**. Many of them would have associated with both. The lower the ID, the higher the prevalence of both epilepsy and autism.
- Much attention has rightly been given to the tuberous sclerosis. In this particular case, a new type of treatment, namely, mTOR inhibitors such as sirolimus and everolimus that **limit cell growth**, can also have an effect in **ameliorating seizures**, in at least some cases.

- Among the genetic abnormalities, there have been a number of **copy number variants**. Some of the abnormalities identified have included **1q21 deletions**, **7q11.23 deletions**, **15q11.1–q13.3 duplications**, **16p11.2 deletions**, **7q11.23 duplications**, **18q12.1 duplications** and **22q11.2 deletions**

- **Abnormalities in corpus callosum connectivity** associated with ASD, about 20% of corpus callosum abnormalities are caused by single or multiple gene mutations or by chromosomal abnormalities*(Margari et al).* In their own study of 61 patients, 4 had ASD and 36 had epilepsy.

Environmental factors

- **Some of which may be associated with ASD/Epilepsy.**
- There is evidence for a deleterious effect of **air pollution**
- protective environmental effect of **maternal folate during pregnancy**
- **Maternal rubella** during pregnancy has long been associated with a high risk of ID, ASD and epilepsy in the offspring
- **Brain damage** arising during delivery and through neonatal factors
- Many **metabolic conditions**

How should the individual with both epilepsy and autism be managed?

- First, ensure that the autistic **features are not the result** of **ESES** or **frequent epileptiform discharges**
- The **diagnosis of epilepsy** may be **more difficult in ASD with or without ID**

- Special cases, **tuberous sclerosis**, specific treatment **sirolimus or everolimus** may decrease the seizures
- Some anti-seizure drugs can have **negative effects on mood, behavior or cognition (LEV, TOP),** whereas lamotrigine tends to be a mood-leveling
- **Neuronal auto-Abs** (seizures, behavioral changes and even psychosis) and **immunomodulators**

How should additional comorbidities be treated in the presence of both epilepsy and autism?

- **ADHD is common** in children with both conditions together
- Should these children be considered for ADHD treatment?
- Some children with epilepsy present with features of ADHD that are the result of **frequent epileptiform discharges**
- Treatment with PB, BZD or Sabril can result in **inattention, distractibility and excitability**

- In those cases with underlying ADHD **standard treatment** with ADHD medication can be of **great benefit**. ADHD treatment is **very unlikely** to precipitate seizures
- About 30% of children with epilepsy have ADHD and about **70% of those with epilepsy and ADHD** will **benefit from** treatment of the ADHD with **methylphenidate**

- **Anxiety** can be **improved** with low-dose risperidone in children with both conditions
- Is epilepsy a contraindication to such treatment?
- it appears that low-dose risperidone is **very unlikely to exacerbate seizures**

- **Cognitive-behavioral therapy** and other psychologic interventions should be the first-line approach to managing anxiety
- There is a **lack of evidence** for a beneficial role of **SSRI** in treating anxiety in children with autism

- **Sleep problems:** If present in a child with both epilepsy and autism, it is clearly important to ensure that nocturnal seizures are not the reason for the sleep disturbance
- Is **melatonin** a contraindication?
- No good evidence was found
- **Animal work** suggests that melatonin might have an anti-seizure effect

Electroencephalographic Abnormalities in Autism Spectrum Disorder: Characteristics and Therapeutic Implications

- An **improvement of autism core symptoms** in patients with **SEAs and ASD** after therapy with Anti-Seizures were shown in literature
- However, in **absence of CDB studies**, it is impossible, to date, to give a final evaluation about the effectiveness and appropriateness of pharmacological treatment of SEAs

Thanks for your attention