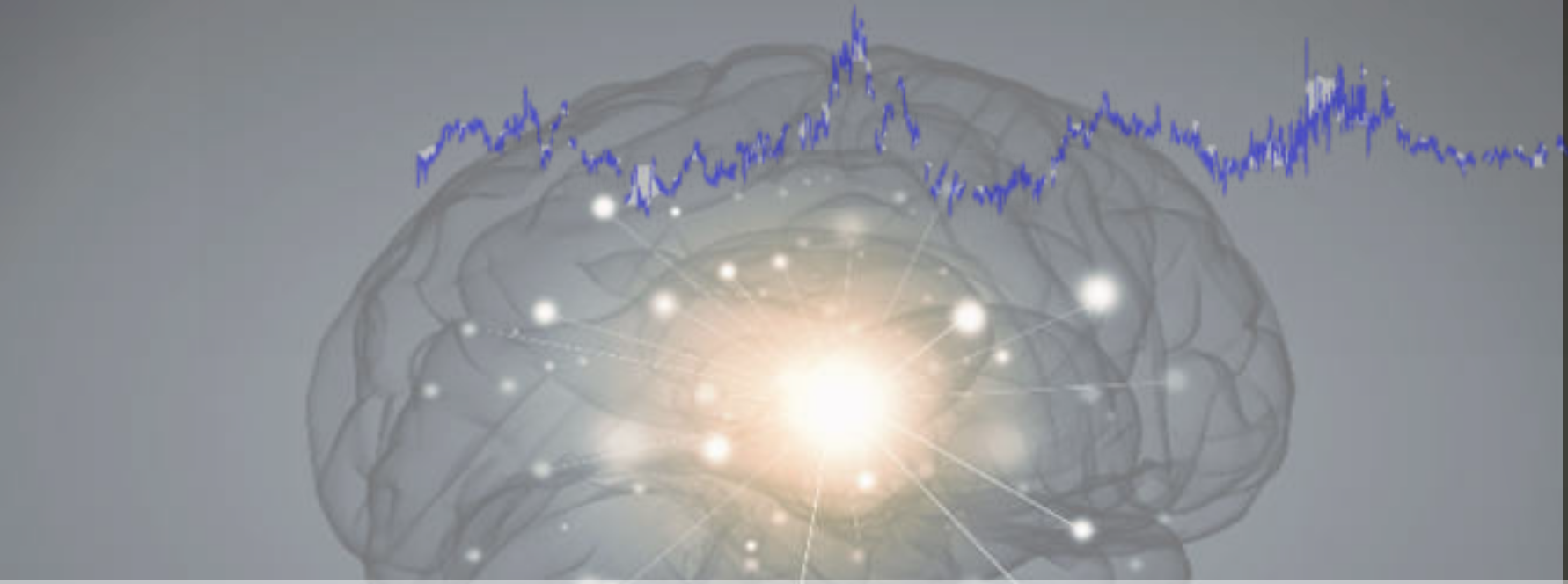

Epilepsia y salud mental en las personas con discapacidad intelectual

Dr. CARLOS PEÑA SALAZAR, MD, PhD
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Parc Sanitari Sant Joan de Déu (UHEDI) Barcelona

COORDINADORA DE CENTRES PER A PERSONES AMB DISCAPACITAT INTEL·LECTUAL DE CATALUNYA

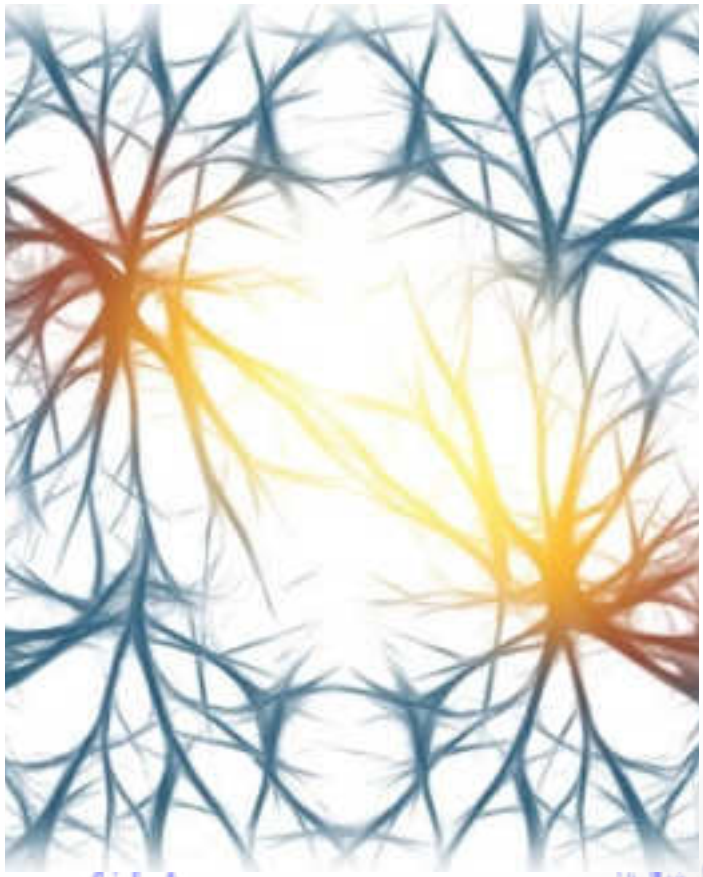

Meryl Streep
Fred Ward
"★★★★!"
"Powerful!"
"...First Do No Harm"
She Went Looking For Help...And Found A Miracle.
DVD


Y dile a Nancy que--

¿Qué es la epilepsia? ¿Y una crisis epiléptica?

- **CRISIS EPILÉPTICA**: Es la presencia transitoria de síntomas y/o signos debidos a una actividad anormal excesiva y sincrónica del cerebro (Kwan P, 2010)

- **EPILEPSIA**: Es una alteración del cerebro caracterizada por una predisposición duradera para generar crisis epilépticas y por sus consecuencias neurocognitivas, psicológicas y sociales. La definición de epilepsia requiere la aparición de, al menos, una crisis epiléptica (Kwan P, 2010)



EPILEPSIA VS CRISIS EPILÉPTICA

- ¿TODO INDIVIDUO QUE HAYA TENIDO UNA CRISIS ES EPILÉPTICO??

Diagnostic Criteria
(ILAE Epilepsia, 2014)

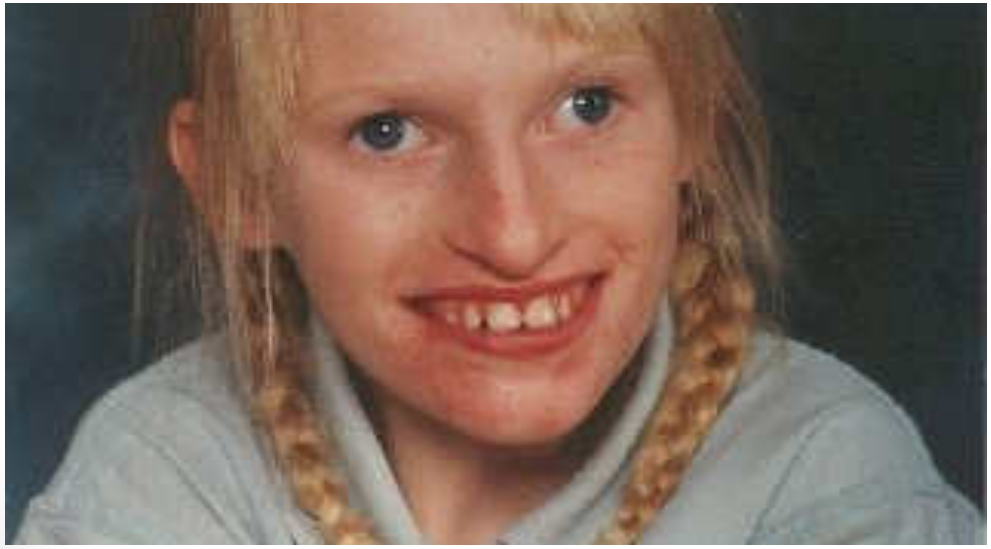
- The task force proposed that epilepsy be considered to be a disease of the brain defined by any of the following conditions:
- (1) At least two unprovoked (or reflex) seizures occurring >24 h apart;
- (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%)
- (3) diagnosis of an epilepsy syndrome.

Etiología de la epilepsia (WHO, 2007)

- Brain damage from prenatal or perinatal injuries (e.g. aloss of oxygen or trauma during birth, low birth weight)
- Congenital abnormalities or genetic conditions with associated brain malformations
- A severe head injury
- A stroke that restricts the amount of oxygen to the brain
- An infection of the brain such as meningitis, encephalitis, neurocysticercosis
- Certain genetic syndromes
- Brain tumor

Síndrome de Down

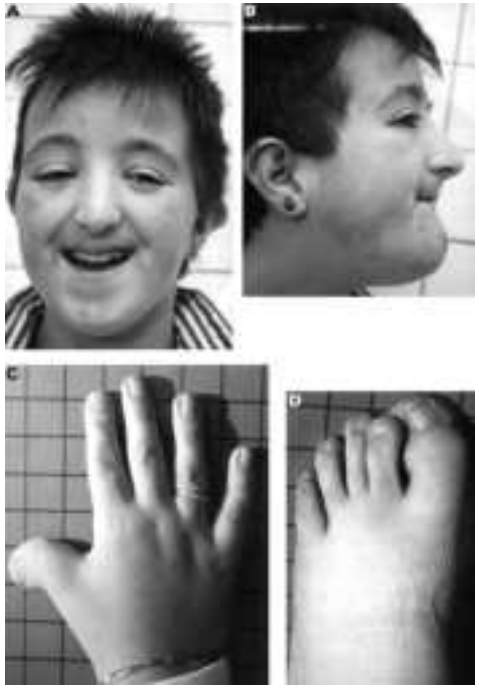
Síndrome de X frágil



Síndrome de Angelman

Síndrome de Bourneville

Smith Magenis



Rubenstein-Taybi

Síndrome de Rett

Research

JAMA Neurology | Original Investigation

Prevalence of Pathogenic Copy Number Variation in Adults With Pediatric-Onset Epilepsy and Intellectual Disability

Felippe Borlot, MD, MSc; Brigid M. Regan, BSc (Hons); Anne S. Bassett, MD, FRCPC; D. James Stavropoulos, PhD; Danielle M. Andrade, MD, MSc, FRCPC

A copy number variant (CNV) is defined as a segment of DNA at least 1 kb in size that differs in copy number compared with a representative reference genome. The term "CNV" does

Mutaciones en el número de copias en pacientes con discapacidad intelectual y epilepsia

¿Qué es una mutación en el número de copias?

American College of Medical Genetics standards and guidelines for interpretation and reporting of postnatal constitutional copy number variants

Hutton M. Kearney, PhD[1], Erik C. Thorland, PhD[2], Kerry K. Brown, PhD[3], Fabiola Quintero-Rivera, MD[4], and Sarah T. South, PhD[5], A Working Group of the American College of Medical Genetics (ACMG) Laboratory Quality Assurance Committee

A copy number variant (CNV) is defined as a segment of DNA at least 1 kb in size that differs in copy number compared with a representative reference genome. The term "CNV" does

Pathogenic

The CNV is documented as clinically significant in multiple peer-reviewed publications, even if penetrance and expressivity of the CNV are known to be variable.

This category includes large CNVs, which may not be described in the medical literature at the size observed in the patient but which overlap a smaller interval with clearly established clinical significance. Although the full clinical effect of

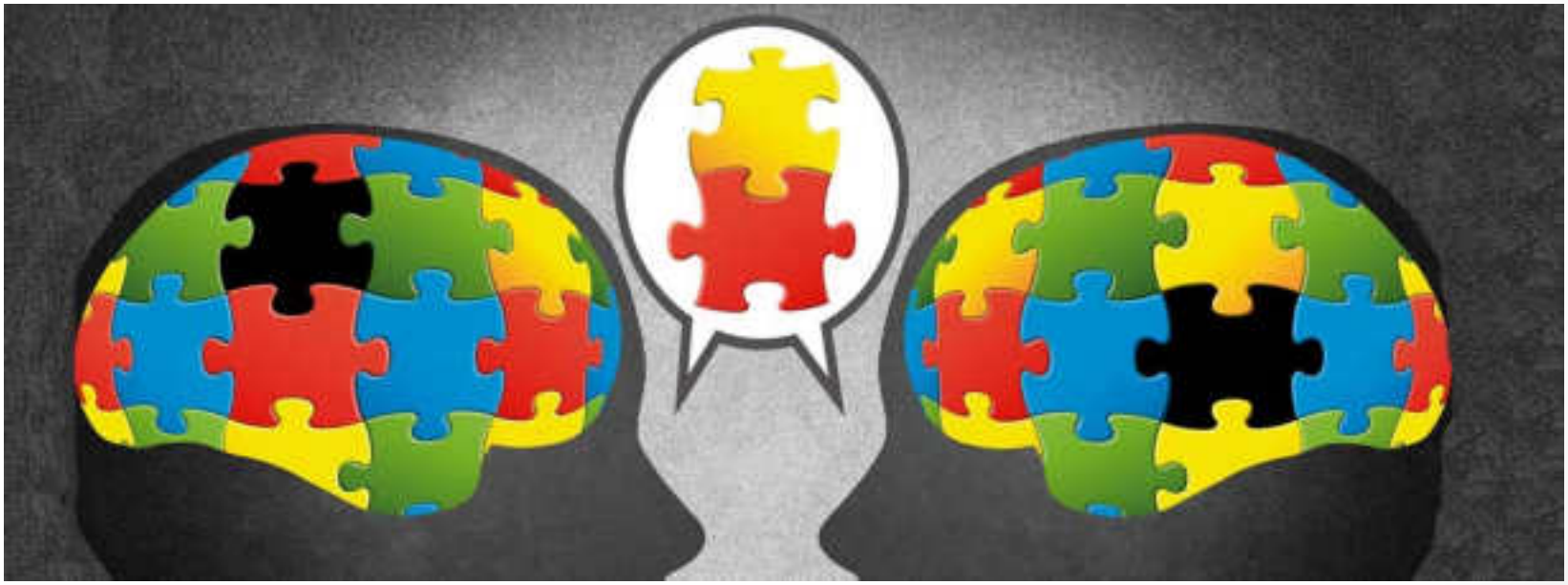
JAMA Neurology | Original Investigation

Prevalence of Pathogenic Copy Number Variation in Adults With Pediatric-Onset Epilepsy and Intellectual Disability

Felippe Borlot, MD, MSc; Brigid M. Regan, BSc (Hons); Anne S. Bassett, MD, FRCPC; D. James Stavropoulos, PhD; Danielle M. Andrade, MD, MSc, FRCPC

RESULTS Of the 2335 patients, 143 probands were investigated (mean [SD] age, 24.6 [10.8] years; 69 male and 74 female). Twenty-three probands (16.1%) and 4 affected relatives (2.8%) (mean [SD] age, 24.1 [6.1] years; 11 male and 16 female) presented with pathogenic or likely pathogenic CNVs (0.08-18.9 Mb). Five of the 23 probands with positive results (21.7%) had more than 1 CNV reported. Parental testing revealed de novo CNVs in 11 (47.8%), with CNVs inherited from a parent in 4 probands (17.4%). Sixteen of 23 probands (69.6%) presented with previously cataloged human genetic disorders and/or defined CNV hot spots in epilepsy. Eight nonrecurrent rare CNVs that overlapped 1 or more genes associated with intellectual disability, autism, and/or epilepsy were identified: 2p16.1-p15 duplication, 6p25.3-p25.1 duplication, 8p23.3p23.1 deletion, 9p24.3-p23 deletion, 10q11.22-q11.23 duplication, 12p13.33-13.2 duplication, 13q34 deletion, and 16p13.2 duplication. Five genes are of particular interest given their potential pathogenicity in the corresponding phenotypes and least tolerability to variation: *ABAT*, *KIAA2022*, *COL4A1*, *CACNA1C*, and *SMARCA2*. *ABAT* duplication was associated with Lennox-Gastaut syndrome and *KIAA2022* deletion with Jeavons syndrome.

CNVs discapacidad intelectual y salud mental



BJPsych | The British Journal of Psychiatry (2018)
212, 287–294. doi: 10.1192/bjp.2017.65

Neurodevelopmental risk copy number variants in adults with intellectual disabilities and comorbid psychiatric disorders*

Johan H. Thygesen**, Kate Wolfe**, Andrew McQuillin, Marina Viñas-Jornet, Neus Baena, Nathalie Brison, Greet D'Haeneris, Susanna Esteba-Castillo, Elisabeth Gabau, Núria Ribas-Vidal, Anna Ruiz, Joris Vermeesch, Eddy Weyts, Ramon Novell, Griet Van Buggenhout, André Strydom, Nick Bass***, Miriam Guitart*** and Annick Vogels***

Background

Copy number variants (CNVs) are established risk factors for neurodevelopmental disorders. To date the study of CNVs in psychiatric illness has focused on single disorder populations. The role of CNVs in individuals with intellectual disabilities and psychiatric comorbidities are less well characterised.

Aims

To determine the type and frequency of CNVs in adults with intellectual disabilities and comorbid psychiatric disorders.

Method

A chromosomal microarray analysis of 599 adults recruited from intellectual disabilities psychiatry services at three European sites.

Results

The yield of pathogenic CNVs was high – 13%. Focusing on established neurodevelopmental disorder risk loci we find a significantly higher frequency in individuals with intellectual disabilities and comorbid psychiatric disorder (10%) compared with healthy controls (1.2%, $P<0.0001$), schizophrenia (3.1%, $P<0.0001$) and intellectual disability/autism spectrum disorder (6.5%, $P<0.00084$) populations.

Conclusions

In the largest sample of adults with intellectual disabilities and comorbid psychiatric disorders to date, we find a high rate of pathogenic CNVs. This has clinical implications for the use of genetic investigations in intellectual disability psychiatry.

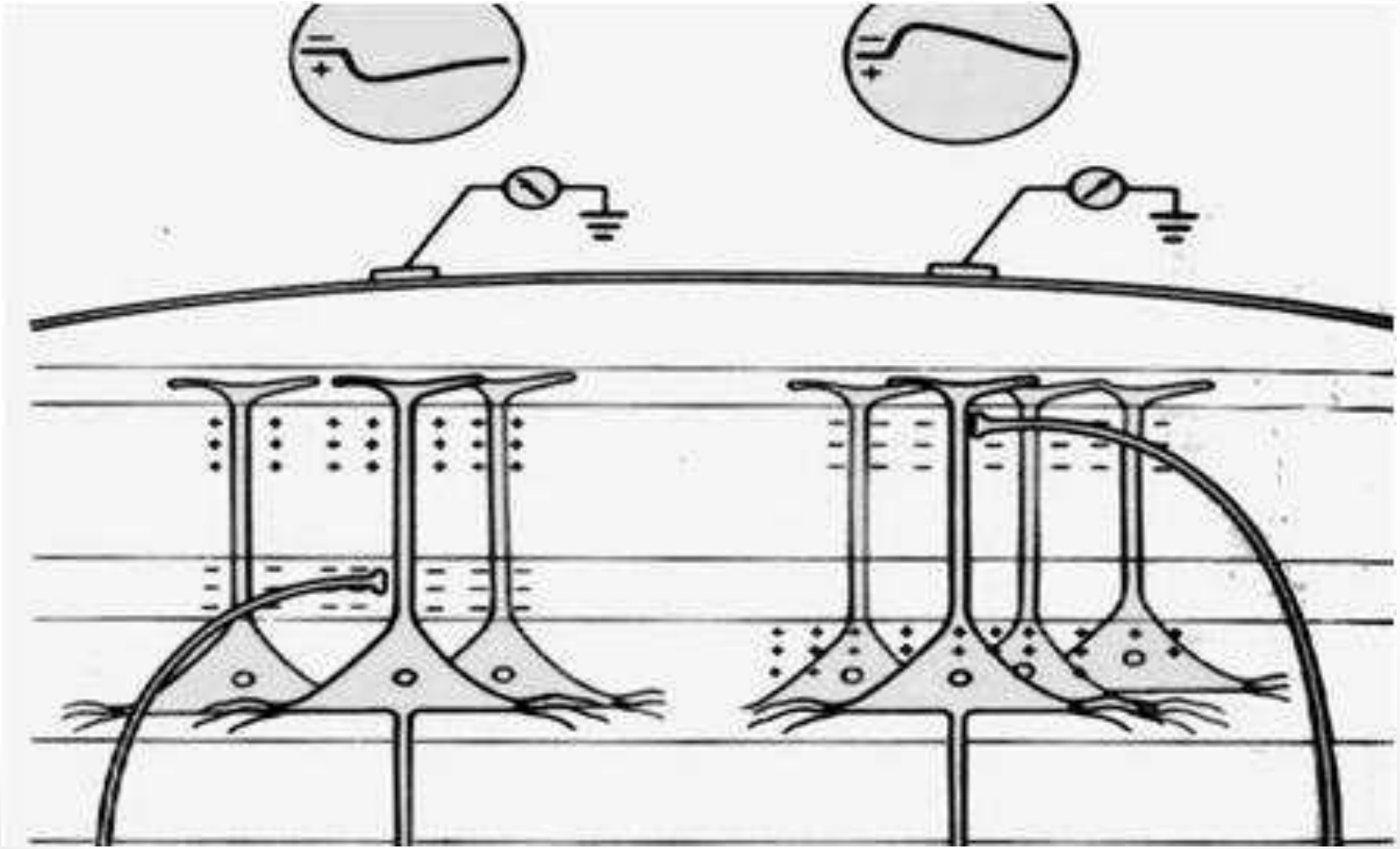
Mutaciones en el número de copias en pacientes con discapacidad intelectual Y trastornos psiquiátricos asociados

Declaration of interest

None.

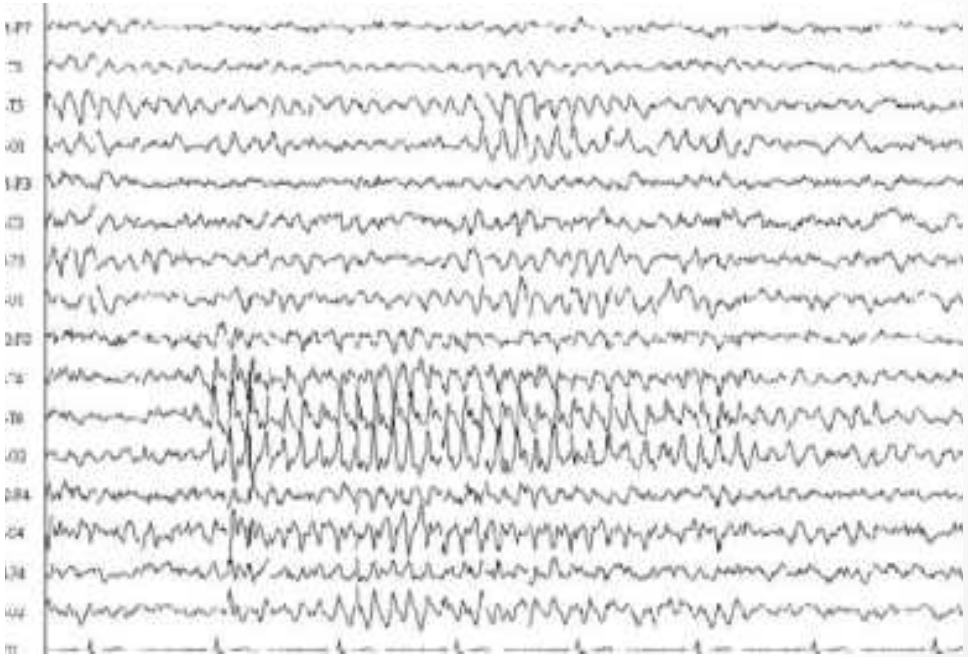
¿Qué pruebas podemos hacer para determinar si existe un foco epiléptico?

¿Qué es el electroencefalograma?

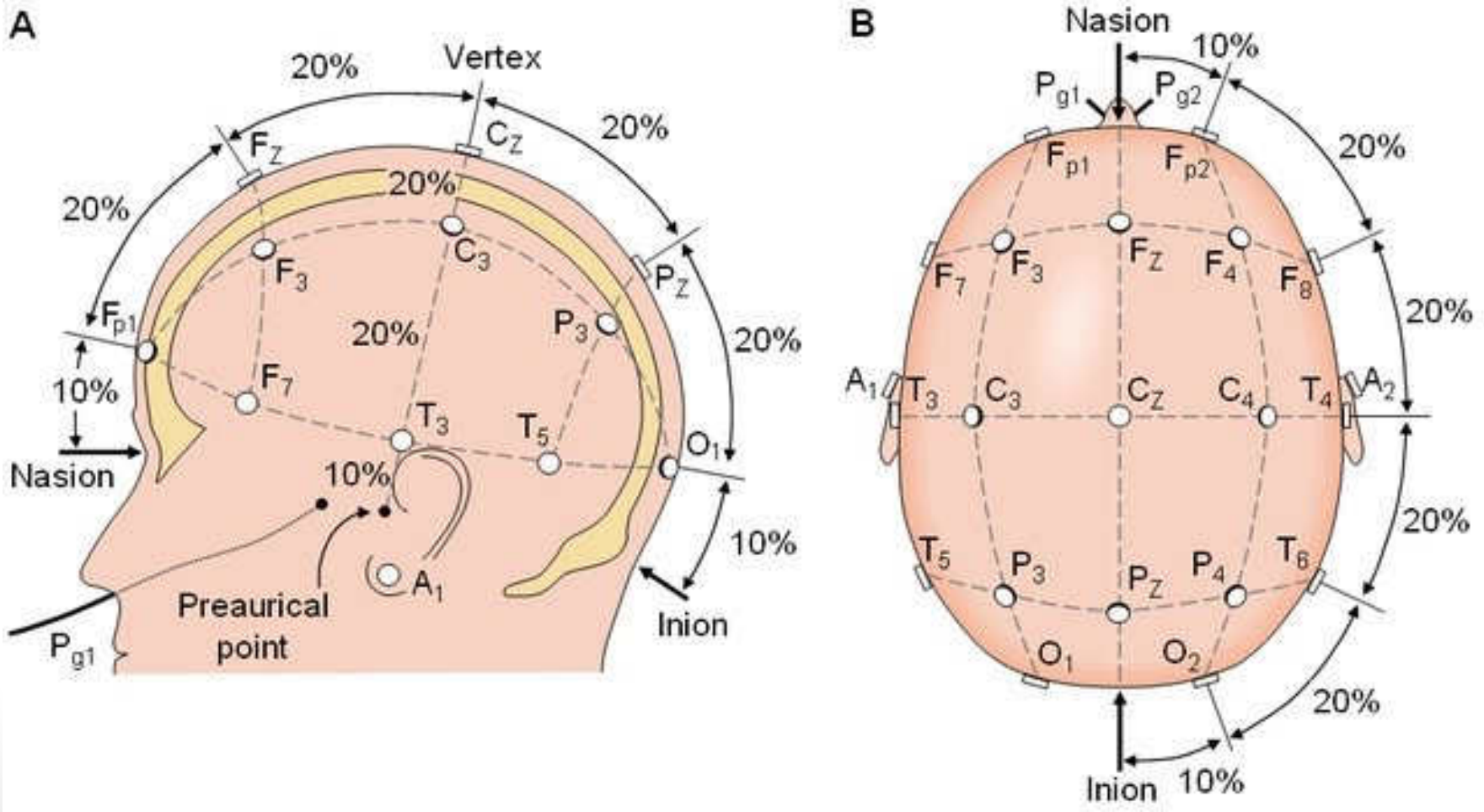


BASES DE ELECTROENCEFALOGRAFÍA

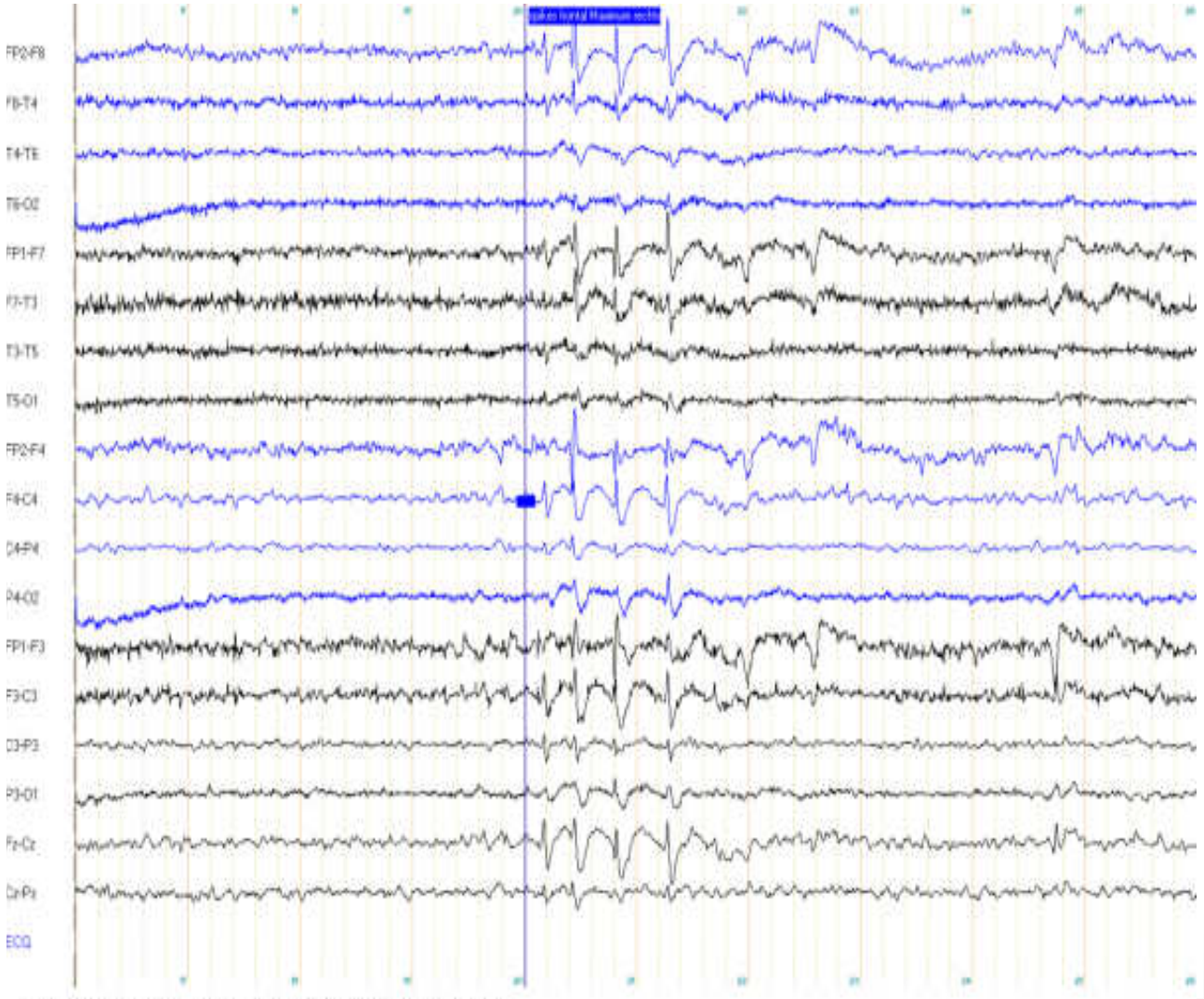
- El electroencefalograma es una prueba neurofisiológica que registra la actividad eléctrica del cerebro generada por la comunicación de las neuronas entre sí. Unos electrodos captan la actividad eléctrica que es amplificada y trasladada a una gráfica que luego es interpretada por el médico.



SÍSTEMA DE COLOCACIÓN DE ELECTRÓDOS INTERNACIONAL



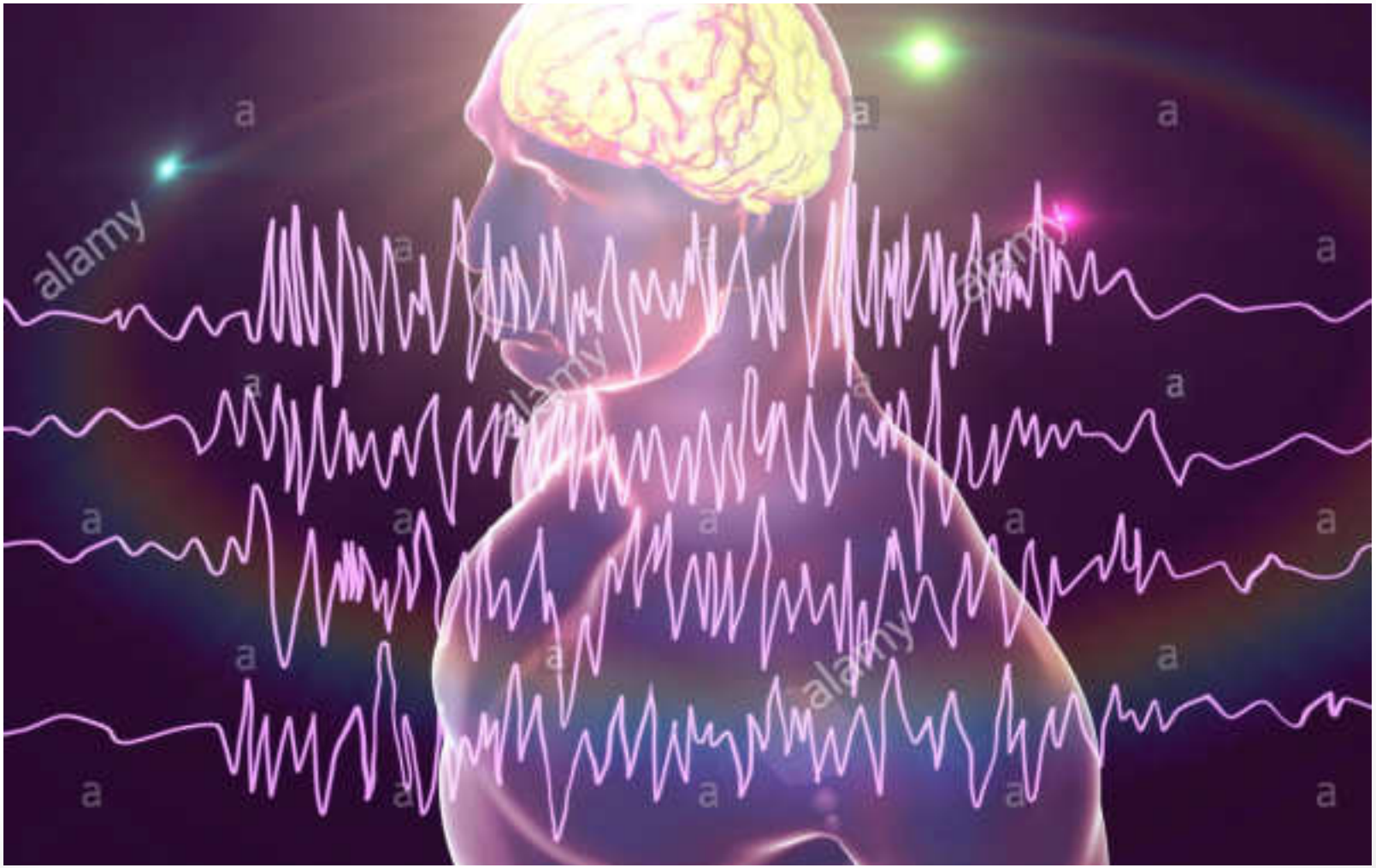
Spike Wave generalizado 3/s



TIPOS DE MONITORIZACIÓN ELECTROENCEFALOGRÁFICA

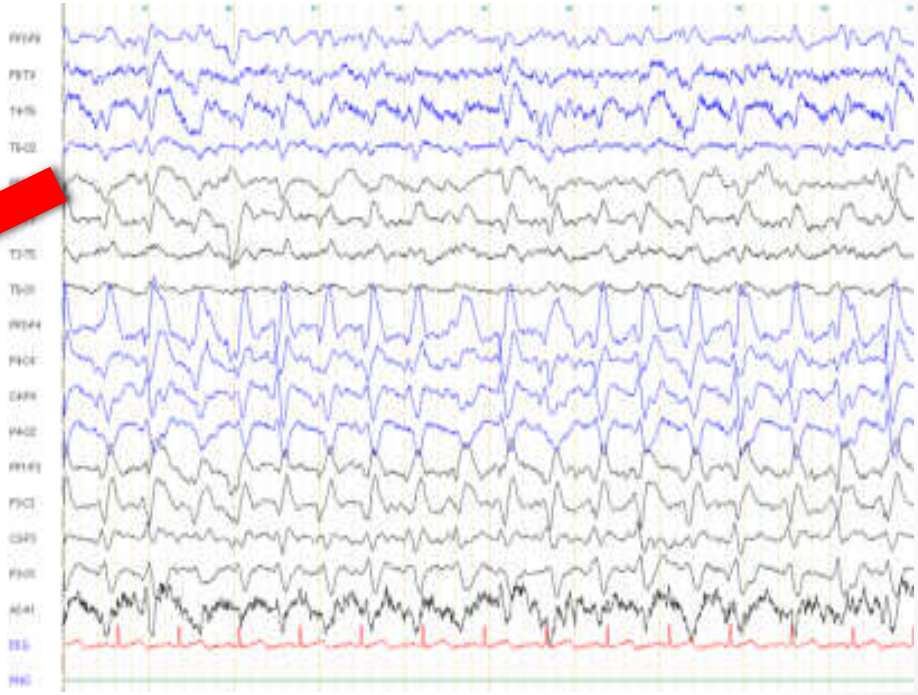
- EEG standard (20 Minutos)
- EEG tras deprivación de sueño (20 Minutos)
- EEG de larga duración (Mínimo 72h) (90% de sensibilidad en detección de potenciales epilépticos)
- Video EEG
- EEG con electrodos implantados (Cirugía de epilepsia)

¿Qué relación existe entre el electroencefalograma y la epilepsia?



SEN (Grupo de epilepsia) 01/2019

- El EEG ayuda el diagnóstico de las epilepsias
  - EEG Standard detecta: 29-55%
  - 3 EEG standard: 69-77%
  - EEG 24h : 80% (ZfP Südwürttemberg).
  - EEG 72h: 98% (ZfP Südwürttemberg).
- Potenciales epileptiformes en población normal (2-3%)
- Falsos diagnósticos en población con migrañas y otras alteraciones cerebrovasculares.



Otras pruebas diagnósticas

- Resonancia magnética nuclear
  - Detección de lesiones cerebrales macroscópicas
- Punción lumbar
  - Descarte de patologías infecciosas que pueden ocasionar crisis epilépticas y deterioro cognitivo
- Test neuropsicológicos
  - Catalogar déficits cognitivos iniciales y tras inicio de tratamientos

Revista de Psiquiatría y Salud Mental

www.elsevier.es/saludmental

Rev Psiquiatr Salud Ment (Barc.). 2019;xxx(xx):xxx–xxx

CARTA AL DIRECTOR

Psicosis como síntoma inicial de encefalitis autoinmune con anticuerpos negativos

Psychosis as an initial symptom of autoimmune encephalitis with negative antibodies

Carlos Peña-Salazar[a,b,c,*], Tanja Erben[b] y Christof Klötzsch[d]

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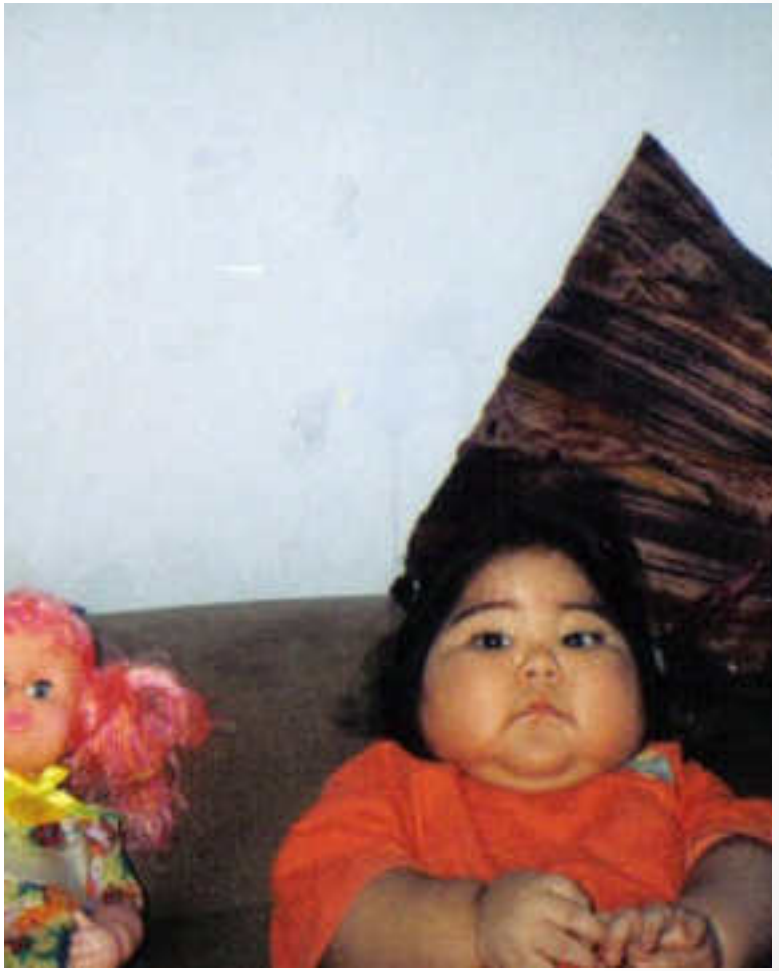
EPILEPSIA CLASIFICACIÓN

- **SINTOMÁTICAS**
  - **Lesión objetivable**
- **CRIPTOGÉNICAS**
  - **Lesión sospechada**
- **IDIOPÁTICAS**
  - **Sin indicios de lesión**

- **GENERALIZADAS**
  - **SÍNDROMES EPILÉPTICOS DE LA INFANCIA**
- **FOCALES**
  - **ALGUNOS SÍNDROMES EPILÉPTICOS DE LA INFANCIA**
  - **AFECTACIÓN FOCAL CON DIFERENTE ETIOLOGÍA**

EPILEPSIA GENERALIZADA

- **SÍNDROME DE WEST**
- Inicio antes del año
- Espasmos en flexión que afectan a cuello, tronco y miembros
- Asociación destacada con DI. Evolución a otras epilepsias más complejas
- Típicamente asociadas a **esclerosis tuberosa**

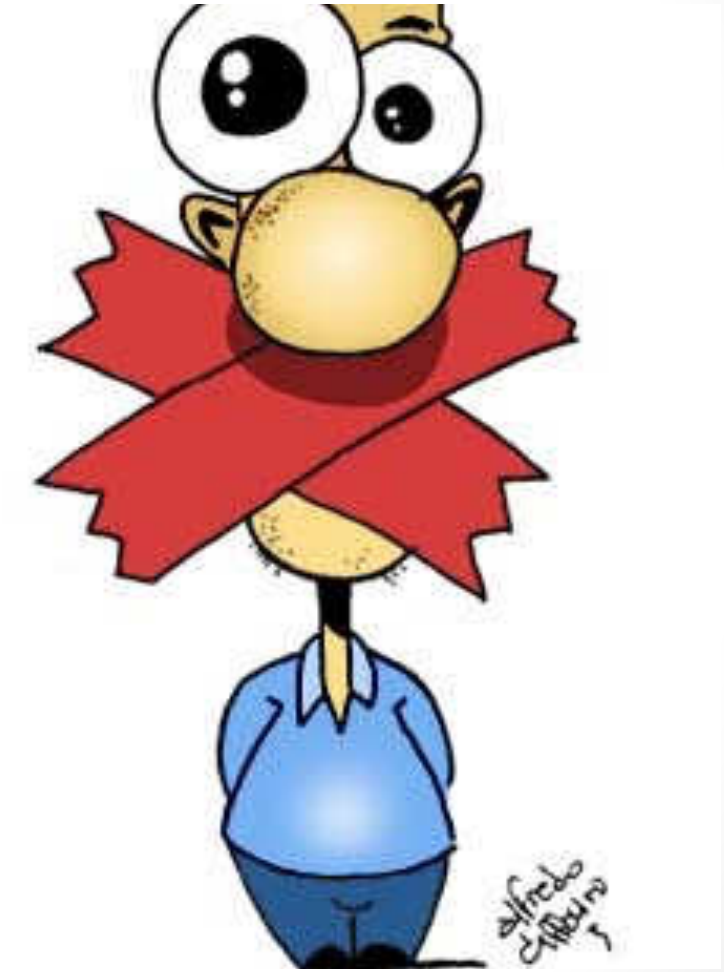


EPILEPSIA FOCAL/GENERALIZADA

- **SÍNDROME DE LENNOX – GASTAUT**
- Inicio entre 2-8 años
- Crisis polimorfas (varios tipos) ausencias + crisis tónicas+ generalizadas
- Asociación con DI
- Mala evolución
- Mala respuesta al tratamiento

Síndrome de Landau-Kleffner

- Afasia que se inicia hacia los 3-5 años de edad de causa desconocida
- Se asocia a alteraciones graves de comportamiento
- Fácil malidentificación con TEA



CRISIS EPILÉPTICAS. CLASIFICACIÓN

- **GENERALIZADAS**
  - **CONVULSIVAS**
  - **NO CONVULSIVAS**
- **FOCALES**
- **SECUNDARIAMENTE GENERALIZADAS**

CRISIS GENERALIZADA

- Descarga excesiva e hipersincrónica de neuronas corticales y subcorticales de ambos hemisferios

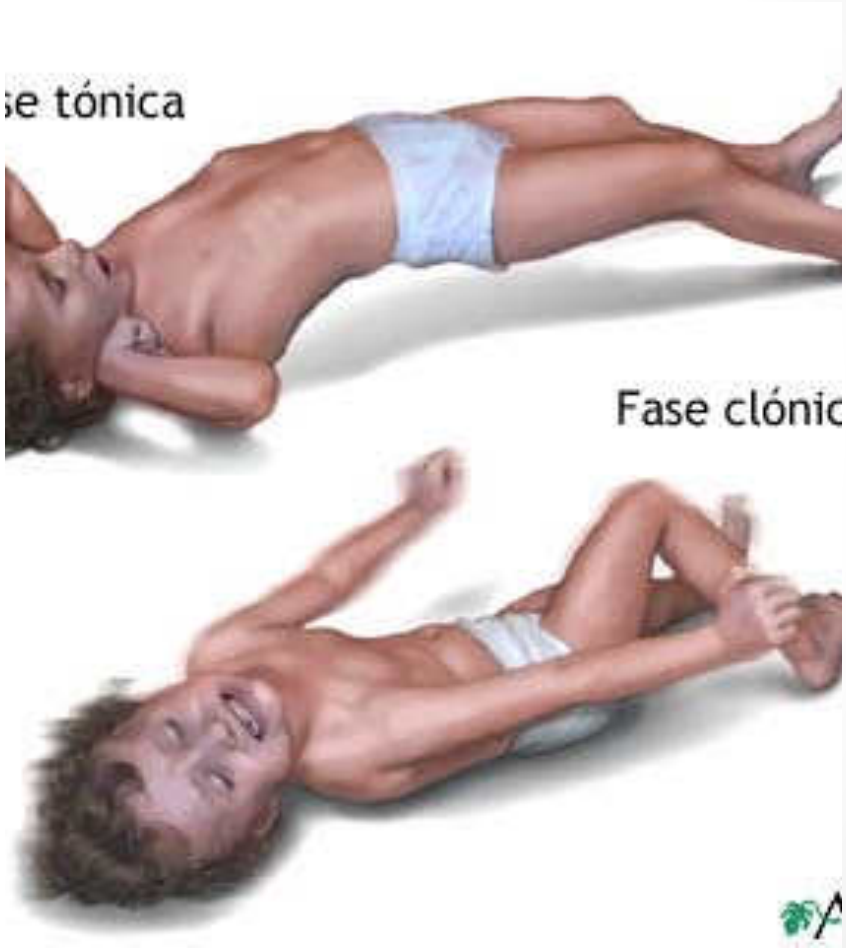
A. **CONVULSIVAS**
    A. Mioclónicas
    B. Tónicas
    C. Clónicas
    D. **Tónico-clónicas**
    E. Febriles(niños)

CRISIS TÓNICO-CLÓNICA

- ✓ Fase clónica
- ✓ Fase tónica
- ✓ Estupor post-crítico

DD: Entre crisis epiléptica y crisis epileptiforme (Psiquiátrica)

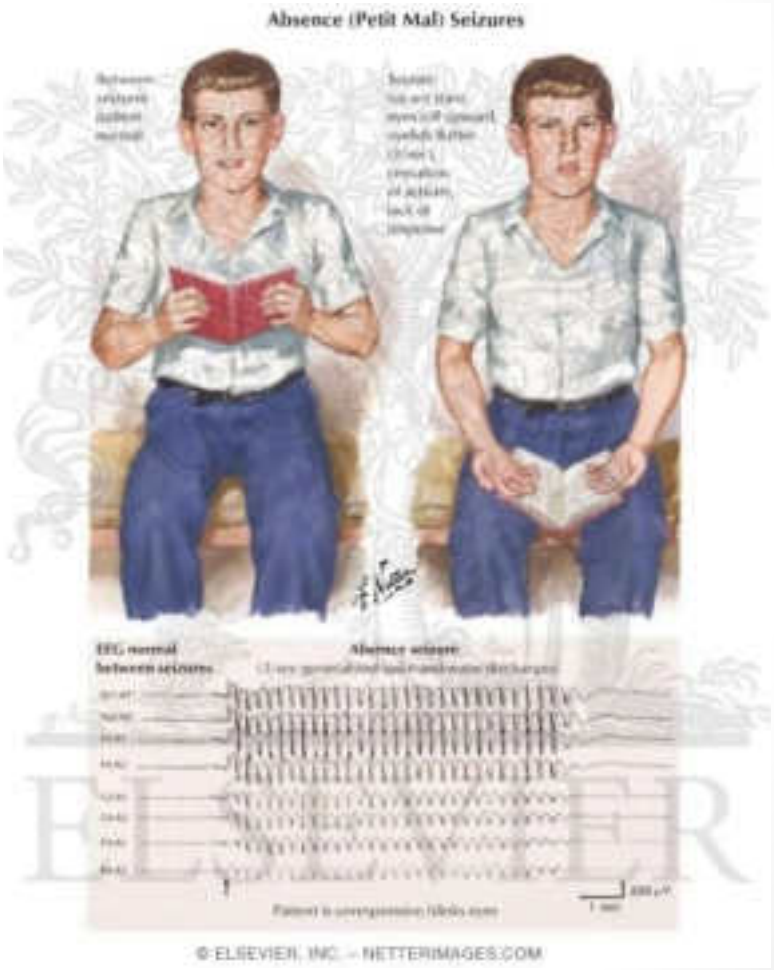
- Mordedura de la lengua
- Pérdida del control de esfínteres
- Elevación de CK
- LZ- EEG (VIDEO EEG)



CRISIS GENERALIZADA

B. **NO CONVULSIVAS**

1. Ausencias

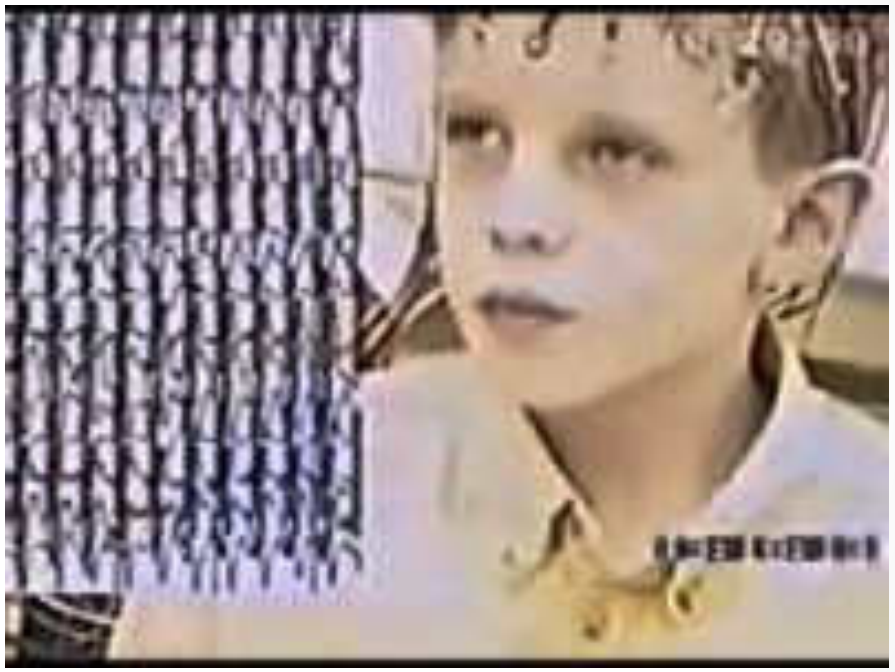


2. Crisis atónicas

CRISIS GENERALIZADA

B. **NO CONVULSIVAS**

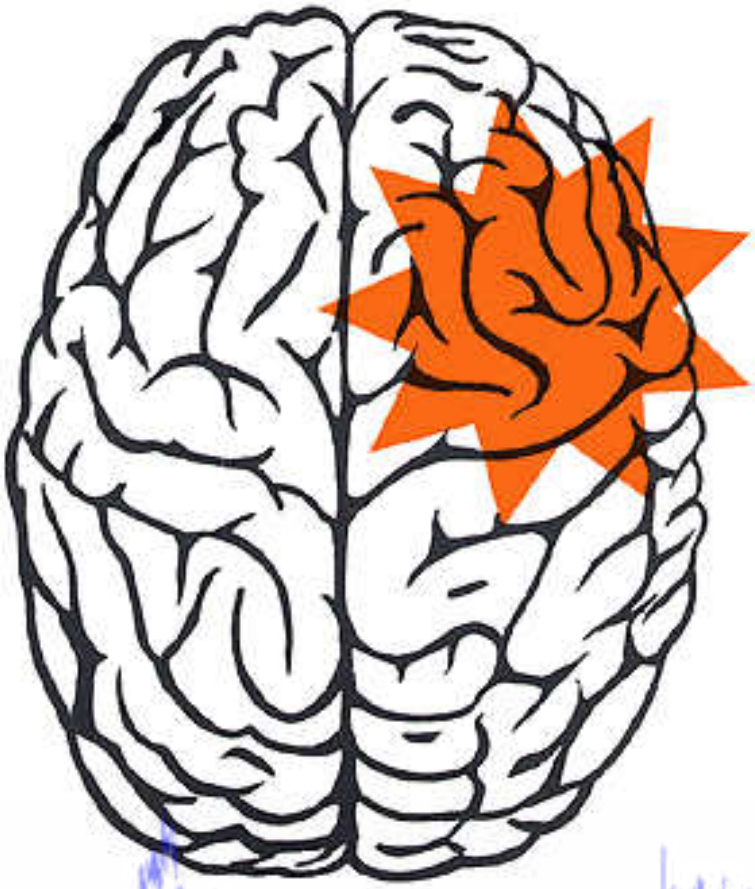
1. Ausencias



2. Crisis atónicas

CRISIS FOCAL

- Descarga eléctrica en una zona concreta del cerebro.
  - A. **SIMPLES**:
    - Motoras
    - Sensitivas
    - Vegetativas
    - Vasomotoras
    - Con síntomas psíquicos (Alucinaciones olfativas/visuales)



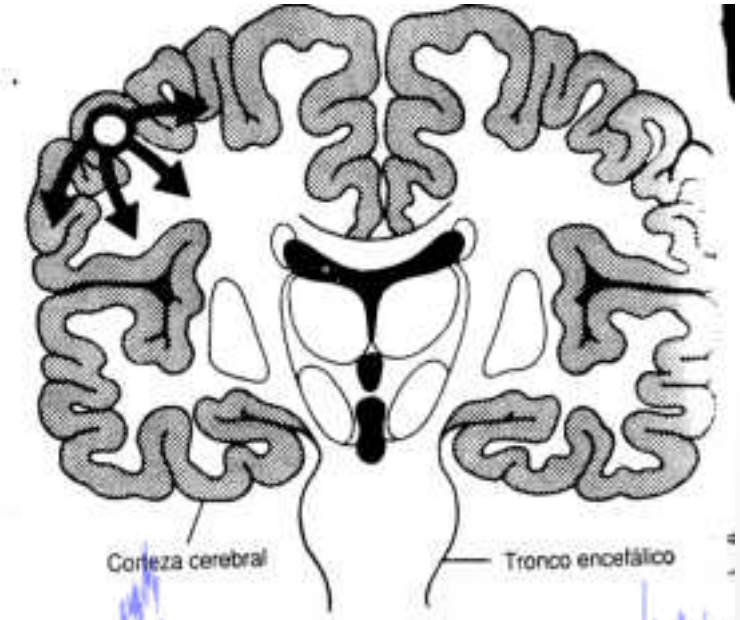
CRISIS FOCAL

B. **COMPLEJAS**

1) Alteración de la conciencia, desconexión con el medio, automatismos, chupeteos, deglutir….

2) **Origen más frecuente en lóbulo temporal y frontal**

- Toda crisis focal se puede generalizar secundariamente (Crisis focal generalizada)



¿QUÉ HACER ANTE UNA CRISIS EPILÉPTICA?

- EVITAR QUE EL PACIENTE SE DAÑE (POSICIÓN DE SEGURIDAD)
- EXTRAER OBJETOS DE LA BOCA
- ESPERAR A QUE PASE LA CRISIS
- ACUDIR A UN HOSPITAL PARA REALIZAR UN ESTUDIO COMPLETO
- ¡OJO CON EL ESTADO CONFUCIONAL POST-CRÍTICO!

- SI SERIE O ESTATUS EPILÉPTICO:
  - DIAZEPAM RECTAL. (EFECTO 7min)
  - Buccolam oral
  - LORAZEPAM E/V – DIAZEPAM E/V (Efecto 1-2 min)
  - IMPREGNACIÓN ANTIEPILÉPTICA (FENITOÍNA/KEPRA/LACOSAMIDA)
  - SINO RESPUESTA, COMA BARBITÚRICO

DIAGNÓSTICO DIFERENCIAL

- Test de Schellong
- ECG
- EEG
- Alteraciones iónicas
  - Hipocalcemia
  - Hipomagnesemia
  - Hiponatremia
  - Hiperglicemias
  - Hiperuricemias

SÍNCOPE CONVULSIVO

- Síntomas prodrómicos
  - Sensación nauseosa
  - Mareo inespecífico
  - “Negro delante de los ojos”
- Duración breve (Excepto cuando ocurren en posición de sedestación)
- Rápida recuperación de conciencia y orientación

CRISIS PSEUDOEPILÉPTICAS DISOCIATIVAS

- Movimientos exacerbados, normalmente no rítmicos
- Inicio y finalización progresiva
- Ojos cerrados
- No incontinencia urinaria
- No mordedura de la lengua
- "Despertables"
- Sugestionables
  - Ojo: DD con crisis hipermotóricas

- Procedimiento:
  - RNM
  - LZ-EEG
  - Video EEG

Prevalencia epilepsia en población con DI

Seizure (2006) 15, 376–386

ELSEVIER

SEIZURE

www.elsevier.com/locate/yseiz

Epilepsy in adults with intellectual disabilities: Prevalence, associations and service implications

Catherine W. McGrother [a,*], Sabyasachi Bhaumik [a,b], Catherine F. Thorp [a], Agnes Hauck [b], David Branford [c], Joanna M. Watson [a,b]

Results: The prevalence of epilepsy was 26%. Among those with epilepsy, 68% experienced seizures despite anti-epileptic medication. Epilepsy showed a significant association with low levels of understanding. Specific morbid associations included wetting (adjusted odds ratio 2.7), soiling (2.2), walking (2.5), daily living skills (1.6), poor speech (2.2), lack of empathy (1.5), mood swings (1.5), being uncooperative (1.6), seeking attention (1.7) and disturbing others at night (1.9). Holistic associations included a wider range of physical and mental problems and global skills deficits.

¿Y en las personas con discapacidad intelectual?

Received: 3 October 2018 | Revised: 23 July 2019 | Accepted: 31 July 2019
DOI: 10.1111/jar.12654

REVIEW

WILEY

Prevalence of co-occurring psychiatric disorders in adults and adolescents with intellectual disability: A systematic review and meta-analysis

Mario G. Mazza[1] | Aurora Rossetti[1] | Giovanna Crespi[2] | Massimo Clerici[1]

Abstract

Background: Subjects with intellectual disability (ID) are vulnerable to experience psychiatric disorders. The present authors performed a systematic review and meta-analysis to estimate the prevalence of co-occurring psychiatric disorders, excluding co-occurring autism spectrum disorders, in subjects with intellectual disability.

Method: The present authors performed a random-effects meta-analysis of the prevalence of psychiatric disorders in adults and adolescents with intellectual disability.

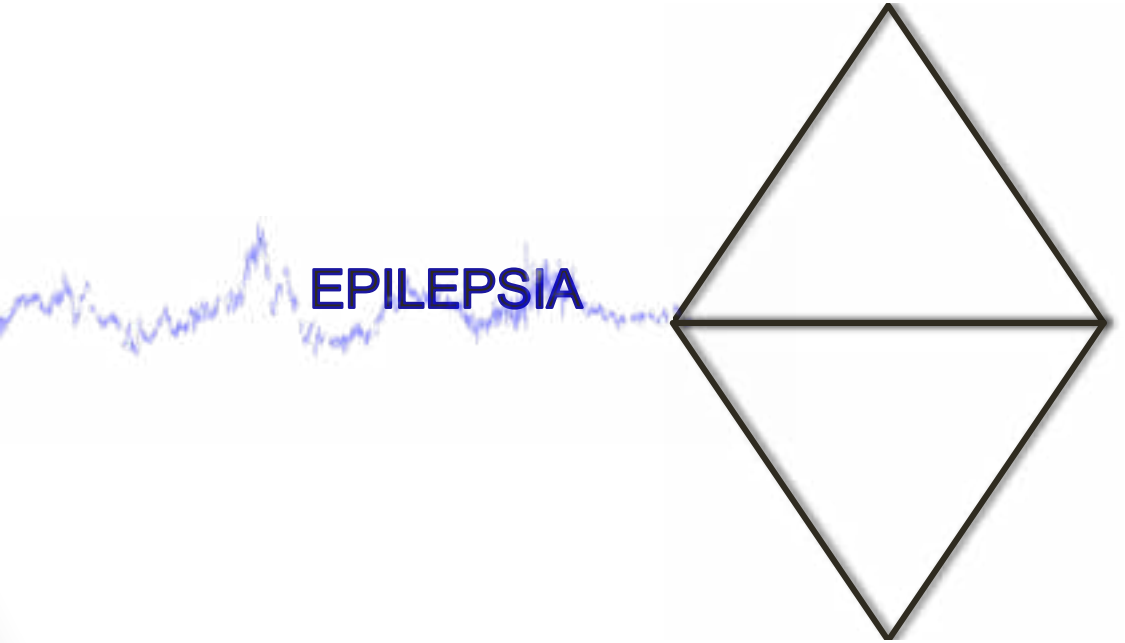
Results: Twenty-two studies were included. The pooled prevalence of any co-occurring psychiatric disorders in intellectual disability was 33.6% (95% CI: 25.2%–43.1%) with high heterogeneity but no publication bias. Prevalence was lower in population-based studies, in studies that used ICD criteria for the psychopathology and in studies with low risk of bias. The prevalence was higher in mild, moderate and severe intellectual disability than in profound intellectual disability.

Conclusions: Psychiatric disorders are common in subjects with intellectual disability, and the present authors found that clinical and methodological moderators affect the pooled prevalence.

RELACIÓN EPILEPSIA Y ENFERMEDAD MENTAL

DISCAPACIDAD INTELECTUAL

EPILEPSIA



ENFERMEDAD MENTAL

Delivery of epilepsy care to adults with intellectual and developmental disabilities

Neurology 85 October 27, 2015

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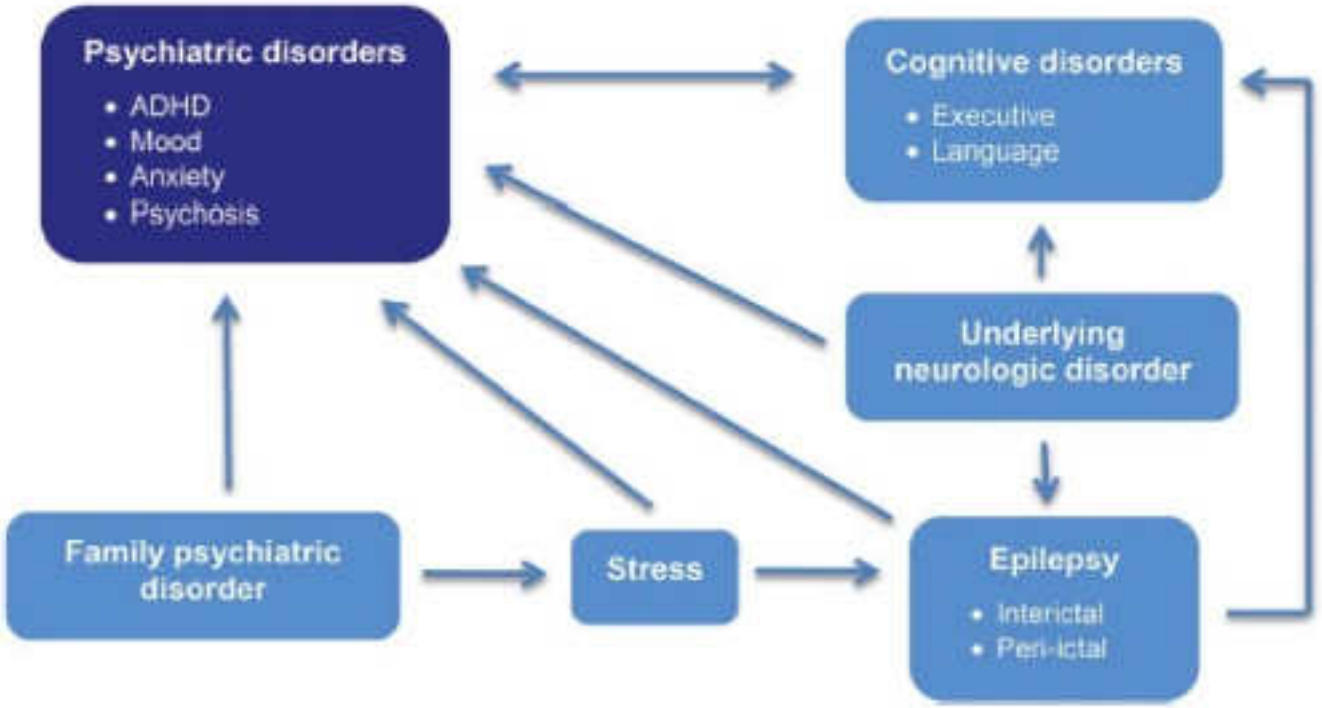
ABSTRACT

Epilepsy is common in people with intellectual and developmental disabilities (IDD). In adulthood, patients with IDD and epilepsy (IDD-E) have neurologic, psychiatric, medical, and social challenges compounded by fragmented and limited care. With increasing neurologic disability, there is a higher frequency of epilepsy, especially symptomatic generalized and treatment-resistant epilepsies. The causes of IDD-E are increasingly recognized to be genetic based on chromosomal microarray analysis to identify copy number variants, gene panels (epilepsy, autism spectrum disorder, intellectual disability), and whole-exome sequencing. A specific genetic diagnosis may guide care by pointing to comorbid disorders and best therapy. Therapy to control seizures should be individualized, with drug selection based on seizure types, epilepsy syndrome, concomitant medications, and comorbid disorders. There are limited comparative antiepileptic drug data in the IDD-E population. Vagus nerve and responsive neural stimulation therapies and resective surgery should be considered. Among the many comorbid disorders that affect patients with IDD-E, psychiatric and sleep disorders are common but often unrecognized and typically not treated. Transition from holistic and coordinated pediatric to adult care is often a vulnerable period. Communication among adult health care providers is complex but essential to ensure best care when these patients are seen in outpatient, emergency room, and inpatient settings. We propose specific recommendations for minimum care standards for people with IDD-E.

Neurology® 2015;85:1512-1521

¿Por qué?

Figure 2 Factors contributing to the genesis and persistence of psychiatric disorders in patients with intellectual and developmental disabilities and epilepsy



ADHD = attention-deficit/hyperactivity disorder.

La relación entre enfermedad mental y alteración de conducta en la poblacion con DI

La relación entre la enfermedad mental y la alteración de conducta

Article

Underdiagnosis of psychiatric disorders in people with intellectual disabilities: Differences between psychiatric disorders and challenging behaviour

Journal of Intellectual Disabilities
1–13

Table 3. Distribution differences between mental disorders and challenging behaviour (Mann–Whitney *U*-test).

Intellectual disability	*n* (%)	ICAP (average) (SD)	*p*
Mild/moderate			
Without mental disorder	76 (83.5)	−9.16 (9.25)	
With mental disorder	15 (16.5)	21.27 (13.55)	<0.001
Total	91 (100)	11.15 (10.96)	
Severe/profound			
Without mental disorder	24 (47.1)	−13.08 (9.39)	
With mental disorder	27 (52.9)	−15.70 (9.96)	>0.05
Total	51 (100)	14.47 (9.69)	
Total	142 (100)		

ICAP: Inventory for Client and Agency Planning; SD: standard deviation.

Peña-Salazar et al, 2018

Epilepsy in Autism is Associated with Intellectual Disability and Gender: Evidence from a Meta-Analysis

Claire Amiet, Isabelle Gourfinkel-An, Anissa Bouzamondo, Sylvie Tordjman, Michel Baulac, Philippe Lechat, Laurent Mottron, and David Cohen

Background: The association between epilepsy and autism is consistently reported, with a wide range of prevalence rates. This may be attributed to the heterogeneity of the samples with respect to age, comorbidity, sex, and intellectual disability (ID). We aimed to compare the prevalence of epilepsy 1) among autistic patients with ID versus autistic patients without ID and 2) among male versus female autistic patients.

Methods: We reviewed all data available from published reports (1963–2006) on autism and epilepsy and conducted a meta-analysis of 10 and 14 studies, respectively, to assess the relative risk (RR) of epilepsy in autism according to ID and gender. The pooled groups included 2112 (627 with IQ ≥ 70, 1485 with IQ < 70) and 1530 (1191 male, 339 female) patients, respectively.

Results: There was a strong discrepancy in relative risk (RR) according to IQ, with more autistic patients with ID having epilepsy (RR = .555; 95% confidence interval [CI]: .42–.73; $p < .001$). The pooled prevalence of epilepsy was 21.5% in autistic subjects with ID versus 8% in autistic subjects without ID. There was a strong discrepancy in RR according to sex, favoring comorbidity of epilepsy in autistic girls (RR = .549; 95% CI: .45–.66; $p < .001$). The male:female ratio of autism comorbid with epilepsy was close to 2:1 whereas the male:female ratio of autism without epilepsy was 3.5:1.

Conclusions: The results of this meta-analysis indicate that risk for epilepsy in autism is a function of ID severity and distinguishes autism associated with epilepsy as a subgroup of autism by its male-female ratio.

BIOL PSYCHIATRY 2008;64:577–582

Review Paper

Is epilepsy related to psychiatric disorders in people with intellectual disability? A systematic review

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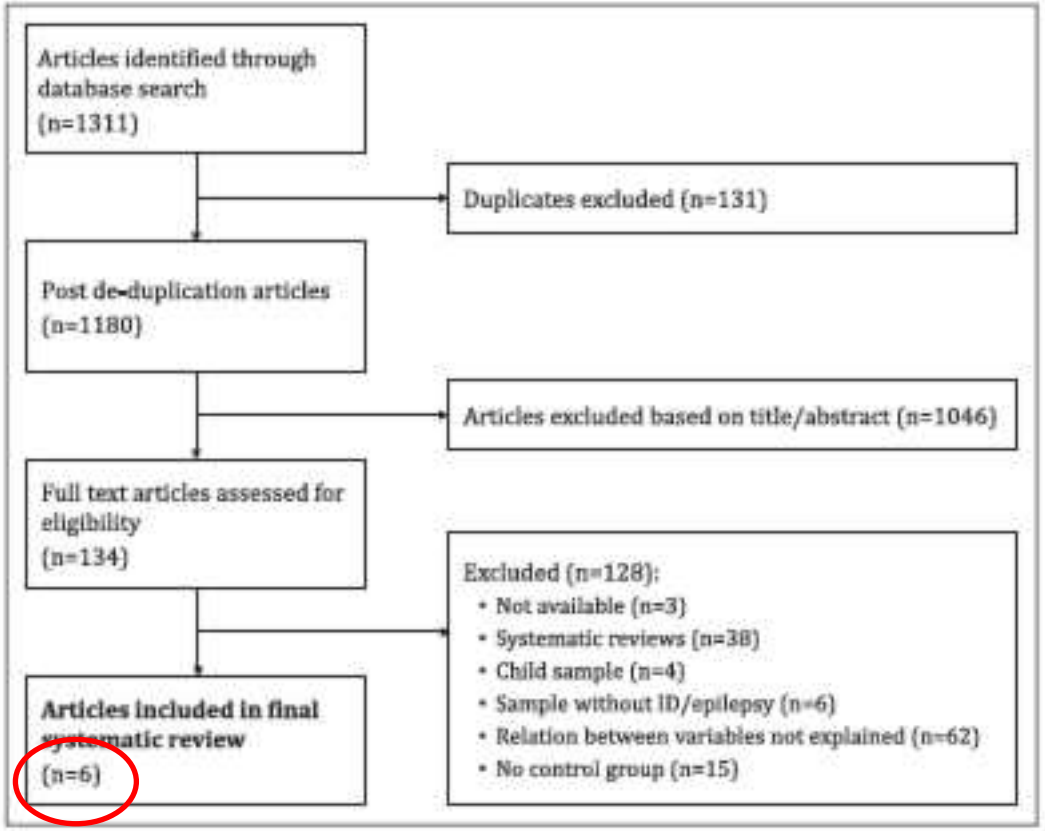


Conclusiones

- 1) No se puede ”corroborar” científicamente una relación entre salud mental y epilepsia en DI
- 2) Existen ciertas evidencias de que la irritabilidad, la clínica depresiva y otros trastornos psiquiátricos sin más frecuentes en las personas con epilepsia y DI
- 3) Existe escasa evidencia científica sobre este tema, a pesar de ser muy frecuente

Factores de confusión

- **Gran heterogenicidad de la muestra**

- Inclusión de ASD dentro del grupo de enfermedad mental en la mayor parte de los casos

- Efecto psicotrópico de diferentes fármacos antiepilépticos
  - Depresógenos
  - Propsicóticos
  - Estabilizadores del ánimo

- Disminución de umbral convulsivo por toma de antipsicóticos

- Fenómeno de normalización forzada

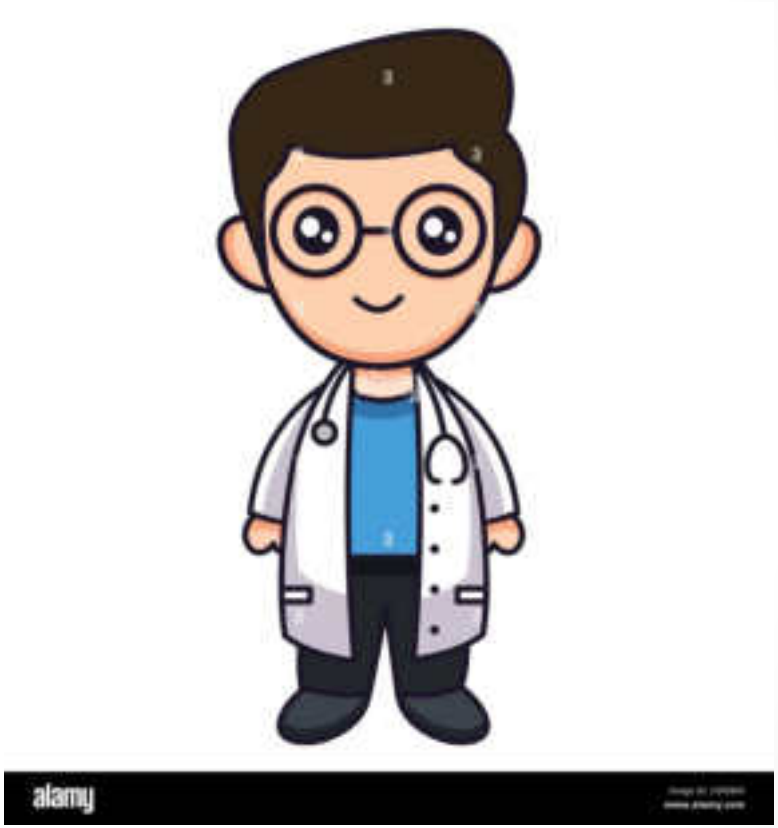
Experiencia profesional

- **Prevalencia muy elevada de epilepsia en las personas con DI**

- Prevalencia muy elevada de enfermedad mental en las personas con DI

- Las personas con DI y epilepsia presentan más enfermedad mental, de mayor complejidad y requiere de un seguimiento estrecho y especializado.

- Es difícil lograr una estabilización de la epilepsia y de la enfermedad mental simultáneamente durante largos periodos de tiempo



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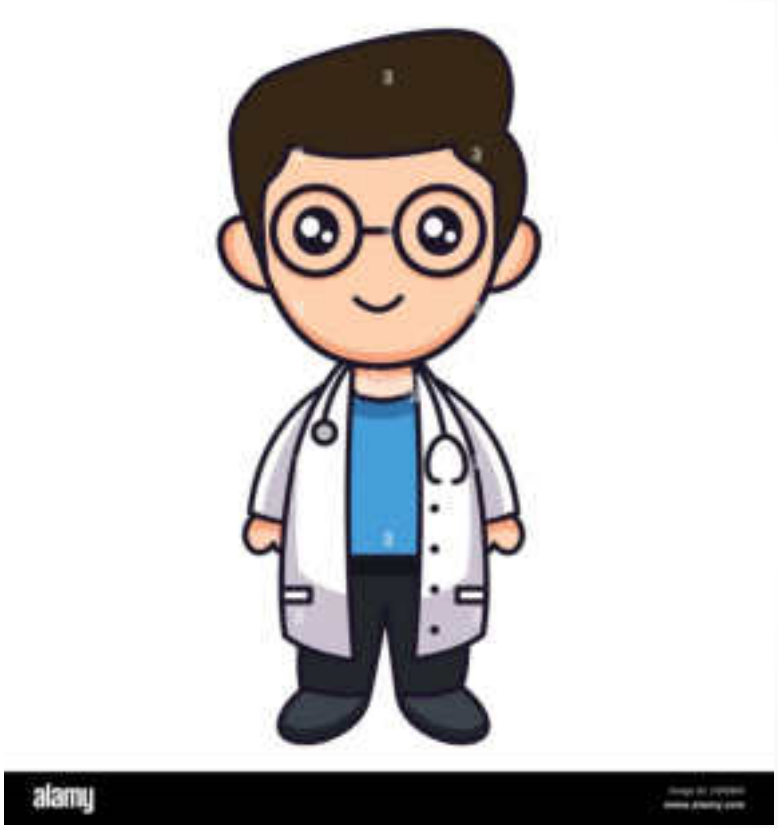

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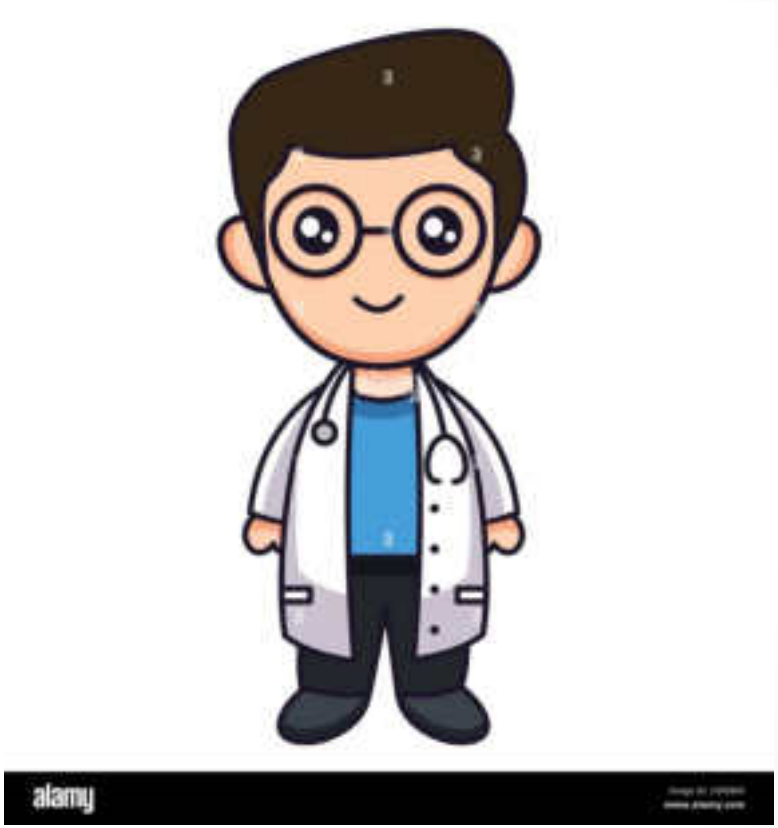

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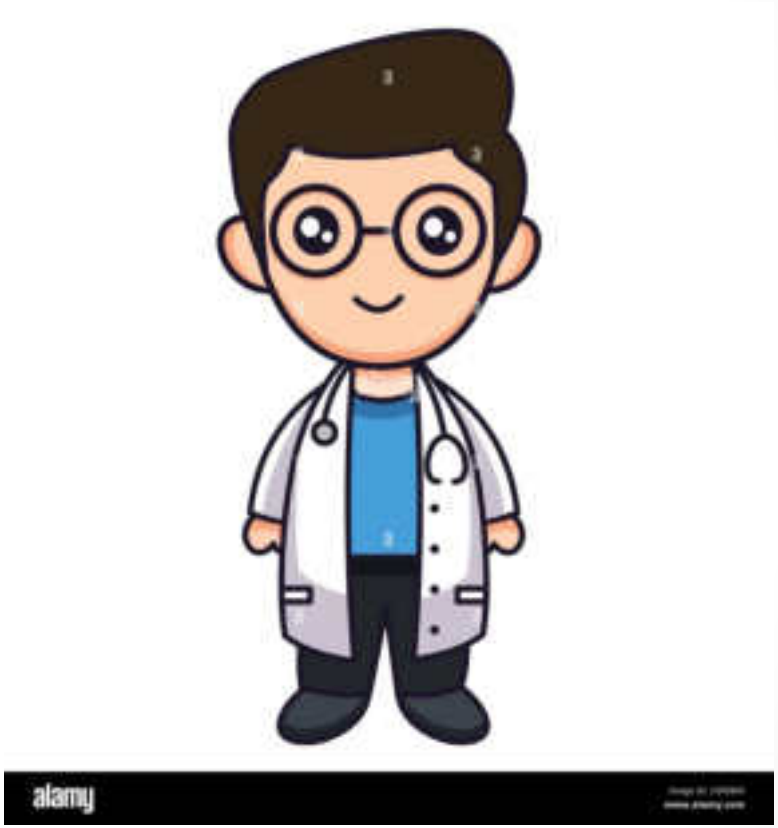

MUCHAS GRACIAS