Actualités en Réanimation 2025
AER
29ème congrès Francophone

Lyon, France
Jeudi 20 Novembre 2025

Encéphalite auto-immune

Pr J. Honnorat
Neuro-Oncologie
Hôpital neurologique de Lyon

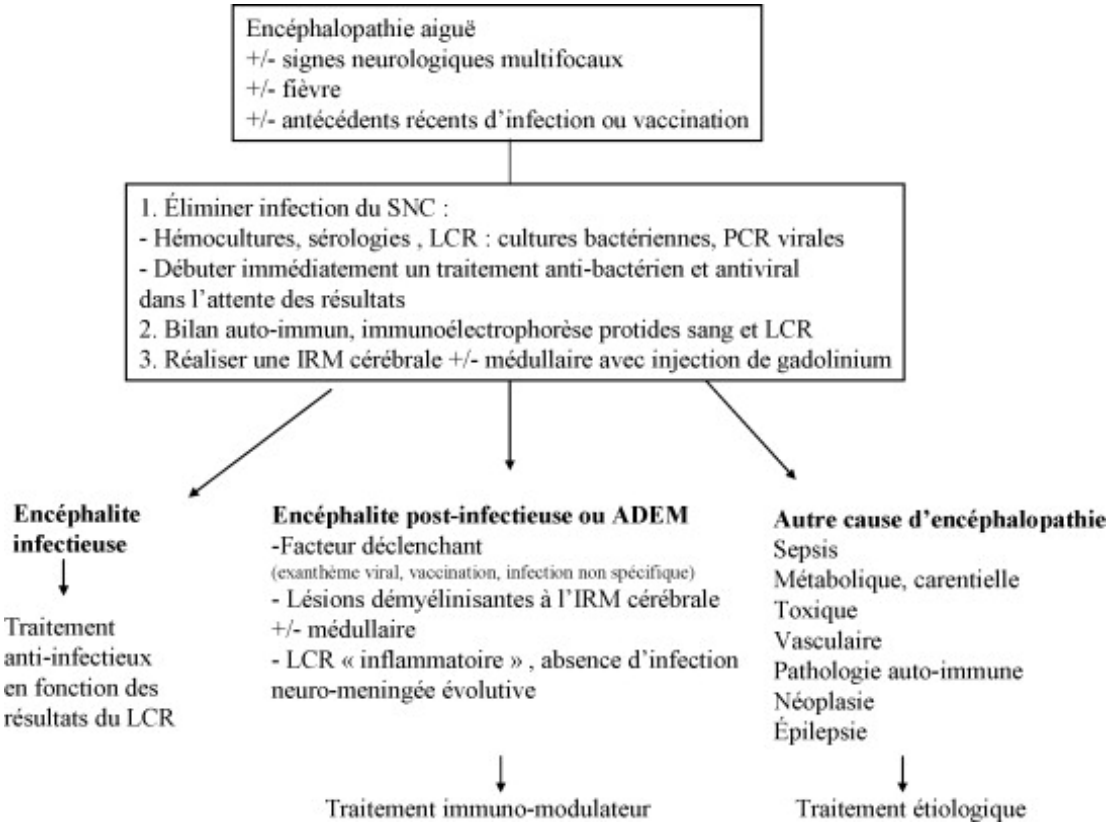
Institut MeLiS
Equipe : «Synaptopathies et Autoanticorps»
Inserm 1314 / UMR CNRS 5284

DÉCLARATION DE LIENS D'INTÉRÊT POTENTIELS

Pr Honnorat Jérôme, Lyon

☑ Je n'ai pas de lien d'intérêt potentiel à déclarer

Evoquer une encéphalite est simple, l'affirmer est plus compliqué

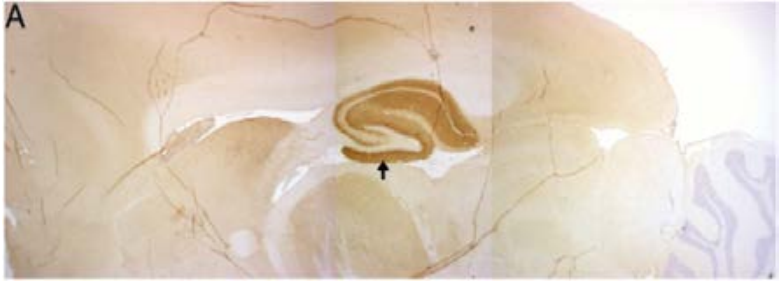


Encéphalites sans cause : 40 à 60%

Sonneville et Wolf, Réanimation 2007;16:452-462

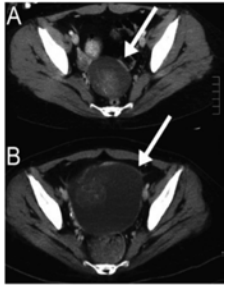
Qu'est-ce qu'une encéphalite auto-immune ?
Premiers cas identifiés : jeunes femmes encéphalite et tératome de l'ovaire

Dalmau et al, Ann Neurol 2007

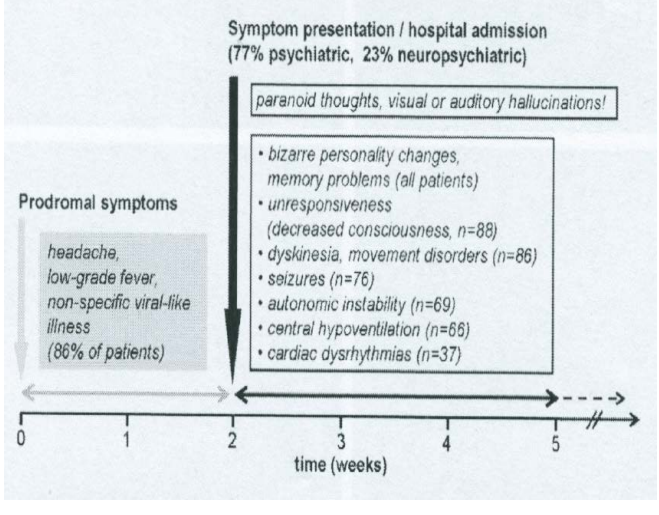


Dyskinésies bucco-faciales
Dysautonomie

Bayreuther et al, Epileptic Disord 2009

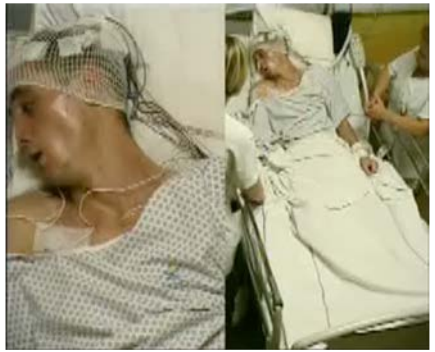


Tératomes de l'ovaire

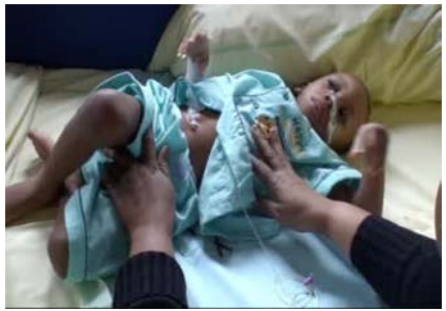


Les Encéphalites avec anti-NMDA-R

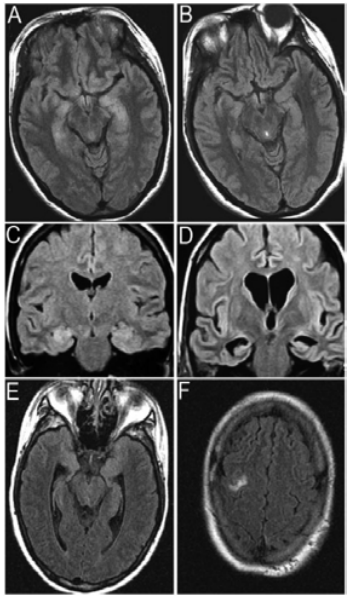
Femme, Mme Y.
Medeline, Colombie.
Dr Reiss.



Homme, Mr X.
Amiens,
France.
Dr Perrin

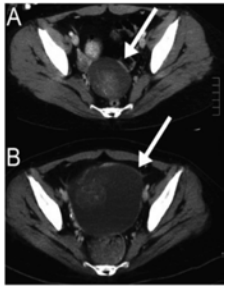


Enfants,
Paris, Trousseau



Anomalies IRM non spécifiques

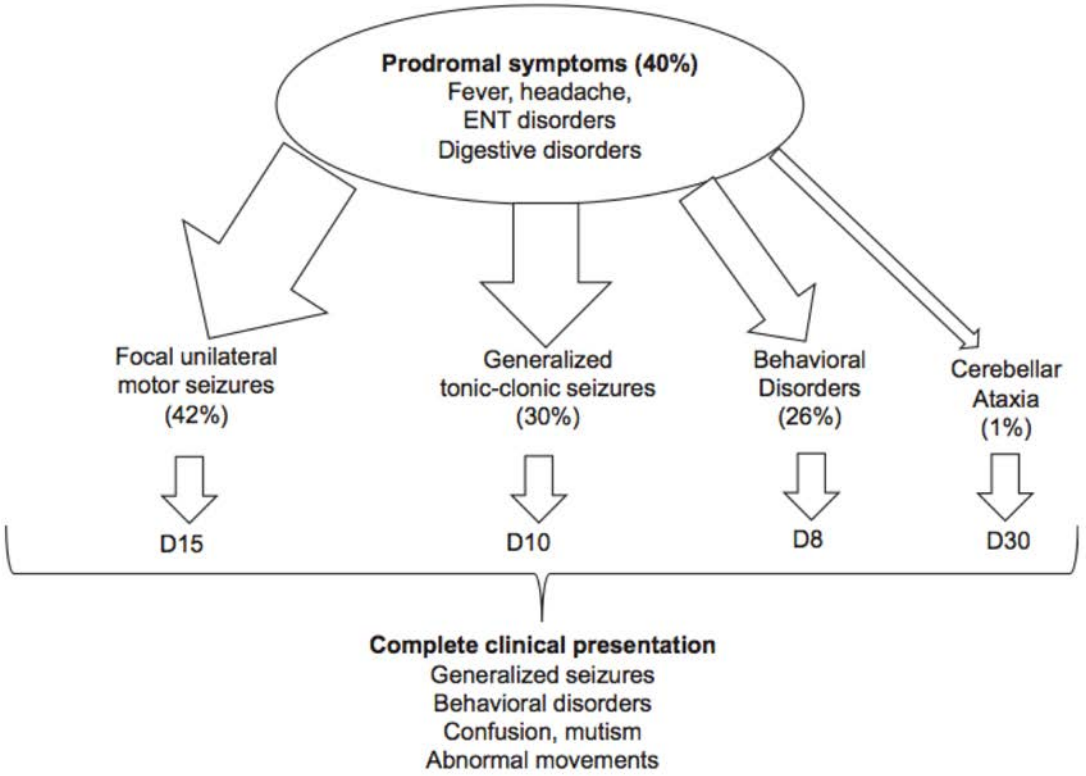
40% des cas sont des enfants



Tératomes non systématiques

Présentation différente chez les enfants

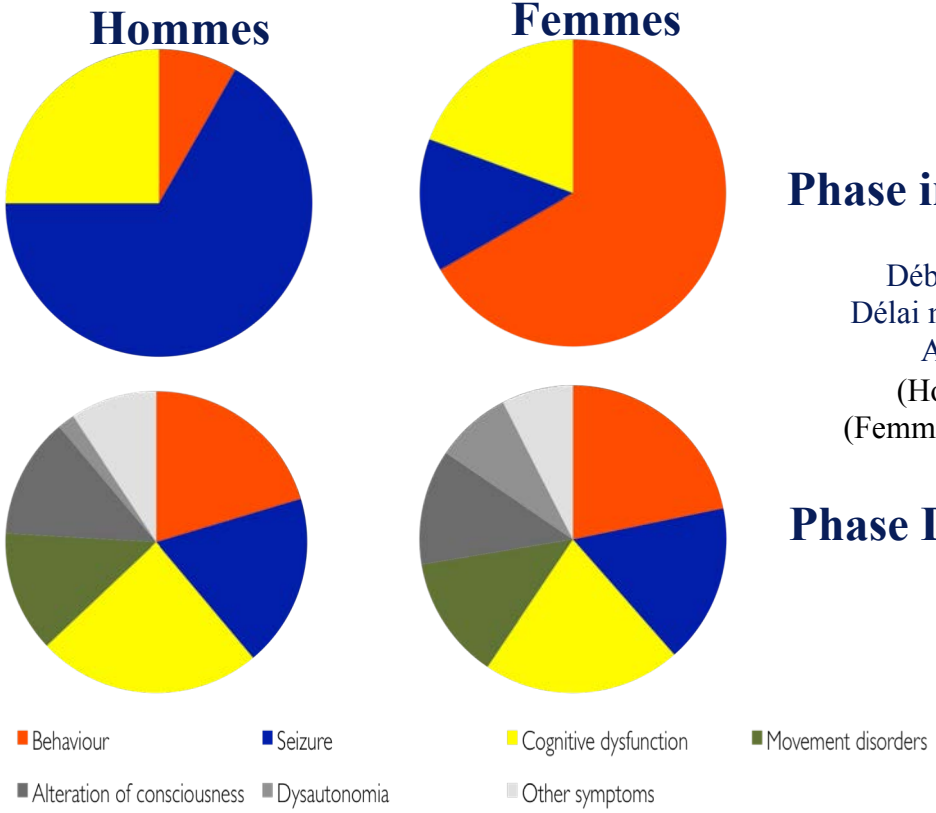
Série française de 50 enfants de moins de 12 ans



Favier et al, Eur J Ped Neurol 2018

Encéphalites à auto-antonticorps anti-NMDAr
Différences Hommes/femmes adultes

(13 hommes versus 58 femmes)



Phase initiale

Début épilepsies partielles
Délai médian de 12 jours (2-17)
Avant la phase d'état
(Hommes : 8/13, 61.5%)
(Femmes : 8/58, 14%, $p<0.001$)

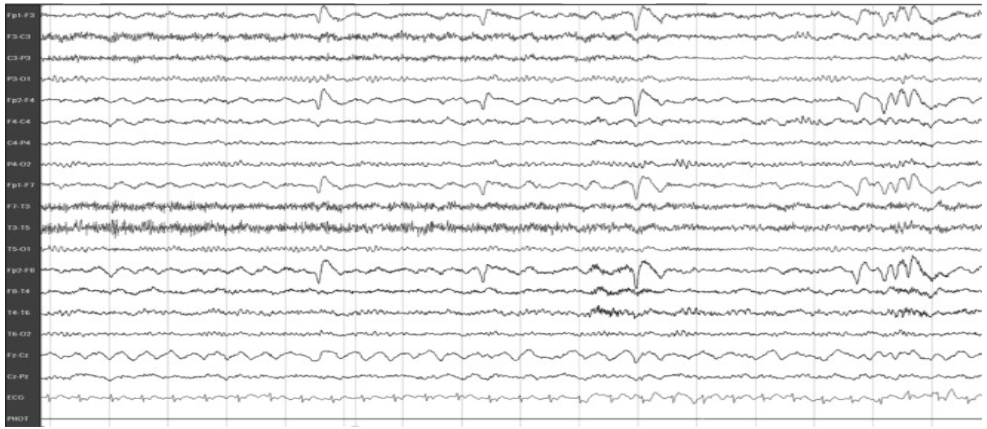
Phase D'état

Viaccoz et al, Neurology 2014

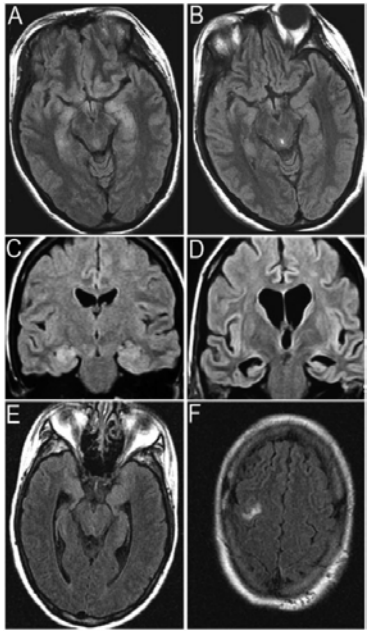
Diagnostic :

1) LCR : inflammation dans 95% des cas

2) EEG anormal dans 92% des cas

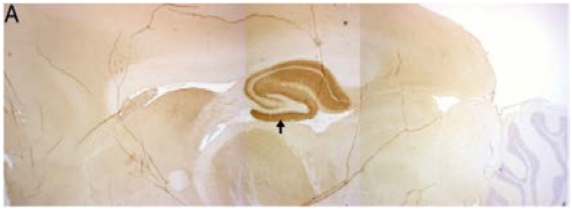


Greiner et al, Seizure 2011;20:266 - 270



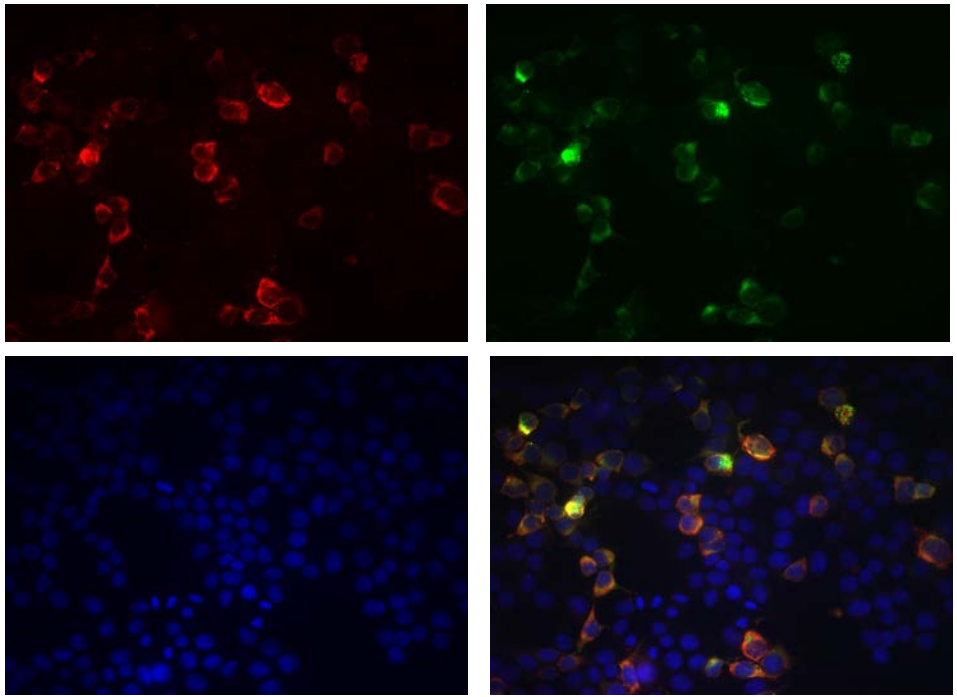
3) IRM encéphalique anormale 20 à 30% des cas, mais non spécifique

La présentation clinique est l'élément majeur du diagnostique



Detection of anti-NMDAR = CSF +++

- Indirect immunohistochemistry on rat brain slices
- Indirect immunohistochemistry on HEK 293 cells transfected with NR1/NR2B plasmids

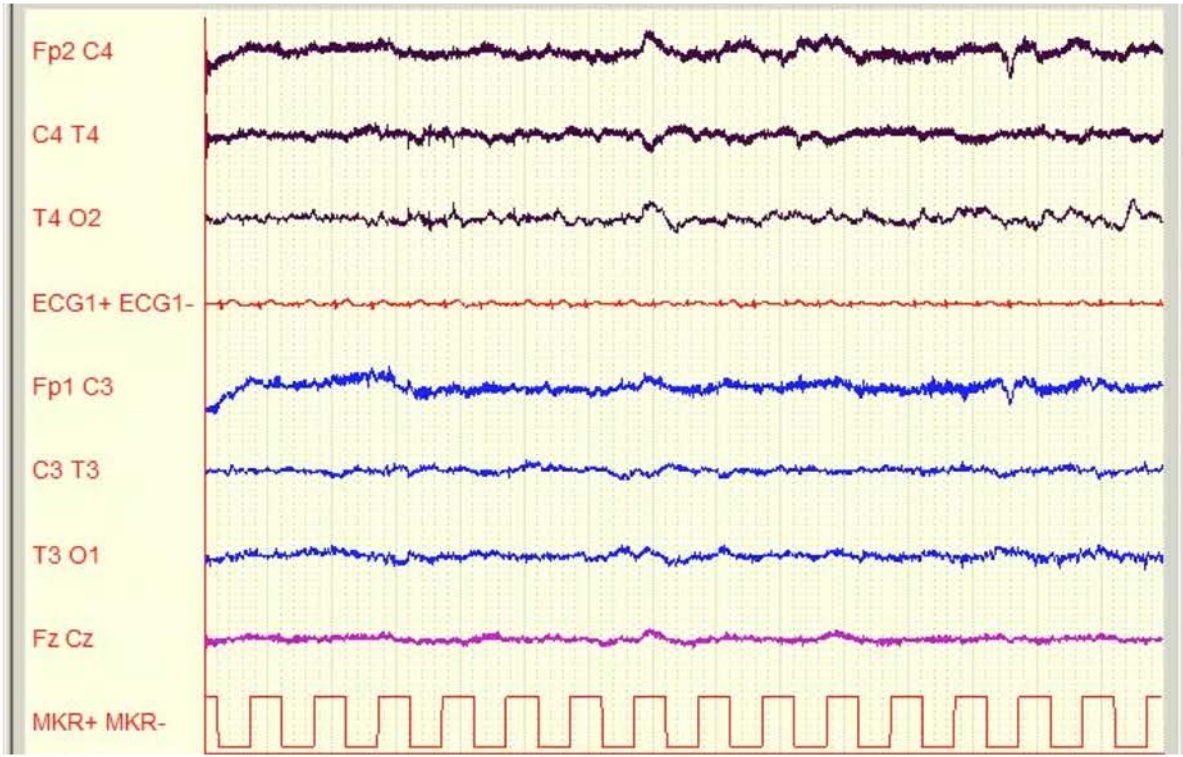


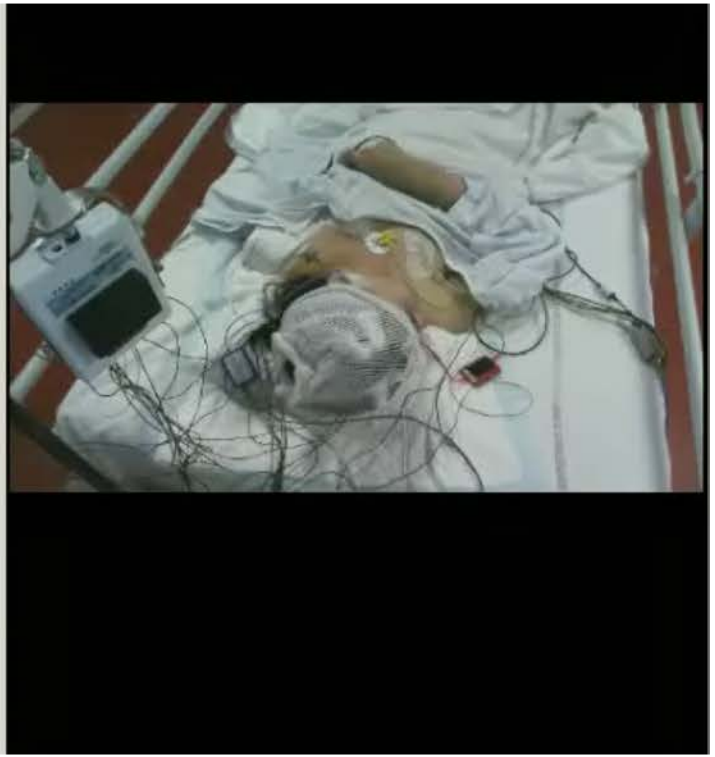
Environ 50 cas par an, en France

Seul moyen du diagnostic et seulement dans le LCR

Most than 70% of patients are initially in ICU and treatment are heterogeneous

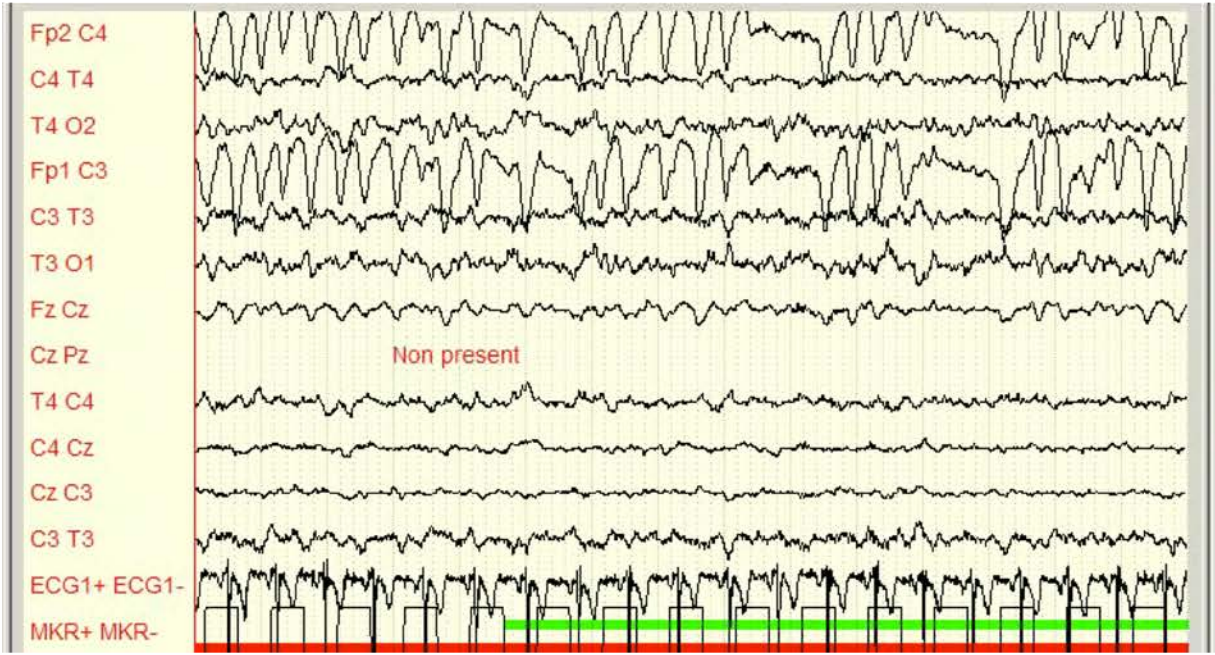
Vegetative crisis are frequent





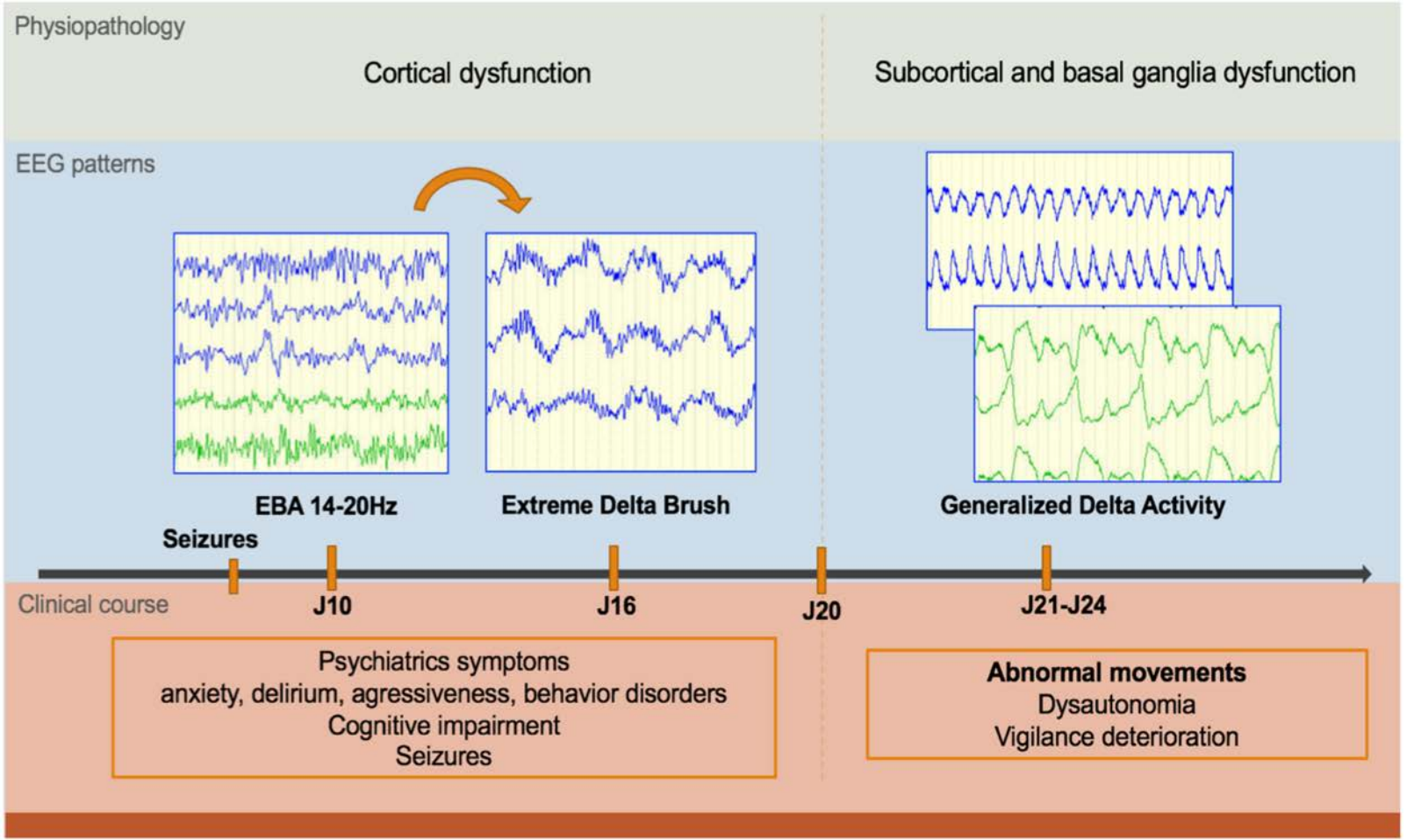
Most than 70% of patients are initially in ICU and treatment are heterogeneous

Abnormal rythmic EEG are not seizure



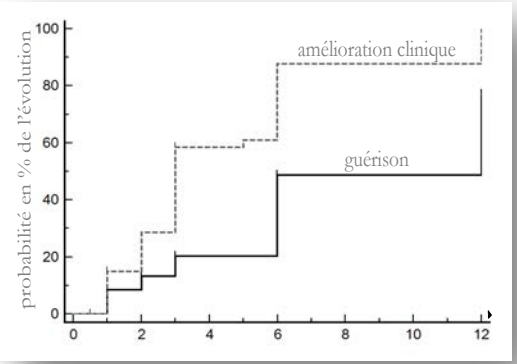
EEG recorded 6 months after the onset of NMDAR encephalitis

EEG patterns in anti-NMDA receptor encephalitis

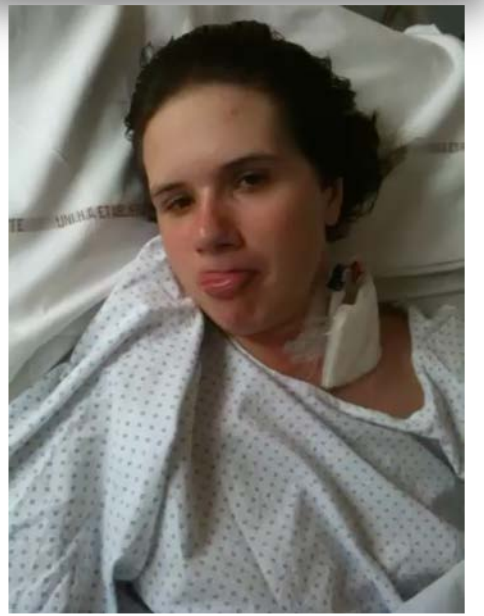


Jeannin-Mayer S, et al. Clin Neurophysiol. 2019 Feb;130(2):289-296.

Dramatic improvement with immunomodulator
(ivIg, plasmapheresis, cyclophosphamide and rituximab)



Complete improvement occurs in 80% of cases
But is very long

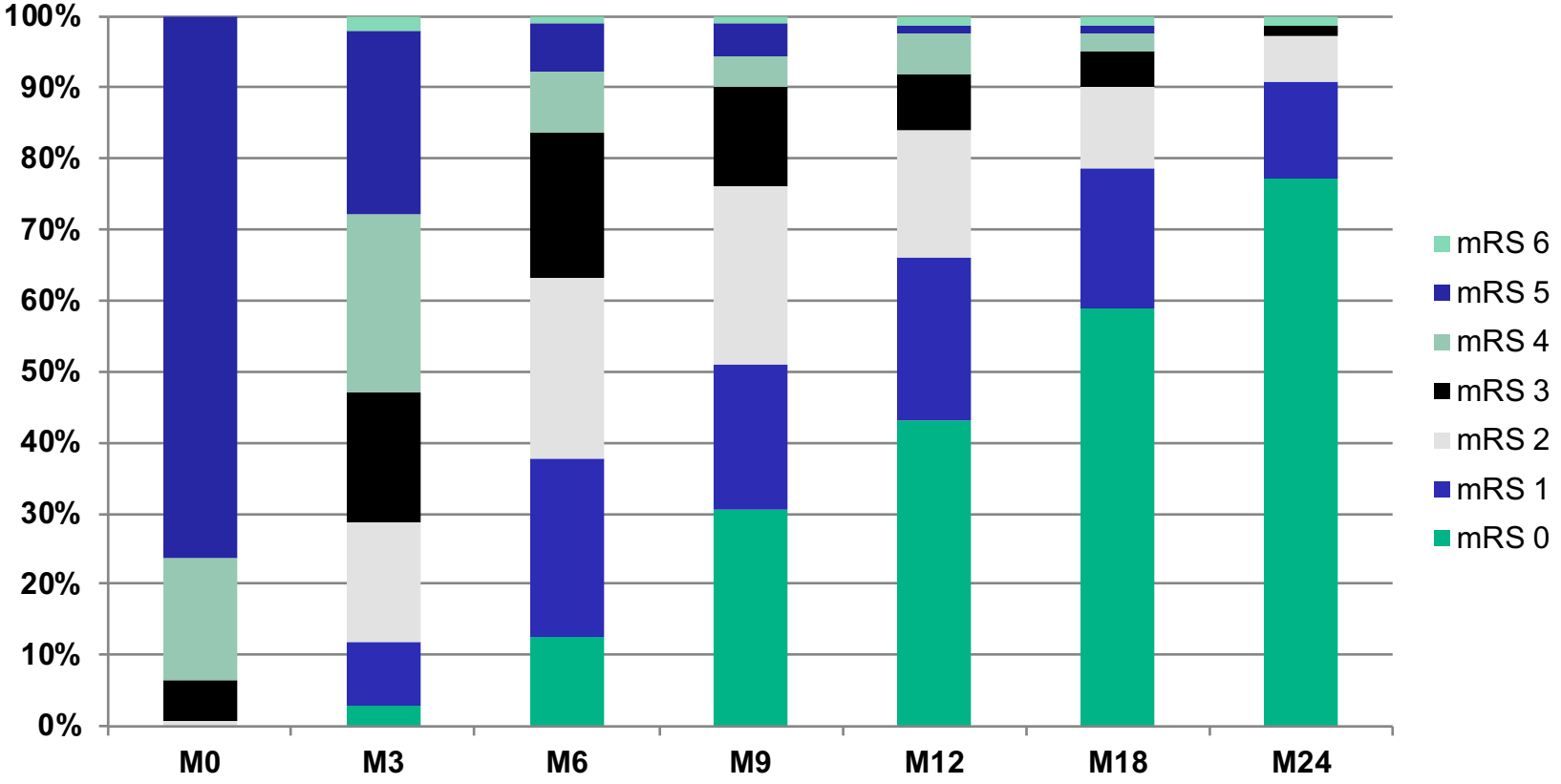


March 2013

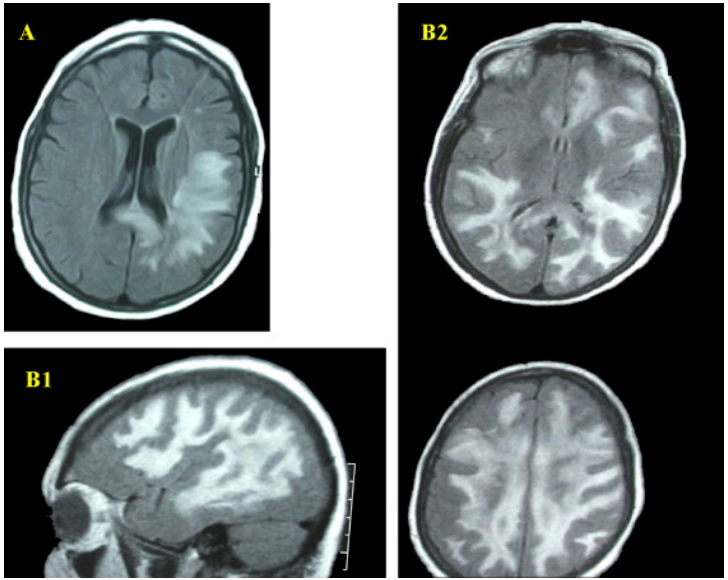
October 2013

March 2014

Clinical outcome of 109 adult patients with NMDAR-Abs encephalitis



Depuis 2007, d'autres encéphalites auto-immunes ont été décrites
Certaines avec des anomalies de l'RM cérébrale



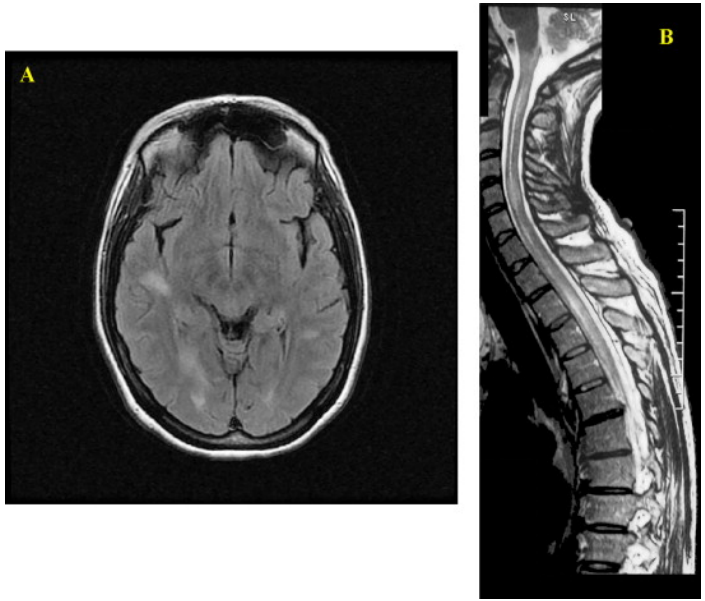
ADEM ?

Femme 68 ans, sept jours après un syndrome grippal.
Coma fébrile et hémiplégie droite.
Atteinte initiale : fronto-pariétale gauche et splénium du corps calleux (A).
Aggravation en quelques jours (B1, B2).

Évolution favorable sous corticoïdes et immunoglobulines polyvalentes

Sonneville et Wolf, Réanimation 2007;16:452-462

Conduite à tenir devant un tableau d'ADEM



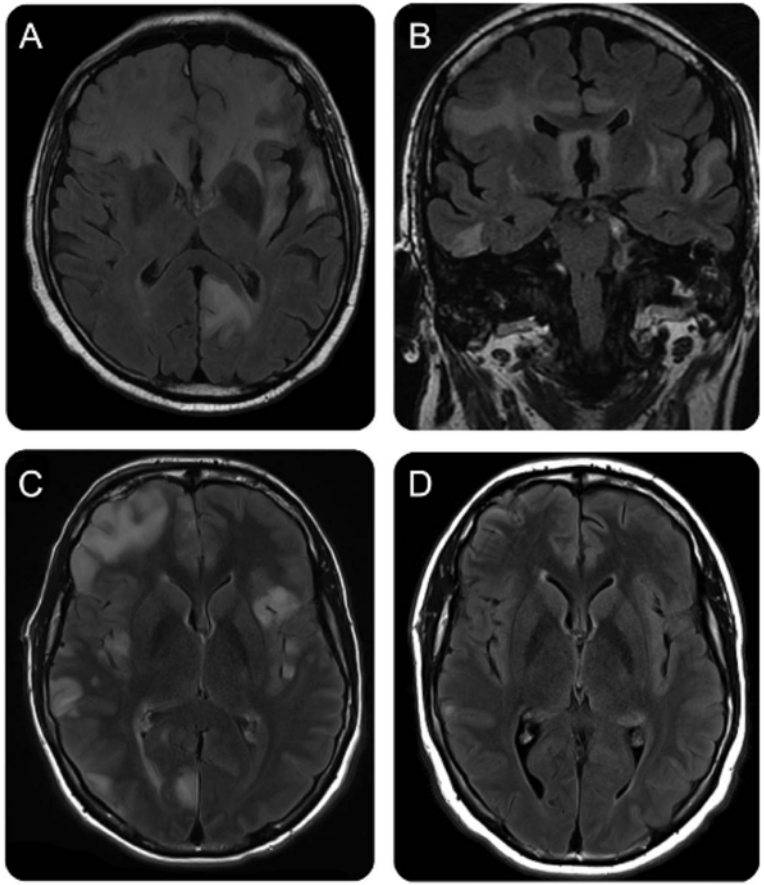
femme de 35 ans, six jours après un syndrome grippal.
Confusion fébrile avec raideur méningée et paraparésie.

Évolution favorable sous corticoïdes et échanges plasmatiques.

Anti-GFAP ?? Anti-AQP4 ?? Anti-MOG ?? Anti-GABAAR ??

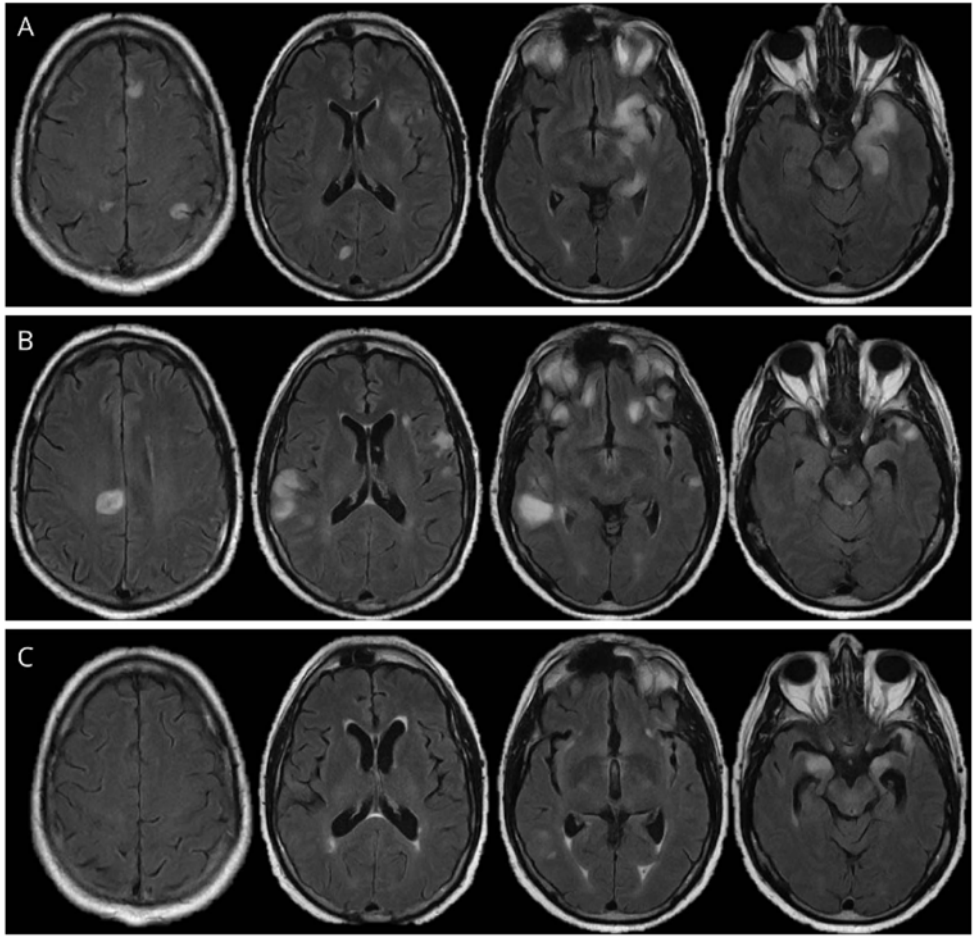
Sonneville et Wolf, Réanimation 2007;16:452-462

Encephalitis with GABAA receptor antibodies



Spatola et al, Neurology 2017;88:1012–1020

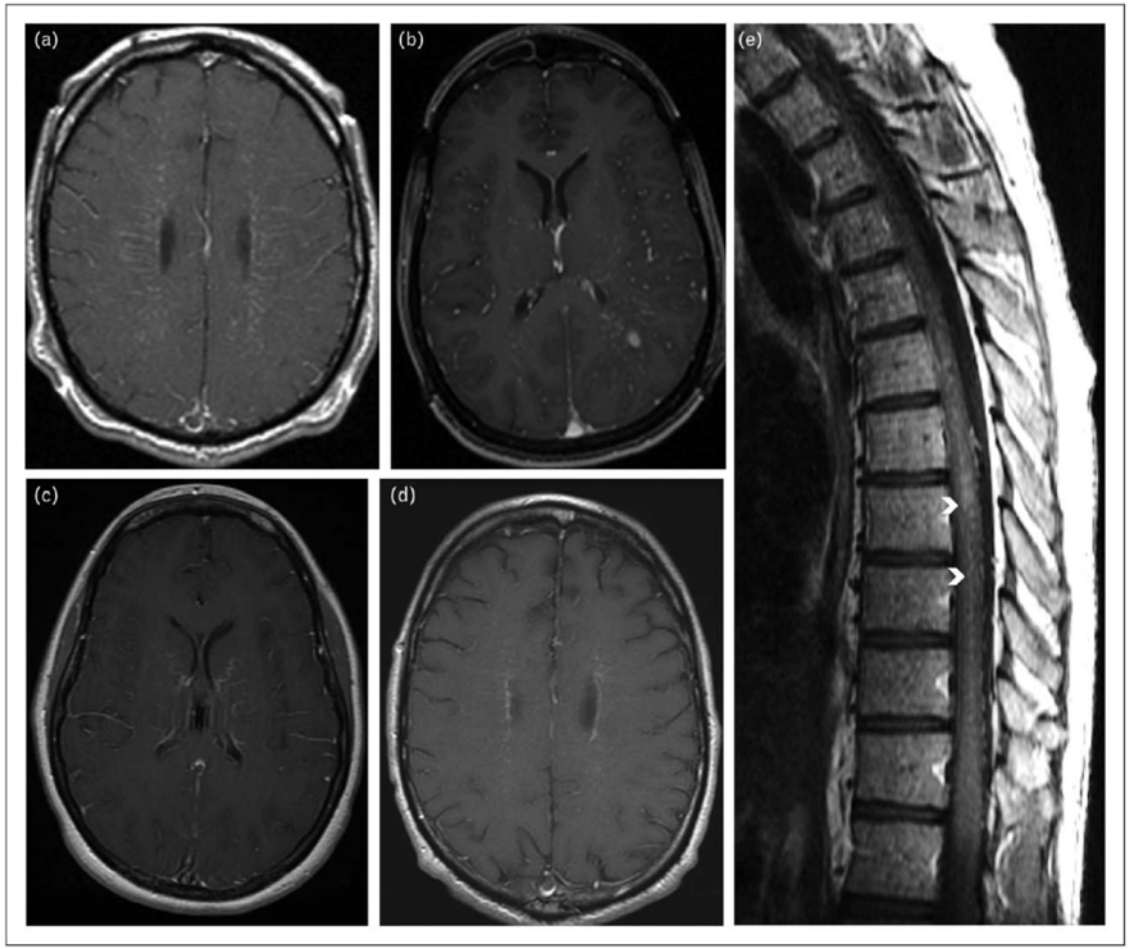
Encephalitis with GABAA receptor antibodies



Très épileptogène comme anti-GABABR

O'Connor et al, Neurol Neuroimmunol Neuroinflamm 2019;6:e552.

Anti-GFAP encephalitis



Kunchock et al, Curr Opin Neurol 2019, 32:000–000

Les encéphalites à anti-GFAP, surtout le tronc et l'encéphale (moelle et racines)

Table 2 Clinical Signs and Symptoms of Patients With Anti-GFAP Antibodies

	French cohort[a]	Flanagan et al.,[2] 2017 (USA)	Long et al.,[4] 2018 (China)	Iorio et al.,[6] 2018 (Italy)	Dubey et al.,[3] 2018 (USA)	Kimura et al.,[7] 2019 (Japan)
Rhombencephalitis	30/46 (65)	NA	NA	4/22 (18)	NA	NA
Ataxia or cerebellar dysfunction	25/44 (57)	10/35 (29)	7/19 (37)	3/22 (14)	32/90 (36)	6/14 (43)
Eye movement disorders	17/46 (37)	6/37 (16)	NA	NA	11/90 (12)	NA
Swallowing problems	5/46 (11)	NA	NA	1/22 (5)	NA	NA
Confusion	29/46 (63)	21/37 (57)[b]	NA	NA	NA	NA
Headache	27/44 (61)	14/36 (39)	12/19 (63)	1/22 (5)	(63)[c]	11/14 (79)
Consciousness disturbance	23/46 (50)	21/37 (57)[b]	1/19 (5)[d]	4/22 (18)	NA	11/14 (79)
Meningeal signs other than headache	20/42 (48)	12/37 (32)	NA	1/22 (5)	(63)[c]	10/14 (71)
Bladder dysfunction	21/45 (47)	2/34 (6)	NA	1/22 (5)	NA	NA
Movement disorders	19/46 (41)	15/37 (41)[e]	3/19 (16)[f]	3/22 (14)	NA	9/14 (64)
Cognitive decline	14/46 (30)	NA	3/19 (16)[g]	NA	NA	3/14 (21)[h]
Psychiatric symptoms	13/46 (28)	10/35 (29)	6/19 (32)[i]	2/22 (9)	NA	5/14 (36)[i]
Dysautonomia	8/46 (17)	8/34 (24)	NA	NA	19/90 (21)	8/14 (57)
Seizures	5/46 (11)	7/37 (19)	2/19 (11)	7/22 (32)	10/90 (11)	2/14 (14)
Extrapyramidal syndrome	5/46 (11)	NA	NA	NA	NA	NA
Abnormal vision	4/45 (9)	12/37 (32)[i]	12/19 (63)	1/22 (5)	NA	NA

Gravier-Dumonceau A, et al. Neurology. 2022 Feb 8;98(6):e653-e668.

Journal of Neurology
https://doi.org/10.1007/s00415-018-9132-0

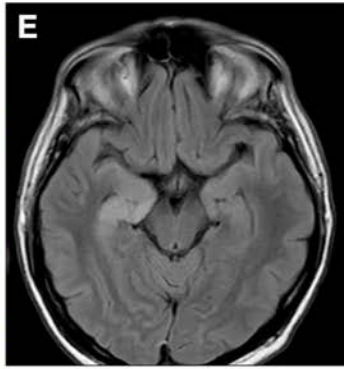
Encéphalites à anti-GABABr

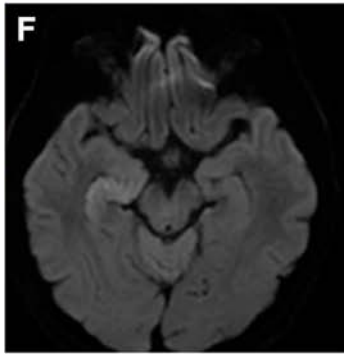
ORIGINAL COMMUNICATION

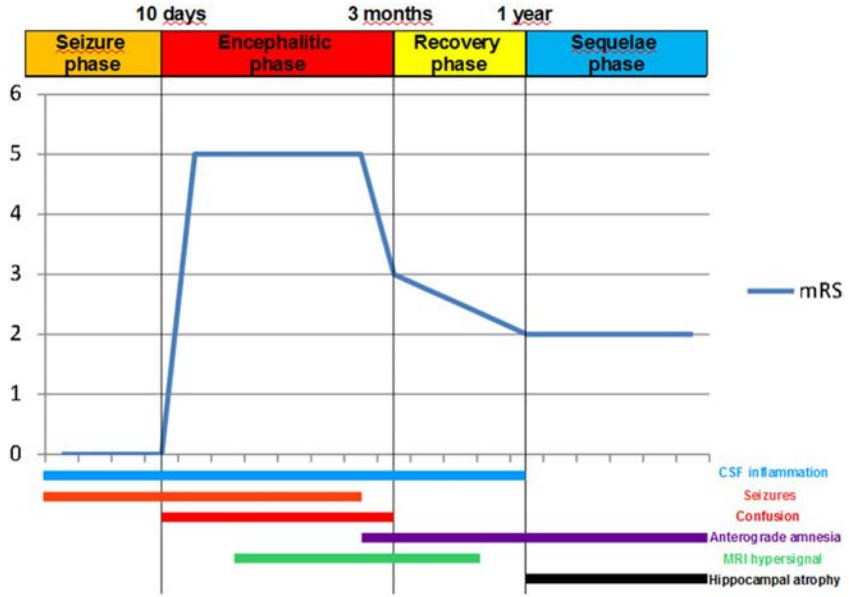
Isolated seizures are a common early feature of paraneoplastic anti-$GABA_B$ receptor encephalitis

Aurélien Maureille[1,2] · Tanguy Fenouil[3] · Bastien Joubert[1] · Géraldine Picard[1] · Véronique Rogemond[1] · Anne-Laurie Pinto[1] · Laure Thomas[1] · François Ducray[1,4] · Isabelle Quadrio[5] · Dimitri Psimaras[1,7] · Giulia Berzero[1,7] · Jean-Christophe Antoine[1,6] · Virginie Desestret[1,4] · Jérôme Honnorat[1,4]

Received: 19 September 2018 / Revised: 21 October 2018 / Accepted: 16 November 2018







Encéphalites et anticorps anti-AMPAR

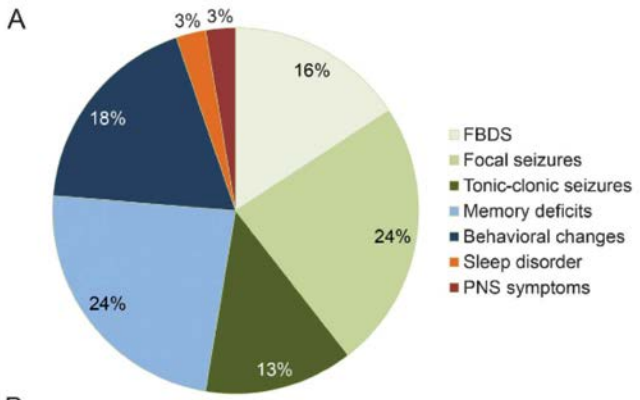
Table 1. Clinical Features and Outcomes in 7 Patients With Encephalitis Associated With Antibodies Against the α-Amino-3-Hydroxy-5-Methyl-4-Isoxazolepropionic Acid Receptor

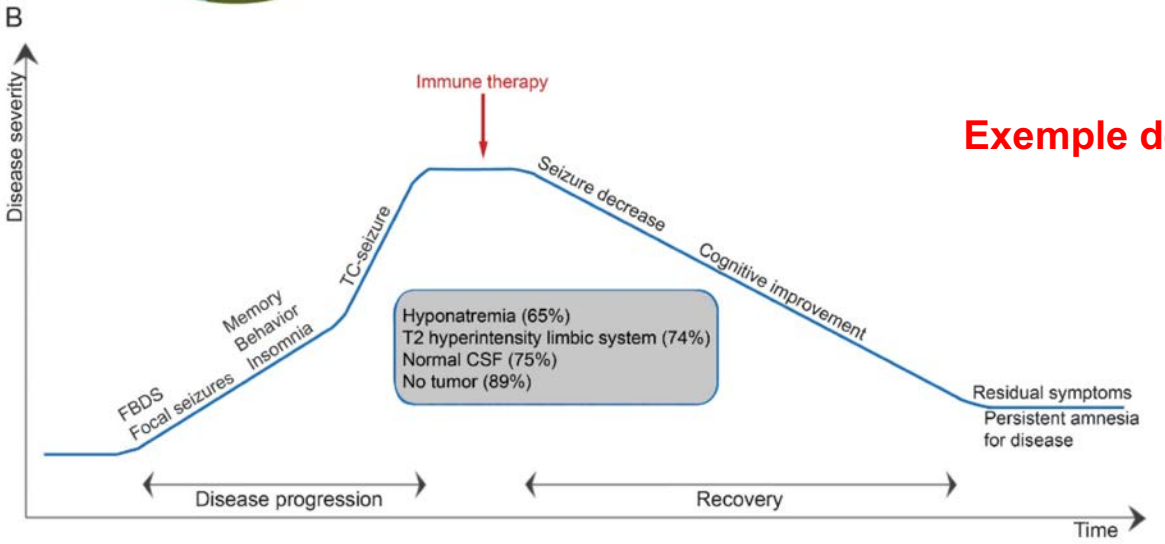
Variable	Mode of Onset			
	Confusion (n = 3)	Epileptic (n = 1)	Amnestic (n = 1)	Fulminant Encephalitis (n = 2)
Age, y	56, 58, 75	43	92	21, 22
Main clinical features	Confusion, psychiatric, behavioral, cognitive (memory, executive)	Temporal seizures	Subacute anterograde amnesia	Stereotypical presentation: (1) confusion, headache, memory problems; (2) hypertonic coma, fever, eye deviation; (3) resolution of behavioral, psychiatric, cognitive disorders
Additional clinical features	Cognitive (aphasia, apraxia), sensory and motor deficits, sleep disorder (insomnia), headache, cerebellar symptoms	Slight memory impairment, dysexecutive features, mild cerebellar symptoms, sleep disorder (insomnia)	Slight ataxia	Motor deficits, downbeat nystagmus, oculogyric crisis, abdominal pain, sleep disorder (insomnia), sphincter dysfunction
Brain magnetic resonance imaging	Temporomesial T2-weighted hyperintensities, complete resolution or slight bilateral HA at 6 mo	Bilateral temporomesial T2-weighted hyperintensities, lateralized HA at 6 mo	Normal	Diffuse T2-weighted hyperintensities, resolution or severe cortical atrophy
Electroencephalogram	Normal	Right temporal seizures	Normal	Bifrontal sharp and slow waves (1 patient)
Cerebrospinal fluid	Inflammation (pleiocytosis, oligoclonal bands) or normal	Normal	Oligoclonal bands	Pleiocytosis
Oncological status	Lung cancer (1 patient)	Thymus hyperplasia	None	Thymus carcinoma (1 patient)
Central nervous system antibodies	Anti-Hu (1 patient)	Anti-Lgi1, anti-GAD65	None	None
Systemic antibodies	Antinuclear, anti-intrinsic factor (1 patient)	Anti-IA2	None	Antinuclear (1 patient)
Follow-up period, mo	2, 9, 15	31	6	18, 12
Outcome	Progressive improvement, persistence of significant cognitive impairment	Seizure control, slight residual memory impairment	Stabilization	Marked improvement (1 patient), death (1 patient)
Modified Rankin Scale score at the last visit	2, 3, 3	1	1	1, 6

Abbreviation: HA, hippocampal atrophy.

Joubert et al, JAMA Neurology 2015;72:1163-1169

Toutes les encéphalites auto-immunes n'ont pas d'inflammation du LCR et peuvent être chroniques

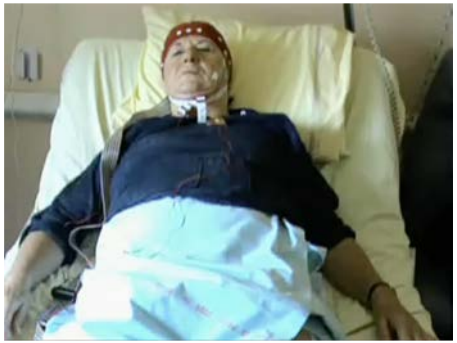


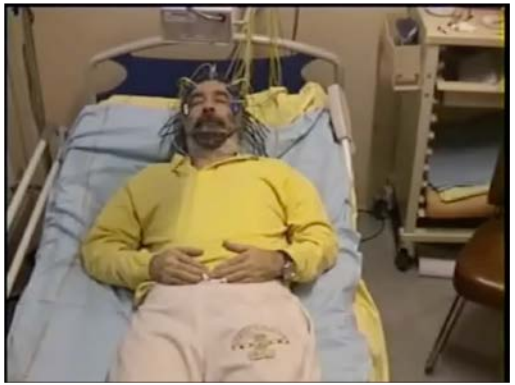


Exemple des encéphalites à anti-Lgi1

Agnes van Sonderen et al, Neurology 2016;87:1–8

Patients with anti-Lgi1 is associated with different syndromes
Ex: bracchio facial dystonia *Irani et al, 2011 & 2013*
may respond to steroids and not to anti-epileptic drugs





Movies from V. Navarro, Pitié-Salpétrière

Chaque encéphalite auto-immune a une sémiologie, une évolution et une association, ou pas, au cancer qui est spécifique Suivant l'âge, le sexe et l'autoanticorps associé

Hu	Old subjects with history of smoking or SCLC; rarely associated with pure LE; frequently accompanied by encephalomyelitis or sensory neuronopathy Children with pharmacoresistant epilepsy
Ma2	Men younger than 45 years, with germ-cell tumor of the testis.. The syndrome develops as LE, upper brainstem or diencephalic encephalitis.
LGI1	Patients older than 50 years, with mild male predominance. In most cases the clinical picture is a typical LE; 60% of the patients develop hyponatremia. Fascio-brachial dystonic seizures.
GABAbR	Usually affect adults; 50% have an underlying SCLC or neuroendocrine tumor. The syndrome presents as typical LE with early and prominent seizures..
AMPAR	Mildly predominates in women. About 50% of the patients present with LE; the rest develop LE combined with other symptoms. Some cases present with pure psychosis. About 65% of the patients have an underlying tumor (mainly SCLC, thymoma).
GAD	May occur as pure or predominant LE. In these cases the syndrome is often paraneoplastic and screening for an underlying tumor is recommended. Possible co-existence of GAD antibodies and cell surface neuronal antibodies (e.g., AMPA or GABAbR)
NMDAR	Predominantly young women with psychiatric symptoms, seizures, abnormal movements and dysautonomia
CASPR2	Pure LE without cancer. Only few described patients. Also described in Morvan's syndrome and Neuromyotonia
CRMP5	Rarely associated with pure LE. Accompanying features may include uveitis, retinopathy, optic neuropathy, chorea, and peripheral neuropathy
DPPX	Patients often have gastrointestinal dysfunction, diarrhea, and loss of weight preceding the neurological syndrome (psychiatric manifestations, confusion, seizures, tremor, myoclonus, nystagmus).
GABAaR	Patients present with multifocal (cortical-subcortical FLAIR MRI changes) or diffuse encephalitis, with prominent seizures and status epilepticus, often requiring induced coma. Presentation as classical LE is unusual. Most patients do not have a tumor; some have thymoma.
mGluR5	Patients present with non-focal encephalitis, and a clinical picture suggesting involvement beyond the limbic system. Most patients have Hodgkin's lymphoma.
AK5	Patients with subacute anterograde amnesia, no epilepsy, bilateral FLAIR hypersignal, CSF inflammation and high tau protein level. No cancer

TOUS CES SYNDROMES SONT TRÈS RARES

Antibodies	2023	2022	2021	2020	2019	2018	2017	2016	2015	2014	2013	
LGI1	57	42	29	46	49	29	25	25	22	15	7	
NMDAR	52	41	44	43	40	56	43	29	47	29	34	✻
GAD	50	50	29	21	32	15	24	28	9	7	4	*
GFAP	49	30	27	25	27	18	3	0	0	0	0	✻
HU	43	27	31	40	35	35	24	29	33	31	27	
CASPR2	23	23	18	17	14	15	17	8	16	11	5	
SOX1	14	5	23	21	32	23	31	13	7	1	6	
CV2/CRMP5	12	10	13	7	11	16	6	13	4	1	10	
YO	10	16	13	15	18	20	11	14	20	6	12	
MA2	10	13	3	8	5	12	5	4	4	1	6	
IgLON5	7	29	7	4	1	2	1	0	1	0	0	✻
GABABR	6	9	16	13	4	4	5	5	3	3	5	✻
DNER	5	2	3	4	3	4	4	4	1	2	1	
KLHL11	4	2	2	10*	0	0	0	0	0	0	0	
Neurofilament	4	2	0	0	0	0	0	0	0	0	0	
Amphiphysine	3	7	4	4	2	1	3	2	5	1	1	
AMPAR	3	0	3	2	2	0	3	1	1	2	0	*
AK5	3	2	0	2	3	0	2	2	7	0	0	
mGluR1	3	0	0	0	2	0	1	0	0	0	0	
RI	2	4	3	7	3	7	2	2	3	2	2	

Données annuelles du centre maladies rares français coordonné par Lyon

- Entre 2 et 7 cas/million/an

IgLon5-Abs encephalitis. A tauopathy with auto-immune disease more challenging to diagnose than other autoimmune encephalitis

A novel non-rapid-eye movement and rapid-eye-movement parasomnia with sleep breathing disorder associated with antibodies to IgLON5: a case series, characterisation of the antigen, and post-mortem study

Lidia Sabater, Carles Gaig*, Ellen Gelpi*, Luis Bataller, Jan Lewerenz, Estefanía Torres-Vega, Angeles Contreras, Bruno Giometto, Yaroslau Compta, Cristina Embid, Isabel Vilaseca, Alex Iranzo, Joan Santamaría, Josep Dalmau, Francesc Graus*

Summary

Background Autoimmunity might be associated with or implicated in sleep and neurodegenerative disorders. We aimed to describe the features of a novel neurological syndrome associated with prominent sleep dysfunction and antibodies to a neuronal antigen.

Lancet Neurol 2014
Published Online
April 3, 2014

5W/3M
Mean age: 59 years old
Clinical presentation looklikes neurodegeneration
REM parasomnia, brainstem involvement, dysautonomia
CSF, MRI, EEG normal
HLA DQB1*501

Séjour en réanimation
Pour hypoventilation

Coma
Syndrome d'apnée du sommeil
Dysautonomie

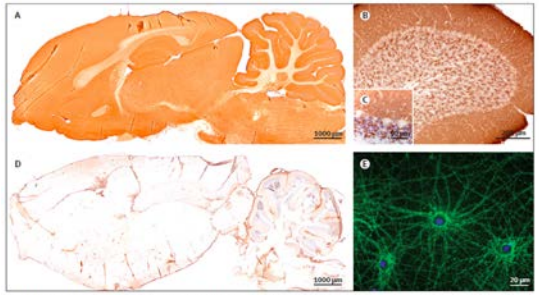
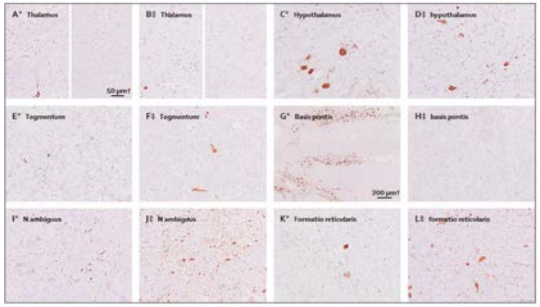


Figure 3: Reactivity of patients' antibodies with rat brain and cultures of hippocampal neurons



Conclusion :

- Concept d’encéphalite autoimmune avec autoanticorps clairement établi
- Les autoanticorps dirigés contre un antigène membranaire jouent un rôle direct
- Existence très probable de formes frustes ou modérées
- La fréquence des formes idiopathiques est supérieure aux paranéoplasiques
- Les tumeurs sont un élément déclencheur parmi d’autres
- Aucun guideline de traitement
- Physiopathologie exacte non élucidée
- Maladies rares, mais importantes à connaitre car curables +++
- Les anticorps peuvent être demandés facilement et faits dans le même temps

BETPSY
Biomarkers in autoimmune EncephaliTis and Paraneoplastic neurological SYndromes

https://www.rhu-betpsy.fr/

Rare disease reference center, Lyon, France	HCL Lyon, France	EFS Lyon, France	Collaborators
Alberto Vogrig	Julie Haesebaert	Valérie Dubois	Aditya Ambati
Anne-Laurie Pinto Marie Benaiteau	Mad-Hélénie Elsensohn		Julien Hedou
Géraldine Picard	Delphine Maucort-Boulch		Vicente Peris Sempere
Macarena Villagrán-Garcia			
Lucie Aliouane			Emmanuel Mignot
Sterenn Closs			
Virginie Desestret			
Le Duy Do			
Bastien Joubert			
Elise Peter			
Véronique Rogemond			
Marine Villard			
Valentin Wucher Sergio Muniz-Castrillo