Claustrum damage and refractory status epilepticus following febrile illness

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Objective: to characterize the clinical, EEG, and brain imaging findings in an adult case-series of patients with de novo refractory status epilepticus (SE) occurring after a febrile illness.

Methods: a retrospective study (2010-2013) was undertaken with the following inclusion criteria:

(a) previously healthy adults (> 16 years of age) with refractory SE;
(b) seizures onset 0–21 days after a febrile illness, and
(c) lacking evidence of infectious agents in CSF;
(d) no previous history of seizures (febrile or afebrile), as well as previous or concomitant neurological disorder.

Among **155 refractory SE** cases observed in the study period, **six** (17 – 35 years-old) fulfilled the inclusion criteria.

Results:

Confusion and stupor were the most common symptoms at disease onset, followed after a few days by acute repeated seizures that were uncountable in all.

Seizures consisted of focal motor/myoclonic events with alternating side involvement and subsequent generalization.

Anti-epileptic drugs failed in every patient to control seizures.

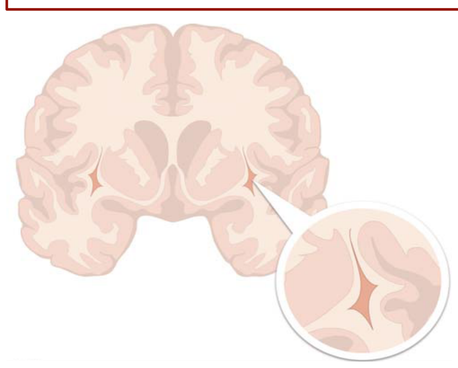
All subjects requiring intensive care unit admission. **Barbiturate-coma** with burst-suppression pattern was applied in four out of six patients for 5 – 14 days.

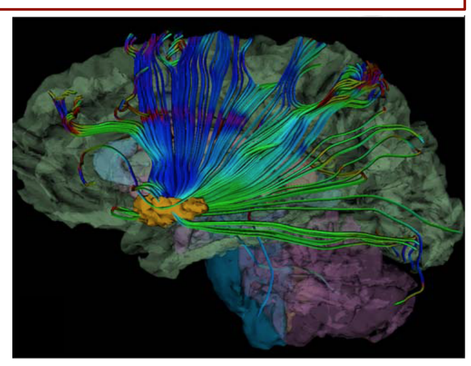
One subject died in the acute phase.

In each patient we observed a reversible bilateral **Claustrum** MRI hyperintensity (FLAIR; T2; DWI seq.) time-related with SE (Figures).

All patients had **negative** multiple neural antibodies testing (Table).

Four out of five surviving patients develop **chronic epilepsy** .

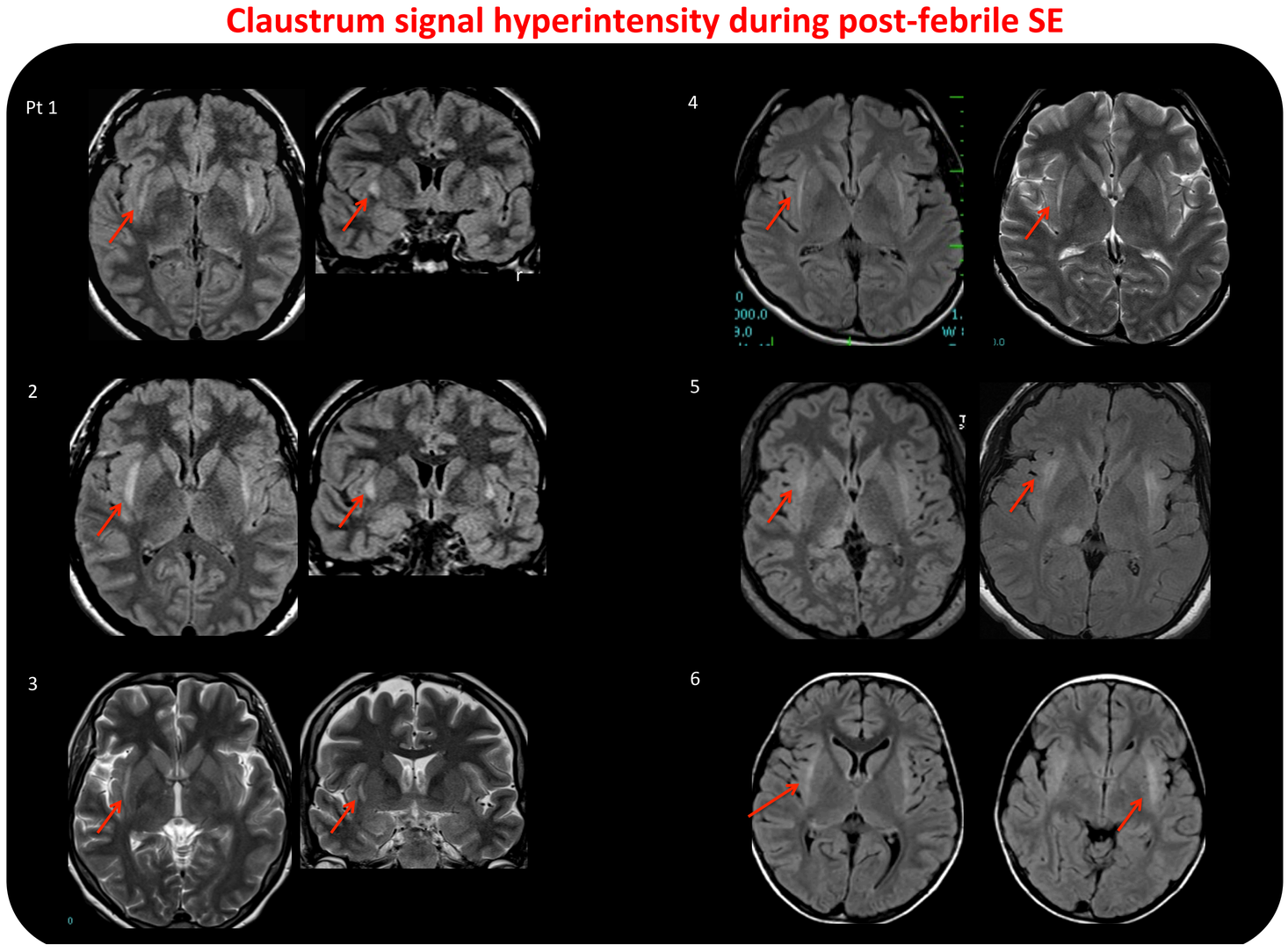


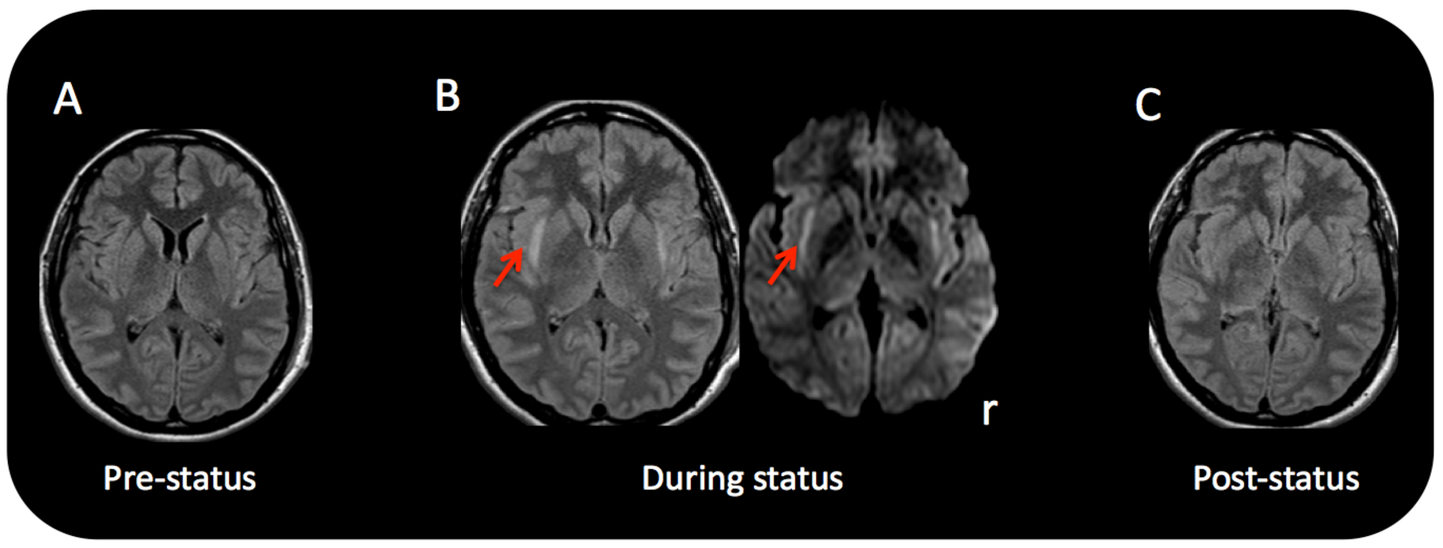


Connectivity of the Clausturm. From Torgerson et al, HBM 2014

The Claustrum can potentially bind together and modulate neural activities (epileptic activity in our case) from and to widespread cortical areas.

Claustrum signal hyperintensity during post-febrile SE





Pt.	Timing from fever (days)	Timing from SE onset (days)	Vigilance at time of "claustrum sign"	Negative laboratory findings
1	17	10	Coma (on anaesthetic treatment)	LGI1, Caspr2, NMDAr, AMPAr, $GABA_{(B)}$, $GABA_{(A)}$, mGlu-R1-R3-R5, POLG1 mutations
2	11	4	Coma (on anaesthetic treatment)	LGI1, Caspr2, NMDAr, $GABA_{(B)}$,
3	9	3	Coma (on anaesthetic treatment)	LGI1, Caspr2, NMDAr,
4	13	9	Stupor	LGI1, Caspr2, NMDAr, VGCC,
5	10	2	Coma (on anaesthetic treatment)	LGI1, Caspr2, NMDAr,
6	10	4	Coma (on anaesthetic treatment)	LGI1, Caspr2, VGCC-Ab, NMDAr

Conclusions: we described a group of **adult patients** with febrile-related status epilepticus and outlined the role of Claustrum damage in this condition. Future prospective studies are needed to delineate the specificity of this imaging biomarker, its pathogenetic role in refractory status epilepticus, and the aetiology of the condition