

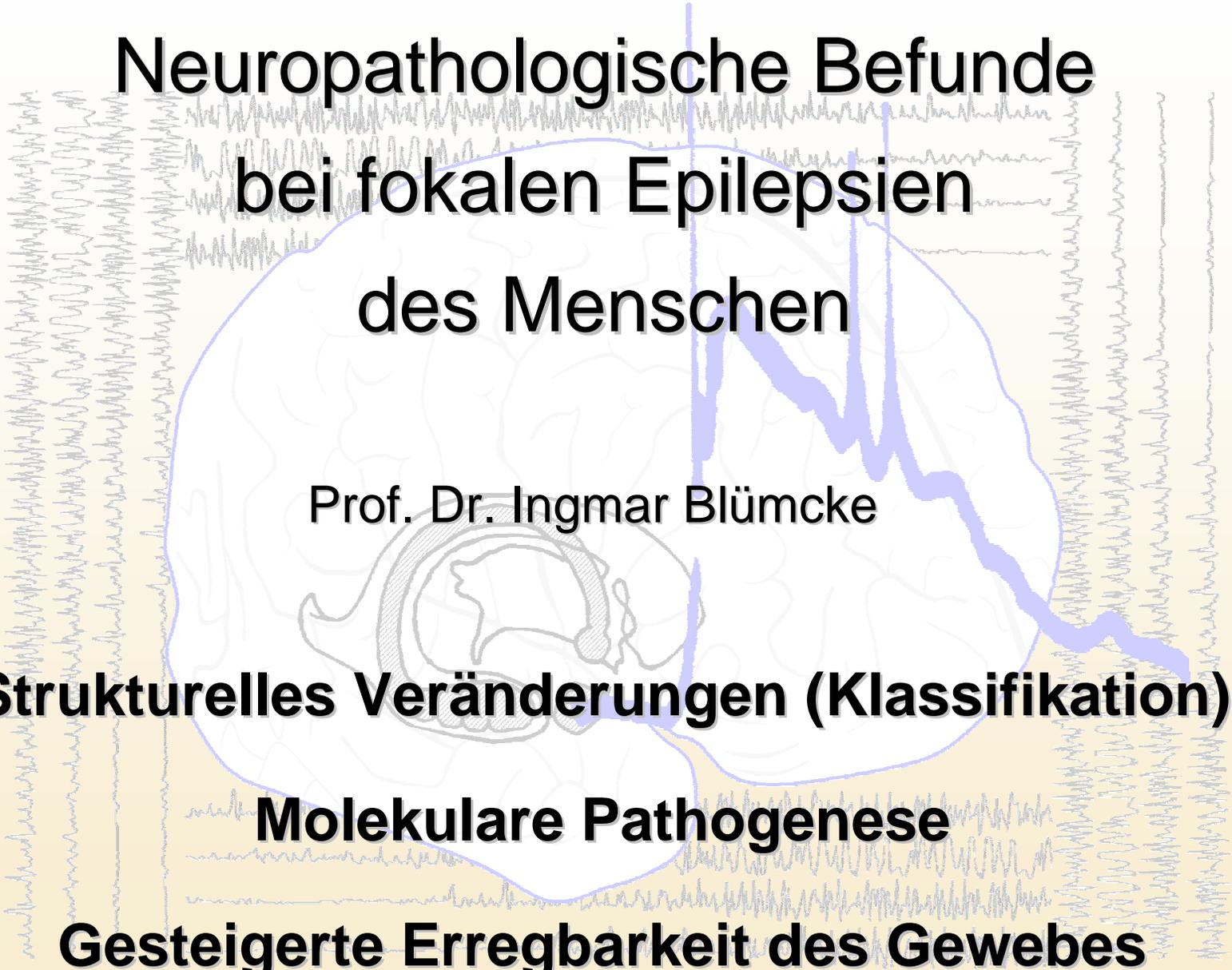
Neuropathologische Befunde bei fokalen Epilepsien des Menschen

Prof. Dr. Ingmar Blümcke

Strukturelle Veränderungen (Klassifikation)

Molekulare Pathogenese

Gesteigerte Erregbarkeit des Gewebes





Neuropathologische Befunde bei Patienten mit fokalen Epilepsien

Hippocampussklerose	(n = 902)
Epilepsie-assoziierte Tumoren	(n = 642)
Fehlbildungen	(n = 303)

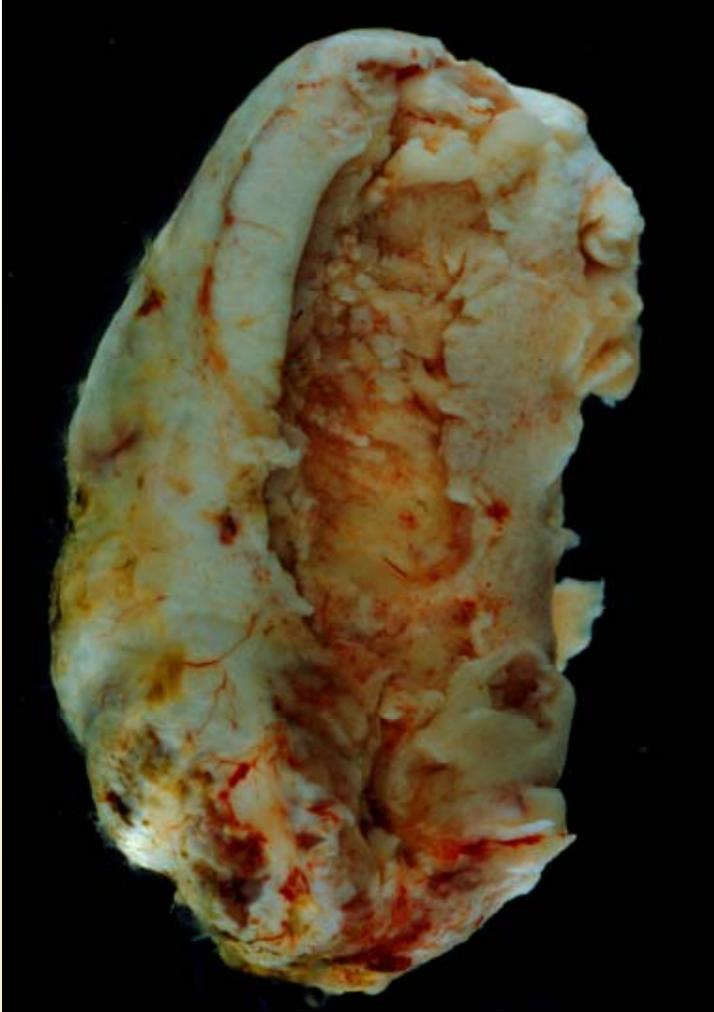
Neuropathologisches Epilepsie-Register
am Lehrstuhl für Neuropathologie der FAU Erlangen (gegr. 2003)

n = 3500 Patienten, davon 2000 ausgewertet

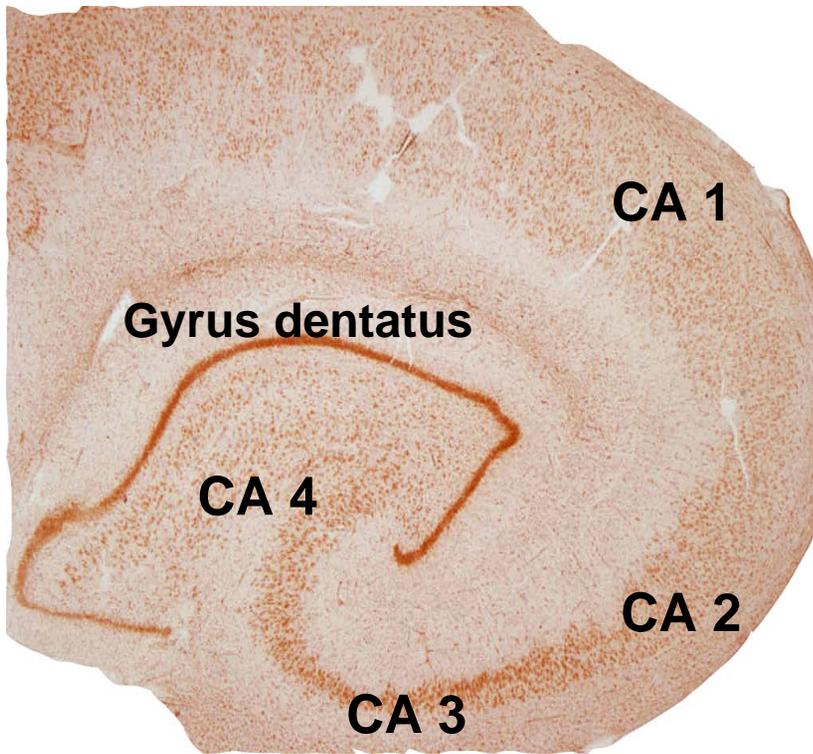
Hippocampusklerose



Hippocampusklerose



Hippocampusklerose



Gyrus dentatus

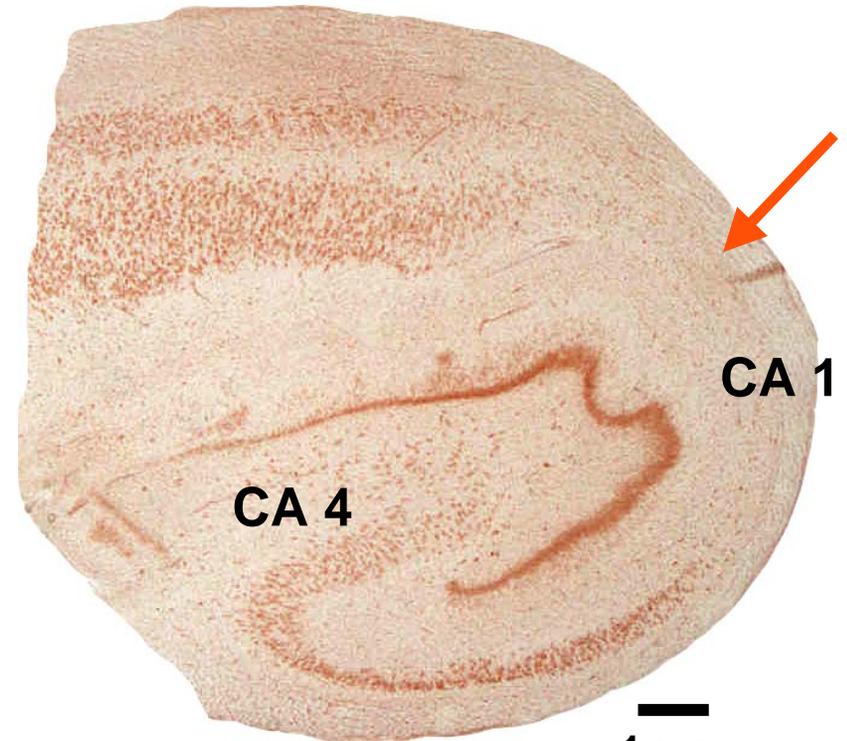
CA 1

CA 4

CA 2

CA 3

Normalbefund



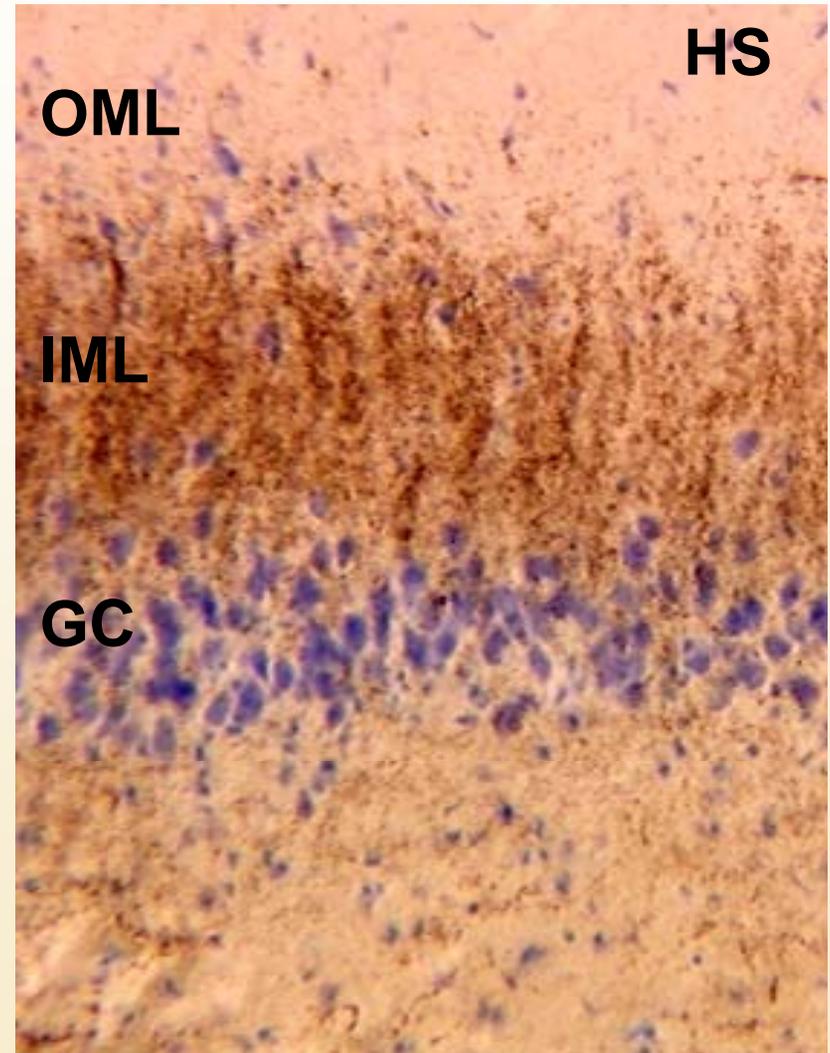
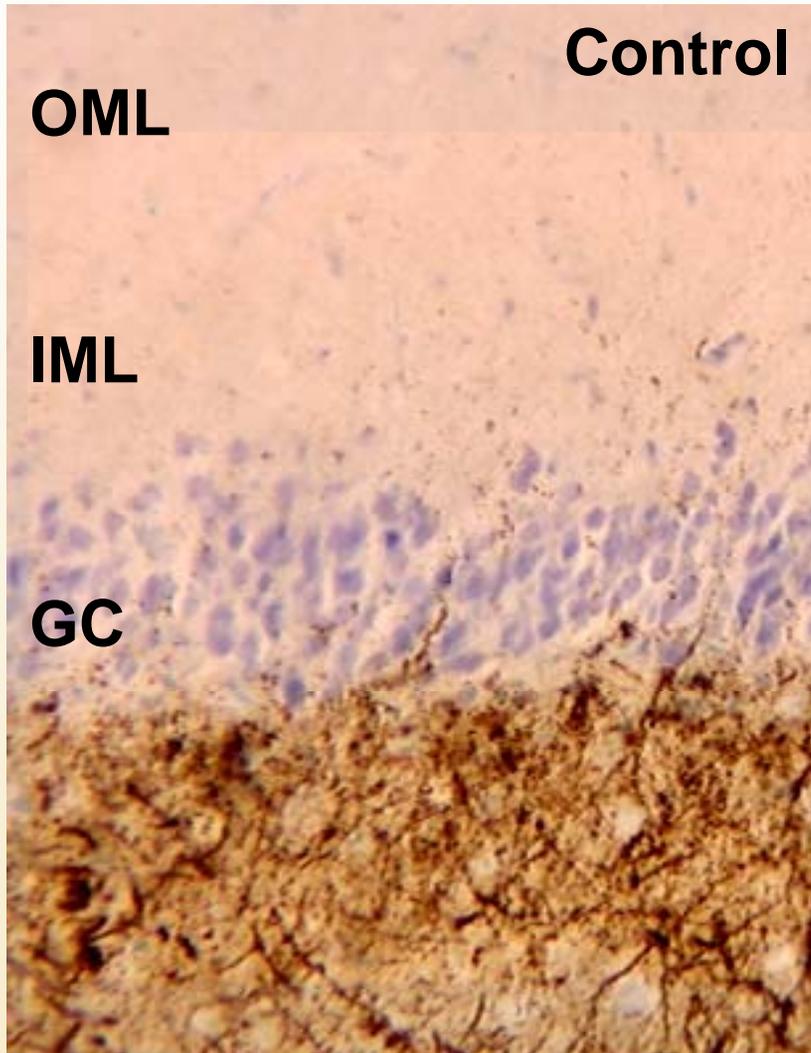
CA 1

CA 4

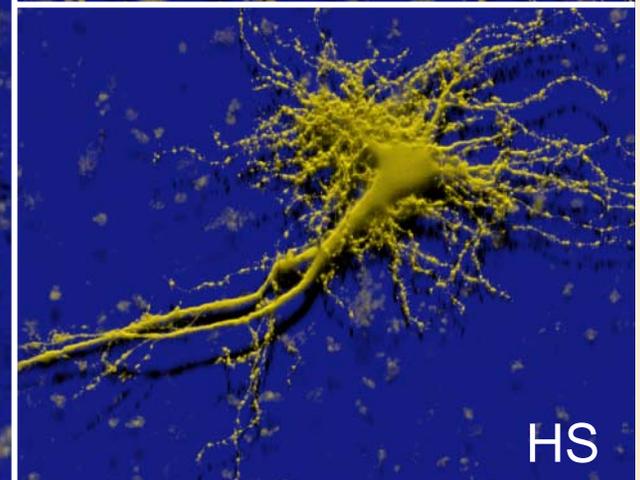
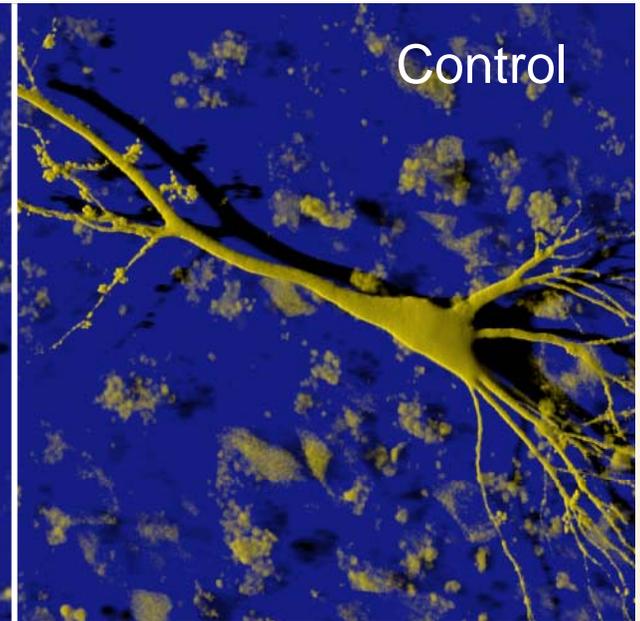
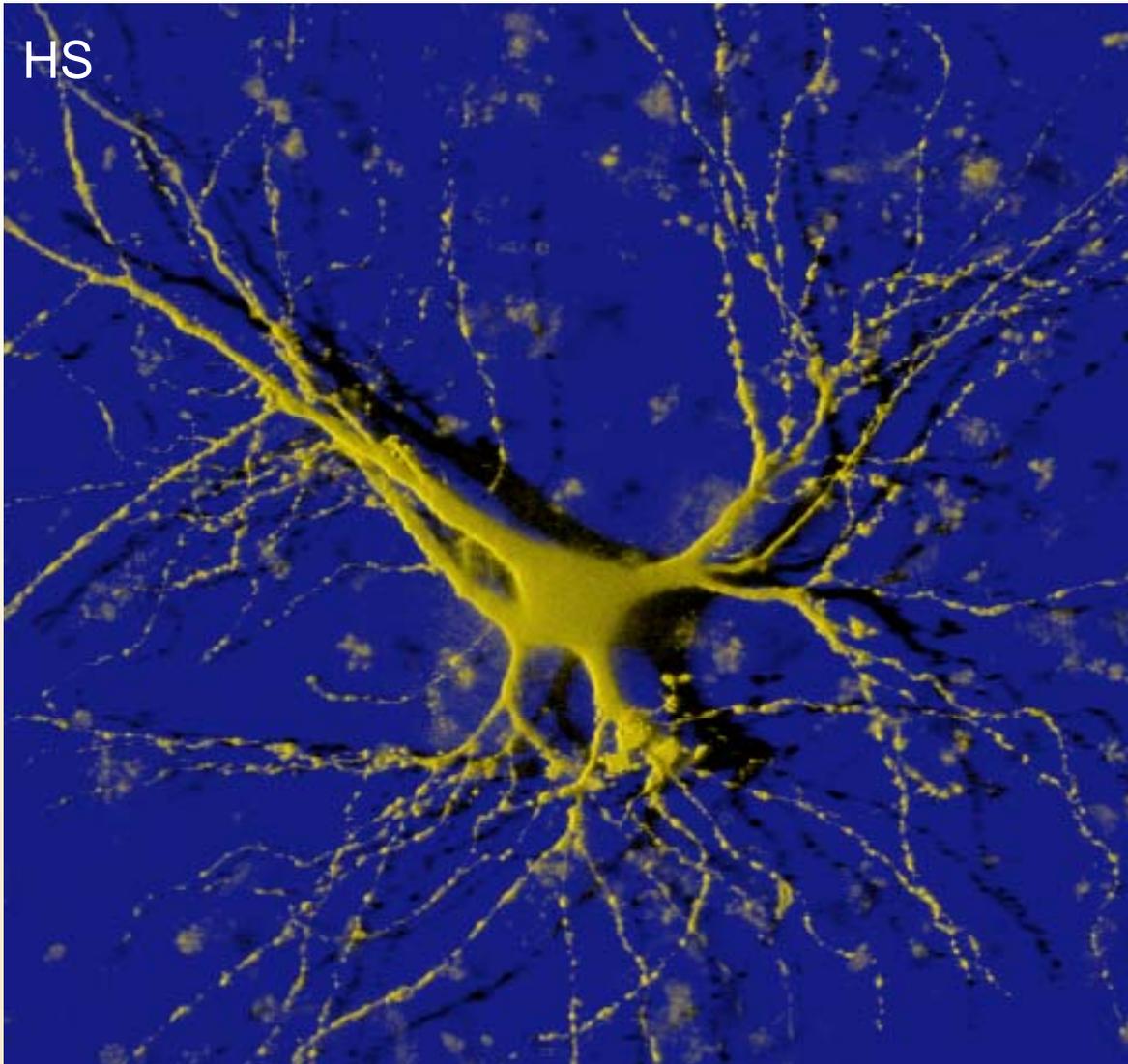
1 mm

AHS

Axonale Reorganisation



Zelluläre Reorganisation



Pathogenetisches Modell Hippocampussklerose assoziierter TLE



frühkindl. Schädigung

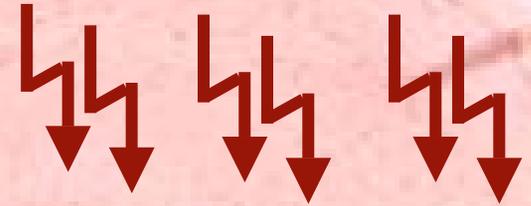
< 4 Jahre

* verzögerte Reifung
(Reelin-Signalweg, Neurogenese)

Latenzperiode

„Teenager“

* molekulare und zelluläre Reorganisation
(z.B. der Neurotransmission)



AHS

Erwachsene

* sekundäre Veränderungen
(Zytotoxizität)

OP

(Alter)

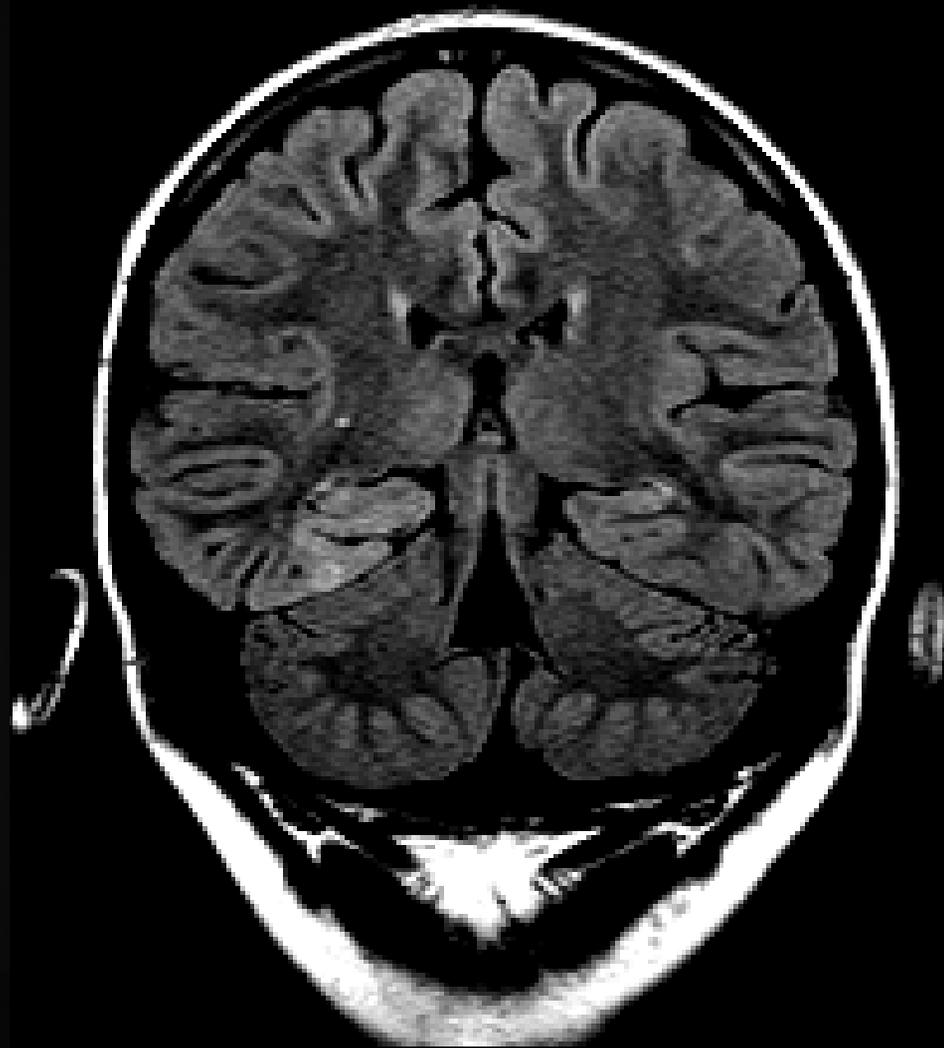
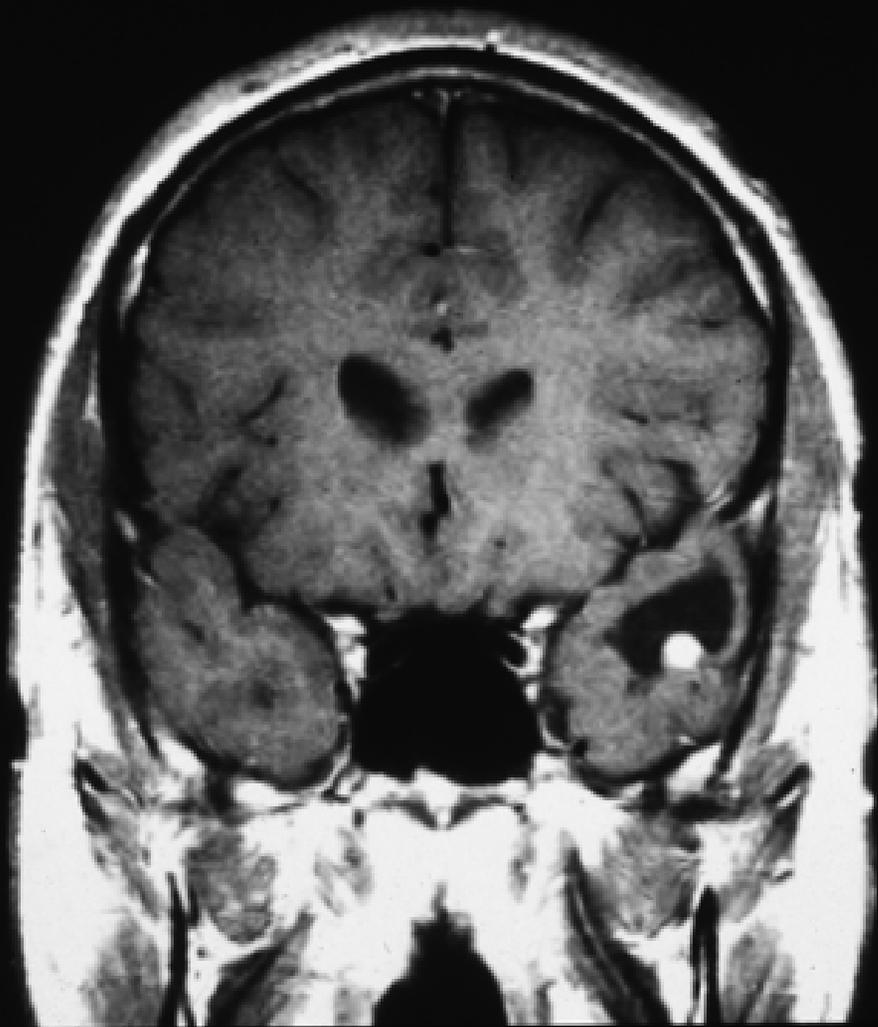


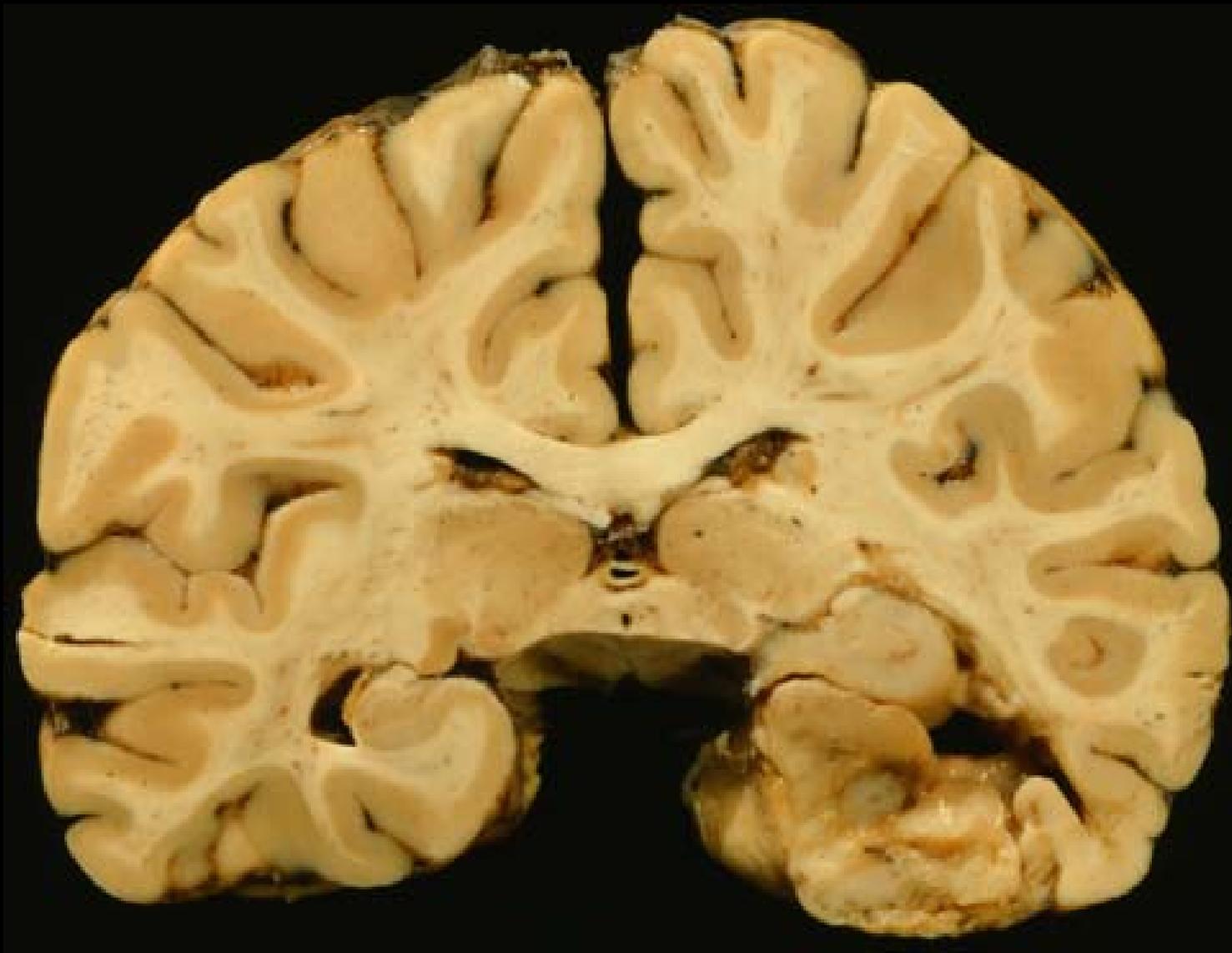
Neuropathologische Befunde bei Patienten mit fokalen Epilepsien

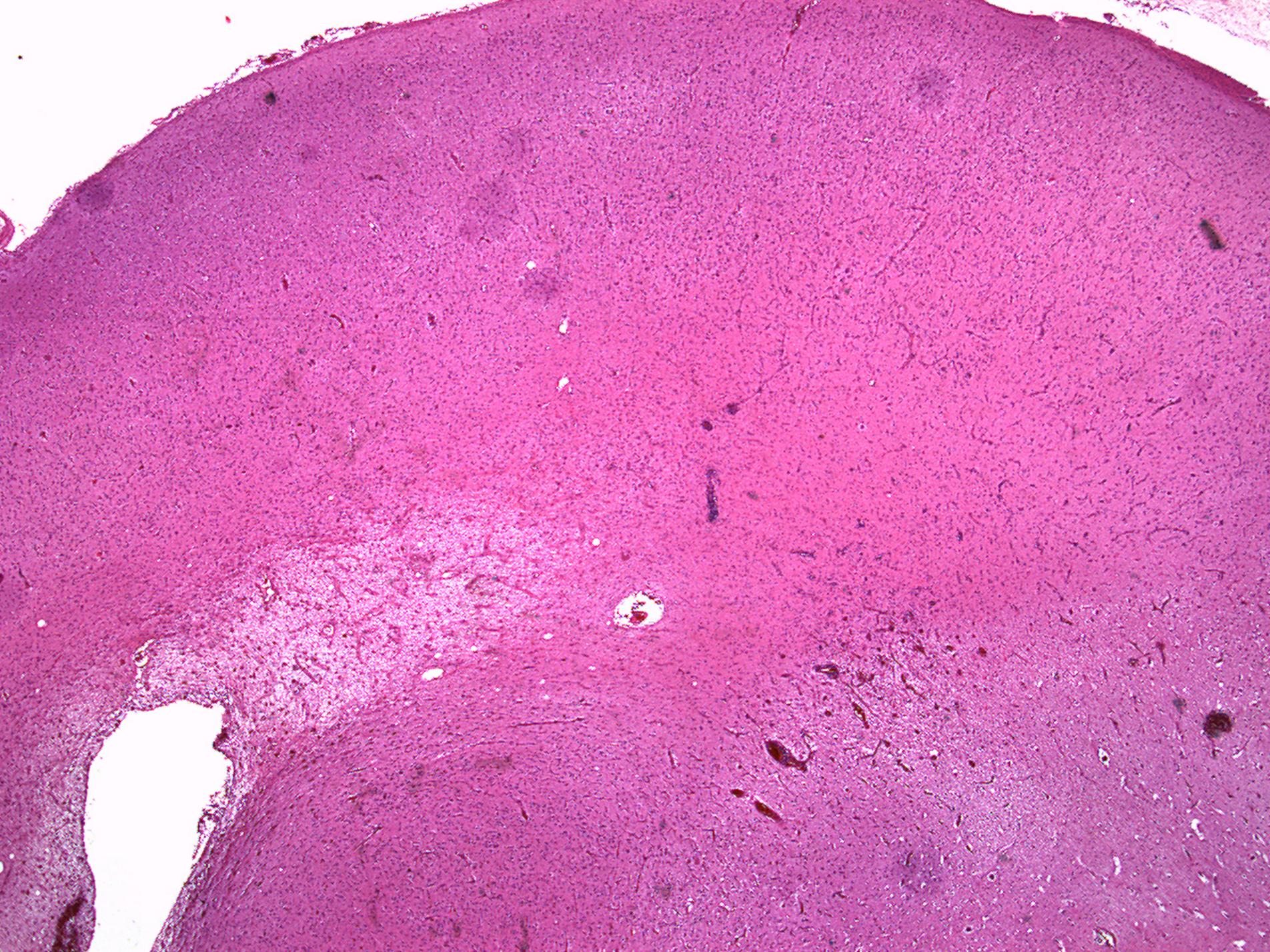
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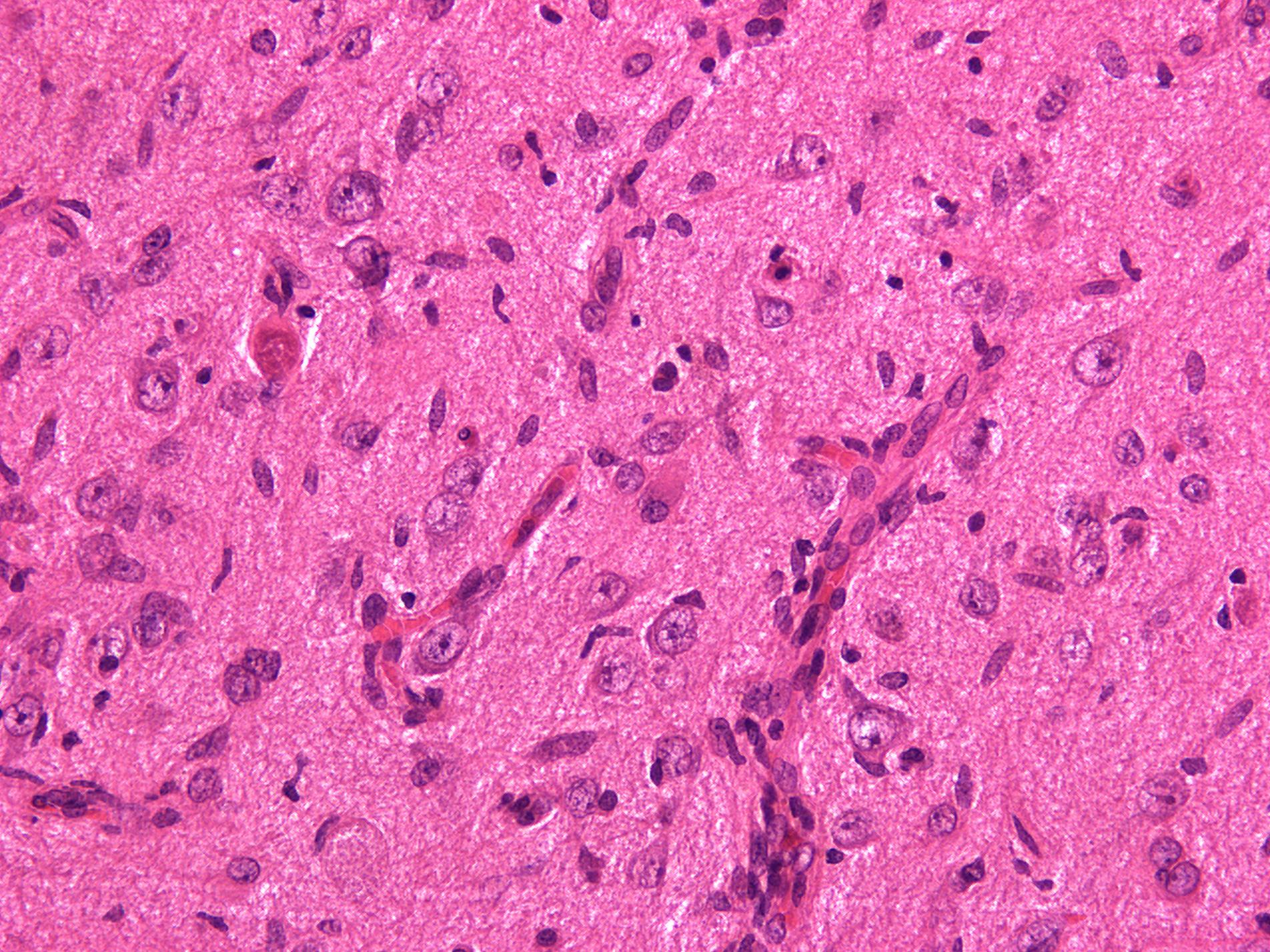
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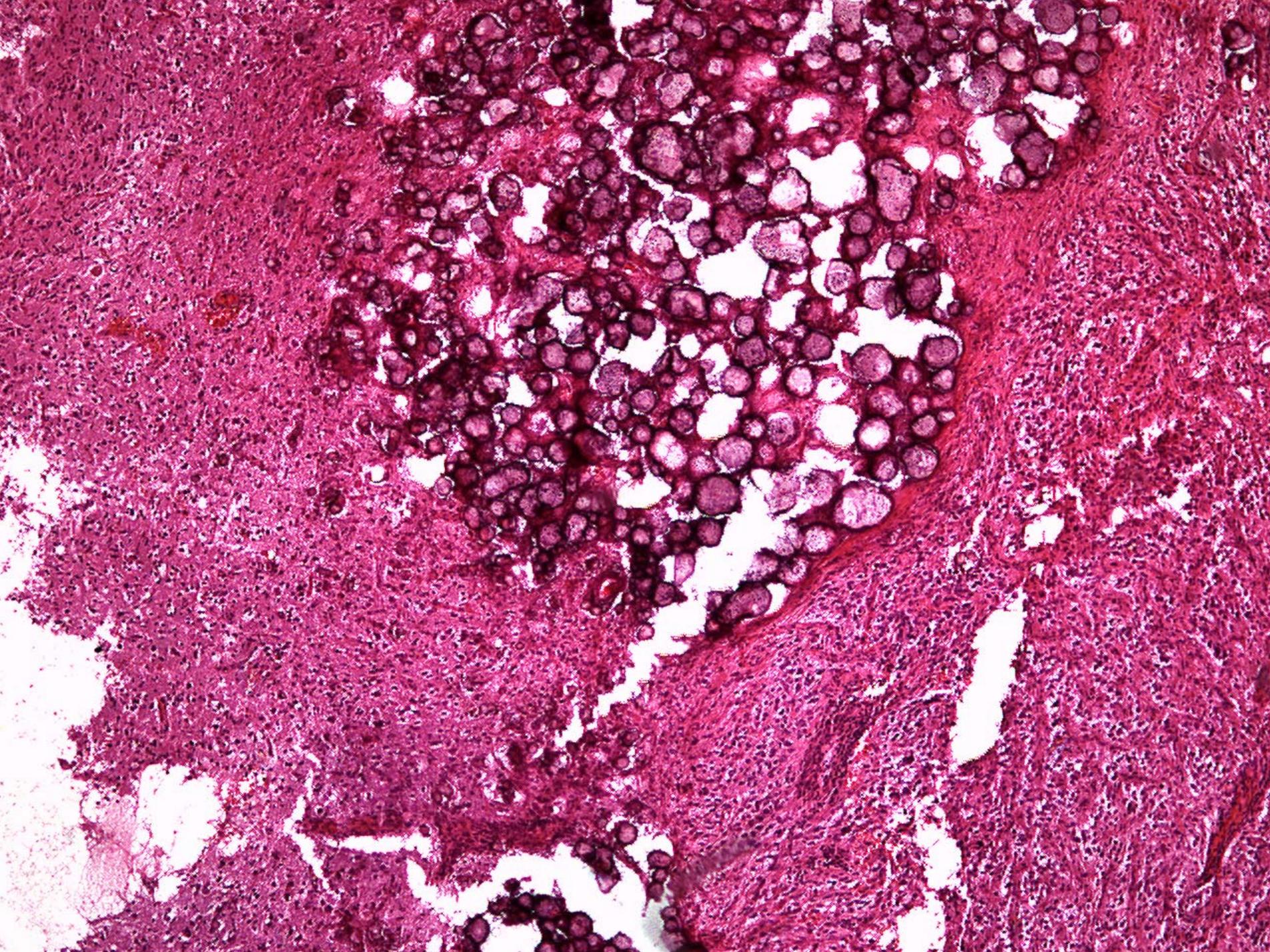
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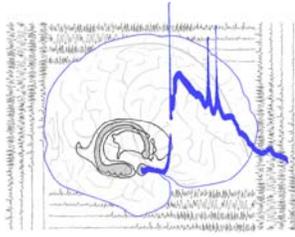












Gangliogliom

- biphasischer Aufbau des Tumors
- molekulare Pathogenese
- Assoziation mit Epilepsie

- Typische Gliom-assoziierte Kandidatengene (z.B. TP53, EGFR, PTEN) sind nicht beteiligt
- Mutationen/Polymorphismen in Entwicklungsgenen z.B. TSC1, TSC2, PS1, CDK5
- **Expression des Stammzellmarkers CD34**
- Erniedrigte Expression der Reelin-Signalkaskade

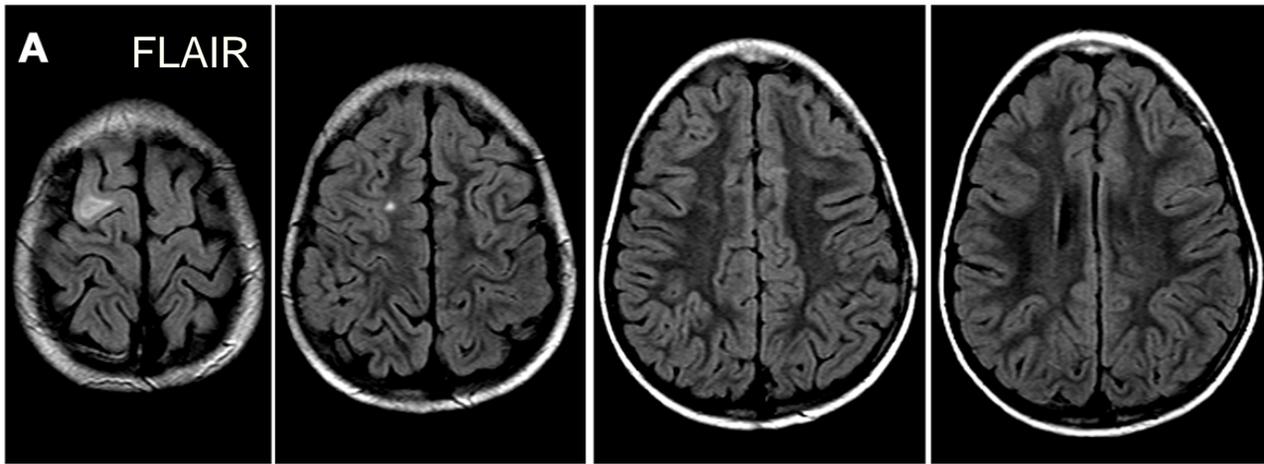


Neuropathologische Befunde bei Patienten mit fokalen Epilepsien

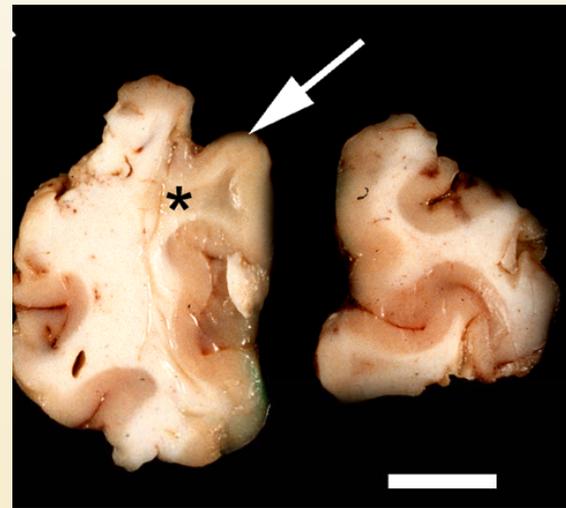
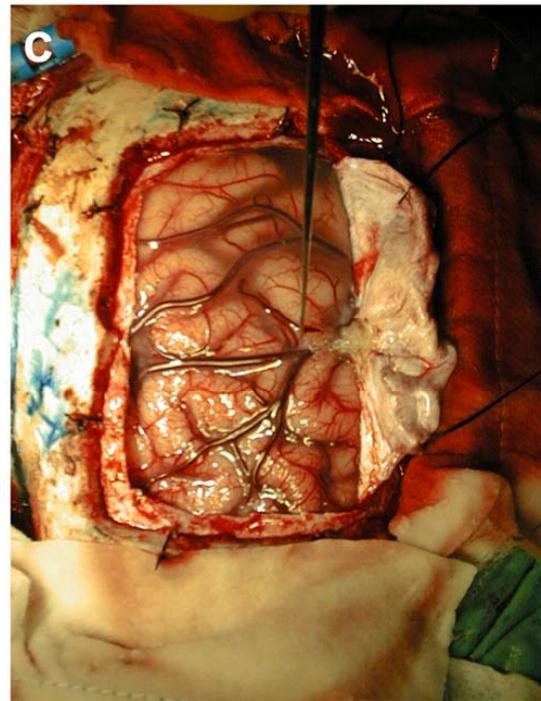
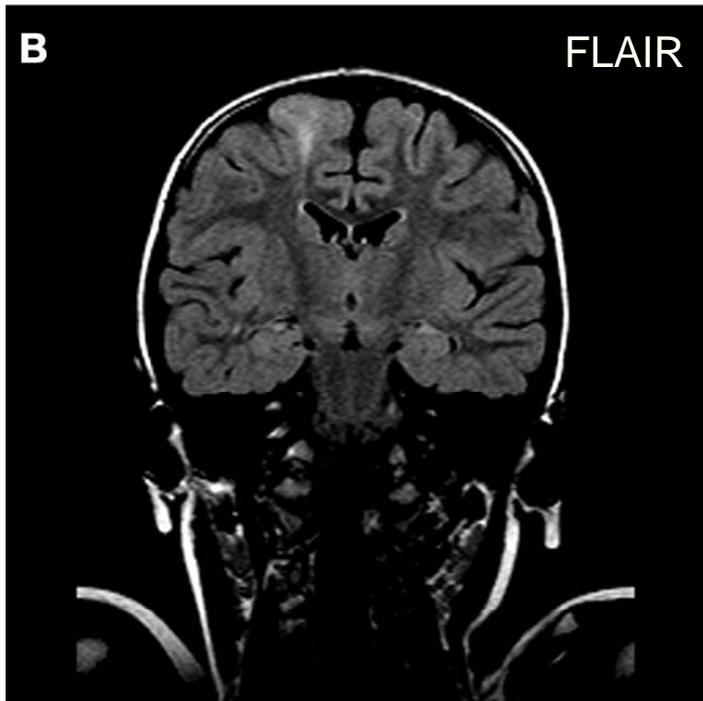
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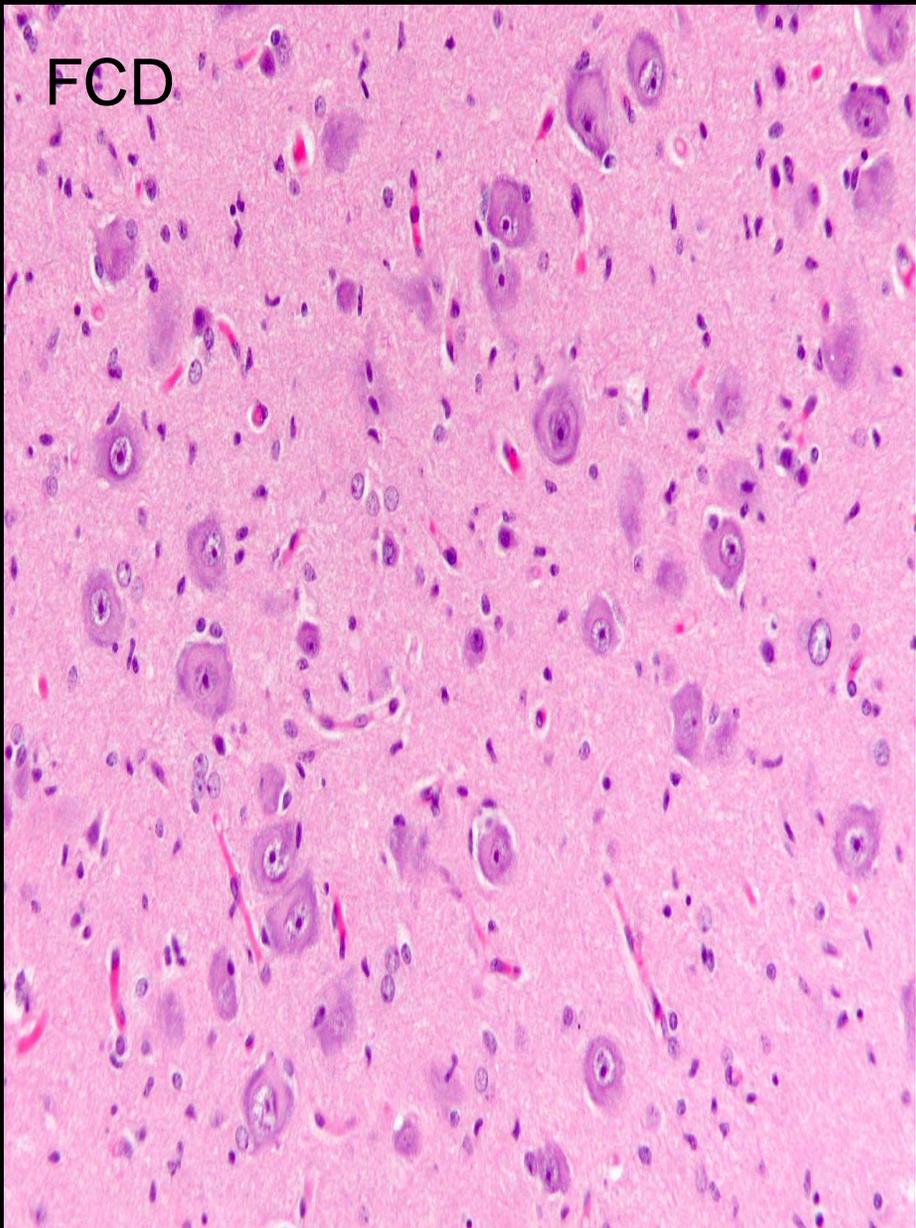
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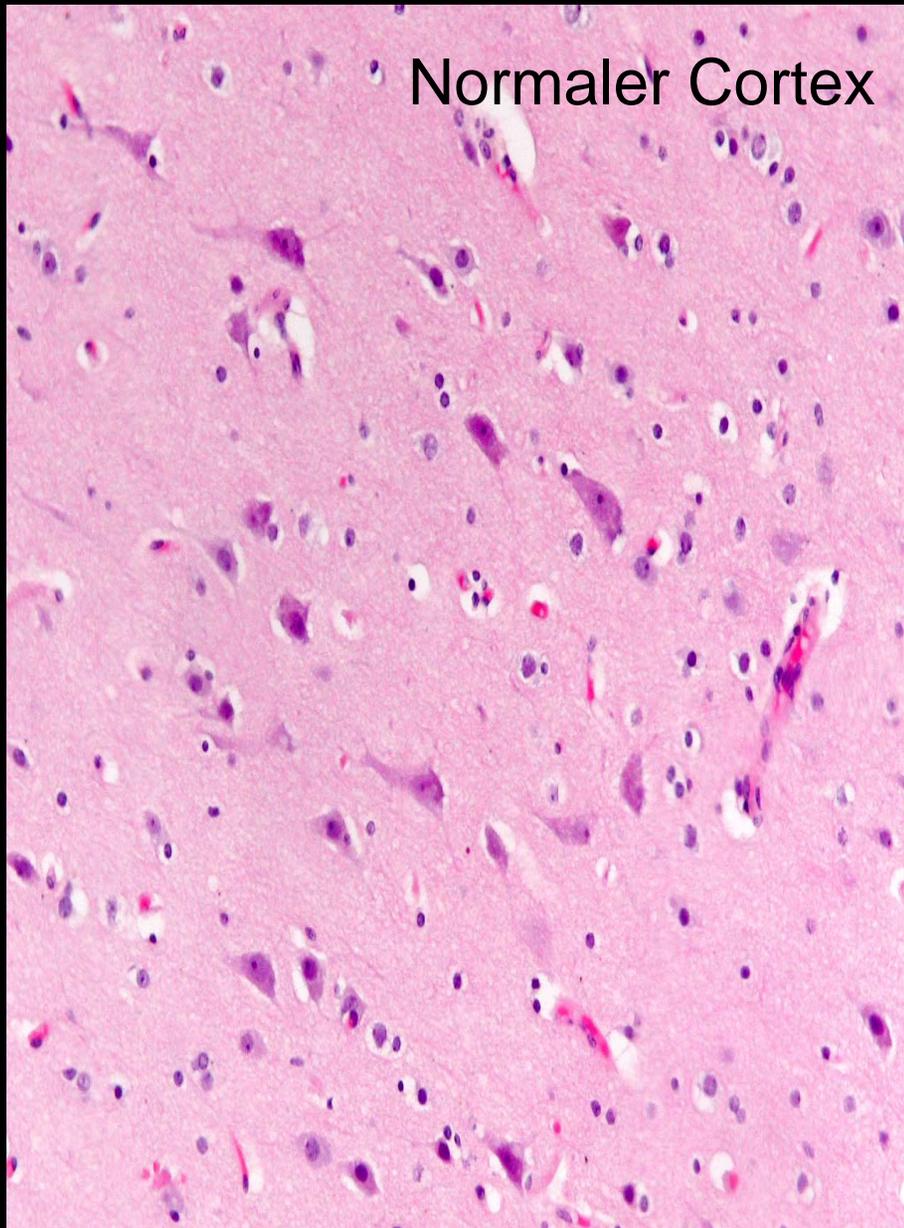
**FCD Typ IIb
(Taylor's
balloon cell
type)**



FCD

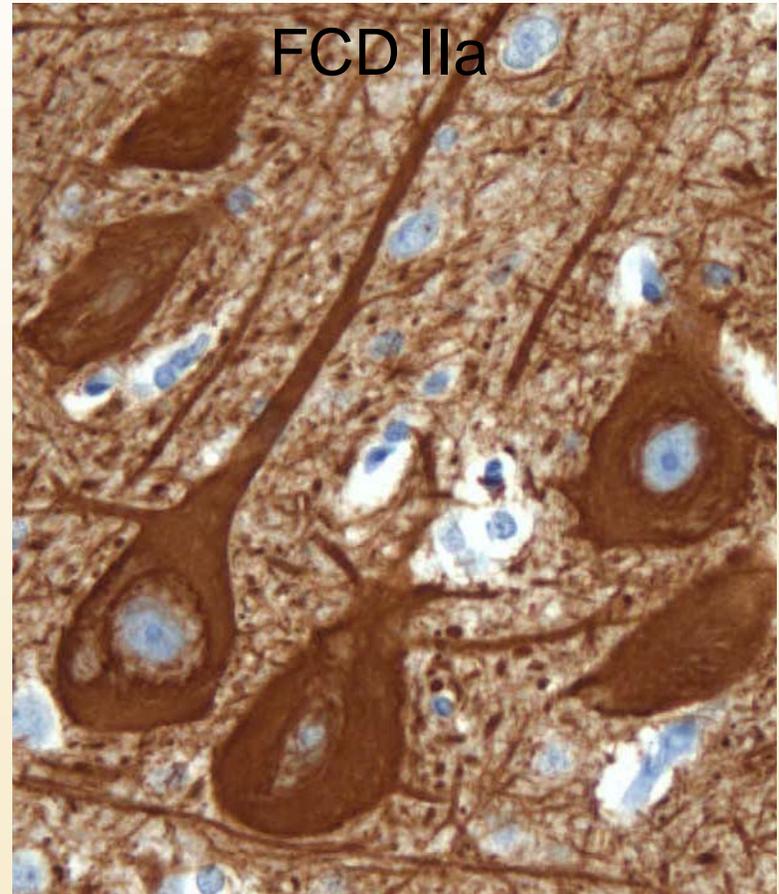
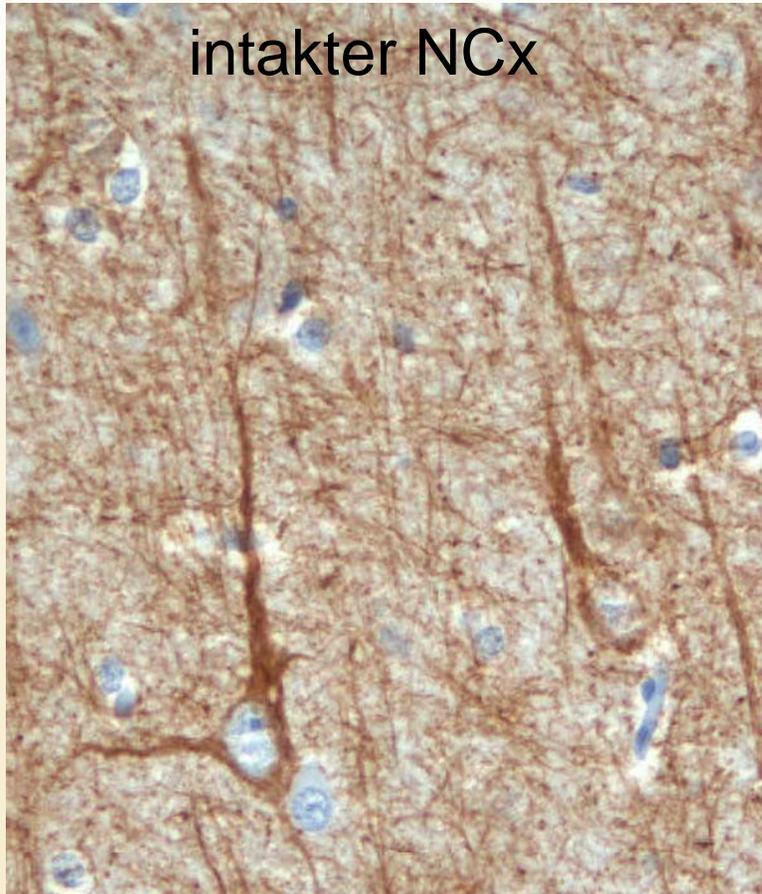


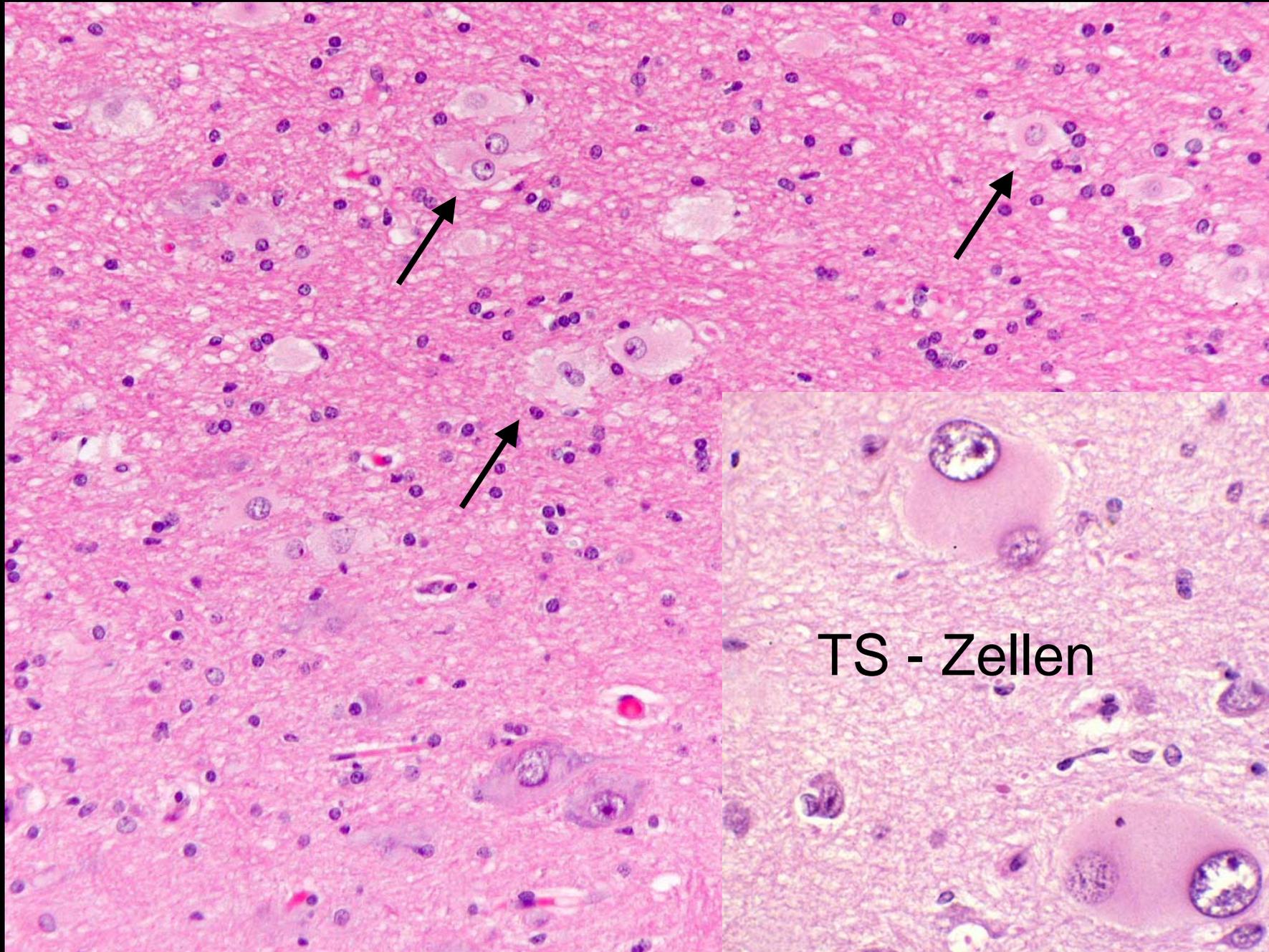
Normaler Cortex



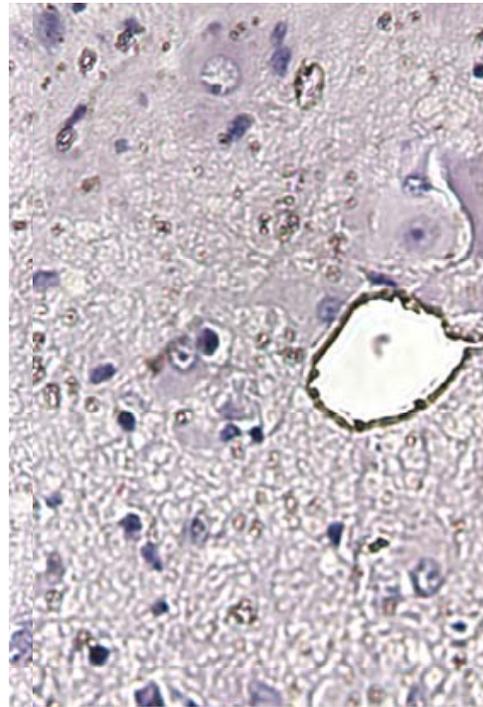
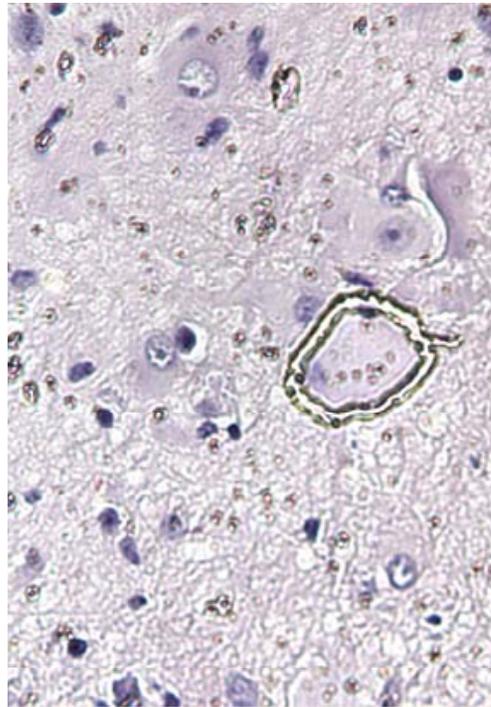
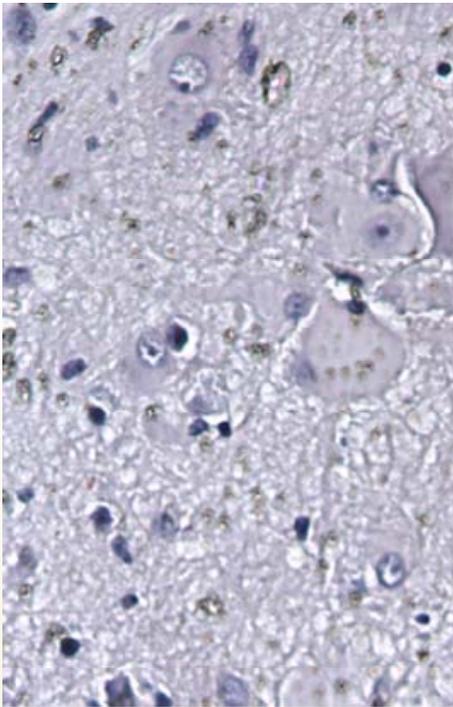
FCD (Type IIa)

Neurofilament-Protein





TS - Zellen

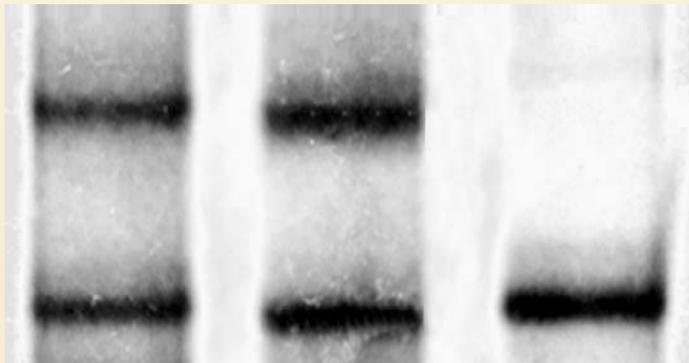


SSCP Exon 14 TSC1

LOH D9S303 TSC1

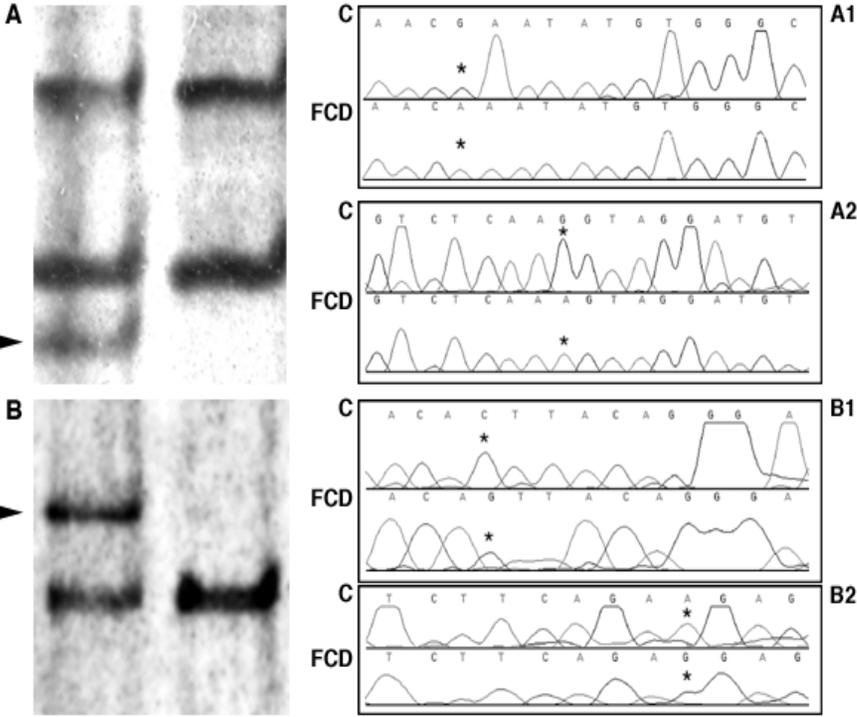
TS N C

N C

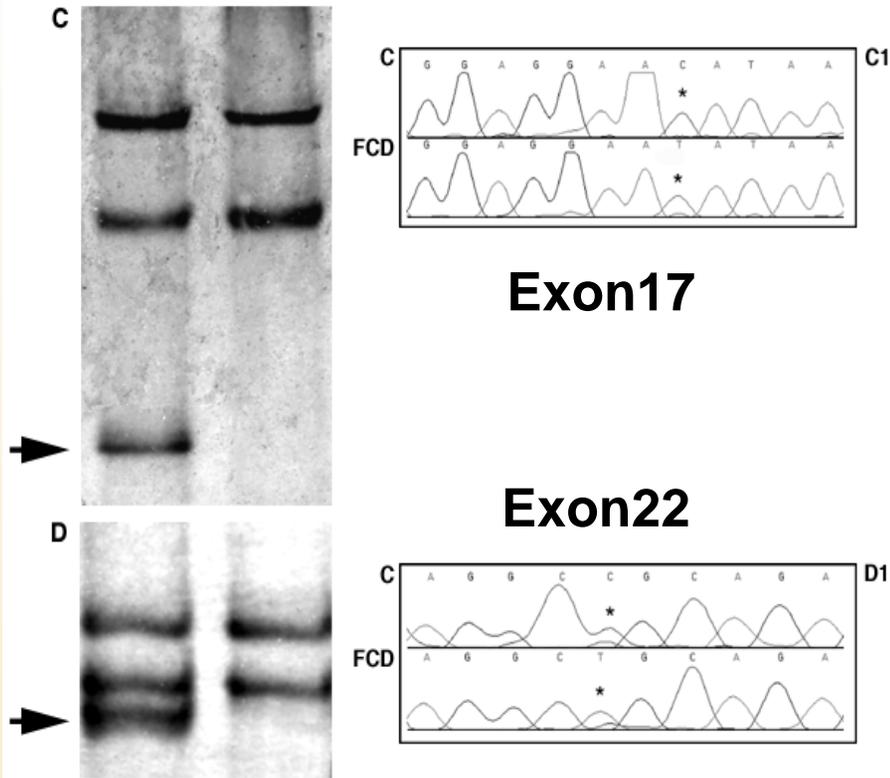


Mutationsanalyse des TSC1-Gens bei FCD Typ IIb (Taylors' balloon cell type)

Exon5



Intron13/Exon14



Exon17

Exon22

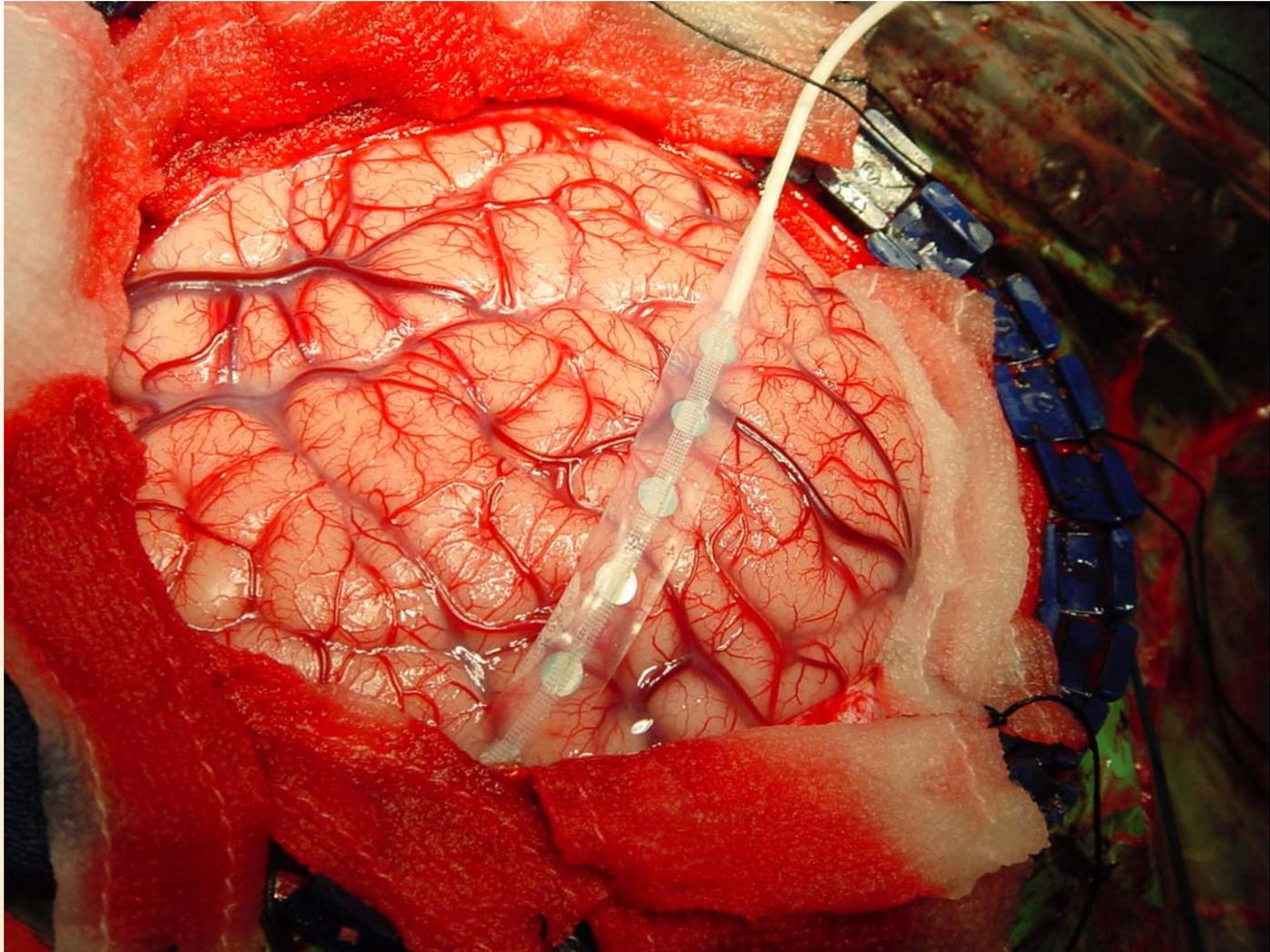
Perspektiven „Pathogenese und Epileptogenese“

Innovative Forschungskonzepte resultieren aus der interdisziplinären Kooperation zwischen

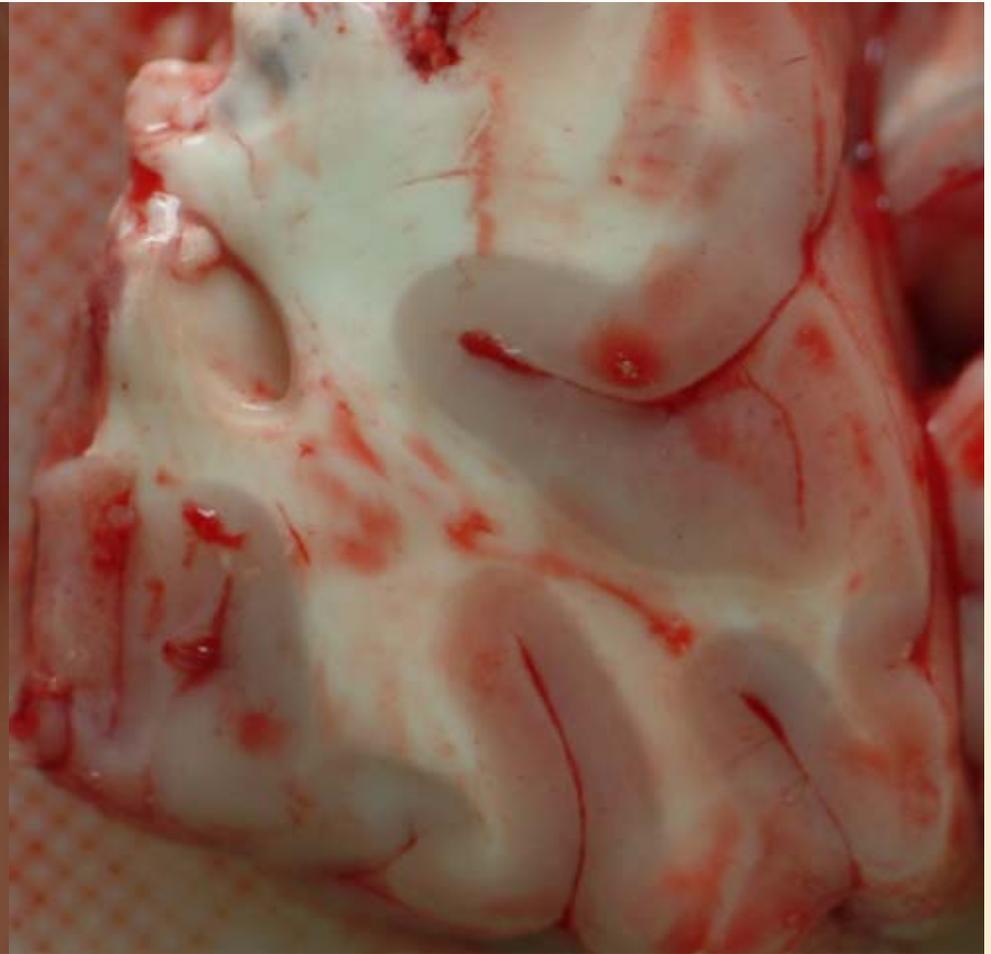
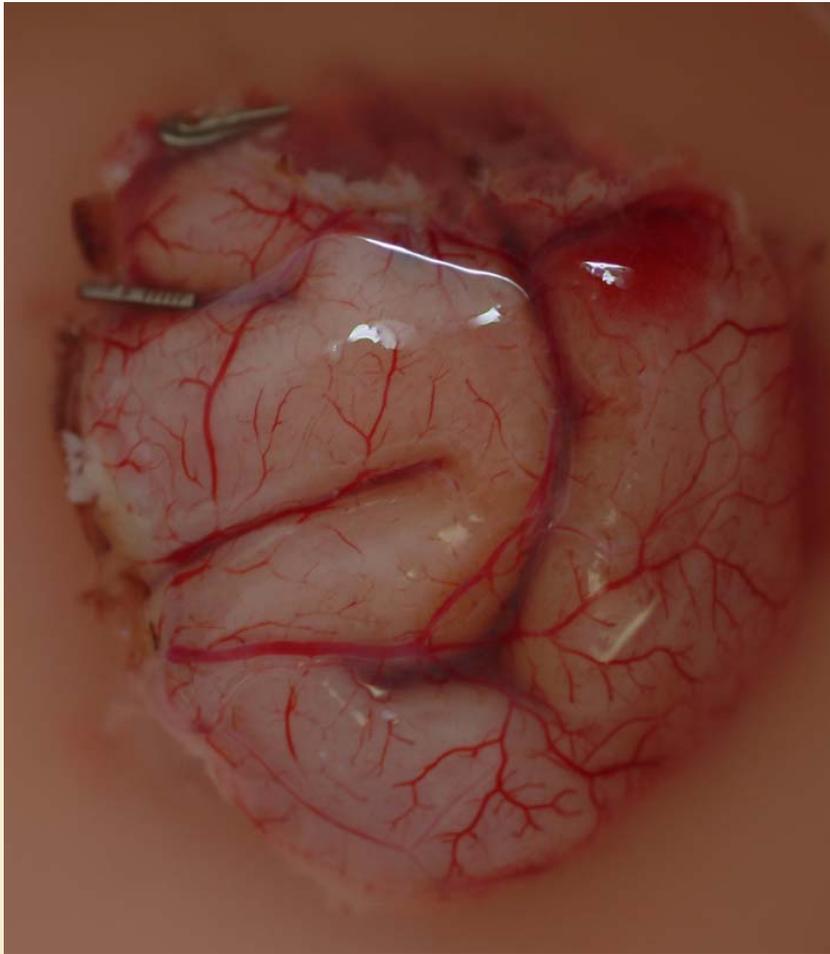
Epileptologie – Neurochirurgie – Neuroradiologie - Nuklearmedizin
- Neuropathologie -
experimentelle Neurophysiologie – Neuro-/Molekulargenetik

Einbindung „funktioneller Genomik“ zur Identifikation
- diagnostisch relevanter Expressionsmuster
- neuer Kandidaten für therapeutische „targets“

Epileptogenese (Monitoring)

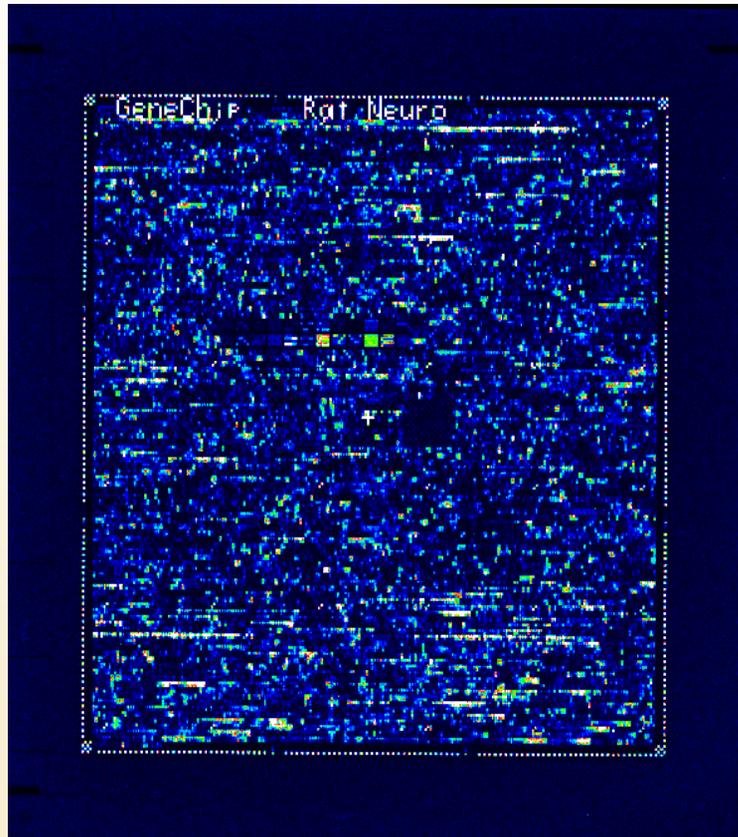


Epileptogenese (Gewebe)

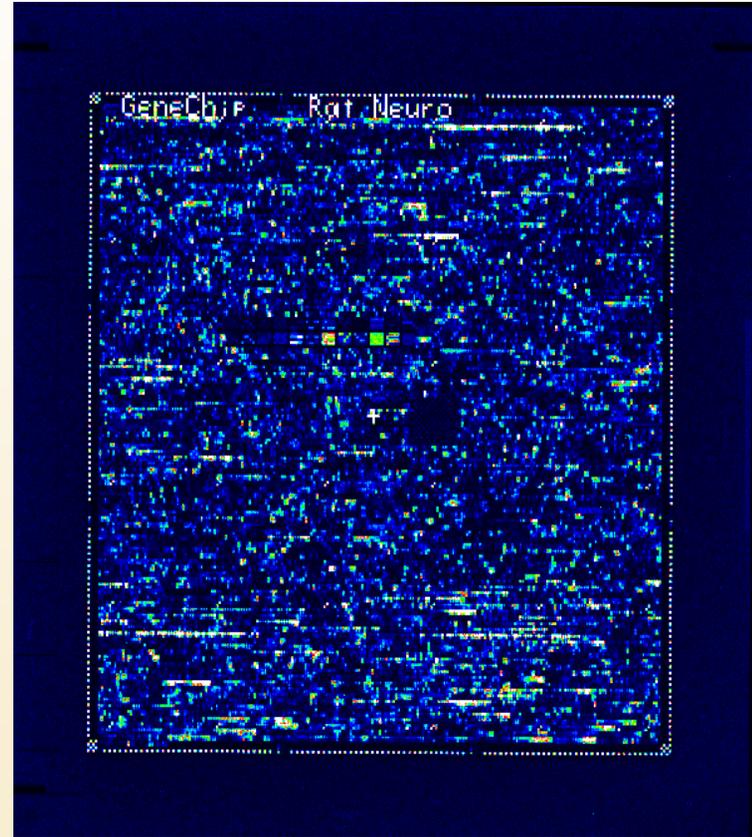


Epileptogenese (Analyse)

Spike-Fokus



Non – Spiking



Neocortex vs. Marklager