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Abstracts
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Cerebrovascular disease and epilepsy – a retrospective study on 2022 patients

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Cerebral ischaemia is a common cause of epilepsy. True frequency, risk factors and prognosis are not well established. We studied 2022 consecutive patients with stroke and/or epileptic seizures between January 2000 and June 2003. 121 patients had seizures due to stroke including 66 patients with one seizure and 55 patients with epilepsy. Only 3 of 19 patients with early onset seizure had recurrent seizures (15.8%) but 52 of 102 patients with late-onset seizure developed epilepsy (51%). After transient ischaemic attacks only 3% of patients had recurrent seizures as opposed to 12.2% of patients after major stroke. Statistical analysis revealed that old age and smoking were associated with a lower risk of developing epilepsy after stroke whereas hypertension, diabetes, hyperlipidaemia or cardioembolic aetiology had no significant influence on seizure recurrence. Twenty-two of 23 patients with an epileptogenic focus after stroke had at least one seizure during follow-up.

In conclusion, 11.8% of patients with cerebral ischaemia had at least one epileptic seizure. More than 50% of patients with late-onset first seizure had seizure recurrence, old age and smoking lowered the risk of developing epilepsy after stroke. Our results have implications on anticonvulsant treatment in patients with high risk of developing post-stroke epilepsy.

Focal cognitive dysfunction as prodromal phase of cortico-basal degeneration

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Cortico-basal degeneration (CBD), a particular tauopathy which associates early extrapyramidal neurological signs such as rigidity, followed by parietal cognitive signs such as motor or melokinetic apraxia, parietal sensory disturbances and alien hand. This complex can evolve towards generalised dementia. In this case, the clinical picture suggests more often a frontotemporal dementia (FTD).

However, there are cases where cognitive signs are by far the earliest, are not characterised by the apraxia and do not evolve in FTD. We present here two cases of focal dementia, which evolves in CBD. The first case is a 76-year-old female, who presented with signs of progressive anarthria, rapidly followed by a progressive aphasia of the non fluent type. In 4 years, she developed agraphia, dyscalculia, melokinetic apraxia and finally rigidity of the right arm and leg. The second case is a 60-year-old travel agent, who developed at the age of 54 a progressive Gerstmann syndrome, with writing difficulties, acalculia, left-right disorientation, but no amnesia. Later parietal signs evolved and extended to the right hemisphere, and the patient presented ideomotor and dressing apraxia, aphasia and amnesia appeared. In both cases, apraxia was melokinetic and ideomotor. However, no specific visuoimative apraxia, suggested to be specific of the disease, was found. Finally signs such as autotopagnosia, as well as left arm and leg rigidity appeared. AchE were of little help, but SSRI improved behaviour in patient 2. These cases illustrate the diversity of presentation of CBD but confirm that amnesia is not the earliest symptom in these patients.

Fatigue in multiple sclerosis is related to sympathetic vasomotor dysfunction

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The authors studied standard autonomic function tests and measures of heart rate variability in 60 patients with multiple sclerosis (MS) and correlated results with the Fatigue Severity Scale and the Modified Fatigue Impact Scale. The authors found that autonomic responses correlated with fatigue resembling a hypoadrenergic orthostatic response, possibly due to a sympathetic vasomotor lesion with intact vagal heart control. Treatments to control sympathetic dysfunction for MS-associated fatigue deserve further study.

Benign course of hypothalamic hamartoma and gelastic seizures

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We present a 28-year-old right-handed female with therapy refractory partial epilepsy. Psychomotor development and sexual maturation was normal. Later focal seizures occurred characterised by epigastric sensations followed by a short, unmotivated laughter (gelastic seizure) with adequate emotions. Some extended to complex partial symptomatology with stereotypic speech production and gastrointestinal sensations followed by altered consciousness and oral automatisms. Seizure control was not achieved by various medications (valproic acid, carbamazepin, vigabatrin, lamotrigin topiramat, gabapentin). *Continuous audio-video EEG monitoring* (foramen ovale electrodes) disclosed 40 seizures all showing low voltage rhythmic fast activity and/or accentuated sharp waves in the right foramen ovale electrodes. *Cerebral MRI* revealed a 4 mm hypothalamic mass – probably a hamartoma – in the right posterior part of the hypothalamus adjactent to the mamillary body. Our patient shows an exceptionally benign course of hypothalamic hamartoma (normal sexual maturation and intellectual development) despite therapy-resistant seizures. We hypothesise that the atypical localisation of the hamartoma at a more posterior region in the hypothalamus may have spared hormonal hypothalamo-hypophyseal tracts enabling thus normal development. Our finding may extend the knowledge of anatomic findings involved in gelastic seizure.

Comparison of sniff nasal pressure (SNP) and forced vital capacity (FVC) to follow disease progression in a randomised controlled clinical trial in ALS

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Introduction: Forced vital capacity (FVC) is a recommended and established measure to follow disease progression in ALS clinical trials. Recently the sniff nasal pressure (SNP) has also been suggested to be a marker of declining respiratory muscle

strength in ALS. However, it is not clear if any of these measures is superior when applied in a randomised controlled clinical trial.

Subjects und Methods: Twenty ALS patients with a mean age of 58.1 (2–75) years were enrolled in the study (Novartis TCH 346A). Inclusion criteria included disease onset less than 3 years and initial FVC more than 70% predicted. Over the 3-month run in period patients underwent respiratory function tests (SNP sitting [SNPsit] and supine [SNPsup], FVC) at regular 4-weekly intervals and ALSFRSR-scoring. All pulmonary function tests were performed by an experienced respiratory technician (DM) familiar with the applied methods.

Results: At study entry mean FVC was 99.1 ± 15.0, mean SNPsit 81.4 ± 26.6, mean SNPsup 79.9 ± 25.0 and mean ALSFRSR 42.4 ± 4.0. After the 3-month period FVC had dropped to 87.8 ± 15.8, SNPsit to 78.7 ± 29.2, SNPsup to 73.8 ± 26.7 and ALSFRSR to 39.5 ± 5.5. These changes were only significant for FVC and ALSFRSR ($p < 0.006$, paired t-test) but not for SNP measures. The correlation between ALSFRSR and SNPsit ($r = 0.37$) and SNPsup ($r = 0.36$) was slightly better than between ALSFRSR and FVC ($r = 0.33$).

Conclusion: The significant change of FVC and ALSFRSR over a 3-month period suggest that these measures are more sensitive to change over this relatively short period than SNP measures. This would argue against SNP measures to be used as markers of disease progression in ALS clinical trials. However, because of an increasing number of missing FVC values with disease progression SNP measures may become more important in advanced disease.

Antikörper gegen Myelin-Oligodendrozyten-Glykoprotein (MOG) und basisches Myelinprotein (MBP) als prognostische Marker bei Patienten mit Clinically Isolated Syndrome (CIS)

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Die Multiple Sklerose (MS) manifestiert sich initial überwiegend als sogenanntes Clinically Isolated Syndrome (CIS) aufgrund einer entzündlich demyelinisierenden Läsion im Sehnerv, Hirnstamm oder Myelon. Durch klinische Verlaufsuntersuchungen bzw. wiederholte Bildgebungen des Gehirns lässt sich im weiteren Verlauf in bis zu 80% die Diagnose MS sichern. Trotz zahlreicher und extensiver klinischer, immunologischer und radiologischer Untersuchungen war aufgrund des sehr variablen Verlaufs der Erkrankung eine Prognose für Patienten mit dieser wahrscheinlichen Erstmanifestation einer MS, u.a. auch in Hinblick auf eine Frühtherapie, nicht möglich.

MOG, dessen Funktion weitestgehend unbekannt ist, bildet ca. 0,01–0,05% des Proteingehaltes des zentralen Myelins und wird ausschliesslich im zentralen Nervensystem exprimiert. Im MOG-induzierten Tiermodell der MS (experimentelle autoimmune Enzephalomyelitis, EAE) kommt es neben der Aktivierung enzephalitogener T-Zellen zur Bildung von demyelinisierenden anti-MOG-Antikörpern. In eigenen T-Zell-Untersuchungen konnte ein deutlich höheres immunogenes Potential der transmembranen und intrazellulären Domäne von MOG nachgewiesen und ein immunodominantes Epitop definiert werden. Aktuelle Daten sprechen dafür, dass durch die Messung von Antikörpern gegen MOG und MBP eine individuelle Prognose in Hinblick auf einen zweiten Schub für Patienten mit Erstmanifestation einer MS besser möglich und damit der Übergang in eine klinisch definitive MS vorausgesagt werden kann.

Neben der longitudinalen Erhebung der Antikörperbefunde, Korrelation der Reaktivitäten zum klinischen Verlauf und MRI-Bildgebung sollen zukünftig auch Erfahrungen hinsichtlich der humoralen Antigenität der intrazellulären MOG-Domäne und Myelinreaktivitäten im Liquor gesammelt werden. Die Messung von Antikörpern gegen MOG und MBP in Serum stellt eine schnelle, kostengünstige und gut reproduzierbare Technik dar, die ab sofort in Basel zur Verfügung steht.

Diese Arbeiten werden von der Schweizer MS Gesellschaft und Schering AG unterstützt.

Utilisation clinique de Tiagabine et états confusionnels récurrents

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Les auteurs présentent le cas d'une jeune femme de 33 ans souffrant d'une épilepsie partielle cryptogénique avec généralisation secondaire de type grand mal. Au bénéfice d'un traitement par agonistes du GABA (GVG et TGB), elle a développé des états confusionnels et amnésiques récurrents, transitoires et indépendants d'une activité critique. Il est démontré une corrélation directe entre la survenue des troubles du comportement et le pic plasmatique de Tiagabine alors qu'un EEG concomittant a exclu une origine épileptique.

Sur la base de cette observation, il est estimé que l'effet thérapeutique gabaergique de la Tiagabine est aussi directement corrélé avec son taux plasmatique. Compte tenu de la demi-vie (1–4 h), son utilisation fractionnée en quatre prises ou davantage devrait permettre une meilleure efficacité clinique en réduisant le risque d'états confusionnels. Des observations anecdotiques confirment cette attitude.

Misdiagnosis of epilepsy

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Aims: To analyse errors that may lead to a false diagnosis of epilepsy in patients with non-epileptic attack disorders.

Method: We examined case histories, seizure recordings and, where available, EEGs of 2697 patients who were referred for Video-EEG-Long-Term-Monitoring to our tertiary epilepsy centre between the years 1978 and 2003.

Results: Non-epileptic attacks were recorded in 642 patients (24%). Of these, 55% suffered from psychogenic attacks, 45% from organic, non-psychogenic and non-epileptic attacks such as syncopes or movement disorders. 233 patients with psychogenic NEAs had a false diagnosis of epilepsy. Diagnostic errors in these patients were related to (1) mis- or over-interpretation of descriptions of the attacks (104 patients) or (2) mis- or over-interpretation of previous EEG-findings (129 patients). False interpretations of EEG-findings could be demonstrated in 63 EEGs that were available for review. 56 false diagnoses were based on unspecific EEG-findings only while mere 10 reports mentioned spikes or sharp waves.

Conclusion: Only Video-EEG-recordings of typical events permit a correct diagnosis in patients suffering from unclear attacks and/or seizures. Thus, the diagnosis should not be based on case history or EEG-findings alone.

Abnormal sleep/wake-patterns in Shapiro's syndrome – a case report

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We present a case of Shapiro's syndrome, characterised by the clinical triad of episodic hypothermia, hyperhydrosis and agenesis of the corpus callosum.

A 74-year-old otherwise healthy woman presented with episodes of generalised flushing followed by profuse sweating culminating in a chill during the last couple of weeks. Her daughter described progressive difficulty with speech, memory and clumsiness on walking as well as general weakness. A similar episode occurred 5 years ago with a symptom-free interval in between. On admission she was awake but mute and motionless showing signs of cerebellar ataxia. Core temperature was 32 °C, blood pressure 90/60 mm Hg. Laboratory investigations showed a slightly increased CRP as a possible infectious trigger, but no focus was found. MRI revealed complete agenesis of the corpus callosum with dilated occipital horns. EEG showed mild diffuse slowing without epileptiform discharges. Polysomnography demonstrated significantly reduced REM-sleep.

The patient was treated with lorazepam and clonazepam which reduced cognitive impairment as well as episodes of hypothermia after an initial two-day period of somnolence.

Conclusion: Abnormal sleep/wake-patterns have been described in Shapiro's syndrome. We present a case of Shapiro's syndrome with significantly reduced REM-sleep so far described in patients with sole agenesis of the corpus callosum.

A case of familial ALS with marked asymmetry

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Introduction: Signs of motor neuron degeneration and ubiquitin-positive inclusions (UPIs) in the primary motor cortex and at the spinal anterior horn cell level are the hallmarks of amyotrophic lateral sclerosis. However, their abundance varies between cases and the relationship of upper and lower motor neuron degeneration in ALS is unclear. Cases with marked asymmetry may help clarify this issue.

Case report: This 72-year-old man whose sister had died of ALS developed slowly progressive clumsiness of his right hand which was followed by weakness of his right leg. On examination his right arm was plegic and severely atrophied. There was moderate weakness in his right leg. On the left mild wasting and weakness were restricted to small hand muscles. Reflexes were exaggerated, sensory examination was normal. One week before the patient died of pneumonia he was still able to stand on his left leg and hold on to a handle bar with his left hand whilst his right side was completely atrophied and plegic. SOD1 gene analysis was normal.

Autopsy findings: Histopathological examination revealed losses of spinal and brain stem motor neurons with UPIs in remaining motor neurons and in granule cells of the dentate gyrus compatible with the diagnosis of ALS. There was severe right-sided predominant axonal degeneration in nerve trunks of the brachial plexus and in anterior spinal roots. The lateral corticospinal tracts showed severe losses of thick axons, more so on the right side. The most striking finding, however, consisted of a severe degeneration of the left precentral motor cortex with neuronal loss, spongiosis, astrocytic gliosis and UPIs in neurons. Only slight changes were observed in the contralateral motor cortex. The prefrontal and temporal cortex only disclosed few ubiquitin-positive neurites.

Discussion: The most prominent feature in this patient is marked asymmetry of weakness and wasting affecting mostly his right side, along with neurodegenerative changes of the type found in frontotemporal degeneration but restricted to the left motor cortex. There was clear asymmetry in corticospinal tract degeneration probably related to the unilateral lesion of the precentral cortex. Although anterior horn cell degeneration was not found to be asymmetrical by simple inspection, clinical evidence together with clear asymmetry of brachial plexus degeneration suggest more severe involvement of anterior horn ipsilateral to the most severely affected lateral corticospinal tract.

Our findings suggest that upper and lower motor neurons do not degenerate independently from each other.

MNGIE in three siblings – clinical, genetic and neuroradiological features

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Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is a rare autosomal recessive disorder in which a nuclear mutation of the thymidine phosphorylase (TP) gene causes mitochondrial genomic dysfunction. Patients suffer from gastrointestinal dysmotility, especially pseudoobstruction, cachexia, ptosis, external ophthalmoparesis, myopathy and polyneuropathy. Brain magnetic resonance imaging (MRI) shows leucoencephalopathy.

We describe a family with three siblings affected with MNGIE. A new mutation (T92N) in the TP gene was identified. Urinary thymidine was elevated in the patients in a dose-related manner according to the severity of clinical disease. Slight increase of urinary thymidine was found in a heterozygous carrier. Brain MRI showed leukoencephalopathy in all patients, however, their cognitive functions were normal. Brain magnetic resonance spectroscopy demonstrated a significant reduction of N-acetylaspartate and choline in the severely affected areas. This might indicate loss of neurons, axons and glial cells.

Volumetry of subcortical nuclei in patients with primary generalised epilepsy syndromes

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By definition, patients with primary generalised epilepsy syndromes (PGES) do not display distinct focal cortical abnormalities as determined by brain imagery or EEG exams. However, functional abnormalities on the subcortical level, e.g. in the thalamus, have always been suspected to play a crucial role in the generation of epileptogenic abnormalities. In the present study, we were interested if PGES are associated to anatomical abnormalities as determined by volumetric measurements. In a preliminary study, 11 patients with a variety of PGES were compared to 15 healthy volunteers. In each subject, the volumes of 8 subcortical nuclei were determined manually, i.e. the caudate nucleus, putamen, pallidum and thalamus in each hemisphere. Volumetric measurements were carried out blinded to the clinical diagnosis. Statistical analysis revealed that overall patients had smaller subcortical nuclei as compared to controls ($p = 0.01$) which is due to significantly smaller caudate nuclei and putamen ($p < 0.01$). Detailed t-tests revealed that in particular the putamen were affected (each side: $p < 0.001$) with left-sided predominance. We concluded that primary generalised epilepsy is associated to subcortical anomalies, in particular to smaller putamen but not to altered thalamic structures. Further studies are needed to determine if this finding is specific to a distinct PGES.

Electric source imaging in a case of hypothalamic hamartoma

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Hypothalamic hamartoma (HH) is a rare condition with onset in infancy, characterised by gelastic seizures, often associated with precocious puberty and mental decline. The pathophysiological relationships between the gelastic fits, other seizure types and the hypothalamic hamartoma are still

unclear and also raise the question if other cortical areas are also recruited. A 2-year-old male patient, suffering from developmental delay and gelastic seizures, due to a left lateralised HH since the age of 6 months, was investigated in our unit. The EEG of his habitual seizures did not show localised alterations at onset, but 8 to 22 sec after clinical onset, left fronto-temporal sharp waves occurred. In the interictal EEG, there were also left fronto-temporal spikes as well as multifocal intermittent slowing. 3D-mapping and source localisation of the epileptic discharges revealed a successive activation pattern that included mainly two cortical areas: left fronto-orbital and left mesial orbital cortex. In fact, these regions have been invoked as predominant outflow in HH without involvement of the mamillary bodies, as is the case in our patient. 3D EEG source localisation is an efficient non-invasive tool to elucidate the underlying network of interictal and ictal discharges.

Out-of-hospital emergency medical care and outcome of patients with severe traumatic brain injury in Switzerland – national population-based prospective cohort study (proposal)

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Background: Severe traumatic brain injury (TBI) is endemic with ~13 cases/100 000 population/year. Severe TBI leads to disability and costs (~1.7 million CHF/patient). Outcomes of TBI may be improved by advanced life support (ALS), i.e. by medical interventions of skilled out-of-hospital emergency medical services (OHEMS).

Objectives: Hypothesis: ALS improves outcome after severe TBI as compared to basic life support. Aim: to investigate the relationship between the components of ALS including the time to specialised care with outcomes of TBI.

Methods: National population-based prospective study on patients with Glasgow Coma Scale (GCS) <9 and Abbreviated Injury Score of head region >3. Consecutive enrolment in the 12 hospitals with neurosurgery. Primary outcome: extended Glasgow Outcome Scale (GOSE) after 12 months; secondary outcomes: survival, GCS after 14 days, GOSE after 2 and 6 months, and health-related quality of life (SF-12) after 2, 6 and 12 months. After a run-in period of 1 year in 3 hospitals, recruitment of ~1500 patients during 2 years.

Rationale and significance: This study will quantify the impact of skills of OHEMS, interventions and timing on outcomes after severe TBI. It will establish a scientific basis for cost-effective, evidence-based care, for standardisation of ALS and planning of services.

Neues zur Pharmakoresistenz bei Epilepsie[1]

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Die Mehrheit der Patienten mit «neu aufgetretenen Anfällen» werden mit dem ersten Antiepileptikum (AED, antiepileptic drug) anfallsfrei oder sind «gut kontrolliert», brauchen aber oft eine lebenslange Prophylaxe. Nach Kwan und Brodie [1] werden mit einem *lege artis* eingesetzten AED der 1. Wahl 47% der Patienten mit neu diagnostizierter Epilepsie anfallsfrei (>1 Jahr Nachbeobachtung), der Wechsel auf ein anderes AED bringt in 13% Anfallsfreiheit.

40% der Patienten sind schwer «kontrollierbar» oder refraktär: das heisst, Wechsel auf ein anderes AED oder die Kombination von AED bringt wenig, nur in ca. 6% wird noch Anfallskontrolle erwirkt. Symptomatische oder kryptogene Epilepsien sind schwerer behandelbar als idiopathische, und eine frühe Aufnahme der AED-Therapie (<10 Anfälle) ist hinsichtlich Anfallskontrolle besser, verglichen mit den Patienten, die >10 Anfälle vor Therapiebeginn hatten. Das Nicht-Ansprechen auf das erste AED ist somit der wichtigste prädiktive Faktor für Pharmakoresistenz. Bei Pharmakotherapieresistenz sollten heute frühzeitig epilepsiechirurgische Massnahmen in Betracht gezogen werden.

Diese Ergebnisse decken sich mit den Resultaten einer kürzlich in England durchgeführten Studie, der zufolge rund die Hälfte der Patienten, die AED einnehmen, im Jahr zuvor noch Anfälle hatten. Die Reihenfolge der Häufigkeit der Verschreibung war wie folgt: Carbamazepin (37%), Valproat (36%), Phenytoin (29%), Phenobarbital oder Primidon (14%) und Lamotrigin (10%). Monotherapie hatten 68% der Patienten. Patienten mit mehreren AED hatten signifikant mehr unerwünschte Nebenwirkungen und auch schlechtere Anfallskontrolle.

Pharmakotherapieresistenz wird üblicherweise klinisch definiert als fehlendes therapeutisches Ansprechen auf zwei AED der ersten Wahl in Monotherapie und in Kombination. Nur vor Implantation eines Vagusnervstimulators fordern einige Autoren auch den Einsatz eines «neuen» AED.

[1] Auszug aus einem Manuskript Wieser HG. Die Behandlung der Epilepsien und verhaltensneurologische Aspekte (in Vorbereitung für Publikation in Schweizer Archiv für Neurologie und Psychiatrie, Sonderheft Neurosciences 2004).

Pharmakotherapieresistenz kann zahlreiche Ursachen haben. Scheinbare Pharmakotherapieresistenz wird oft durch mangelnde Compliance vorgetäuscht. Bei echter Pharmakotherapieresistenz werden heute folgende biologische Faktoren diskutiert [2]: Schwere und Art des Syndroms beziehungsweise der zugrundeliegenden Neuropathologie (z.B. epileptische Enzephalopathien des Kindesalters), abnorme Reorganisation neuronaler Schleifen (z.B. Hippokampussklerose, kortikale Dysplasien), übererregbare oder disinhibierte Netzwerk-Reorganisation (z.B. Moosfaser-Sprossung), Rezeptor-Veränderungen von Neurotransmittoren (Komposition/Funktion von GABA/Glutamat-Rezeptoren), Pathologien der Ionenkanäle Natrium, Kalzium, Kalium («ion channelopathies», sowohl liganden- und spannungsabhängig; zum Beispiel bei genetisch bedingten Epilepsien, wie bei der autosomal dominanten nächtlichen Frontallappenepilepsie [ADNFL] mit dem mutierten nikotinischen Rezeptor), reaktive Autoimmun-Prozesse (z.B. Autoantikörper gegen Glutamatdecarboxylase oder – wie bei der Rasmussen-Enzephalitis vermutet – gegen GluR3) und gestörte AED-Penetration in den epileptischen Herd (z.B. P-Glykoprotein-Expression an der Blut-Hirn-Schranke). Daneben sind auch genetische Ursachen zu diskutieren.

Ein derzeit intensiv beforschter zellulärer Faktor der Therapieresistenz ist die vermehrte Aktivität von Efflux-Pumpen, wie sie z.B. ATP-abhängige Transporter darstellen. Der Efflux-Transporter P-Glykoprotein (Pgp), enkodiert durch das «multidrug resistance (*MDR*)»-Gen, ist im Gehirn vorwiegend in der dem Lumen zugewandten Endothel-Membran von Mikrogefässen lokalisiert, die die Blut-Hirn-Schranke formen. Lipophile AED sind potentielle Substrate für Pgp. Überexpression von Pgp im Endothel der Blut-Hirn-Schranke wurde bei Epilepsiepatienten mit Pharmakotherapieresistenz festgestellt und lässt vermuten, dass dies zu einer verminderten Aufnahme von AED ins Gehirn führt.

Tierexperimentell fanden Volk et al. [3] Pgp-Expression in Neuronen des Hippokampus (CA3- und CA4-Regionen) nach experimentell erzeugtem limbischem Status epilepticus. Beim Menschen wiesen Sisodiya et al. [4] nach, dass MDR1 und MRP1 im Hirngewebe von chirurgisch behandelten pharmakotherapieresistenten Patienten mit dysembryoneuroepithelialen Tumoren (DNET), fokaler kortikaler Dysplasie (FCD) und Hippokampussklerose (HS) überexprimiert sind, und zwar in Glia und Nervenzellen: Bei allen 8 DNET-Fällen und bei 5/8 HS-Patienten dieser Studie fanden sich reaktive Astrozyten, die MDR1 und MRP1 exprimierten. MDR1- und MRP1-Expression wurde aber auch nachgewiesen in dysplastischen Neuronen bei FCD und DNET, akzentuiert um Gefässe. Da neue Pgp-Inhibitoren in Entwicklung sind [5], hegt man Hoffnung, dass sich aus ihrem Einsatz therapeutischer Nutzen bei pharmakotherapieresistenten Epilepsien ziehen

lässt. Dass Therapieresistenz bei Epilepsien mit einem Polymorphismus im Drug-Transporter-Gen ABCB1 (3435) assoziiert ist, wurde kürzlich in der Studie von Siddiqui et al. [6] gezeigt. Die wichtige Rolle von genetischen Polymorphismen wird sich möglicherweise zukünftig bei der Entwicklung von AED – besonders hinsichtlich Vermeidung von unerwünschten Nebenwirkungen – positiv auswirken («individuell ausgewählte Medizin, massgeschneidert nach Genotyp»).

Kurative Epilepsiechirurgie bewirkt nicht nur in einem hohen Prozentsatz der Operierten vollständige Anfallskontrolle, sondern kann auch von Epilepsie vollständig heilen, in dem Sinne, dass die AED ohne Anfallsrezidiv abgesetzt werden können. In der Zürcher Amygdala-Hippokampektomie-Serie liegt der Prozentsatz der Patienten, die ihre AED postoperativ vollständig absetzen konnten, im 7. bis zum 11. postoperativen Jahr zwischen 40 und 43% [7]. Bei jenen Patienten, die *seit der Operation* vollständig anfalls- und aurenfrei blieben, waren im 8. postoperativen Jahr über 90% ohne AED.

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Neurologist-in-training

Answers to MCQ

1 E **2** E **3** E **4** A **5** C

Answers to Neuroradiology/Neuroanatomy

1 Type of image: venous magnetic resonance angiogram, in a slightly rotated lateral view.

2 Anatomical structures:
- **A** Superior sagittal sinus
- **B** Left transverse sinus
- **C** Left sigmoid sinus

3 The lesion is in the deep venous system which is nearly completely obstructed by thrombosis. Usually, the following deep venous structures can be identified in a venous MRA, venous CT-angiography or conventional angiography:
- Straight sinus (sinus rectus) (single)
- Internal cerebral veins (pair)
- Basal veins of Rosenthals (pair)
- Thalamostriate veins (pair)

This 18-year-old woman presented with 3 days of non-lateralised headaches, followed by mutism and a stuporous state. Plain CT showed bilaterally oedematous and hypodense thalami, and T_2W-MRI showed bilateral diffuse thalamo-lenticular hyperintensities. A protein S-deficiency was found on hypercoagulable work-up, and the patient recovered completely within 2 months on anticoagulation.