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Epilepsy Surgery for Remote Symptomatic Epilepsies
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P1. The investigation of insulin resistance in two groups of epileptic patients treated with sodium valproate and carbamazepine

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Objectives. Valproic acid (VPA) is a widely used broad-spectrum antiepileptic drug (AED) for treatment of generalized and focal epilepsies. Cross sectional studies have suggested that valproate treatment may be associated with hyperinsulinemia. The aim of this study was to investigate this health-threatening side effect in the Iranian population.
Methods. Body mass index (BMI), lipid profile, fasting serum insulin, fasting blood sugar (FBS) and homeostasis model assessment insulin resistance(HOMA-IR) were measured in 30 VPA-treated epileptic patients and 30 controls [carbamazepine (CBZ)-treated].
Results. BMI was higher in the VPA group than in the control group (25.7± 3.5>21.7± 4.1) (0.000<0.05).
Prevalence of obesity was 16.6% in the VPA group which was almost the same but lower than that of the general Iranian population. Serum TG (150± 77.2) was higher than CBZ group (114± 35.2) (p=0.023). Serum High density lipoprotein (HDL) level was lower in the VPA group than controls (45.2± 11.7<54.4± 13.9) (p=0.008). Serum insulin, FBS, HOMA-IR, cholesterol and Low density lipoprotein (LDL) did not demonstrate in a statistically significant difference between the two groups (P>0.05).
Conclusion. Although VPA therapy is associated with significantly greater BMI and an increase in lipid profile, despite several previous studies hyperinsulinemia and insulin resistance did not occur in any of cases.

P2. Symptomatic epilepsy with partial complex seizures caused by hippocampal mesial sclerosis: case report

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Objective. We report good outcome of neurosurgical treatment in a 17-year-old boy who had drug resistant epilepsy with complex partial seizures. The data of pregnancy and delivery, psychomotor and intelectual development were normal. The patient had normal neurological findings during early follow-up. Febrile seizures occured twice in infancy. Since the age of 4 years very frequent seizures occured with epigastric aura, vegetative symptoms, automatisms and masticatory pantomime. Seizures persisted for years with secondary generalisation several times per year despite all mono and polytherapy with numerous antiepileptic drugs. After 13 years of unsuccessful treatment, advantages and complications of neurosurgical treatment were explained to the patient and his parents.It was emphasized that neurosurgical treatment leads to seizure freedom in more than 70% of patients who suffer from temporal lobe epilepsy.
Methods. EEG showed slow and poorly defined activity in the begining with the discrete focal discharges over the left temporal region later on. Computerised brain tomography and brain nuclear magnetic resonance were normal at the age of 7 years. Repeat brain MRI recordings at the age of 12 and 15 years showed left hippocampal sclerosis. Interictal single photon emission computerised tomography revealed reduced perfusion in the left hippocampal region. The finding was confirmed with positron emission computerised tomography. During the long-term video-EEG monitoring, an epileptic lesion in the left temporomesial area was recorded. Preoperative brain MRI showed the

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reduction of the left hippocampus together with loss of its internal structure. 18F fluorodeoxyglucose-PET studies showed hypometabolism of the left temporal region.
Results. The obtained diagnostic data were congruent with the clinical semiology of seizures in our patient. Subtemporal left osteoplastic craniotomy was performed together with selective amygdalohippocampectomy and sclerotic left hippocampus with uncus and left enthorinal cortex removed. Postoperative follow-up was without complications with normal EEG and normal brain MRI 5 months after surgery.
Conclusion. 12 months after neurosurgery, the patient was seizure free and continued treatment with antiepileptic drugs. Seizure freedom improved the quality of his life. We expect a good final outcome following surgical treatment and the discontinuance of the antiepileptic therapy.

P3. Extratemporal epilepsy surgery around eloquent cortex using noninvasive presurgical evaluation

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Objective. To assess surgical outcome in refractory epilepsy (RE) patients with extratemporal lesion (ETL) around eloquent cortex, who underwent epilepsy surgery based on data from noninvasive presurgical evaluation.
Method. A retrospective analysis of clinical data of 14 patients with RE due to ETL around eloquent cortex, who underwent surgery at KEM hospital Mumbai, India between 2008-2010, was performed. Presurgical evaluation included dedicated MRI brain (1.5/3 tesla), ictal and interictal video-EEG, neuropsychology and psychiatric assessment. Due to financial constraints we do not have facilities for any preoperative invasive monitoring. Patients who require invasive monitoring are informed about these constraints and refused surgery. A subgroup of patients who were refused surgery but who were highly affected, reproached the center and voluntarily requested for epilepsy surgery, making an informed choice to accept suboptimal outcome. From this group only 14 patients who had concordant data on MRI and video-EEG were selected and they were operated under intraoperative electrocorticographic guidance. The type of surgery was corticectomy with or without MST. Postsurgical outcome was assessed in terms of postoperative deficit and seizure freedom and graded according to modified Engel's classification.
Results. 14 patients with age range 8-34 years were assessed. Average seizure duration up to surgery was 12.2 years (range 3 to 25 years). Patients were followed for max. 24 mths and min. 6 mths. Seven patients had a new postoperative neurological deficit during immediate post-operative period but which recovered completely within the next 2-3 weeks. All patients showed improvements, 11 in Engel class I and 3 in II. The seizure outcomes were comparative in patients with neoplasm and cortical dysplasia. The cost of full presurgical evaluation and surgery was Rs.15-20,000 (300-400$).
Conclusion. Patients with RE due to ETL around eloquent cortex can achieve good outcome with surgery done on the basis of noninvasive presurgical evaluation. Factors that possibly contributed to good outcomes may include well defined lesion on MRI brain, concordant EEG and MRI data, intraoperative identification of epileptic zone by corticography and area of resection targeted around eloquent cortex. This poster emphasizes the need for considering surgery in such patients even if invasive presurgical evaluation is not feasible, as the result could be very gratifying in well selected patients.

P4. Long-term prognosis of resective epilepsy surgery for infants with foreign-tissue lesions

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Early epilepsy surgery for infants with foreign-tissue lesions has not been commonly indicated during infancy unless seizures become intractable and show a catastrophic nature, which may partly be because the operative risks and post-operative prognosis of epilepsy surgery in infancy are not well understood.
We performed a retrospective review of eight consecutive cases of infants (male 6, female 2) with foreign-tissue lesions operated at less than 24 months old in our institute between 2001 and 2010. The etiology was ganglioglioma (3 in temporal lobe, one in cerebellum), astrocytoma (2 in temporal lobe) and Sturge-Weber Syndrome (1 in temporo-occipital and 1 in fronto-parietal region). The age of seizure onset was from 1 day to 15 months (av. 4.8 mo) and the age of surgery was from 4 to 23 months (av. 15.5 mo) after birth. The follow-up period was from 1 to 8 years (av. 5.0 y).
Seizure semiology was variable depending on the lesion site. Patients with temporal lesions showed apneic spells (n=3), complex partial seizures (n=2), spasms (n=1) and generalized tonic clonic convulsion (n=1). Eyelid jerks were observed in the patient with cerebellar ganglioglioma. Pre-operative development was normal in six and mildly delayed in two infants. Complete removal of the MRI-visible lesion

was performed in all the cases and Engel class I outcome was obtained post-operatively in all the eight patients and medication was stopped in four. Developmental status during follow-up was normal in five and mildly delayed in three patients; *i.e.* one gained, five stable and two delayed postoperatively. No permanent morbidity or mortality was experienced except for the initial case, which developed small basal ganglia infarction because of a complication of the intra-operative transfusion line resulting in hypotension. Preoperative central vein catheterization became mandatory.
Long-term seizure and developmental prognosis of resective epilepsy surgery for infants with foreign-tissue lesion was favorable. All the patients became seizure free, 50% of them were off medication, and 63% of them developed normally.

P5. Outcome of extratemporal epilepsy surgery and hemispherectomy after evaluation with a non-invasive protocol

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Introduction. Surgery is an accepted choice of therapy in patients with refractory epilepsy. Selection for surgery is based on a battery of invasive and non invasive investigations. In countries with limited resources, extensive presurgical evaluation may not be possible.
Objective. To assess the outcome of surgery in patients with medically refractory extra-temporal epilepsy (ETLE) and hemisperectomy patients evaluated with a non-invasive protocol and to determine the predictors of outcome following surgery.
Patients and methods. Retrospective analysis of presurgical (ictal EEG, MRI, fMRI, SPECT, FDG PET, neuro-psychology and pathology) data was performed in 48 patients who underwent surgery for ETLE and 12 patients following hemispherectomy and who had at least one year post surgery follow-up. WADA, invasive monitoring was not done. Outcome was assessed according to Engel's outcome classification. Stepwise multiple logistic regression analysis was employed in data analysis.
Results. Mean follow-up was 32 (12-68) months. 36 (60%) were males. Intra-operative electrocorticography was used in 42 and cortical stimulation in 23. Frontal resections were the commonest (28), followed by parietal resections. The pathology showed cortical dysplasia in 21, gliosis in 8 and low grade tumoral lesions in 10. Transient postsurgical complications occurred in 3. At last follow-up visit, seizure free outcome was noted in 37 (77%) with ETLE and 9 (75%) after functional hemispherectomy. After stepwise multiple logistic regression analysis, the variables found to be significant ($p \leq 05$) and predicting favourable outcome were normal IQ and absence of acute post-operative seizures.
Conclusion. Favourable outcome after epilepsy surgery can be obtained in patients with extra-temporal epilepsies after evaluation with a non-invasive protocol if presurgical evaluation is carefully planned.

P6. Individual, automated MRI classification in temporal lobe epilepsy based on diffusion tensor imaging

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MR imaging has an important role in identifying structural causes of seizures that may be amenable to surgical treatment. Automated MRI classification is a desirable tool to augment the interpretation of images especially in patients with cryptogenic epilepsy. Support vector machines (SVM) based on volumetric MRI datasets have recently been described to be useful for voxel-based MR image classification (Focke *et al*., 2010, 2011). In the present study we sought to evaluate this method based on diffusion tensor imaging (DTI) in temporal lobe epilepsy.
We studied 38 patients with hippocampal sclerosis and unilateral (mesial) temporal lobe epilepsy (20 left=LHS, 18 right=RHS) undergoing presurgical evaluation and 22 neurologically normal control subjects. DTI scans (b=1,200 s/mm/mm and TE=73 ms, $1.875 \times 1.875 \times 2.4$ mm, 61 b1 directions) were acquired at 3T (GE Excite) and processed with FSL-FDT yielding fractional anisotropy (FA) and mean diffusivity (MD). The SVM analysis was done with the libsvm software package separately for FA and MD maps with leave-one-out cross-validation. Local weighting was applied by SPM F-contrast maps.
Prediction accuracies (percentage of correct classifications/attempted classifications) for FA were 93% (LHS *vs* controls), 85% (RHS *vs* controls) and 51% (LHS *vs* RHS). For MD, accuracies were 95% (LHS *vs* controls), 97% (RHS *vs* controls) and 97% (LHS *vs* RHS).
These findings show that automated SVM image classification based on DTI data can achieve high prediction rates in mTLE at the individual subject level. MD-based classification showed slightly better results compared to the FA-based variant in the patients against controls setup; in the lateralization design (LHS *vs* RHS) the MD-based SVM also showed excellent accuracy whereas the FA-based method could not separate both groups.

Table. SVM classification results.
Overall accuracy, sensitivity, specificity and correctness (where applicable) for the leave-one-out classification are shown in percent. Rows represent different comparisons (two-way or three-way SVM).

	FA		**MD**	
Local weights	No	Yes	No	Yes
	LHS *vs* controls			
Accuracy	92.86%	92.86%	88.09%	95.24%
Sensitivity	85%	85.00%	80.00%	90.00%
Specificity	100.00%	100.00%	95.45%	100.00%
	RHS *vs* controls			
Accuracy	79.49%	84.62%	87.18%	97.44%
Sensitivity	64.71%	70.59%	82.35%	94.12%
Specificity	90.91%	95.45%	90.91%	100.00%
	LHS *vs* RHS			
Accuracy	48.65%	51.35%	64.86%	97.30%
LHS correct	50.00%	60.00%	70.00%	95.00%
RHS correct	47.06%	41.18%	58.82%	100.00%

FA: fractional anisotropy; MD: mean diffusivity; LHS: left hippocampal sclerosis; RHS: right hippocampcal sclerosis; SVM: support vector machine.

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P7. Ictal SPECT perfusion patterns in temporal lobe epilepsy: correlation with ictal EEG, MRI and surgical outcome

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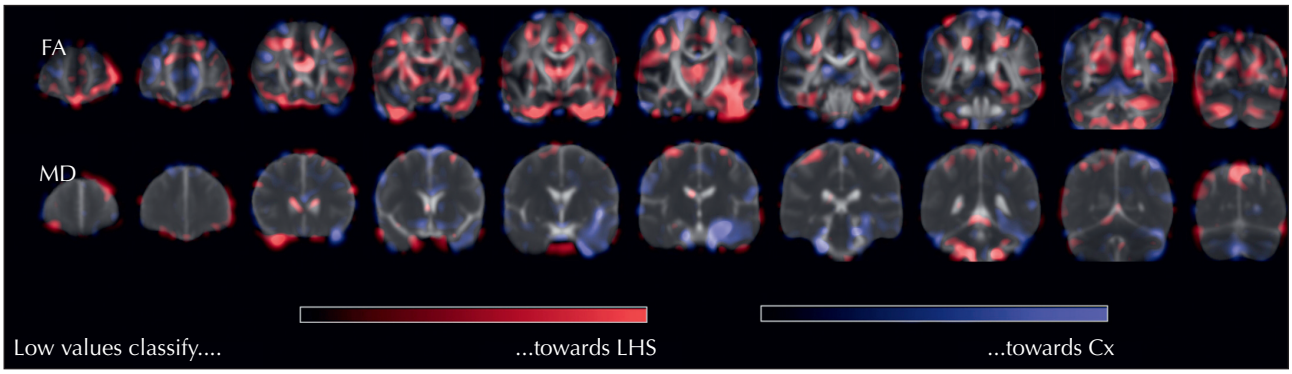
Aim. To identify ictal SPECT perfusion patterns and to correlate with ictal EEG, MRI, and surgical outcome in patients with refractory temporal lobe epilepsy (TLE).
Materials and methods. Retrospective analysis of SPECT, IctalVEEG and MRI data was performed in 114 patients with refractory TLE with at least one year follow-up after surgery. The mean injection time was 22.4 seconds. The SPECT perfusion patterns were classified as typical (anteromedial, anterolateral and inferior) and atypical (extended and extratemporal) patterns.
Results. Mean follow-up was 32 (12-62) months; 63 (55%) were males; mean age at surgery was 26.5 (5-52) years. Pathologically verified hippocampal sclerosis (HS) was found in 85. The sensitivity of ictal& interictal SPECT was 93% and 67% and specificity 97% and 50%, respectively. The commonest ictal perfusion pattern was typical (79%), with predominant anteromedial and lateral hyperperfusion. The ictal EEG onset was discordant with MRI in 20 and surgery was done after concordant ictal SPECT and interictal PET. MRI was normal in 19; surgery was done after concordant ictal EEG, SPECT and interictal PET, 10 (53%) had favorable outcome. Typical perfusion pattern was commonest among patients with Engel class 1, and atypical pattern was seen in those with class 2& 3 outcome (OR: 9.717; CI: 2.919-32.342; p=0.002). After multiple regression analysis using the McHenry's algorithm, abnormal imaging, unilateral interictal spikes and typical ictal SPECT pattern were predictors of favorable outcome.
Conclusion. Ictal SPECT is a highly specific and sensitive noninvasive modality during presurgical evaluation of patients with refractory TLE. It obviates the need for invasive EEG in resource-poor countries.



P8. Application of intraoperative angio CT for implantation of SEEG in intractable epilepsy patients

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In the 1950s, Talaraich and Bancaud introduced the technique of stereotactic implanted EEG (SEEG) electrodes for evaluation in patients with medically refractory epilepsy. In the mean time, SEEG has become a well established procedure for a large number of these patients prior to resective epilepsy surgery. The most feared complication is a hemorrhagic complication due to vascular injury during the insertion of the EEG electrodes. This study investigated the usefulness of Angio CT during implantation of the SEEG electrodes.

In 12 patients, 146 implanted SEEG electrodes were investigated. Fifty were left- and 96 right-sided. All brain lobes were involved: frontal (n=47), hippocampal/insular (n=16), parietal (n=43), temporal (n=30) and occipital (n=10). All patients suffered from medically refractory epilepsy. The indication for invasive monitoring with SEEG was confirmed by the patient management conference at the Epilepsy Center of Cleveland Clinic Foundation, unrelated to this study.

Surgical planning of each trajectory was performed with matching of preoperative contrast enhanced MRI, MRA and non-contrast CT. Intraoperatively, each trajectory was approved by matching the intraoperative angio-CT. In case of suspected vascular collision the trajectory was changed. Such a replacement was mandatory for 27 electrodes (18%) according to the additional information gained by the live intraoperative CT angio.

The mean accuracy of entry point was at 0.88 mm $\pm$ 0.92 (range: 0-2.9 mm) in the remaining electrodes which were implanted as preoperatively intended. Mortality rate was zero. Hemorrhagic or infective complication occurred in none of the patients.

These findings underline the usefulness of intraoperative CT angio. Beyond the preoperative imaging and anatomical landmarks, respecting the detailed vasculature in each individual patient by application of intraoperative CT angio offers a complementary, live and accurate method to reach a most valuable level of safety.

P9. Indication and follow-up of hemispherotomy in 3 adult patients

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One female patient with a right-hemispheric epilepsy (onset: 13 yrs) presented with left homonymous hemianopsia. Aetiology was Sturge-Weber-Syndrome. EEG-findings and lesion on MRI (angiomatosis, right temporo-parieto-occipital) were congruent. Neuropsychologically, she had average IQ and low unremarkable short-term memory. In 11/09, aged 17, a modified right hemispherotomy was done. After one year of follow-up the patient presented with 3 early seizures and has been seizure-free since (ILAE 1). She had new spastic hemiparesis of the left foot/leg. The patient showed better verbal skills and improved short-term memory. Her attitude towards the operation remained positive.

A male patient (20 yrs) had right-hemispheric epilepsy (onset: 14 yrs). He presented with left spastic hemiparesis, left homonymous hemianopsia and hydrocephalus. Aetiology was a prenatal porencephalic cyst DD schizencephaly. EEG showed right parietal pathology. MRI displayed a defect in the right MCA-territory with polymicrogyria. Cognitive functions were below average with deficits in attention, verbal memory and executive functions. Visuospatial functions and nonverbal memory were spared. Hemispherotomy was conducted in 08/07. Two years after, the patient remained seizure-free (ILAE 1) and had no new neurological deficit. He showed decreased visuospatial short-term and nonverbal memory while attention improved. He is now in vocational training to be a clerk.

The third patient (28 yrs) had Rasmussen syndrome (onset: 10 yrs). EEG showed right-hemispheric pathology. MRI showed right hemiatrophy. Cognitive decline began after the age of 10 and the patient switched to a school for the disabled and a sheltered workshop. IQ was below average with individual strengths in figural material. Deficits in memory were non-material-specific. Hemispherectomy was conducted in 08/08. After two years of follow-up the patient remained seizure-free (Engel 1). He had no new neurological deficits but presented initially with anxiety and psychotic symptoms. Verbal remained better than figural skills. An individual decline in word fluency was observed.

Discussion. Seizure onset was relatively late in all patients (10-14 yrs). All of them had a good seizure outcome (2 Engel 1a, 1 Engel 1). Quality of life improved in two patients; one initially had severe psychiatric symptoms which are currently under remission. Hemispherotomy should be considered a therapy option for remote epilepsies even in adults.

P10. Borna disease virus infected TNF-transgenic mice: an inflammatory model of epileptic seizures

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Objective. Experimental infection of tumor necrosis factor (TNF)-transgenic mice with the neurotropic Borna disease virus (BDV) serves as model to study the role of neuroimmune interactions and reaction patterns of brain cells for seizure induction. Dysregulated neuromodulatory systems such as dynorphin expression have already been found in human epilepsy forms. Initial studies revealed disturbances of the anticonvulsant dynorphin system in the transgenic mice per se and a relationship between reduced prodynorphin mRNA levels and seizure development in TNF-transgenic BDV-infected mice.
Material. TNF transgenic C57BL/6 mice with selective TNF-overexpression in cerebral cortex, hippocampus, striatum and thalamus and wild-type mice were infected neonatally with a mouse-adapted BDV strain and necropsied between 21 and 42 days post infection (p.i.) to obtain freshly frozen and formalin-fixed paraffin-embedded tissue of the central nervous system. Immunohistochemistry (IHC) and Western Blotting (WB) were used to visualize dynorphin A protein expression and NFkappaB nuclear translocation.
Results. TNF-transgenic BDV-infected mice developed complex partial and generalized epileptic seizures from day 21 p.i. on accompanied by encephalitis and glial cell activation. Dynorphin A was detectable either by IHC or WB in non-infected and BDV-infected transgenic mice as well as wild-type mice on day 21, 35 and 42 p.i. in the same brain areas. Interestingly, increasing nuclear NFkappaB translocation as part of downstream TNF signaling and dynorphin gene induction was not observed in BDV-infected neurons at 42 days p.i.
Conclusion. These initial qualitative studies indicate that dynorphin A protein is not completely absent in the TNF-transgenic mice which developed epileptic seizures despite downregulation of prodynorphin mRNA. Further investigations will address the morphological characterization of cells containing either prodynorphin mRNA and/or dynorphin A protein and NFkappaB nuclear translocation to analyze a relationship between enhanced TNF levels, virus infection, and the NFkappaB signalling and dysregulated dynorphin system to determine its role in seizure indcution.

P11. Forced thinking in two cases of electrocortical stimulation of the left frontal operculum

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Objective. There are no previous reports of psychic perceptual phenomena elicited by stimulation of the frontal operculum (Selimbeyoglu and Parvizi 2010). Here we report two cases in whom "forced thinking" occurred upon electrocortical stimulation of the left deep anterior frontal operculum.
Methods. Two right-handed female patients (age 38 and 21 years) with intractable epilepsy underwent invasive monitoring in our Video-EEG-monitoring-unit including implantation of depth electrodes (diameter=1 mm, interelectrode distance=2.5 mm, 12 contacts) into the left insular lobe using a tangential mediodorsal-to-lateroventral technique. Postsurgical cCT and presurgical cMRI were superimposed to localize the electrode contacts (iplan-stereotaxy 2.6 Brainlab, Munich, Germany) *(figures 1, 2)*. Electrical stimulation was applied with an Ojemann current stimulator and repeated if the initial stimulation produced any symptom (stimulation frequency=50 Hz, pulse width=0.5 ms, duration of stimulation=3-5 sec, stimulation intensities=1.5-14 mA).
Results. Stimulation of two electrode contacts in close proximity to the deep frontal operculum and the dorsal anterior insula did elicit forced thinking in both patients. One patient reported hearing the phrase ". . .so, how do you know. . ." in English with an Italian accent upon stimulation of an electrode contact with $\geq$7.3 mA in 3 out of 8 stimulations.
A second patient reported the feeling of "thinking out loud", the sense of saying own thoughts directly after initiating stimulation of an electrode contact with $\geq$7.4 mA 9 times in 3 different stimulation sessions.
With repetition, this phenomenon developed an affective component and was described as unpleasant and as "chaos going on in my head". No oral movements were witnessed with stimulation. These phenomena were elicited in the absence of after-discharges and did not resemble the patients' habitual epileptic seizures.
Discussion. These signs may correspond most closely to the symptom of forced thinking which has been described as a type of psychic aura in patients with left frontal lobe epilepsy (Mendez *et al*., 1996). Also, there

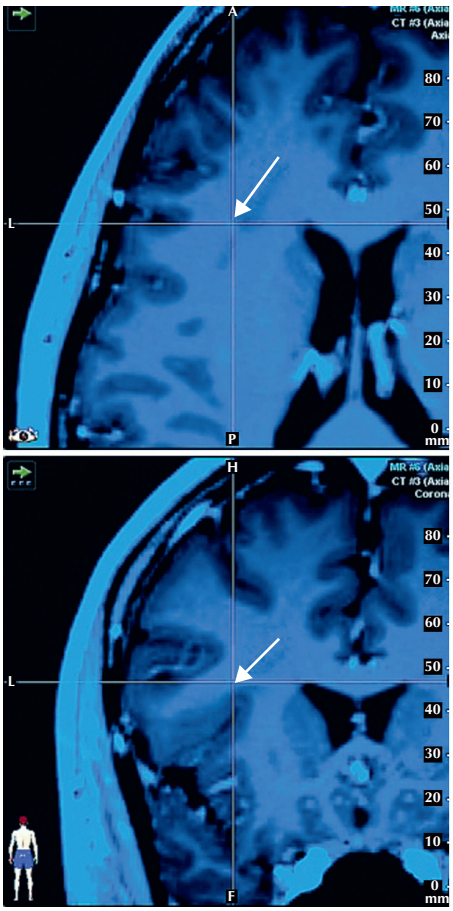

Figure 1.

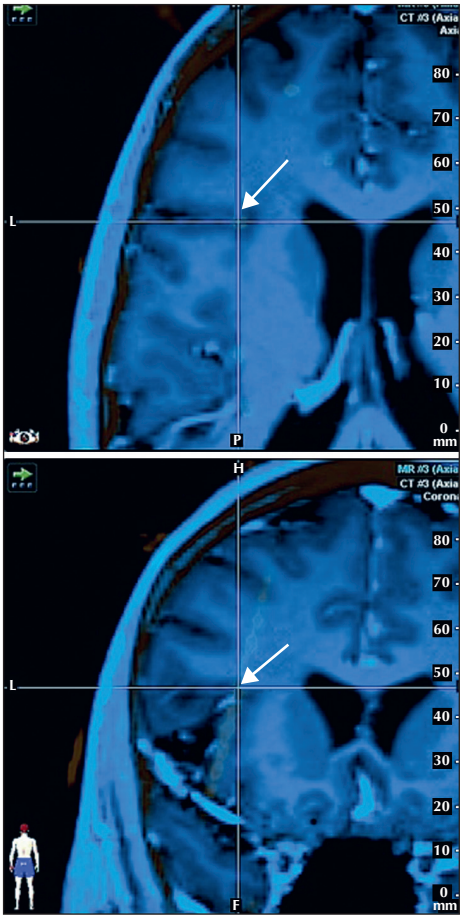

Figure 2.

is similarity to complex acoustic verbal hallucinations including feelings of audibility and alienation as frequently seen in patients with schizophrenia (Sommer *et al.*, 2010). Our results support a functionally distinct role of the left deep frontal operculum within the speech processing network of the frontal lobe (Friederici *et al.*, 2006).

P12. Granule cell dispersion in two mouse models of temporal lobe epilepsy is associated with changes in dendritic orientation and spine distribution

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Objective. Temporal lobe epilepsy is associated in the most patients with hippocampal sclerosis. It is histologically characterised by neuronal death in CA1 and the hilus. Granule cells of the dentate gyrus survive but show a dispersion of the usually tightly packed granule cell layer. This is associated with a decreased expression of the glycoprotein Reelin, which acts as a stop protein for neuronal migration and dendrite outgrowth. Here, we studied dendritic orientation and the distribution of dendritic postsynaptic spines on granule cells in two mouse models of temporal lobe epilepsy, namely the p35 knockout mutant and mice with unilateral intrahippocampal kainate injection.

Methods. Granule cells were Golgi-stained and analysed using a computer based camera lucida system. The granule cells of wild-type, p35 knockout and kainate-injected mice were categorised as proximal or distal to the hilus (GCprox, GCdist).

Results. We found that GCprox in the densely packed granule cell layer of wild-type mice exhibited a mainly vertically oriented dendritic arbour with a small bifurcation angle (31°) between branching dendrites. In contrast, GCdist showed a wider bifurcation angle (90°), suggesting a widening of the dendritic field during the migratory process to superficial positions. Granule cells of p35 knockout- and kainate-injected mice showed a dispersed granule cell layer, exhibiting recurrent basal dendrites and a wider bifurcation

angle of their dendrites (GCprox: 96°; GCdist: 152° and GCprox: 294°; GCdist: 286°, respectively). The spine density on dendrites of GCprox in the two epilepsy models was increased compared to wild-type mice. In contrast, dendrites of GCdist extending into the molecular layer showed a reduced spine density in the two epilepsy models.
Discussion. We hypothesise that adult granule cells start to migrate in temporal lobe epilepsy, creating new dendrites with specific angular spread and new synaptic spines in areas proximal to mossy fibre sprouting and loose spines on distal dendrites. These results in the epilepsy mouse models are in accordance with our recent findings in human controls and epilepsy patients.

P13. Modification of EEG recordings by local antiepileptic polymers in a rat epilepsy model combining neocortical tetanus toxin and cobalt chloride application

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Objective. Patients with pharmacoresistant epilepsy caused by an epileptogenic focus in an eloquent brain area are difficult to treat. An operative resection or multiple subpial transections may result in severe neurological deficits (hemiparesis, aphasia). Therefore, we have developed a novel experimental technique for local antiepileptic therapy by implantation of biodegradable valproate-containing polymer matrices on the cortex of rats with tetanus toxin/cobalt-chloride-induced focal neocortical epilepsy.
Methods. We tried to use a recently described rat model of tetanus toxin-induced neocortical epilepsy. Unfortunately, we were not able to reproduce the reported seizures or interictal activity. Therefore, we have developed another model by combining (1) three repeated tetanus toxin injections and (2) local application of cobalt chloride onto the area of the tetanus toxin injections. Subsequently, intracortical encephalography electrodes (EEG) were implanted in all rats and long-term video-EEG recordings were performed. Valproate-containing polymer matrices were then implanted on the cortex. Antiepileptic effects were evaluated by reduction of clear-cut epileptiform potentials per hour.
Results. (1) According to the reported epilepsy model, 50 nanograms of tetanus toxin were neocortically injected, but reliable seizures or interictal activity could not be reproduced. (2) After three 50-nanogram tetanus toxin injections, seizures were observed only in two out of five animals without interictal activity. In two other animals interictal spike-waves were only rarely seen. (3) In animals with three 50-nanogram tetanus toxin injections plus 20 mg CoCl2 application, continuous spike-wave discharges were observed in all recorded animals. This interictal epileptic activity was reduced in animals treated with valproate implants.
Discussion. We show for the first time a reduction of epileptiform activity through local application of valproate polymers.