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Parasomnia and arousals. A. C. DECLERCK.

Undesirable physical behaviour during sleep can be caused by epilepsy or sleep disorders (parasomnia). Distinction between these two is difficult to make according to Broughton. Parasomnia is defined as a group of undesirable physical phenomena, either exclusively appearing during sleep or exacerbated by sleep. These events are the manifestation of CNS activation usually transmitted into skeletal muscle and/or autonomic nervous activity. Epilepsy is defined as a chronic brain disorder of various etiologies, characterized by recurrent seizures due to excessive discharges of cerebral neurons associated with a variety of clinical and laboratory manifestations. Parasomnia can be categorized in nonREM and REM parasomnia. NonREM parasomnia is characterized by young age (4-12 years), occurring during the first half of the night and associated with distinctive motor and autonomic symptoms. The patient is very difficult to arouse and has no memory afterwards. REM can occur at any age, occurring during the second half of the night, without outspoken symptoms : more mental activity, spontaneous awakening and vivid memory. Unfortunately these two categories can overlap. There are also parasomnia's occurring during shallow nonREM sleep and those that occur during transition sleep/awake. Case reports are presented to illustrate this. The conclusion from these case reports is that it is indeed very difficult to differentiate between types of parasomnia and epilepsy. Besides long term EEG-video-monitoring it takes sufficient knowledge and experience on sleep disturbances and epilepsy to make an accurate and correct diagnosis. The specialist has to realize the medical and legal repercussions, that the diagnosis can have.

Parasomnia or frontal lobe epilepsy. P. H. M. VELTMAN.

Nocturnal frontal lobe epilepsy can be diagnosed in those cases where seizures usually start during sleep. The movements start abruptly and are frequently accompanied by vocalizations. They vary from one individual to the next but they are stereotyped in each individual patient. Usually, the seizure lasts less than 1 minute and seizures occur with a high frequency per night. They will mostly occur during more than one night per week. The patient either does not lose consciousness at all or regains consciousness quickly. In general no disturbances are seen on EEG. The seizures start in childhood or in (young) adults and continue after childhood. In approx 30% of the patients the seizures are therapy resistant. Sleep terror is characterized by a loud scream, followed by uncoordinated arm and leg movements. The patient has a terrified facial expression and sometimes sweats profusely, followed by 5-10 minutes of disorientation. Sleep choking causes leads to an intense fear of dying. The patient has a choking sensation and feels a pressure on the chest, accompanied by tachycardia. This episode lasts from seconds to minutes. The patient vocalizes with distinctive mouth movements and raises his head up and down. The patient remains conscious. Symptoms, duration, frequency, MRI abnormalities and occurrences in the past that can cause epilepsy, are clues for an epileptic origin of the events during the night. One should always be on the alert for nocturnal frontal lobe epilepsy when brief events during sleep are accompanied with abrupt movements, occur frequently and are individually stereotyped.

Parasomnia or breathing disorders. K. E. SCHREUDER

Parasomnias are undesirable phenomena, which occur predominantly during sleep and are disorders of the dynamic aspects of sleep ; they are manifestations of CNS activation. Primary parasomnias can be categorized in wake-sleep

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transition phenomena, unstable sleep parasomnias, deep NREM sleep parasomnias, REM sleep parasomnias and as proposed by our group : sleep related laryngospasm and sleep choking syndrome. The secondary parasomnias can be divided in arousal disorders by cardio-respiratory regulation disorders (with perhaps sleep related breathing disorders) and epilepsy. Cardiorespiratory regulation is based on the CNS and the autonomic nerve system, on metabolic signals from chemo-receptors and on the baro-receptors. The card io- respiratory network theory of Richter and Spyer (1990) presumes a respiratory rhythm generator in the pre-Botzinger nucleus. After discussing the theories some examples of the clinical practice are reviewed. The first patient snores, has apnoeas, displays sudden stereotyped movements with vocalisations and sits up with wide open eyes. These symptoms suggest obstructive sleep apnoea syndrome (OSAS), frontal lobe epilepsy or confusional arousal. After additional investigations the conclusions are that this patient has NREM 2 desinhibition phenomena, there is no relation to the epileptic EEG signals and he has OSAS, which reacts moderately on CPAP. The second patient has apnoeas, makes swallowing noises, turns around, eyes opened and staring, pales with cyanotic lips and with a loud snore starts breathing again. These symptoms suggest epilepsy, sleep related gastro-esophageal reflux, sleep related abnormal swallowing syndrome, laryngospasm or sleepchoking. After additional investigations the conclusions are that this patient has a right temporal complex partial epilepsy and he is treated accordingly. The last patient has an increase in excessive daytime sleepiness, restless sleep with snoring, sudden movements and incontinence. The symptoms may suggest psychomotor epilepsy, REM parasomnia, instable sleep parasomnia, arousals from superficial and deep sleep or narcolepsy. After additional investigations the conclusions are that this patient has parasomnia from instable sleep and NREM 3 sleep provoked by paradoxal breathing and oxygen desaturations. During BPAP no parasomnias occurred. In general a possible breathing-related arousal disorder should be considered both when primary and secondary parasomnia are present.

Sensory-motor disorders : restless legs syndrome (RLS) and periodic limb movement disorder (PLMD). J. H. M. GROEN.

Patients with RLS have a desire to move their legs, which leads to motor restlessness. Symptoms are worst at rest, in the evening and night. The neuronal structures involved in RLS/PLMD have been studied on basis of fMRI studies. With PLMD an activation takes place in the nucleus ruber en surrounding structures. With RLS an activation of the cerebellum, and of the contralateral thalamus takes place. On the basis of clinical findings, it is clear that, besides the central nervous system, the peripheral nervous system is involved. Data from multiple sclerosis patients indicate the importance of the brainstem in the etiology of PLMD. Neuropharmacological research implicates the dopaminergic system especially, but also the opiate, and – the adrenergic system. On the basis of polygraphic registrations, PLMD is usually triggered by a respiratory event, but the data is conflicting with regard to cause and effect. Medically PLMD can be induced by dopamine D2 receptor blockers, by drugs and on the rebound after stopping sedatives. It is so hard to differentiate between PLMD and RLS that it is doubtful that they encompass two entities. There is a strong hereditary component, but the genes involved are not yet known. At the moment, the treatment of choice are dopamine agonists. Pergolide has nausea and reduction of deep nonREM sleep as side effects, ropinirol and pramipexol have sleepiness during the day as side effect. A double blind, randomised, placebo-controlled trial with pergolide was performed in 100 patients during 1 year. The mean effective dose was 0.52 mg resulting in a reduction in PLM index from 39.6 to 9.0/hour and in of the PLMD-arousal index from 15.2 to 2.6/hour. Despite a better sleep the amount of deep nonREM sleep decreased and about 40% of the patients complained of nausea.

Sleep pathology in epilepsy and mental retardation. A. C. DECLERCK.

The function of sleep is to recuperate after daily activities. The need for sleep differs greatly for each individual. From research with EEG and polygraphs it became apparent that sleep can be classified. First sleep can be divided in REM and nonREM. REM is characterized by rapid eye movements, fast and low amplitude EEG waves and practically no muscle activity. Non REM is the period without rapid eye movements and can be subdivided in 4 categories, differing in the depth of sleep. Category 1-2 is superficial slow sleep and category 3-4 is deep asleep. REM sleep is necessary for ones psychic and cognitive well-being. NonREM (3-4) is used to recuperate physically : the so called core sleep. NonREM (1-2) is probably a fancy sleep. During sleep several cycles, lasting about 90-110 minutes, with nonREM and REM sleep take place. In the mentally retarded the sleep pattern is different from healthy individuals. They have insufficient (quantity and quality) deep nonREM 3-4 sleep, an unstable nonREM 1-2 sleep with to many arousals and a decrease in REM sleep. This causes a lack of recuperation during the night. Sleep and sleepiness can lead to an increase of epileptic phenomena. A seizure during sleep will decrease the quality of the sleep : a complete disorganisation of sleep structure occurs during $^1/_2$-3 hours after a tonic-clonic seizure. Even subclinical seizures disrupt the sleep pattern resulting in insufficient recuperation. An adequate treatment is therefore necessary, but anti-epileptic drugs usually have a negative influence on sleep quality as well. When mentally retarded epilepsy patients exhibit excessive sleepiness during

the day it is rational to evaluate their sleep/wake pattern. A standardized observation with 3 criteria (awake and active ; awake and passive ; asleep) can yield meaningful data.

Neuroendocrinology of epilepsy. J. ISOJÄRVI.

Epilepsy, hormones and antiepileptic drugs (AEDs) influence each other to a greater or lesser degree. Therefore it may be important to evaluate the hormonal state in epileptic patients on AEDs.

Women

Reproductive dysfunction and reproductive endocrine disorders are unusually common among women with epilepsy. Symptoms seen in women are menstrual disorders, infertility and weight gain. These reproductive disorders probably contribute to the decreased fertility in women with epilepsy. Therefore the reproductive function should be screened regularly, looking for menstrual disorder, infertility, obesity or weight gain, hirsutism and galactorrhea. Even further assessment may be necessary such as endocrine testing, pelvic ultrasound or pituitary imaging. The diagnosis of a reproductive endocrine disorder should be considered in terms of etiology and potential contributory factors, including epilepsy and AEDs (valproate in particular). If the disorder is caused by or enhanced by an AED, the possible benefits of a change of AED treatment must be balanced against efficacy in terms of seizure control and the side effects of alternative agents. Conclusion is that the comprehensive management of women with epilepsy includes counselling about reproductive issues that relate to epilepsy and AED use, as well as monitoring of reproductive function.

Men

Reproductive dysfunction and reproductive endocrine disorders are also common among men with epilepsy. Symptoms seen in men are infertility, sexual dysfunction and weight gain. If these problems emerge, hormonal evaluation, sperm analysis and an examination of testicular structure should be done, when indicated. Epilepsy itself and the older AEDs (valproate, phenytoin, carbamazepine) may have effects on reproductive hormones and reproductive function in men with epilepsy. At the moment there are no data suggesting that the newer AEDs affect reproductive functions in men.

New antiepileptic drugs ; efficacy. J. A. CARPAY.

In the last decade quite a few new antiepileptic drugs (AEDs) have been introduced. There are several efficacy factors to study in these new AEDs.

1) There have been no comparative trials in resistant patients so the results of different trials have to be compared. From a clinical point of view the best way to do this is compare retention rates because this reflects clinical practice and displays the balance between efficacy and tolerability. After 3 years the retention rate in resistant patients varies between < 10% with gabapentin, 37% with levetiracetam and 29% with lamotrigine. The speed of titration and effect is also important. Use of levetiracetam and gabapentin results in rapid clinical improvement in contrast with lamotrigine and topiramate.

2) In the Netherlands lamotrigine and topiramate have been registered for monotherapy. In monotherapy efficacy is not the most important issue because there is a high chance of remission with the first AED used. More important therefore is tolerability.

3) It is an advantage if an AED is effective both in partial and generalized seizures. Lamotrigine, topiramate and probably levetiracetam have such a broad spectrum whereas oxcarbazepine, gabapentin and vigabatrin have a narrow spectrum.

4) There are several mechanisms through which the new AEDs work : sodium channels, calcium channels, GABA mimetic, glutamate. The need to know the mechanism is relevant when polytherapy is considered. It is rational to combine different mechanisms. Levetiracetam has an unknown mechanism, different from the others, and is easy to combine with other AEDs.

5) Complete remission is a relevant quality of life outcome from a patients point of view. Unfortunately in resistant patients the chance on complete remission is only about 2-10%. The conclusion is that all new AEDs represent important additions to the therapeutic armamentarium.

New antiepileptic drugs ; tolerability. A. P. ALDENKAMP.

The efficacy and tolerability of an antiepileptic drug (AED) should be in balance. Tolerability in drug trials is measured as percentage of patients complaining and in clinical practice it is measured by long term retention : the percentage of patients still taking the drug after 3 or 5 years. The old AED had a 3 year retention of about 50% in the period that new AED were not yet available. Three year retention for gabapentin is 24%, for lamotrigine 42%, for topiramate 39% and the 5 year retention for levetiracetam is 32%. Patients stop using an AED if it has too many side effects or if it

hasn't enough effect. Side effects can be acute, dose related (trade-off), due to drug interactions, idiosyncratic (individual) or chronic. Chronic effects may increase with prolonged therapy and are usually CNS related (learning/ memory problems). Most patients (90%) still receive the old AEDs with reasonably controlled seizures, but 75% of the patients complain of side effects. The neurologists note about 40% of these complaints and only 25% of the patients have had a change in drugs in the previous year. The new AEDs have better possibilities with regard to side effects and their use should be considered more often. Characteristics of individual new AEDs :

Vigabatrin : mood disorders, irreversible nasal constricted visual field defects (> 0%). Oxcarbazepine : rash, hyponaetremia (20%, elderly), pharmacokinetic equivalence ?

Lamotrigine : rash, psychotropic effect, activating cognitive effect.

Topiramate : cognitive impairment, idiosyncratic behavioural reactions, weight loss, kidney stones (1/1200 patients).

Gabapentine : no effects, however studies done with lower dose than currently used. Tiagabine : mood changes (psychosis), lack of clinical experience.

Levetiracetam : mood disorders such as nervousness, hostility and emotional lability.

Antiepileptic drugs and co-medication ; suggestions for clinical practice. H. P. BOOTSMA.

Epileptic patients on carbamazepine or phenytoin used to get midazolam before going to the dentist. Any effect seen was a placebo effect because only 7% of the midazolarn enters the bloodstream. Carbamazepine and phenytoin promote the synthesis of CYP3A4 and this enzyme breaks down midazolam. To avoid this problem a parenteral administration could be chosen or a benzodiazepin, which isn't broken down by CYP3A4 or use an AED that does not accelerate CYP3A4 production. There are a few important definitions with regard to drug interactions : enzyme induction, enzyme inhibition and substrate. *Enzyme induction* is dose dependant, its effect reaches a maximum after a few weeks, it is enzyme specific, independent of substrate and reversible. *Enzyme inhibition* has the same characteristics except its effect starts immediately. *Substrate* is the drug that is metabolised by a certain enzyme. If an enzyme is induced this leads to an accelerated degradation of the substrate and if an enzyme is inhibited the degradation of the substrate is decreased. More than 50% of the drugs, that are broken down by the cytochrome P450 system, are substrates for CYP3A4. It is therefore clinically relevant to know the degradation mechanism of each drug ! For instance the combination cisapride (substrate CYP3A4) and erythromycine (CYP3A4- inhibitor) may lead to arrhythmias. The effect of oral contraceptives is diminished by most AEDs. Of the calcium antagonists only Nifedepine has no link with the CYP3A4 system. Erythromycin can raise the carbamazepine levels by 200-400%. It is crucial to know the metabolic pathways of each drug in order to predict the interactions. Though the interaction can be predicted the magnitude of the effect can not. The interactions are always substrate specific, so it is usually possible to find a comparative drug, that bypasses the interaction. Interactions in the P450 system give rise to huge increases or decreases in blood levels. The potent induction of CYP3A4 by phenytoin and carbamazepine precludes the use of certain drugs as co-medication.

Psychopharmacological treatment strategies in mentally retarded patients with epilepsy. W. VERHOEVEN.

Difficulties encountered when treating mentally retarded patients with epilepsy are : increased vulnerability for behavioural toxicity and stress-related disorders, virtually no information about biotransformation of psychotropics and enhancement of drug metabolism (P450 iso-enzymes) may induce ineffectiveness, active or toxic metabolites. The behavioural toxicity of anticonvulsants expresses itself in sedation with phenobarbital, phenytoin, valproic acid, vigabatrin, tiegabine, gabapentin and benzodiazepines. Sedating agents appear to be associated with depression, just as activating agents (lamotrigine, felbamate) appear to be associated with psychosis. Limited data is available about oxcarbazepine and levetiracetam. Carbamazepine is associated with motor CNS effects such as dyskinesias, tics, increase of akathisia and tardive dyskinesia. In phenobarbital, carbamazepine and phenytoin the behavioural toxicity is also secondary to P450-related interactions. Chronic treatment with anticonvulsants increases the risk for behavioural side effects and necessitates regular evaluation. Anticonvulsants affect the efficacy of psychotropics via adverse neuropsychiatric effects, via changing plasma concentrations and via direct psychotropic effects. However, all psycho-active compounds have an effect on the seizure threshold by way of : rapid dose changes, altering metabolism, changing protein binding or direct effect on epileptogenesis. General guidelines for prescribing psychotropic compounds in mentally retarded subjects are the following. Choose a low anticholinergic profile, a known and simple pharmacokinetic profile. Avoid long term administration of antipsychotics for indications other than psychoses. Choose a favourable and known profile of interactions, consider half-life and monitor plasma levels. Taking all this into consideration first choice compounds as antipsychotics are : risperidone and haloperidol ; as antidepressants : citalopram, venlafaxine, nortriptyline ; as mood stabilizers : lithium, valproic acid and perhaps gabapentin ; as benzodiazepines : lorazepam, temazeparn and oxazepam.

Advantages and disadvantages of different modes of action of anti-epileptic drugs. J. FRENCH.

The reasons why mechanisms of action might matter are : efficacy, pharmacodynamic interactions, utility in different populations, pharmacogenetics and antiepileptigenesis. Several mechanisms of action of AEDs are known, like blocking voltage-dependant Na^+ channels, enhancing GABA inhibition, blocking voltage-dependant Ca^+ channels and modulating K^+ currents. But the problem is, that there is no guarantee, that these mechanisms of action are responsible for the observed clinical effect. Does a certain mechanism predict a certain effect and is this dependant on the seizure type ? Lamotrigine and oxcarbazepine both work through the Na^+ channels, but lamotrigine has a broad spectrum and oxcarbazepine doesn't. The use of two AEDs in combination wasn't very successful in the past because the old AEDs had almost the same mechanisms. Perhaps the new AEDs will have more success but it is not yet known if two different mechanisms together would enhance each others effect or lessen it. The underlying pathophysiology might influence this. Pharmacogenetics may be important as well : some patients may have a genetic inability to respond to a given mechanism. Some mechanisms might improve certain seizure types while worsening others. And perhaps some mechanisms might be antiepileptogenic. It is evident that much is not known about the impact of mechanism of action and that more preclinical and clinical investigation is needed.

Clinical experience with levetiracetam in adults. J. FRENCH.

Despite the fact that new AEDs have several advantages, the old AEDs are still often selected, mainly because they are well known and comfortable to use. Levetiracetam has important characteristics for different populations : a novel mechanism, favourable pharmacokinetics, rapid onset of action, broad spectrum, rapid titration, good tolerability and confirmed long-term benefit. The use of levetiracetam as first add-on is rational. In 1422 refractory patients levetiracetam was used with a retention rate of 40% during a mean period of 622 days. The median seizure frequency dropped from 2.3 to 1.3 per week, with a seizure free period of at least 6 months in 13% and 8% for at least one year. One very interesting finding was that the median seizure frequency continued to decrease during the follow-up period to about 80% of baseline rate after 4 years, in patients continuing on the drug. An open study in 36 drug resistant patients with generalised epilepsy also showed promising results with levetiracetam. During the 8 month treatment period 42% became seizure free and 75% had their seizure frequency more than halved. The fact that levetiracetam is renally excreted, has less than 10% protein binding, no hepatic metabolism and low intersubject variability makes it very useful as add-on therapy. This also accounts for the fact that levetiracetam does not interact with oral contraceptives, digoxin or warfarin. Woman, elderly or chronically ill patients and probably newly diagnosed epilepsy patients can profit from levetiracetam's pharmacokinetic profile. Most adverse events during treatment with levetiracetam are based on CNS effects like somnolence, asthenia, headache, dizziness and behavioural changes. This last effect is seen as anxiety, irritability, hostility and emotional lability in 13-15% of the patients and causes discontinuation in about 5%. Suggestions for optimal use are : start slow (250 mg bid), go slow ; warn in advance of the two most common side effects (sleepiness and irritability) ; if side effects occur, drop down to previous dose, re-escalate as tolerated and only titrate up when necessary.

Clinical experience with levetiracetam in children. G. HOLMES.

Special issues are evident in children with epilepsy. The pathophysiology of epilepsy varies as function of age, there are age-related epilepsy syndromes and there are also age-related responses to antiepileptic drugs. In spite of this knowledge there has been virtually no testing of drugs in immature animals and little testing of AEDs in children. After a drug is released it is very difficult to perform phase III studies in children. In general the AED pharmacokinetics in children differ from adults in : faster absorption, lower protein binding, higher metabolic rate and higher clearance. Levetiracetam has some appealing features for children besides antiepileptogenic properties. It has a brain-specific binding site, it is likely to have an unique mode of action, it has a high safety margin and it lacks drug interactions. The body clearance of levetiracetam is about 30-40% higher in children and its $t^1/_2$ is ± 6 hours. In 23 children with partial seizures up to 40 mg/kg levetiracetam was given with only one concomitant AED. Two children discontinued early and 12/23 had a 50% response, 2/23 had a complete remission. In 13 children with resistant juvenile myoclonic epilepsy levetiracetam 2000-4000 mg/day was given with a 50% responder rate in 12/13 children and 7/13 had a complete remission. In other generalized epilepsies similar results were obtained. An assessment study was done with levetiracetam as add-on therapy in 65 children. These children were previously treated with a mean number of 7.6 AEDs and therefore very resistant to treatment. In 23/65 children levetiracetam was stopped : 15/65 due to lack of efficacy and 8/65 due to adverse effects. The drug had a broad spectrum of action and was effective in atypical absence, myoclonic, tonic, atonic, generalized tonic-clonic, and partial seizures. From a pediatric perspective positive characteristics of levetiracetam are : renal excretion, no drug interactions, probably broad spectrum and well tolerated. Negative characteristics : limited data in children,

behavioural changes, unclear mechanism. This last item can been seen as a positive effect as well since it likely discriminates levetiracetam from the other available AEDs.

New developments in presurgical evaluation. H. STEFAN.

The point of surgery in epilepsy is to stop the seizures without causing neurological damage. Successful surgery depends on patient selection, optimal diagnosis, interactive benefit/risk balance and a multi-methodological approach. The timing of pre-evaluation should be after 2-3 years of medical treatment with insufficient result. To define the epileptogenic region a multi dimensional focus localisation has tot take place to determine if it is only focal, multifocal or localised in a hemispheric region, resulting in the following flow-chart :

A) Pharmacoresistance ? diagnosis (EEG, MIRI, SPECT, PET)
serum concentrations
neuropsychological and social status
B) Phase 1 : intensive video/EEG monitoring, functional tests,
interdisciplinary discussions
C) Phase 2 : invasive evaluation. – subdural depth recording
– angiography
D) Operation

MRI has revolutionized detection of the structural basis of uncontrolled epilepsy but the lesion shown is not invariably the site of epileptogenesis. The advances in structural and functional imaging show that high resolution imaging more often shows multiple lesions, which necessitates the requirement for intensive electrical studies. New developments are : digital image analysis which gives a quantitative interpretation of size, shape and signal changes allowing the development of objective measures of pathological changes. Also new is diffusion weighted MRI allowing early detection of tissue damage. Next are MR perfusion imaging, functional MRI (FMRI), magnetic resonance spectroscopy (MRS) and magnetoencephalography (MEG). Magnetic source imaging (MSR) combines MEG and MRI.

When the data of Phase 1 offers converging data with no functional risks, surgery can follow without going to Phase 2. However the finding of conflicting data or a possible functional risk necessitates the invasive evaluations of Phase 2. Only when an adequate localisation without functional risk is detected, surgery may follow. Otherwise electrostimulation is the treatment of choice.

Ictal and interictal SPECT activation studies. K. VAN LAERE.

Single-photon emission computed tomography (SPECT) is a non-invasive imaging technique which allows imaging of functional parameters. Commonly, technetium-99m ligands are used for this purpose, which show the advantage of low cost and ease of use compared to PET (positron emission tomography). Technetium-99m-labeled brain perfusion ligands allow imaging of cerebral blood flow as a “frozen image” since this is weighted towards the first 30-60 seconds after injection. Therefore, the ictal phase can be captured. Non-invasive localization of epileptogenic foci is important to minimize morbidity and extent of (possibly subsequent) subdural electrode placement. Studies have demonstrated variable results from interictal perfusion studies with fairly low sensitivity for epileptic focus localization. Ictal studies are far more sensitive (89-92%) as long as strict documentation is kept of the temporal relationship between time of injection and EEG seizure activity. Peri-ictal studies enable reliable localization in 70-95% of the patients. Subtraction analysis between ictal and interictal studies show the highest promise. SISCOM (subtracted ictal SPECT coregistered to MRI) is the technique where this subtraction image is overlaid on the structural MRI information and has a specificity of 95%. In extratemporal epilepsy, ictal SPECT has a sensitivity of 70% depending on the location and injection timing. Use of automated injection systems improves timing and therefore probably also clinical results. EEG and MR correlation remains absolutely indispensable to prevent “SPECTectomies”. Daily clinical performance of the SISCOM method requires dedication of both neurology and nuclear medicine departments.

Anticipation and prediction of epileptic seizures. P. BOON, E. GYSELS, K. VONCK, M. DHAVE, M. LE VAN QUEN, J. MARTINERIE, V. NAVARRO, C. ADAM, B. RENAULT, M. BAULAC.

Non-linear analysis of EEG signals may allow prediction of seizures minutes before the occurrence of the seizure. Early work has focussed on the feasibility in intracranial EEG recordings. The purpose of the present work was to show the feasibility and reliability of performing anticipation of seizures based on the analysis of scalp-EEG recordings. The

validation was performed by comparing results of intracranial and scalp EEG recordings in the same patients. Long-term changes before seisure onset were identified by a measure of non-linear similarity that is rather independent of EEG-runs and artifacts. In a series of 23 patients with temporal lobe epilepsy, some of whom also underwent intracranial EEG recording with amygdalohippocampal depth electrodes, a mean anticipation time of 7 minutes was achieved..Pre-ictal changes in the scalp EEG corresponded well to those found in intracranial EEG. Scalp EEG recordings contain relevant dynamical information and can be used to anticipate seizures by showing consistent pre-ictal changes.

Epilepsy surgery in mentally retarded patients with refractory epilepsy. O. VAN NIEUWENHUIZEN.

Mental retardation (MR) is a necessarily lifelong disorder, characterised by low cognitive ability and diminished social and adaptive competence. MR combined with epilepsy can be permanent or state-dependant. The basic principle of epilepsy surgery is to remove the epileptic focus or to disconnect it. Indication for surgery is intractable epilepsy. It was always thought that epilepsy surgery in children with MR would be hazardous under the assumption that they already have bilateral, diffuse brain damage. This assumption is not correct ; the brain abnormalities found in MR-epilepsy are : developmental abnormalities, vascular disorders, brain tumours, encephalitis or metabolic diseases. MR children with intractable epilepsy can be candidates for surgery with the objective to reduce seizures without compromising intellectual development and quality of life. Gleissner found that after resective surgery 64% became seizure free of the 16 patients with an IQ < 85, without change of status. Our experience is with 12 patients (4 mths-17.1 yrs) who were followed for 1.5-5 years. Two approaches were used : file analysis with parental perceptions and structured interviews with parents and children. The results were that the seizure reduction was comparable to non MR patients, intellectual development did not deteriorate or improve and the quality of life was considerably improved. The resulting postulation is that epilepsy surgery in mentally retarded children is not more hazardous than in children with normal intelligence.

Ketogenic diet. W. C. G. OVERWEG-PLANDSOEN.

As early as 500 B.C. people suspected a relationship between food and epileptic seizures. In 1921 Wilder theorised that ketonemia might cause the benefit. To produce ketogenesis the diet had to be very rich in fat and very low in carbohydrates. The classical diet was hard to eat, so Huttenlocher proposed a modification with medium chain triglycerides (MCT-diet). After the introduction of carbamazepine and valproic acid the ketogenic diet went out of use. In 1992 however the Abrahams family were searching for a treatment for their son, who had not responded to all available drugs or to surgery. They started the ketogenic diet and their son became seizure free. Nowadays the ketogenic diet is an alternative for children with refractory epilepsy. The precise mechanism of action is not known. Animal studies revealed that a ketogenic diet results in a prompt rise of plasma ketone bodies, then during several days the brain shifts to utilisation of the ketone bodies as energy source, which leads to an anticonvulsant effect. This process is more efficient in the young. In 1989 Schwartz compared several diets. They produced a build up of ketones during the day in contrast with a normal diet. The classical ketogenic diet reached the highest levels. The two accepted indications for ketogenic diet are : refractory epilepsy and unacceptable side-effects caused by antiepileptic drugs. The overall results of clinical studies are a remission rate varying from 29-55%. In myoclonic seizures rates are as high as 70-80%. Which diet is used, does not seem to make a difference. Side effects can be categorised as medical, social, practical and financial (expensive). The acute medical side effects are : blood level changes of AEDs, hypoglycemia. Long term effects : vitamin and mineral deficiencies, hypercholesterolemia, liver dysfunction, hypocalcemia, kidney stones, cardiomyopathy and excessive bruising. Ketogenic diet is recommended for refractory epileptic children with cooperative parents and the availability dedicated dietitian and pediatrician. Within 2-4 weeks an effect should be seen. In case of a positive effect the diet has to be used for two years before it can be withdrawn.

Vagal nerve stimulation in children with therapy-resistant epilepsy. H. J. M. MAJOIE.

Population : children with a 'Lennox-Gastaut-like' syndrome characterized by therapy-resistant epilepsy, multiple seizure types, mental handicap (IQ 25-80), not eligible for epilepsy surgery and slow spike waves & disturbed occipital activity on EEG were included in a vagal nerve stimulation study. The aim of this study was to evaluate cost effectiveness, efficacy and tolerability of vagal nerve stimulation. After a baseline period of 6 months the children were followed for 2 years. Nineteen children, age 6-18 years, entered the study : 15 male, 4 female with a mean duration of epilepsy of 8.1 years. Neuropsychological findings were a moderate improvement of function, behaviour and mood. The largest seizure reduction occurred in the group with the highest baseline mental function. The scores for mental age improved independent of seizure control. Side effects reported were : coughing (4), hoarseness (7), strange feeling in the throat (2)

and swallowing difficulties (1). Vagal nerve stimulation significantly reduces seizure frequency and severity, without serious side effects . The seizure type has no influence on the outcome. Patients with less disturbed EEG show the highest seizure reduction. The final conclusion is that vagal nerve stimulation is effective in patients with pharmacotherapy resistant epilepsy, though its effectiveness is limited. Additional basic and clinical research is needed as well as cost effectiveness studies with attention for quality of life.

Feasibility and efficacy of amygdalo-hippocampal deep brain stimulation in temporal lobe epilepsy. K. VONCK, J. CAEMAERT, E. ACHTEN, P. CLAEYS, J. DE REUCK, P. BOON.

Short-term hippocampal deep brain stimulation (DBS) has recently been shown to be efficacious in patients with medically refractory temporal lobe epilepsy. The purpose of the present study was to evaluate the efficacy and safety of long-term DBS in medial temporal lobe structures and to evaluate the feasibility of using chronic DBS electrodes for the localisation of the ictal onset zone prior to DBS.

In four patients with refractory complex partial seizures (CPS) and negative MRI findings four DBS, electrodes were bilaterally implanted in the amygdalohippocampal region to identify and subsequently stimulate the ictal onset zone. Mean monthly CPS frequency was compared before and after chronic DBS. Side effects were carefully monitored.

DBS electrodes yielded high-quality EEG recordings that showed unilateral focal or regional seizure onset in medial temporal lobe structures. In all patients unilateral amygdalohippocampal stimulation was performed. The first 3 patients have a sufficient follow-up (range : 3-6 months) for analysis. In these patients there was a reduction in seizure frequency of > 50%. None of the patients reported side effects.

This study shows the feasibility of consecutive EEG recording and amygdalohippocampal DBS using DBS electrodes implanted during a single surgical procedure. Chronic DBS is an efficacious and safe treatment for refractory temporal lobe epilepsy and may become an alternative treatment for patients who are less successful candidates for resective surgery.
