

50 YEARS EPILEPTOLOGY: RECENT SITUATION AND FUTURE ADVANCEMENTS

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50 years are an extended epoch to consider for developments in epileptology. Therefore only a selection of important milestones can be covered with regard to available space. After looking back to the past current activities and important aspects for future research will be discussed.

Concerning epidemiology one of the first important studies investigated the role of precipitation of epileptic seizures. 26 to 50 % (Pond et al. 1960) recognized triggering mechanisms. Electrophysiology for epilepsy was used by Gibbs (1935) demonstrating epileptiform activities in the EEG. Functional anatomy of the brain was studied by Foerster (1936) and Penfield and Jasper (1945). Whereas x-ray roentgenography was used early after Roentgen's discovery. Pneumoencephalography was systematically investigated by Dandy (1916). The window to neurobiology and epilepsies was opened by Meyer (1954) suggesting for epileptogenesis a dual component theory with genetic disposition plus injury. Gastaut (1954) influenced later international classification approaches by defining a dichotomy of partial vs generalized seizures. Modern drug treatment using bromide was started by Locock (1854) and epilepsy surgery by Horsley (1886).

Developments in the last 50 years permit nowadays predominant research activities concerning genomics, computation, neuroscience, network analysis, neurochemistry, neurobiology, data base classification, innovative treatment approaches and comprehensive patient care.

Very important electrophysiological milestones in the 60ies were the definition of paroxysmal depolarisation shift by Matsumoto and Ajmonemarsan (1964), the clinical use of video EEG (simultaneous double picture registration = SDA) by Penin (1966) and stereoactic electroencephalography (SEEG) by Bancaud and Talairach (1969). Imaging of epilepsies came up in the 70ies using computertomography (Banna et al., 1975) and Gastaut (1976). The experiences indicated that computertomography is very helpful for the detection of lesions in epilepsies, but the quality of images as well as the first MRI images in epilepsies still was insufficient to detect small lesions at the beginning of its use (Huk et al. 1984).

In the 80ies two new classification concepts at a major input into epilepsy research and clinical management. These are the international classifications of epileptic seizures 1981 and classification of epileptic syndromes 1998. Seizures were classified in partial or generalized seizures using ictal sings and EEG. In addition etiology, age and prognosis were used to define epileptic syndromes. After collecting these data a differentiation into symptomatic epilepsies, cryptogenic and idiopathic is performed. The knowledge of different epileptic syndromes with their age distribution led to an improvement of the estimation of prognosis.

In a next step definitions were used for epileptic seizures and epilepsies by Fisher et al. (2005) indication that in special situations epilepsy requires only the occurrence of at least one epileptic seizure. An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. Epilepsy is a disorder characterized by enduring predisposition to generate epileptic seizures. The relation of epileptic seizures,

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syndromes and cognition is influenced by impaired erroneous perception, interictal epileptic activity, seizures, location and type of lesions and also treatment. Different epileptic syndromes are related to different cognitive outcomes. Further research indicated that in special epileptic syndromes encephalopathies lead to cognitive decline. The cognitive decline correlates for instance with spike wave discharges especially during sleep and their amount and degree of generalisation (benigne, focal, centro temporal epilepsies and electric status epilepticus and sleep) (Halasz et al. 2005).

For the diagnosis of epileptic activities and structural as well as functional pathologies investigation techniques with high time resolution, EEG, MEG and higher spatial resolution MRI, SPECT and PET were developed. This improved the localisation of focal epileptic activities and functional important cortex. In addition to spikes and rhythmic activities up to beta range high frequency oscillations were detected at seizure onset and super imposed spikes which are nowadays also detectable by means of non-invasive MEG frequency analysis (Rampp et al. 2010). Masked epileptogenic lesions in MRI "negative" cases can be detected by voxel based morphometry (Huppertz et al. 2010).

In addition to the improvement of the diagnostic techniques patient attitudes became more self confident and was strengthened by establishing self help-groups. Top priority for patients were seizure freedom and quality of life facts like driving licence, independent employment, medication dependence (Gilliam et al. 1997). Furthermore comprehensive care for epilepsy patients was established and anticonvulsant drugs of the first, second and third generation developed. In addition to drug treatment surgery was performed not only as standard resection but also tailored resections, transections and invasive stimulation techniques. The correlation of postoperative outcome and hippocampal pathology after temporal lobe surgery showed that severe hippocampal sclerosis had the best outcome with 98.3 % Engel 1 and 79 % Engel 1a (Stefan et al.

2009) in a group of patients with different types of hippocampal sclerosis.

Epilepsy treatment of the 21st century is engaged not only with new development of anticonvulsive drugs but also with nerve and brain stimulation, local application of anticonvulsants and transplantation approaches, radio surgery was performed in patients with temporal lobe epilepsy and 67 % of patients were free of seizures for the prior 12 months (Barbaro et al. 2009). Different locations for brain stimulation were used. A survey is provided by Jobst (2009).

For the understanding of epileptogenesis the interference of genetic disposition and realisation factors leading to increased neuronal excitability is of major interest. Genetic analysis has shown several monogenetic epileptic syndromes, but still in most epileptic syndromes a complex polygenetic disposition exists. The time course of biochemical, anatomic and functional changes of the seizures with acute ion influx, early gene activation, protein expression, glial activation and later neuronal cell loss and susceptibility to recurrent seizures was demonstrated by Col (2000). These investigations stimulate the approach to find a rational intervention in the epileptogenesis in which upregulation of gene expression alteration of messenger, RNS of neurotrophins, neuronal loss, sprouting and synaptic remodelling takes place. Considering treatment, dosing of anticonvulsants, their absorption, distribution, passing the blood brain barrier, finding the CNS target and their metabolism and elimination are of importance. For absorption and distribution polymorphic transporters and the blood brain barrier have to be considered. In addition to the clinical phenotype and epilepsy syndrome the genotype may be able to aid predicting of clinical outcome: drug response, adverse effects, comorbidity and health status (Löscher et al. 2009). In the new therapeutic age instead of purely symptomatic therapy modification of disease pathogenesis has to take place (Villoslada et al. 2009).

References with the author.