Second Edition

Student's guide to Epilepsy

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Contents.

Preface			1
Abbreviations			2
Chapter	**1**	Fundamentals of epilepsy	3
Chapter	**2**	Historical perspective on epilepsy	5
Chapter	**3**	Classifying epilepsy	5
Chapter	**4**	Diagnosing epilepsy	8
Chapter	**5**	Epidemiology of epilepsy	9
Chapter	**6**	Complications of epilepsy	11
Chapter	**7**	Treatment of epilepsy	15
	7.1	Treatment with drugs	15
	7.2	Treatment by surgery	17
	7.3	Treatment with diet	18
Chapter	**8**	Models of epilepsy	19
	8.1	In vitro models	19
	8.2	In vivo models	19
	8.3	Genetic models	20
	8.4	Models based on drugs/metals	22
	8.5	Electrical stimulation models	24
	8.6	Infection models	25
	8.7	Lesion models	25
Chapter	**9**	Summing up on epilepsies and their models	27
References			28

Preface.

One of the subjects for my PhD dissertation was a new animal model of genetic reflex seizures so I needed to also prepare a brief introduction to the epilepsies in general. When I started to dig into the literature, I was at first confirmed in the belief that scientists had indeed made significant progress in this field, simply because the first many papers I read included a myriad of detailed informations in addition to figures of brain waves during seizures, and the routinely use of complex names for all types of different seizures and syndromes.

However, after a while the little details started to stand out, just as they usually do after you have read enough papers on a given subject, and I had to adjust my understanding. The epilepsies are basically still a mystery, and the main problem for any researchers involved in studies of the brain is of course its immense complexity. Anyway, I decided to try to get a little behind the usual headlines. The result you are about to read now is more or less a direct copy of the introduction to the epilepsies I presented in the above-mentioned dissertation [1].

My intention with this review is primarily to provide a compact and no-nonsense aid for students of biology or medicine interested in achieving a factual overview of the epilepsies. I also include a description of the literally countless and most diverse models of seizures and the epilepsies as a service for those who might consider doing some actual research and I provide plenty of references for those interested in further studies.

This second edition of *Student's guide to Epilepsy* only adds minor revisions to the first edition. I hope you will enjoy the reading and that you afterwards will also feel a little enlightened on the subject.

Bryan Schønecker.

Hareskovby, Denmark, April 2014.

Abbreviations.

5-HT	Serotonin (5-hydroxytryptamine)
AEDs	Anti-epileptic drugs.
CNS	Central nervous system (brain and spinal cord)
EEG	Electroencephalograph.
ELmouse	"Epilepsy" mouse. Named "ep" in 1959; "E1" in -64 and "EL" in -92 [2].
FSIQ	Full-scale intelligence quotient.
GABA	Gamma-aminobutyric acid.
GAD	Glutamic acid decarboxylase (two isoforms: GAD65 and GAD67).
GEPR	Genetically epilepsy-prone rats.
ILAE	International league against epilepsy.
MRI	Magnetic resonance imaging.
PET	Positron-emission tomography**.**
SE	Status epilepticus.
SSRI	Selective serotonin re-uptake inhibitors.
SUDEP	Sudden unexpected death in epilepsy.
TLE	Temporal lobe epilepsy.
WHO	World health organization.

Chapter 1 - Fundamentals of epilepsy.

Epilepsy is basically any disorder characterised by uncontrolled excessive and synchronous electrical discharges in various brain areas resulting in spontaneously recurrent seizures which typically last from seconds to minutes [3].

Several authors consider epilepsy a heterogeneous group of disorders best characterised as different syndromes (i.e. defined by types of seizures, onset ages, eliciting causes if possible to access, complications, family history and other variables), which is why the terms “the epilepsies” and “epilepsy” often are used interchangeably (see e.g. [3-5]).

The part of the brain attracting the main interest as origin of seizures is the anterior part of the forebrain (the cerebrum) which outermost portion (the cerebral cortex) in one study were found to weigh approximately 82% of the total brain mass while just containing 19% of the roughly 86 billion neurons in the total brain [6]. The cerebrum is divided in two cerebral hemispheres, linked by a massive structure of axons (the *corpus callossum*). Each hemisphere constitute a clear physical structure which is further, more or less arbitrarily, divided in four lobes, named and demarcated by the bones which overlie them. The frontal lobe is the foremost and largest of the lobes and is bordered posteriorly by the central sulcus and inferiorly by the lateral sulcus. It is positioned anterior to the parietal lobe and above/anterior to the temporal lobe. The parietal and temporal lobes are separated by the lateral sulcus and they both border the occipital lobe (no distinct boundaries) which is the smallest of the four lobes and located in the posterior portion of the hemisphere [7].

The defining feature of the epilepsies is the “seizure” which to a casual bystander can include unusual movements and inappropriate behaviours. Seizures are named “convulsions” if they manifest as violent shakes of the body/limbs and “absence” or ”spell” if the person just stares indifferently without gross movements and reactions to the surroundings. Other frequently used terms are e.g. “fit” and “attack” [3]. A seizure might originate from a specific localization in any of the lobes (so-called partial seizures) and later spread to include parts of the second hemisphere (i.e. secondary generalized seizure) or start from multiple loci in both hemispheres (i.e. primary generalized seizures).

There are in principle four distinguishable components to a seizure and whether they are present and, if so, their presentation are both important for the subsequent diagnose.

The prodromal phase can last hours or sometimes days and is accompanied by headache, irritability, insomnia, bad temper, depression, or increased activity [8]. It should not be confused with the aura, which precedes the seizure by seconds or minutes.

The aura signals the onset of a partial seizure and dependent on where in the brain the seizure originates, patients will experience different "strange" sensations and feelings which can persist for minutes/hours and sometimes be followed by a generalized seizure [4]. Presence of an aura is therefore indicative of a partial seizure. The feelings are often vague and the most common manifestations include indescribable visceral symptoms, unpleasant smells, flushings, dizziness, hallucinations, fear, etc [3, 4, 8].

Third phase is the seizure (ictus) itself and if it includes impairments of consciousness the patient may have no recollection of the seizure where an aura is remembered very well. More than 30 different types of seizures and 37 types of epilepsy syndromes are named [9] and the most common types have been reviewed by the International League Against Epilepsy (ILAE) in 1981 [10] and 1989 [11].

Citing from Dekker [8], the last phase, the post-ictal phase, "*may be absent, brief or may last several hours, and sometimes even days. There is usually a deep sleep and waking up with headache, tiredness, irritability, vomiting, confusion, muscular aches or ataxia. Transient paralysis of a part of the body, known as Todd's paresis may occur for a few hours or days. Altered speech or aphasia may occur when the dominant hemisphere of the brain has been involved. Altered behaviour and emotional outbursts may occur, and if these are interfered with, violent behaviour is likely*."

Chapter 2 - Historical perspective on epilepsy.

Epilepsy is one of the oldest conditions known to mankind. Two tablets, one in Neo-Assyrian and the other in Neo-Babylonian cuneiform writings from around…

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