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Summary

This article describes the history of EEG and epileptology in Geneva, characterised first by the early semiological work of Herpin in the XIXth century and, later, by the installation of one of the first 3 EEG systems in Switzerland in the beginning of the 1940’s. The role of the principal actors in the field is described with a particular focus on the important increase in the epileptological and electrophysiological activity in Geneva in the past 20 years. The epilepsy surgery program, in strong collaboration with Lausanne, and the combined work of clinicians and neuroscientists have transformed EEG into a modern tridimensional neuroimaging technique. Geneva has also pioneered the combination of 3D EEG with functional MRI. The article finishes by browsing current activities and future perspectives.

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The early years

The early history of epileptology in Geneva is personalised by Théodore Joseph Dieudonné Herpin (1799-1865). Born in Lyon, France, he studied in Geneva and Paris before returning to Geneva where he practised as a medical doctor and surgeon in Geneva and the nearby city of Carouge. Besides his clinical activities, Herpin exerted several mandates for the local government as a deputy and vice-president of the “Conseil de santé” (Health Board). On top of being the founder and director of the Medical Society of Geneva (1823),
Herpin shall be remembered essentially for two of his publications that contain pioneering observations and interpretations on patients suffering from epilepsy, notably with respect to juvenile myoclonic epilepsy and to the semiology of focal onset seizures.

In his work, Herpin precisely describes the semiological features “peripheral motor seizures” (Jacksonian), “visceral” (“epigastric aura”) “encephalic” (sensory seizures, “déjà-vu”) and “concussions” (myoclonic jerks). Herpin also introduced the concept of localisation and propagation, usually attributed to John Hughlings Jackson whose description was done later than Herpin’s: “Chez la même personne, toutes les crises commencent toujours de la même manière, bien que le développement d’une crise peut par la suite varier d’une crise à une autre”. (In the same person, all seizures always start in the same way, although the development of a seizure can thereafter vary from one seizure to another) (translated by the authors) [1].

Indeed, Jackson, more often remembered in the epilepsy textbooks than Herpin, insisted on the heritage of Herpin:

« I take this opportunity of advising the younger medical neurologists to study carefully Herpin’s writing on epilepsy. I have long known his valuable work “Du pronostic et du traitement curatif de l’épilepsie” (1852) but I have only recently heard of his still more valuable work “Des accès incomplets d’épilepsie” (1867)” (John Hughlings Jackson, 1899 [2]).
Electroencephalography (EEG) and modern epileptology in Geneva

In 1941, the neurophysiologist PD Dr Marcel Monnier (Figure 2) and the engineer Marc Marchand provided the first description of the installation of an EEG equipment in Geneva, in the Institute of Physiology. The system was based on an electrocardiogram coupled to a preamplifier and a powerful amplifier allowing the recording of electrical activity in a bipolar or monopolar montage, as proposed by Berger and Tönies. Monnier and Marchand initially presented the localisation of head trauma using EEG. In 1952, Monnier became director of the newly created “Laboratoire d'EEG clinique neurologique” and the “Laboratoire de recherche en neurophysiologie appliquée”[3].

In 1958, Prof. François Martin took over from M. Monnier. Under his direction, Geneva partnered the University Hospital of Zurich in EEG teaching: the Swiss School of Electroencephalography and Epileptology. Between 1970-72 Martin also served as president of the Swiss Society for Clinical Neurology, founded in 1948 (as the “Schweizerische Arbeitsgemeinschaft für Elektroencephalographie”) [4].

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In 1966 Dr Annette Beaumanoir, a French neurologist, took the lead of the EEG laboratory in the hospital cantonal of Geneva (Figure 4). A. Beaumanoir had been trained in the famous epileptology school of Marseille under Henri Gastaut. She contributed to the characterisation of paroxystic occipital discharges of idiopathic focal occipital epilepsies, today referred to as “Gastaut syndrome” and “Panayiotopoulos syndrome”. The arrival of A. Beaumanoir in Geneva is strongly related to her political activities. Member of the French Resistance at age 18, she was a member of the Communist Party and later supported the war for Algeria’s independence (“Front National de Libération”). She became a member of the Algerian cabinet before being forced to leave the country after a coup in 1965, and found refuge in Geneva where she directed the EEG Unit until her retirement. She continued working with Gastaut, notably in descriptions of the Lennox-Gastaut syndrome with an interest in pediatric EEG, installed the first EEG-telemetry with videographic recordings in Switzerland (and one of the first in Europe) and also reported important observations on non-convulsive status epilepticus, “état de mal à expression confu-
In 1989, she was followed by Prof. Pierre Jallon, another French epileptologist, trained in Bordeaux and former director of the EEG unit of the French military hospital of Val de Grâce in Paris. Interested in epidemiology, Jallon conducted several prevalence and incidence studies in Switzerland, notably and on the incidence of status epilepticus (EPISTAR) [5], new-onset epilepsy (EPIGEN) [6] as well as similar studies in French overseas territories (EPIREUN, EPIMART). From an EEG perspective, he reported toxic-metabolic encephalopathies related to the accumulation of the antibiotic agent cefepime in patients with concomitant renal failure [7] as well as work investigating the origin of periodic lateralised discharges [8]. Jallon was also dedicated to educational aspects and destigmatisation of epileptic patients, as reflected by his activity in “l’Ecole de l’Épilepsie” and two mountaineering expeditions to 4000m summits uniting patients and epileptologists (“Sport et Épilepsie” at the Bishorn 4153 m, Valais and the Gran Paradiso 4061 m, Piedmont, Figure 5). Jallon witnessed the transition from ink and paper EEG to digital recordings at the very end of the XXth century. This radical evolution offered not only an easier offline clinical interpretation, but opened new avenues for EEG research.

**Epilepsy surgery and EEG-based neuroimaging**

In 1995 the Unit for Presurgical Epilepsy Evaluation was founded by Prof. Theodor Landis, head of Neurology. Its direction was given to Prof Margitta Seeck, a German epileptologist trained in Germany and Boston, USA. Under her leadership, in close collaboration with Prof. Paul-André Despland, head of the EEG laboratory in the Centre Hospitalier Universitaire Vaudois (CHUV), the presurgical evaluation unit (Figure 6) and the epilepsy surgery program was quickly established. A sophisticated multimodal electrophysiological and imaging platform flourished with intense collaborations with clinical experts in the Neuroradiology, Nuclear Medicine, Neuropsychology and Psychiatry as well as neuroscientists for the development and application of new imaging techniques. The surgical program is placed in the context of an intense and fruitful collaboration with the CHUV and the Institution of Lavi-gny (see the Lausanne contribution in this issue) defining a Geneva-Vaud epilepsy surgery program with the partnership of the surgical teams of Prof. JG Villemure, Prof. N. de Tribolet and Dr C. Pollo, followed by Prof. K. Schaller and Prof. R. Daniels, PD Dr Momjian.

The program, celebrating its 20th anniversary in 2015, currently offers all aspects of epilepsy surgery including invasive peroperatory and extra-operatory EEG recordings using subdural electrodes or stereotactically placed depth electrodes tailored to the clinical need. Resective potentially curative surgery as well as palliative surgery such as corpus callosotomy can be proposed. Functional surgical approaches using vagal nerve stimulation and deep brain stimulation, in the amygdalo-hippocampal structures or the nucleus anterior of the thalamus are also part of the therapeutic armamentarium. Cognitive studies involving some patients of our centre with intracranially implanted electrodes have led to some important scientific contributions for the understanding of brain functions. Probably the most striking is the localisation of feelings of “out-of-body experiences” to the temporo-parietal junction [9, 10], giving an unambiguous organic substrate to these symptoms often perceived as having a
purely psychiatric origin.

Approximately at the same time as the Presurgical Evaluation Unit was founded, Professor Landis also founded the Functional Brain Mapping laboratory (1994), led by Prof. Christoph M. Michel, a neuroscientist and EEG expert, trained by Prof. Dietrich Lehmann in Zurich. C. Michel became a renowned international figure in the analysis of scalp voltage topography and Electric Source Imaging, consisting in the estimation of the brain electric generators of scalp EEG. This approach largely benefitted from the development of high density EEG systems with up to 256 scalp electrodes, initially used only for non-clinical human research. Dr L. Spinelli, physicist, developed a head model called SMAC (Spherical Model with Anatomical Constraints) describing the propagation of electromagnetic fields across the head and allowing the localisation of electrical sources taking into account the individual brain anatomy [11]. This model has proved very reliable in clinical studies and not inferior than more sophisticated later models [12].

More broadly, the presurgical evaluation unit and the functional brain mapping lab established a very strong collaboration that led to pioneering methodological advances and clinical applications, in the field of functional and structural brain imaging in patients with epilepsy, while pursuing stringent validation as a clinically relevant imaging tool. A seminal study showed that even in the absence of visible interictal epileptic spikes, epileptogenic activity can be identified and localized [17]. The current brain imaging research focuses on the mapping of functional and structural relationships between brain regions involved in the occurrence of epileptic activity (Figure 7) [18]. Nowadays, ESI and EEG-fMRI are routinely performed in the presurgical work-up of patients with focal epilepsy and their results integrated in the clinical case discussion.

The pediatric aspect of epileptology and electroencephalography and epilepsy surgery has also increased in recent years, corresponding to about a third of the presurgical evaluations. Geneva has the largest Swiss pediatric presurgical evaluation program, performed on children referred from most parts of the country under the joint supervision of Prof. Seeck’s team and neuro-pediatricians. Initially, the pediatric part of the program was developed together with Prof. Eliane Roulet-Perez in Lausanne who has special interest in the role of epilepsy in the development of the child and potential of children to catch up developmental retardation if the operation is carried out early and successfully [19]. The pediatric epilepsy surgery team was later joined by PD Dr Christian Korff, expert in pediatric epileptology trained in Geneva and later in Chicago and Dr Joël Fluss, expert in cognitive aspects trained in Paris and Toronto.

PD Dr Fabienne Picard, a French neurologist trained in Strasbourg, is particularly interested in specific genetic forms of epilepsies, notably Autosomal Dominant Nocturnal Frontal Lobe Epilepsy syndrome that she has contributed to characterise in several large families [20] and which is related to a mutation in the nicotinic receptor. These studies led her to further investigate the functional aspects of the insula and the distribution of nicotinic receptors in the brain, using nuclear imaging.

Psycho-social and education aspects have been further developed by Dr Anne-Chantal Héritier Barras, a Swiss epileptologist trained in Geneva and expert in therapeutic education of patients with chronic medical conditions. She introduced modern methodology in pa-
tient’s interviews [21] and management to offer them better strategies to understand and accept their condition and improve their care for themselves and their quality of life.

Other more recent developments in epileptology include a first seizure clinic aiming to rapid extensive diagnostic evaluation and follow-up of patients with first seizure of probable epileptic origin.

Beyond their joint epilepsy program, the centres of Geneva and Lausanne have also strongly collaborated since 2006 by organising the “Université d’Eté d’EEG”, a yearly training program for Neurologists and EEG technicians.

Conclusion and perspectives

The complementarity of the medical, nursing and technical team as well as the strong local, regional, nationwide and international clinical and scientific collaborations allow our centre to continue evolving to offer patients the best diagnostic and therapeutic approaches, from diagnostic clarification to presurgical evaluation and to comprehensive care of the patients’ condition. A great number of clinical and non-clinical collaborators worked towards this goal over the years. They could not be explicitly named in this article but their contribution should be strongly acknowledged.

The proximity of a strong methodological and clinical research team with internationally recognised EEG expertise ensures that new development in EEG-based neuroimaging are rigorously validated and then rapidly integrated into the clinical work-up for an increased quality of care.

The very recent large reorganisation of the neurosciences in Geneva in the Biotech Campus in 2014, joining engineering, neuroscientific and clinical teams from the University of Geneva and the Ecole Polytechnique Fédérale de Lausanne will enhance multidisciplinary collaborations with a special focus on new imaging techniques and neuromodulation. New implantable diagnostic and therapeutic devices using electrophysiological recordings and electrical stimulation, as well as neuroprosthetic tools developed in the Geneva-Lausanne area will hopefully be part of epileptological care in the not so far future.

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