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The history of invasive EEG evaluation in epilepsy patients

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ABSTRACT

Modern invasive EEG recording techniques are the result of an interdisciplinary research process between neurologists and neurosurgeons that began in the 19th century. In the beginning, stimulation studies were the basis of our understanding of cortical functions. After the introduction of EEG in humans by Hans Berger and its implementation in diagnostic procedures in epilepsy patients, a new era began when Forster and Altenburger performed the first invasive EEG recording five years later. The fruitful work of Wilder Penfield and Herbert Jasper was the basis of a new understanding of epilepsy and influenced the investigations of the next generation of researchers. The development of stereotactic devices advanced by Jean Talairach and Jean Bancaud was fundamental to the understanding of deep brain functions and pathophysiological processes in epilepsy patients. In subsequent decades, new recording techniques were established and long-term video-EEG-recordings became the gold standard in presurgical evaluation. The development of imaging techniques allowed a combination of structural and electrophysiological data and restricted the indications for invasive evaluations, but also led to new concepts in the diagnostic process, including the epileptogenic network and the pathophysiological understanding of epileptogenic tissue. The following article provides an overview of the history of invasive EEG evaluation in epilepsy from the 19th century until today.

1. Characterization of the brain cortex: early stimulation studies and their transfer to humans

In the first half of the 19th century, the assumption of the brain as a single unit was challenged by observations that a focal cerebral lesion can lead to a focal deficit [1]. Based on the hypothesis of Jean Baptiste Bouillaud that speech is localized in both frontal lobes, Pierre Paul Broca was the first to describe a man with frontal lobe lesions and an expressive aphasia in 1861 [2]. His observations resulted in the localization of the speech area in the left frontal lobe, the so-called "Broca Area" (BA 44 and 45). In the following years, Hughlings Jackson's investigations of epileptic patients assumed that focal seizures are induced by local cortical discharges [3]. This was supported by the results of stimulation studies in animals by Theodore Fritsch and Eduard Hitzig showing focal motor activity after galvanic stimulation of the cerebral cortex [4]. Influenced by these findings and their confirmation three years later by David Ferrier, Robert Barthlow conducted the first electrical stimulation in a human brain in 1874 [5,6]. In the first years of the 20th century, more detailed results of cortical stimulation in the human brain were published. Using the technique of faradic stimulation, Harvey Cushing reported on two cases of patients with focal epilepsy in 1909 [7]: Stimulation of the postcentral gyrus intraoperatively resulted in sensory sensations of the contralateral hand. In 1911, Fedor Krause published the first detailed cortical map of the motor area of the brain [8]. During the First World War, traumatic brain injuries and the resulting epilepsy increased dramatically. Otfrid Foerster, a German neurologist from Breslau, was frustrated by the results of neurosurgical procedures conducted by his surgical colleague and started to operate himself [1]. He had already used intraoperative electrical stimulation during local anaesthesia to identify the epileptogenic focus in traumatic brain injuries. Driven by Foerster's success, Wilder Penfield, a Canadian neurosurgeon, joined him. As a result of their work, they published an expanded map of the human cortex in 1930 [9]. The so-called "epileptogenic

Abbreviations: BA, brodmann area; ECoG, electrocorticography; ETLE, extra temporal lobe epilepsy; MNI, Montreal Neurological Institute; mTLE, mesial temporal lobe epilepsy; TLE, temporal lobe epilepsy; DC, direct current.

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cortical areas" showed detailed information about motor, sensory, acoustic and visual representations of the brain surface [9].

2. EEG recordings in humans and their implementation in neurosurgical procedures

With studies of the EEG in humans by Hans Berger in 1929, a new technique for functional analysis of the brain was introduced [10]. Inspired by Berger's results, Otfrid Foerster and Hans Altenburger postulated the necessity of intracranial recordings for further investigations. In 1934, they published results from 30 intraoperative EEG recordings in different regions of the brain [11]. The localizing value of EEG in cases of brain tumour was stressed and an ictal seizure pattern during invasive recording was described for the first time [11].

As a consequence of the Second World War and the initial lack of notice of Berger's discovery, the impact of epilepsy research in Europe, and especially in Germany, declined. Adrian and Matthews reported on Berger's discovery in the English-speaking community in 1934 [12]. Meanwhile, Gibbs and Lennox systematically demonstrated the importance of EEG in the characterization of epileptic patients [13]. In 1940, Schwartz and Kerr confirmed the results obtained by Foerster and Altenburger as they showed characteristic EEG changes in the cortex adjacent to brain tumours [14]. They demonstrated the electrical silence of intratumoral tissue and the importance of the superficial brain cortex in the generation of electrical potentials measured by EEG [14].

In 1937, the successful cooperation between Wilder Penfield and the neurologist Herbert Jasper in the Montreal Neurological Institute (MNI) began [15]. They combined cortical stimulation with EEG recording technique and established an interdisciplinary approach at the institute [16]. Influenced by his earlier work with Foerster, Penfield advanced his studies on the mapping of cortical functions and used them to better understand seizure semiology. During that time, not only the concept of the "Homunculus" but also precise characterizations of the insular cortex and its integrative function of frontal, parietal and temporal input were described. Intraoperative stimulation studies demonstrated the representations of gastric, motor and sensory functions by insular tissue, but also their variable representation [17–21]. A first serial invasive EEG recording over several days using epidural electrodes was performed in 1939 at the MNI and showed the importance of invasive EEG techniques in the delineation of the epileptogenic area [16].

Between 1939 and 1944, epilepsy surgery was performed in 76 cases at the MNI. Pre- and postoperative EEG were established routinely to identify the epileptogenic area as "the surgeon's best guide" and the relevance of the EEG in localizing cerebral lesions started to surpass that of the pneumencephalogram [22]. Provoking procedures such as hyperventilation, hydration and metrazol were used to activate the epileptogenic focus during extraoperative recordings [23]. In a next step, acute intraoperative ECoG was routinely executed during awake surgery. According to this interictal approach and the rare recordings of seizure patterns during ECoG, Jasper proclaimed that "random spikes" generated by local epileptogenic lesions of the brain had the highest probability of identifying the epileptogenic focus [24]. Other epileptiform discharges, such as sharp and slow waves, had a lower localization value because they were typically found more distant from the epileptogenic lesion. Jasper used the term "primary and secondary foci" to describe these phenomena. He characterized the affected tissue as "normal cortex in which the epileptic discharge is conducted from a distant buried focus" and pointed out the dilemma to differentiate the primary from secondary epileptogenic foci, especially in deep and inaccessible brain structures [25]. Also, after-discharges or seizure patterns induced by electrical stimulation were recognized as useful to detect epileptogenic tissue [26]. Even though their distribution did not completely correspond with the expansion of interictal spikes [24], stimulation-induced phenomena resembling the patients' initial seizure signs were applied to define the resection area intraoperatively [27]. Penfield and Jasper confirmed that epilepsy was not produced by the cortical lesion itself but by the surrounding, partially destroyed tissue, a notion initially proposed by Jackson. In cases of epilepsy surgery, Penfield and Steelman summarized that "the epileptogenic focus in the marginal partly involved gyri must also (be) removed" by cortical excision [23].

3. Investigation of deep structures and the beginnings of sEEG

Over the course of time, it became clear that not only surface grey matter was involved in the generation of epileptic seizures. Subcortical and deep brain lesions like the thalamus, basal ganglia and other regions were identified as sources of slow EEG and epileptiform activity [28]. Furthermore, the influence of thalamocortical circuits was discussed as a result of stimulation studies in animals and their impact on generalized epilepsies [29]. In temporal lobe epilepsy (TLE) the importance of the resection of mesial TL structures was recognized [25,26]. Jasper discovered the phenomena of initial EEG suppression, especially in seizures with a deep anterior or mesial focus [25]. Additionally, the interhemispheric connectivity between homologue regions and the observation of a fast shift of pathological EEG patterns in TLE highlighted the necessity of a better understanding of subcortical regions and tracts and their function in seizure generation and propagation [25]. Robert Hayne and Russel Meyers published the first report about stereotactically implanted EEG electrodes in humans with epilepsy in 1949 [30]. They described combined and independent seizure activity in cortical and subcortical structures and advanced the importance of expanded simultaneous investigations of superficial and deep brain tissue. However, at that time, the implantation system was not individualized enough, resulting in inaccuracy in investigations of small nuclear structures [31].

At the same time, Jean Talairach, a French neurosurgeon, gained his first experience with stereotactic procedures. He improved the implantation technique and used the pneumencephalogram to adapt the implantation coordinates with respect to ventricular position and size [32]. He defined a system of reference lines and structures that allowed an individualized and optimized approach for investigations of deep brain structures and their anatomical localization. His work culminated in the publication of the first atlas of stereotactically defined brain structures in 1957, followed by a second edition 10 years later [33,34]. Working in the St. Anne Hospital in France, he met Jean Bancaud, a neurologist and neurophysiologist interested in EEG and influenced by the French pioneer on epileptology, Henri Hécaen, who had previously worked with Wilder Penfield at the MNI [35]. Comparable to the MNI, the interdisciplinary approach to the investigations in epilepsy and epilepsy surgery at St. Anne Hospital was the basis of successful work over the next decades. Together with Jean Bancaud, he advanced stereotactic techniques in epilepsy patients. The application of depth electrodes allowed not only the recording of deep brain structures; it also offered the possibility of a three-dimensional analysis of seizure patterns, their distribution and propagation and correlation to clinical features. The technique allowed longer and serial terms of recordings as well as the separation of diagnostic and surgical procedures [36]. Due to the good tolerance of intracranial stereo-EEG (sEEG), "chronic" investigations with a duration of days up to weeks became possible.

Talairach and Bancaud developed new concepts in the definition of seizure-relevant tissue. The resections of Penfield initially were, in most cases, guided by interictal spikes and

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