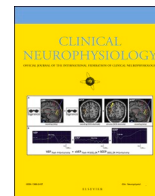




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## 1924–2024: First centennial of EEG

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### A B S T R A C T

On July 6th of 1924 Hans Berger –a German psychiatrist- first recorded electric signals from the human brain via scalp electrodes. This date marks the beginning of Electroencephalography. In this review a representative panel of past and present Officers of the International Federation of Clinical Neurophysiology (IFCN) and of its Official Journal briefly summarizes the past, present and future of Electroencephalographic and related neurophysiological techniques' impact and the role of the IFCN in global collaboration, education, standardization, research innovation, and clinical practice.

### 1. The discovery of electroencephalography

The roots of EEG can be traced back to the late 18th century when Luigi Galvani discovered “animal electricity” by demonstrating that short circuiting two metals with the frog legs serving as electrolyte (building together a “Galvanic element”) could cause muscle contractions. The first direct precursor to EEG came when Richard Caton, a British physiologist, measured electrical activity from the exposed brains of animals in 1875 (Caton, 1875). He observed fluctuations in electrical potentials related to brain activity, which laid the groundwork for future studies. On 6th of July 1924, one century ago, German psychiatrist Hans Berger made in Jena the first recording of spontaneous electrical activity from a human brain by placing electrodes on the scalp. The results were published in a paper 5 years later, summarizing the state of art in animal experiments, a detailed methodological discussion and many considerations excluding alternative sources of the reported EEG signals (Berger, 1929).

In the present Review article (which follows an analogue publication – by Mushtaq et al. (2024), in which a survey from a large panel of electroencephalographers was reported on the occasion of the 1st centennial of EEG discovery, mainly focusing on future applications) we aim to summarize the history of EEG and derived techniques, mainly in terms of clinical applications, and to review the role of the International Federation of Clinical Neurophysiology (IFCN) and of its official journal

(Clinical Neurophysiology, formerly Electroencephalography & Clinical Neurophysiology) in fostering and promoting EEG and all its technological evolutions.

Hans Berger also noticed EEG brain waves with a typical frequency of 8–13 Hz seen predominantly when a person is awake but relaxed, especially with eyes closed, which were later termed alpha, (Berger, 1929).; He also demonstrated that the presence and amplitude of these alpha waves were suppressed by cognitive brain activity (i.e., reasoning, mathematical calculations). Following his discovery of alpha waves, Berger also identified beta waves, which typically have a frequency of 14–30 Hz and are associated with active thinking, concentration, and mental activity. The impact of his publication was initially seen more in the media than the scientific community, with fantastical ideas on potential utility of these novel signals, from telepathy to the possibility to explore and unravel mysteries of the mind with a non-invasive method. It was, however, left for Lord Adrian, Nobel laureate for his studies on nervous propagation along peripheral nerve fibers and olfactory perception, to turn the scientific doubters into believers (Adrian, 1932). Together with H.C. Matthews, Adrian replicated Berger's experiments in early '30 s, opening the avenue for a new field of study and enlarging previous observations on the reactivity of EEG to visual stimuli and its relationship with sleep.

William Grey Walter (IFCN president from 1953 to 1957)) became the pioneer of clinical applications of EEG (Walter, 1963). He built an

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oscilloscope able to record 3 EEG channels and began to be used to aid the diagnosis of cerebral tumors and as a rudimentary monitoring system, both during surgery and to confirm the effects of anesthesia. Following Berger's example he identified with the Greek letters "delta" and "theta", the slow rhythms of EEG activity and, as early as 1943–1944, introduced the first methods for automatic analysis of the cerebral bioelectric signal.

## 2. Introduction of EEG into routine clinical practice

After the Second World War EEG developed even further, both in Europe and in America. In 1947, the first International Congress of EEG was held in London, followed by the second Congress in Paris in 1949, at which time the IFCN was also established. These two pivotal congresses helped to define the first international parameters to be used in EEG recordings (including the so called *international 10–20 system* of electrodes positioning/labeling), parameters that were later published on the journal *Electroencephalography and Clinical Neurophysiology* (better known as the "EEG Journal", now *Clinical Neurophysiology*).

Thanks to the introduction of EEG in the clinical routine, epilepsy – previously seen as a personality trait – was repositioned as an electrophysiological disorder of brain functioning. This work, pioneered by William Lennox, and Erna and Frederic Gibbs, was a considerable success in the development of biomarkers of neurological disorders (Gibbs et al., 1935; Lennox, 1936). A further seminal contribution was by Henri Gastaut and the 'School of Marseille' who described in detail several types of primary/secondary epilepsies, defining the EEG and clinical phenotypes of the seizures and the interictal EEG patterns. Gastaut (IFCN President from 1957 to 1961) made crucial advancements in identifying the role of EEG in diagnosing different forms of epilepsy.

During the second world war, because of the growing amount of brain injuries in soldiers, post-traumatic and focal epilepsies were explored in detail. Studies performed at the Montreal Neurological Institute by Penfield and colleagues recorded pre- and postoperative EEGs to identify the epileptogenic area, with greater accuracy than with pneumoencephalogram, a remarkably invasive diagnostic method for localizing cerebral lesions (Jasper, 1941). Provocative or activation procedures, including hyperventilation, hydration, and metrazol were introduced to activate the epileptogenic focus. Subsequently acute electrocorticography (ECoG) performed during awake surgery was carried out to localize epileptogenic lesions and it was found that "random spikes" in ECoG recordings directly from the exposed cortex were most reliable for identifying the epileptogenic focus; on this basis the distinction between primary and secondary epileptogenic foci was emphasized (Jasper & Penfield, 1949). These two giants of electroencephalography, Penfield and Jasper, concluded that epilepsy does not originate from the cortical lesion itself but from surrounding, partially destroyed tissue, and that removal of all the involved cortical gyri was therefore evidently necessary for successful epilepsy surgery (Jasper & Penfield, 1949). Herbert Jasper, founding president of IFCN (from 1947 to 1953), promoted the use of EEG in clinical settings, particularly in epilepsy treatment and helped establish international collaboration in neurophysiology, which laid the foundation for the IFCN's mission of standardizing clinical neurophysiology globally. Jasper's contributions to EEG, especially through his work with Wilder Penfield, shaped the modern understanding of brain wave analysis and its application in surgery. It is interesting to notice that the main use of EEG, 100 years after its discovery, remains clinical and still centered in the diagnosis and assessment of treatment of epilepsy.

In the late '60 s, the success of organ transplantation from deeply comatose subjects led to the introduction of the concept of 'brain death' defined by irreversible damage of the brainstem vital centers. Since then a growing body of evidence has accumulated on the role of EEG recordings in comatose patients with unrecoverable brain damage. With this the need of doctors and technicians with expertise in EEG recordings and interpretation expanded to all the major hospitals. EEG recordings

and Evoked Potentials were routinely introduced in intensive care units, for this and for monitoring comatose and vegetative states, as well as in surgical theaters for those neurosurgical procedures which are potentially harmful to central and peripheral nervous systems structures. In this field the contribution of one of the former IFCN presidents – Mark Nuwer (president IFCN from 1997 to 2011) – was of paramount importance.

Focal slow-waves during wakefulness have been described as a hallmark in presence of brain lesions of various etiologies (e.g., stroke, neoplasms, encephalitis). In the present era of studies on brain connectivity it is surprising to observe how researchers who pioneered in EEG analysis were able to interpret focal slow EEG waves during wakefulness as a sign of disconnection.

Following the pioneering studies by Moruzzi and Magoun on the reticular formation which included EEG recordings, (Moruzzi & Magoun, 1949), the neural characteristics of sleep were quickly defined. Soon after, new laboratories started enlarging EEG boundaries of clinical/research applications. The neural characteristics of sleep were quickly defined, mainly in the US, with Albert Einstein contributing to the scientific debate in these early studies (Rechtschaffen & Kales, 1968). Polysomnographic studies were carried out and the different sleep stages were described (Gottesmann, 2009). Meanwhile, the progressive changes of the hypnographic profile across the life span were first observed.

## 3. Computers and further development of EEG

Quantitative analysis of EEG (qEEG) was born when Mary Brazier and Norbert Wiener (Wiener, 1961) modeled the EEG as a stochastic process using analogue computers. Brazier, (IFCN president from 1957 to 1961), was one of the first women in neurophysiology. In addition to her work on EEG analysis methods in both normal and pathological conditions, she also supported the growth of clinical neurophysiology education under the IFCN's leadership, being the Editor-in-chief of the EEG Journal (Brazier et al., 1975). Such approaches were quickly superseded by digital computers, which opened the way for evoked potential recordings, EEG spectra via Fast Fourier Transform analysis, event related activity evaluation and the study of brain ageing, brain connectivity and normative modeling. Because of the possibility of qEEG analysis, pharmaco-EEG (namely, the possibility to explore the effects on the EEG characteristics of neuro- and psychoactive drugs) became particularly popular in the '70 s and '80 s.

After the early studies by Duncan George Dawson (1951) the introduction of microprocessors and digital computers in the '70 s allowed recording of stimulus-related EEG potentials by averaging single trials time-locked to a trigger. In this way, EEG signals not related to the stimulus were canceled out, while those with a fixed temporal relation to the stimulus (i.e., the stimulus response) were preserved. This allowed the recording of clear brain (subcortical and cortical) responses to external (e.g., visual, auditory, somatosensory) or endogenous (e.g., cognitive) stimuli. Their use in a clinical setting became a diagnostic routine (e.g., in multiple sclerosis, for screening of deafness in neonates, testing of acoustic neuroma, spinal cord compression). In addition Evoked Potentials and EEG monitoring became a pillar of intraoperative and ICU assistance to patients with central nervous system damage/disease. Members of the IFCN were pivotal in the development of Evoked Potentials generators and mechanisms with some of its Presidents major figures for spinal, brainstem and cortical somatosensory evoked potentials; Martin Halliday (Carroll et al., 1980), John Desmedt (Desmedt & Cheron, 1981a, 1981b), Jun Kimura (Kimura, 1985) and Francois Mauguire (Mauguière et al., 1983).

A non-invasive brain-computer interface (BCI), sometimes called a brain-machine interface (BMI), is a direct communication link between EEG and an external device, most commonly a computer, domotics (or home automation refers to all the technologies and automated systems used to control and manage a home's equipment and infrastructure) or

robotics. This approach has been used to assist, augment, or repair sensory-motor functions in severely neurologically impaired patients. They are often conceptualized as a human-machine interface that bridges the intermediary of dysfunctional moving body parts (hands...). Research on BCIs began in the 1970s by Jacques Vidal at the University of California, Los Angeles. Vidal's 1973 paper (Vidal, 1973) introduced the expression brain-computer interface into the scientific literature. More recently, BCI has been enriched by the application of machine learning to statistical temporal features in order to distinguish/classify mental states (relaxed, neutral, concentrating), mental emotional states (negative, neutral, positive), and movement programming/execution. Brain-muscle interactions have been also studied via advanced EEG analysis methods providing insightful information on movement mechanisms in health and in the pathophysiology of movement disorders. In this area the contribution of one of the former IFCN presidents –Mark Hallett- has been remarkable.

#### 4. Transcranial Magnetic Stimulation and EEG

About 30 years ago it became possible to record EEG responses to non-invasive transcranial magnetic brain stimulation (so called transcranial evoked potentials, or TEPs), (Ilmoniemi et al., 1997). The combination of transcranial magnetic stimulation (TMS) and EEG is a noninvasive tool to measure the electrical brain reaction to direct cortical stimulation and provides several advantages. Recordings can be collected at the patient's bedside at low cost; they provide information on brain excitability, even outside motor cortex (MEPs) or visual cortex (phosphenes) and the TEPs follow the temporal order of activations of distant cortical areas, allowing the tracing of the dynamics of causal interactions within functional brain networks. They also have good spatial resolution when high-density EEG is combined with individual structural neuroimaging.

TMS-evoked activity spreads from the stimulation site ipsilaterally via association fibers and contralaterally via transcallosal fibers and to subcortical structures via projection fibers (Ferreri et al., 2011; Ilmoniemi et al., 1997). Therefore, TMS-EEG enables the study of cortico-cortical interactions by applying TMS to one area and observing responses in remote, but interconnected areas, and the study of how the activity in one area affects the ongoing activity in other areas (Ferreri et al., 2014; Ilmoniemi & Kicić, 2010). Several neurotransmitter receptors (including NMDA, GABA<sub>A</sub>/GABA<sub>B</sub>) are likely involved in the generation and/or modulation of TEPs (Darmani & Ziemann, 2019; Ferreri et al., 2011). Several recent findings have opened up use of this technique to assess directly whether and where in the cortex long-term potentiation or depression plasticity phenomena can be induced with several different paradigms (Esser et al., 2006; Huber et al., 2008; Veniero et al., 2013).

Detection of the natural frequencies of TEPs with TMS-EEG (Rosanova et al., 2009) may also have diagnostic potential and clinical applications, as it opens up possibilities to map the natural frequency of different cortical areas in various neuropsychiatric conditions such as depression, schizophrenia, epilepsy, dementia or disorders of consciousness (Ferreri & Rossini, 2013; Ferreri et al., 2017; Kimiskidis et al., 2014).

#### 5. Brain connectivity, EEG and neurodegenerative diseases

Neuronal assemblies in the cortical layers and subcortical nuclei continuously exchange information, via anatomical and functional connections along which neuronal assemblies cooperate/communicate. One way this cooperation/communication is represented is in the amount and timing of synchronization of the oscillatory firing of the neuronal assemblies as they go in and out of phase, defined as 'binding/unbinding' of the neuronal oscillatory firing (Pina et al., 2018). Within this theoretical framework, the brain can be considered the 'container' of a huge number of networks, each network being represented by nodes

(neuronal assemblies) and edges (connections; .....). Binding/unbinding can be a transient and extremely rapid phenomenon (in the order of tens of milliseconds), which often does not require changes in energy consumption (as a result of in phase without changes in firing frequency). These two aspects preclude the analysis of binding/unbinding phenomena via fMRI, which is exquisitely linked to the relaxation time of hemoglobin for the brain oxygenation level dependent (BOLD) signal generation. The organization, topography, strength and weight of nodes and edges are shaped by several factors including genetic background, age, training and lifestyle. In recent years, mathematical procedures, which include graph theory and entropy analysis, have been successfully employed to evaluate in research and – most importantly – in clinical fields (e.g., early diagnosis of dementia) the network architecture and chaotic organization of brain EEG activity (Stam et al 2023; Cacciotti et al., 2024).

#### 6. Present and future of electroencephalography in the clinical context

Today, EEG is supported by scientific and professional societies (with the IFCN the largest and oldest) that foster its use across the globe. Indeed, EEG is often the only method exploring brain function available in resource-limited clinical settings and remains the only imaging modality shown to be successful for mass screening of brain dysfunction. Moreover, EEG has a time discrimination in the millisecond range, which cannot be reached by any functional brain imaging modality and represents a unique opportunity to investigate brain dynamics and hierarchies with sufficient temporal resolution. Last, but not least, EEG can also follow changes in brain activity that do not require energy consumption and which are undetectable with other modalities such as fMRI. For applications in future routine daily activities, scalp EEG signals recorded with portable devices will allow the analysis of direct environmental interactions deriving from the presently available BCI experiments without the need of invasive systems which –besides requiring neurosurgical approaches- will never allow a holistic vision of the brain activities particularly where complex networks organization is required with simultaneous involvement of different (and often remote) brain areas.

In the near future EEG and TMS-EEG may also become sensitive tools in detecting early electrophysiological abnormalities in neurodegenerative disorders, such as dementias, which show as an initial pathophysiological hallmark alterations in synaptic transmission, excitability and connectivity even at the preclinical or early clinical stage. It is worth noting that EEG development efforts are still mainly focused on signal definition, analysis and interpretation, while the technical part of installation and recording is partly neglected. In this perspective, it can be emphasized that facilitating installation and recording could also be considered as a development axis in practice, with the use of dry electrodes, pre-glued headcaps, wifi or blue tooth transmission EEG might represent not only a matter for neurologists and neuroscientists, but also for laboratory technicians, nurses and emergency and intensive care units, which makes the democratization of the technology a valuable objective.

Emerging technologies are opening new possibilities for EEG analysis and clinical applications, provided that this is also perceived and fully understood by the clinical community and that international standards for digital tools, data formats and hardware/software solutions are implemented. Increasingly affordable hardware, coupled with advances in artificial intelligence algorithms and virtual reality, holds immense potential for EEG-based brain-computer apparatus. There is a general consensus that the low cost, non-invasive nature, portability, and temporal resolution of EEG will secure its unparalleled value in long-term studies. It is striking that the application of EEG as a biomarker for global brain health is therefore seen as a possibility in the near future. It is one of the major aims of the IFCN to support and follow-up clinically-oriented research activity to invigorate and further develop the field of

EEG and related neurophysiological techniques.

## 7. Conclusions

Despite EEG being the most widely used direct measure of brain function worldwide, it is still not or little accessible in many developing countries of the world; in the research field the majority of studies come from a small number of countries and a small section of the world population from therein, but the EEG field can now tackle these challenges. Devices are becoming cheaper, more portable, and user-friendly; the EEG signals can be easily posted on web-based platforms to facilitate remote analysis from expert centers both for research and clinical purposes. This is allowing scientists and clinicians to engage with communities that have traditionally been excluded from EEG research. It is sufficiently robust a technique and affordable to be useful in the acquisition of large data sets in low and middle income countries for example. AI-driven analyses, based on large representative (i.e., multi-ethnic generalizable) datasets, is ready to overcome the substantial barriers in accessing training and expertise to support interpretation in clinical settings. We are confident that all these aspects will drive future applications of EEG towards a second centennial of a vivid and bright history in promoting brain health and tackling brain diseases.

We hope that, with this brief review, we have provided to our readership some awareness of the origins and development of electroencephalography, mainly in the clinical arena, but also a perception of the research potentialities of future studies based upon EEG and related techniques. In addition to complex analysis of EEG, in many clinical departments EEG recordings have increasingly moved to ambulatory ones taken over 24 h or more at home, and increasingly with video. This has led many EEGers to become experts not simply in EEG signal analysis but also in seizure semiology, especially in some neonatal practice. Since AI may well become a valid companion of human medical expertise in EEG analysis within the next decade, the interpretation of EEG with each patient's video semiology, which is likely to require human judgement suggests a continuing need for clinical neurophysiologists. Even 100 years after its first discovery, EEG continues to have new and important uses.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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