THE IFCN-EC, CO-ORDINATED BY PROFESSOR WALTER PAULUS, OUTLINES THE CHAPTER'S POSITION PAPER

Clinical neurophysiology

Clinical neurophysiology (as defined by the International Federation of Clinical Neurophysiology) is 'a medical specialty, or sub-specialty, concerned with function and dysfunction of the nervous system, caused by disorders of the brain, spinal cord, peripheral nerve and muscle, using physiological and imaging techniques to measure nervous system activity. When interpreted in relation to the clinical presentation of patients, data from these techniques can either diagnose or assist in the diagnosis of neurological or psychiatric conditions and quantify, monitor, and follow progression of such conditions. Clinical neurophysiology also encompasses physiological methods for therapy of neurological and psychiatric disorders.'

Research in clinical neurophysiology

Clinical neurophysiology encompasses a broad array of methods to study the peripheral and central nervous system, and targets virtually all diseases in neurology and psychiatry. Clinical neurophysiology bridges basic neuroscience closely with clinical neuroscience. It is a typical translational part of brain research. Investigation of human brain function is possible from single cell recordings during epilepsy surgery or deep brain stimulation to recording activity of large-scale brain networks during electroencephalography (EEG), magnetoencephalography (MEG), single-photon emission computed tomography (SPECT), positron emission tomography (PET) or functional magnetic resonance imaging (fMRI). These investigations are often combined with psychophysical and neuropsychological investigations.

Methods

Multichannel recording of brain electrical (EEG) and magnetic activity (MEG) is a necessary adjunct to the diagnosis of epilepsy and delineation of its type and frequency, and in the analysis of wake/sleep conditions and reduced states of consciousness. Refinement with modern source analysis methods will allow improved precision, in particular in conjunction with multimodal imaging. The introduction of ambulatory recording of EEG and video now means that patients can be recorded over days at home, improving yield and the patient experience. In cognitive neuroscience, EEG and MEG are the only real-time recording techniques presently available and are thus often essential for data acquisition and are complementary to functional imaging (the neurophysiological signals have a time discrimination thousands of times higher than techniques based on blood-flow/metabolism). Though EEG has been considered a clinical tool, over the last decade or so it has moved beyond this to also be frequently used in neuroscience laboratories.

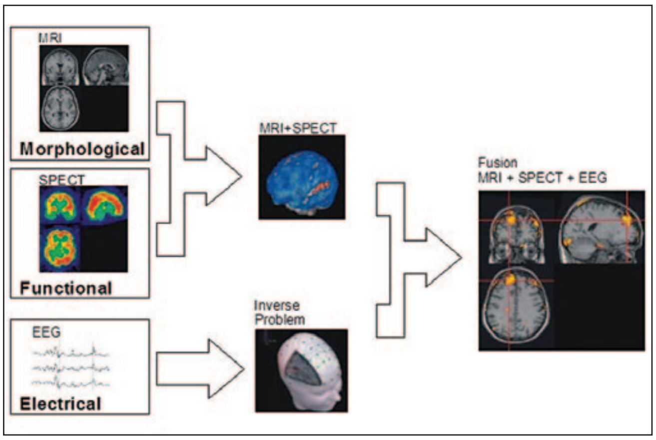
Subdural and intracerebral EEG recordings are techniques that are currently indispensable in defining surgical targets during the pre-surgical assessment of pharmaco-resistant epilepsy. In an increasing number of cases, the electrode contacts used for recording can be subsequently used to perform micro-thermocoagulation procedures that can avoid major resection (therapeutically interventional neurophysiology).

Multimodal evoked potentials (VEP, ERG, BAEP, SEP, MEP, LEP, AEP, etc.) are employed in the diagnosis of the causes of sensory and motor disturbances, for instance in multiple sclerosis, in coma prognosis and in investigation of ophthalmic and auditory disease, while multimodal event-related potentials (ERPs), being long latency evoked potentials, reflect cognitive processing and therefore allow the recording of brain responses during tasks involving different types of memory, problem solving, decision making etc.

Intraoperative monitoring of brain, spinal cord and nerve function during surgery is improving the safety of these procedures and, indeed, is becoming mandatory medico-legally. The monitoring of ICU patients is becoming more widespread and standard.

Optimising neurological care during emergency and intensive care treatment has become a priority through all age groups. In particular, neonatal brain monitoring with long-term EEG is already a standard in most European tertiary level centres in neonatal intensive care. Brain monitoring is also a key component of paediatric and adult intensive cares, as well as an increasingly used method in the emergency medicine of neurologically compromised patients.

EEG, together with other measures such as polysomnography, is the only way to accurately measure sleep stages and is the backbone of the diagnostic investigation of sleep disorders. In addition, electromyography, quantitative motor unit studies, nerve conduction studies, and reflexes (spinal, brainstem, transcortical) are standard extensions of the neurologic examination to diagnose patients with anterior



Co-Registration and Data Fusion to define the Epileptic Focus (Courtesy from JM Fernandes, UA-Portugal

horn cell, peripheral nerve, neuromuscular junction or muscle disorders and to determine the extent and severity of such conditions. Reflexes are of paramount importance for research as well as for evaluation of clinical conditions including muscle tone abnormalities. Quantitative motor unit studies such as motor unit number estimate (MUNE) are valuable endpoints in clinical trials on motor neuron diseases and motor neuropathies. Channelopathies can be diagnosed by excitability testing with threshold tracking providing information about the activity of a variety of ion channels, energy-dependent pumps and ion exchange processes activated during the process of impulse conduction in the nerve.

Neurophysiological techniques are used to record various parameters associated with autonomic disturbances including heart rate variability, postural blood pressure and cutaneous blood flow useful in the assessment of small fibre nerve damage, which can occur in diabetes and other conditions. Specialised techniques, (contact heat evoked potentials and laser evoked potentials) can assess the pathways from skin to brain involved in perception of pain.

Signal plus imaging methods in clinical neurophysiology

Within the area of structural imaging, MRI in clinical neurophysiology provides high resolution data of the brain for many functional purposes (such as guidance of electrode position for deep brain stimulation, dipole source calculation of multichannel EEG data and identification of epileptic foci). Ultrasound plays an increasing role in diagnostics of peripheral nerve and muscle disease, supplementary to MRI imaging and electrodiagnostics. Further new fields include the diagnostic ultrasound investigation of the brain in Parkinson's disease. In focused ultrasound therapy non-invasive stereotactic brain surgery is performed during simultaneous thermosensitive MRI imaging.

Similarly, within the area of functional imaging, fMRI by using the BOLD and other techniques provides a most promising link to brain physiology on a systems level. Though primarily a neuroradiological tool, it can be used simultaneously or in series with EEG to provide complementary information about brain structure and function.

Stimulation

Deep brain stimulation (DBS) is now a routine method approved in the EU for improving symptoms in movement disorders such as Parkinson's disease, dystonia and epilepsy. In DBS, electrodes are implanted into nuclei such as the thalamus, subthalamic nucleus or other basal ganglia regions. Currently, new targets in the brain and novel stimulation protocols are being tested to treat other frequent diseases, such as epilepsy, intractable pain and a variety of psychiatric disorders. Future challenges encompass improvement of stimulation parameters, introduction of closed-loop stimulation, discharge for interruption of epileptic activity and seizure prevention by patterned brain stimulation, directional sensitive electrodes and others.

Transcranial magnetic stimulation (TMS) can be used for the investigation of the functional properties of the nervous system. Direct continuous electrical stimulation of the brain by either weak alternating or direct current or pulsed short duration stimulation mediated by TMS allows the manipulation of brain function non-invasively for research, for clinical diagnosis, and for the purpose of treating neurological and psychiatric diseases. Repetitive TMS is now a standard treatment for depression (and is reimbursed by insurance in the USA). It will be a main research task to further develop and refine these stimulation methods for treatment of other neurological diseases such as epilepsy, stroke sequelae, and others.

Elsewhere, many integrative multimodal assessment techniques can be combined for more power, including brain imaging in conjunction with electrophysiological techniques and clinical or behavioural measures, whilst brain-computer interface (BCI) enables those with profound paralysis, e.g. locked-in syndrome, and some tetraplegics to communicate and/or control external manipulanda.

Finally, clinical neurophysiology in the context of recordings during epilepsy research or deep brain stimulation is important because it allows reducing the need of animal experiments. In particular, when compared to non-human cognitive primate research it allows the design of much more complex experimental paradigms. In general this research provides fundamental information on how the human brain works on levels from systems to cells.

Promising future research topics

Using invasive recordings in humans during epilepsy monitoring or deep brain stimulation for acquisition of neurophysiological data holds a lot of potential for future research. The implantation of invasive electrodes in patients with epilepsy or movement disorders provides a unique possibility to acquire data on human brain function with a high potential to reduce the amount of non-human primate research in this area.

Diseases assessed by clinical neurophysiology approach

- Epilepsy;
- Stroke;
- Disorders of consciousness;
- Intraoperative monitoring;
- Movement disorders;
- Migraine;
- Multiple sclerosis;
- Myasthenia;
- Tics;
- Dementia;
- Schizophrenia;
- Depression;
- Neuropathies and myopathies;
- Motor neuron disorders;
- Spinal and nerve root disease;
- Sleep disorders; and
- Chronic pain;

Europe-wide networks between clinicians and basic scientists would have a high potential for advancing knowledge of human brain function by minimising animal studies.

Providing database infrastructure for the collection of clinical data of rare patients is also an area which should be further investigated. The prognosis of rare neurophysiological patients is frequently unclear due to the lack of a sufficient number of patients. Europe-wide studies could provide a sufficient number of patients. Clinical neurophysiology seems to be particularly well suited: many exact measures such as nerve conduction velocities etc. allow a quantitative follow-up, in conjunction with clinical and imaging data. A central EU-funded database would contribute to closing this knowledge gap.

Interventional clinical neurophysiology

Interventional clinical neurophysiology (transcranial and deep brain stimulation, focused ultrasound) provides a promising tool for treatment of many neurological and psychiatric diseases beyond the state reached so far. In particular, improving the efficacy of transcranial stimulation methods requires a better understanding of underlying neurophysiology. A network bridging basic and human studies would advance this field to a great extent.

Brain monitoring during intensive care

Brain-oriented care is rapidly advancing as a standard in the emergency and intensive care settings of all age groups. European academic centres have pioneered in this area for decades. In the past, European manufacturers of brain monitors have developed most of the technology that is currently sold around the world; hence Europe is in a clearly commanding position with strong competitive advantages.

To continue European excellence in the field, there is a need to prospectively support the building of pan-European networks with clinical studies on brain monitoring, as well as to encourage their linkages with European-based medical device industry for the next generation brain monitors.

Clearly, many clinical, technical and commercial challenges related to brain monitoring are shared by other modalities of neurophysiology, especially EEG, intraoperative monitoring, integrative multimodal assessments, invasive EEG studies, and multimodal evoked/event-related studies.

Human consciousness

Human consciousness remains a major challenge in basic as well as in clinical neuroscience. Human consciousness depends on brain function. Impairment of consciousness may occur after focal or systemic brain lesions, after functional disturbances such as epilepsy or, for example, in the context of anesthesia.

Inevitably, clinical neurophysiology at the interface to diseases can play a central role bridging basic neuroscience, neuropsychology, computational neuroscience and other areas by the methods described above whilst also incorporating aspects such as selective attention, memory, decision making and task monitoring.

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