Interventional neurophysiology: A new frontier in investigation, treatment and research

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1. ABSTRACT

In this short review, we highlight and reference the new developments in the newly emerged field of Interventional Neurophysiology in relation to neurosurgery, particularly the functional neurosurgery. The review covers clinical aspects of neurophysiological interventions into investigation, treatment and research on the pathophysiological mechanisms of neurological disorders.

2. INTRODUCTION

The concept of Interventional Neurophysiology reflects the changes in clinical practice as many surgical procedures require more use of neurophysiological methods. Neurophysiologists integrate themselves as a part of team, particularly in functional neurosurgery, where intracranial recordings of neural activity are increasingly needed, and electrical modulation of brain activity becomes an alternative to ablative and pharmacological treatments. New frontiers are created as the emergence of Interventional Neurophysiology aids clinical research on the pathophysiological mechanisms of neurological disorders, their investigation and treatment.

Interventional Neurophysiology emerges from the clinical need in an increasingly large number of neurosurgical procedures (involving brain, cranial nerves, spinal cord and the peripheral nervous system) to achieve maximal efficacy and safety by applying neurophysiological methods. Traditional ‘Clinical Neurophysiology’ has consequently extended its participation not only in the pre-operative stage, playing a diagnostic role to help select the patients, but also in the operating room during the surgical procedure itself. This is largely reflected by the increase in use of the various procedures generally termed as ‘Neurophysiological monitoring’ or ‘Surgical neurophysiology’ in the literature. The term "neurophysiological monitoring", as defined by the American Society of Neurophysiological Monitoring (ASNM, http://www.asnm.org/), refers to any measure that is used to assess the functional integrity of the peripheral or central nervous system in the operating room, the intensive care unit or other acute care setting. The participation of neurophysiology in operating room has been highlighted by Aage R. Møller’s book “Intraoperative Neurophysiological Monitoring” of the 1st edition in 1995 (1) and the 2nd
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Figure 1. Timeline. Milestones in the history of invasive recordings from the human brain. Reproduced with permission from (67).

edition 10 years later (2). A clear emphasis on the motor system is seen in a book from Deletis and Shils, (3). The new international association ‘International Society for Intraoperative Neurophysiology’ has been established recently in Rome, (http://www.ptsroma.it/isin/) reflecting the expanding of the field.

With the resurgence of functional and stereotactic neurosurgery, some neurophysiological procedures are practically integrated as an essential part of surgical procedures, not only to achieve efficacy and attain safety, but by detecting the spontaneous or evoked potential signals to provide functional markers for target localisation, and more profoundly, to deliver the final therapeutic outcome by electrically modulating neuronal activity via the implanted electrodes. This makes the neurophysiology become therapeutic in itself, as represented by the terms of ‘Neurostimulation’ and ‘Neuromodulation’. The latter has been used to name the official journal of the International Neuromodulation Society (INS, http://www.neuromodulation.com/)..

In this short review on the frontiers of neurosurgery research, we will provide an over view with highlights and references on developments in the newly emerged field of Interventional Neurophysiology in relation to functional neurosurgery, covering clinical aspects of investigation, treatment and research into the pathophysiological mechanisms of neurological disorders.

3. NEW ROLES IN CLINICAL INVESTIGATION PLAYED BY INTERVENTIONAL NEUROPHYSIOLOGY

Interventional neurophysiology plays new roles in diagnostic investigations beyond the boundary of conventional procedures, largely based on the advances of technology. Clinically, the new roles have been very much led by the needs and opportunities associated with functional neurosurgery (Figure 1). Firstly, various types of neurophysiological investigations involving transitional surgical procedures have been developed in order to get a close access to the pathological sources for more accurate identification and quantification so that the selectivity on the extent of a permanent ablation and accuracy of the target localisation can be enhanced. For examples, “stereotactic electroencephalography, SEEG” (4-6), cortical mapping (7), and depth microelectrode (8-12) and macroelectrode recordings (13-17) have been integrated with the procedure of ablation or stimulation. Secondly, in order to predict the long-term outcome of surgery, transient alleviation of symptoms may be induced by neurophysiological means, such as magnetic stimulation to the cerebral cortex at pre-operative stage (18-22) or electrical stimulation to the deep brain structures during operation (23-25).

4. NEW ROLES IN THERAPEUTIC INTERVENTIONS PLAYED BY INTERVENTIONAL NEUROPHYSIOLOGY

The new roles of neurophysiological techniques in therapeutic interventions are mainly reflected by achieving therapeutic effects using electrical or magnetic modulation of the neural activity. Since 1970s, (26) spinal cord stimulation has been widely used for control of intractable pain and spasticity. High-frequency electrical deep brain stimulation has been widely used to treat epilepsy, with progressively greater success, (27-30) and ‘closed loop’ systems, where a discharge is detected, and high frequency stimuli applied to abort a seizure, are being developed. Movement disorders also respond to high frequency stimuli, (31-40) as may neuropathic pain, (41-50) and psychiatric disorders. (51-53) Transcranial magnetic stimulation as a treatment has been attempted in movement disorders (22, 54-58) and various psychiatric disorders. (59-66)

5. RESEARCH INTO THE PATHOPHYSIOLOGICAL MECHANISMS

Interventional Neurophysiology provides new approaches in clinical research on the pathophysiological mechanisms of brain disorders by directly investigating the function of deep brain structures in conscious patients, as highlighted by a recent review on invasive neurophysiological recording in human brain (67). The obvious advantages of this approach are the greatly
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enhanced spatial resolution and signal to noise ratio, and the ability to correlate the neural signals with either the symptoms (13, 15, 68-76) or the performance of specifically designed behavioural or cognitive tasks (77-84). Recently, the neural control of the systemic blood pressure has been investigated in the patients with electrode implanted in the periventricular/periaqueductal region (85-87). New area of research has also been created in association of the treatment of deep brain stimulation. One distinctive example is the studies on the effects of neuromodulation to increase our understanding of its actions, and to refine the indications for this therapy. This may extend the range of relevant applications and lead to increased availability, as the objectives set by the International Neuromodulation Society (http://www.neuromodulation.com/). Studies have been carried out to investigate the mechanisms of deep brain stimulation at neuronal (88) and system levels (89), and have ranged from clinical studies (31, 90-94) to experimental studies focusing on the depth electrode-brain interface (95-100). Some recent studies have focused on optimising stimulation parameters, including frequency, pulse width, intensity, and the pattern settings of either electrical or magnetic stimulation to ensure therapeutic effects become more selective, effective and with fewer complications (35, 37, 101-105). Last but not least, given the nature of the neurophysiological procedures mentioned above as of many other interventional procedures, safety is an important issue. A clear therapeutic need assessed against other treatment options, with favourable benefit-risk ratio, will be mandatory for deploying any interventional neurophysiology procedure. This has provoked much discussion concerning the safety and efficacy. For example, using microelectrode recordings in movement disorder surgery has been strongly challenged (106). Efficacy and safety issues on various procedures during deep brain stimulation (107-113) or surface brain stimulation (107, 114, 115) have been vigorously investigated and assessed.

6. THE MULTI-DISCIPLINARY NATURE OF INTERVENTIONAL NEUROPHYSIOLOGY

The development of interventional neurophysiology have been largely based on the interactions from a wide range of clinical specialities, including neurosurgery, neurology, anaesthesia, and intensive care. Due to the rapid expanding of interventional neurophysiological procedures in response to the needs of developments in functional neurosurgery, there has been a vacuum of trained specialists playing the newly developed interventional roles. It was surveyed that, before the 90’s, a large proportion of the simple procedures for intraoperative monitoring were carried out without involvement of specialised neurophysiologists (see the Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology (116). This vacuum has been initially (and, to a large extent, is still) filled by one individual from a team of neurosurgeons and neurologists with an interest in neurophysiology. Helps also come from experimental neurophysiologists or medical engineers with an interest in the clinical application of their skills. For instance, electrical/magnetic neurostimulation procedures have been adapted from an experimental tool to an alternative therapeutic intervention for psychiatric disorders (117, 118). In addition, neurophysiologists have been interacting with other clinical disciplines such as anaesthesia and intensive care for monitoring neuronal activity in a clinical setting (119, 120). The speciality has also been assisted by the expertise of laboratory-based neurophysiologists and by the advances in basic scientific fields of medical physics and neural engineering. All of these interactions with other clinical and scientific disciplines have become the fundamental guiding force for developing and defining the multi-disciplinary nature of Interventional Neurophysiology. Encouragingly, the involvement of clinically trained neurophysiologists with an interest in playing a more interventional role has been steadily on the increase.

7. CONCLUDING REMARKS

Neurophysiology has gone beyond the traditional boundary of playing diagnostic roles in assessing brain functions. It now becomes more interventional and creates a new frontier in investigation, treatment and research related to functional neurosurgery and neurosurgery as a whole.

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