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REVIEW

Innovations, advances, and updates in neurosurgery

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Abstract

Neuroscience plays an important role in the basic study to control the coordination of the human body, thinking, and behavioral patterns that keeps pace with time. It is a complex and multidisciplinary scientific body of knowledge related to the nervous system. There are different and overlapping aspects in this field, which are closely interconnected to several elementary professional subjects such as science, technology, engineering, and mathematics. The number of aging population is expected to rise abruptly in the future, such that more than one in six adults globally will be 65 years or older by the year 2050. Advancing age of the elderly would obviously correlate to a rise in the burden of neurological diseases.

Neurosurgery comprises surgical interventions involved in the management of central and peripheral nervous system diseases. Rapid technical and technological advances in the neurosurgical field in the past decades have revolutionized better outcomes and prognoses for patients. The present paper discusses selected relevant innovations, advances, and updates in neurosurgery. Further theragnostic strategies and perspectives to treat victims with neurological deficits are also summarized. We hereby outline some noteworthy, major, plus recent innovations, advances, and updates in the field of neurosurgery.

Keywords

Neurosurgery; Innovations; Advances; Updates; History; Technology

1. Introduction

The history of neurosurgery began in North America about 10,000 B.C. "Trepanation", another name for "trephination", is derived from the Greek word "trypanon", which means creating a burr hole in the skull. Dating back in ancient Egypt, the god of medicine, Imhotep studied neurons in the mummification process. Forty-eight cases of trauma including detailed descriptions of the brain were documented in detail. After around 2200 years, Hippocrates of Kos, an outstanding figure in the Age of Pericles and known as the "Father of Medicine", became one of the most influential physicians in the history of medicine. He also wrote a record of skull perforation to treat fractures, epilepsy, or paralysis. Harvey Cushing (1869–1939), a famous contributor in the field of neurosurgery, was an innovator and the earliest known scholar to report Cushing's disease [1]. John Hughlings Jackson (1835–1911), founder of Cerebral Localization and Neurology, was a frontline neuroscientist who focused on epilepsy. Sir Charles Scott Sherrington, who was the father of modern neurophysiology, coined the unprecedented word "synapse", and served as president of the Royal Society from 1920 to 1925. He wrote two classic literary works—"The Integrative Action of the Nervous System" in 1906 and "The Reflex Activity of the Spinal Cord" in 1932, which affected the progress of neurosurgery [2]. Finally, Walter Edward Dandy (1886–1946), who was a pioneer in hydrocephalus studies, used a cystoscope, which was normally applied to examine the urinary bladder, to visualize the internal structures of the cerebral ventricles in 1922 [3].

Development of neurosurgery includes theories of cerebral localization, sanitized concept, and general anesthesia. Cerebral cortical localization explains the different cortical functions. Current sanitized concept is derived from the previous antiseptic technology including washing hands. Later, carbolic acid was introduced as an antiseptic, which diminished the incidence of surgical site infections. Thereafter, complications following operations were drastically decreased on account of the introduction of a clean environment. In 1804, a Japanese surgeon, Hanaoka Seishū, first conducted surgery under general anesthesia [4]. The emergence of major advances in pharmacology and physiology has accelerated the development of general anesthesia and pain control. Currently, almost every operation routinely uses tracheal intubation and advanced anesthesia depth monitoring apparatuses to improve its safety and efficiency (Fig. 1).

Additionally, application of high-level imaging can accurately locate the surgical target before surgery. Interventions using endoscopes allow us to treat lesions in a minimally invasive manner. In a previous study, it was discussed that

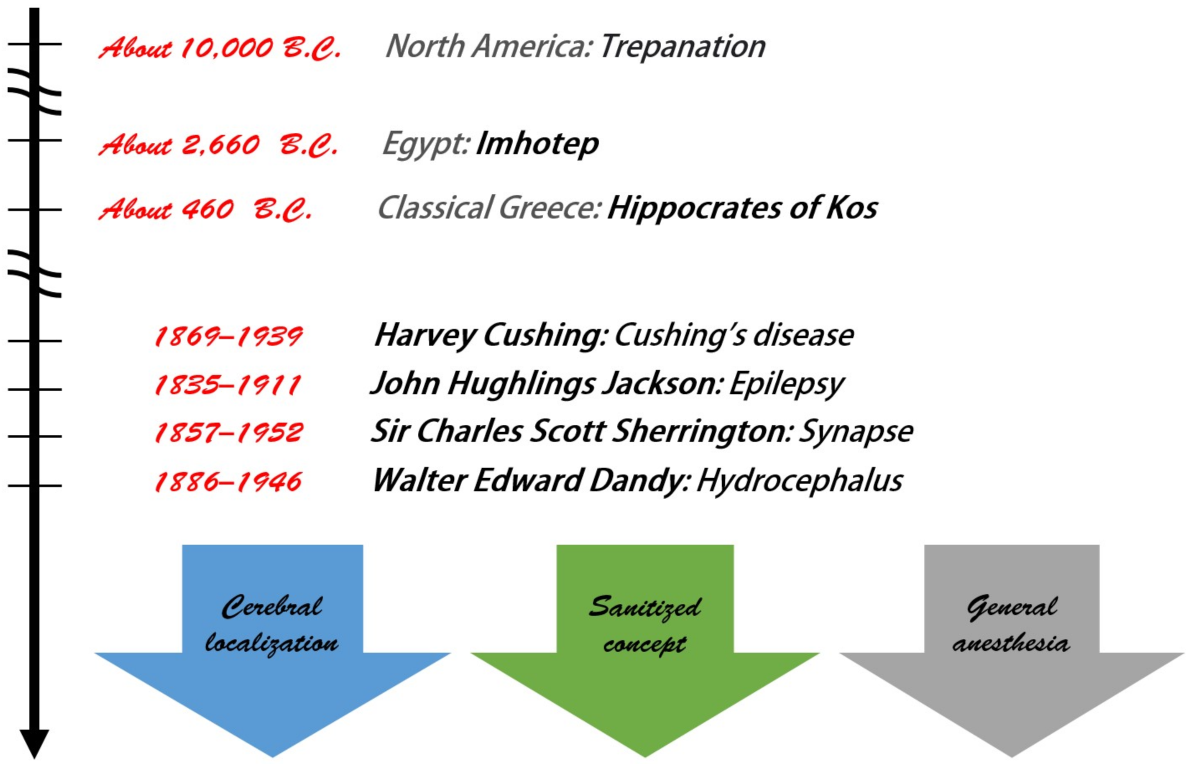

FIGURE 1. Representative historical timetable of neurosurgery.

basal ganglia hemorrhage is a common type of cerebral hemorrhage with high mortality and poor prognosis. The authors compared whether the use of craniotomy or endoscopic surgery has significant differences in neurological recovery. They found that there were lower intraoperative blood loss, shorter operation time, and higher hematoma clearance rate in the endoscopic group when compared to the craniotomy group. In addition, endoscopic group showed better recovery in listening comprehension and speaking ability [5]. On the other hand, Ram Ishwar Yadav *et al*. [6] pointed out that micro-endoscopic discectomy had a better prognosis in terms of (1) a reduction of time in bed, (2) shorter surgery time, and (3) lesser blood loss then open discectomy.

Currently, combined chemotherapies and/or radiosurgical approaches are often considered as adjuvant treatment to control malignancies. Interventional therapies performed in a modern hybrid operating room allow us to treat patients with neurovascular conditions without delay, even in emergent situations. The development of tissue neuronal engineering and cell transplantation facilitates the production of new diverse biomaterials. The combination of biotechnology, big data, artificial intelligence, and telemedicine facilitates the use of information and communication technologies for healthcare providers in the future to improve medical care and quality of life. The primary aim of this article is to narrate the history, present state, and expected tomorrow of neurosurgery.

2. Neurosurgery - clinical

2.1 Neuroimaging

Structural imaging shows the anatomy of our neurological system reached from current image synthesizer, including computed tomography (CT) and magnetic resonance imaging (MRI). It is practical to distinguish lesions and design treatment plans perioperatively. Nowadays, CT-guide 3D modeling further investigates those obscure anatomical organizations. Recent literatures have also revealed its application in spinal surgery [7]. It can even be integrated with MRI in the management of head injury [8].

Functional imaging, which is mainly used in neuroscience and psychological research, is also gradually being widely used to diagnose certain neurological conditions. Positron emission tomography (PET) is performed to paint the cerebral network changes under metabolic continuity patterns in different neurological disorders [9]. Furthermore, multimodal PET/MRI or PET/CT could be an appropriate approach to jump off the limits of traditional image modalities [10, 11].

2.2 Fluorescence imaging technology

It is a challenging task to resect malignant brain tumors safely for neurosurgeons. They have to enable maximal tumor resection and to minimize surgery-induced neurological deficits simultaneously [12]. Thus, a large molecular weight dye is emerged and approved to visualize the boundary between tumor and normal tissue under intraoperative fluorescence imaging [13]. Ahmed Mansour *et al*. [14] even reported a technical note to clip an anterior spinal artery aneurysm with difficult endovascular embolization using a novel endoscopic fluorescence imaging system.

2.3 Augmented reality (AR) system

AR is considered to be the future of the gaming industry. The US Food and Drug Administration permitted the first AR image navigation system "Xvision" for surgical operations in 2019, and it is expected to bring significant changes. Through a head-mounted display headset, the position of the target is superimposed and displayed on the patient's CT scan. This allows the surgeons to intraoperatively track the anatomies and surgical tools in real time as if they have acquired "see-through" capabilities [15, 16].

2.4 Brain multimodality monitoring

At present, a simple way to understand early neurological changes in neurosurgical patients is through intracranial pressure (ICP) monitoring. ICP-guided strategy has been the keystone for postoperative monitoring in severe traumatic brain injury and postoperative brain surgery before fatal neurological deteriorations happened. Modern technologies enable clinicians to detect brain hypoxia with swift corrective therapies in multimodal neurocritical monitoring [17, 18]. A growing body of literature demonstrated that the combination of ICP and partial pressure of brain tissue oxygen (PbtO2) monitoring can reduce the extent of brain tissue hypoxia in head injury victims to achieve more favorable outcomes [19].

2.5 Endovascular embolization technology

Endovascular embolization is considered to be one of the treatment options, where individuals may have high risk of intraoperative bleeding. Hybrid operating room is a suitable place for perioperative monitoring and treatment. Doctors may perform thrombectomy, coiling, and even clipping surgery at the same time in the same theater. An interesting study compared cerebral arteriovenous malformation patients with and without prior endovascular embolization. It showed a reduction in operation time and shorter hospitalization period [20]. Yet, Sophia F Shakur *et al*. [21] reported a large carotid body tumor treated by transarterial glue embolization with the liquid embolic agent N-BCA (N-butyl cyanoacrylate).

2.6 Minimally invasive three-dimensional (3D) endoscope

This fascinating tool removes the lesion through a small opening under the appropriate depth of field, in such a manner that the front and back distance are precisely anticipated. Compared with traditional surgery, 3D endoscopy can access various parts of the brain and spine without leaving conventional large scars. Endoscopy is widely used by clinicians in third ventriculostomy, pituitary surgery, as well as spinal surgery [22–24].

2.7 Surgical navigation system

Navigation technology uses perioperative real-time imaging to provide robotic guidance to surgical instruments. However, robotic control of the instruments may not be as experienced as a trained surgeon. Navigation in surgery has been proven to be used in minimally invasive spinal surgery to place pedicle screws during posterior lumbar fusion surgery to avoid screw misplacement, which can lead to catastrophic complications [25].

2.8 Telesurgical robotic system

This device involves a handheld control to operate from a remote command station, so that the surgery can be performed with an instrument directly operated by a robot. The main advantage is that the surgeon may operate elsewhere or even far away from the operating table [26].

2.9 Functional surgery using deep brain stimulation (DBS)

This method starts with creating a burr hole in the skull, followed by inserting tiny electrodes into the specific deep portion of the brain. The electrodes are subsequently connected to the battery, which then supply energy and stimulate the brain with electrical signals to relieve symptoms of diseases such as Parkinson's disease (PD) and epilepsy. DBS opens up new treatment possibilities for neurological and psychiatric diseases, enabling neuroscientists to directly measure cell activity and probe the function of neural circuits [27].

2.10 Woundless stereotactic ablative radiotherapy (SABR)

SABR involves the non-surgical precise use of radiation therapy to the nidus part of a lesion. Some reformed equipments are frameless and the radiation dose may even be fractionated to minimize injuries to normal tissues. SABR has been used to treat intracranial tumors, trigeminal neuralgia, and refractory epilepsy, especially when the focuses are too deep in the brain, preventing a thorough removal with traditional craniotomies. The several advantages of SABR include its high accuracy, non-invasiveness, no loss of blood, and convenience in operation, as the task can be achieved at outpatient services [28].

2.11 Neural engineering

A brain-computer interface (BCI) allows the brain to communicate with the outside world without transmitting signals via the peripheral nerves and muscles. Jonathan Wolpaw proposed that BCI consists of the following three elements: signal acquisition, feature extraction, and translational algorithm [29]. Neuroprosthetics refers to an artificial implant that replaces the damaged part of the human nerve pathway using prostheses. Nerve prostheses use artificial electrical stimulation to excite the nerve tissue, thereby replacing damaged nerve functions. Specifically, sensory nerve prostheses convert external information into electrical stimulation signals to act on sensory nerve pathways, such as cochlear implants and visual prostheses [30].

2.12 Gene therapy

Gene therapy is a new management technique, which applies genes or short oligonucleotide sequences as therapeutic molecules, as an alternative for traditional drug compounds [31]. These methods include transgenes encoding therapeutic

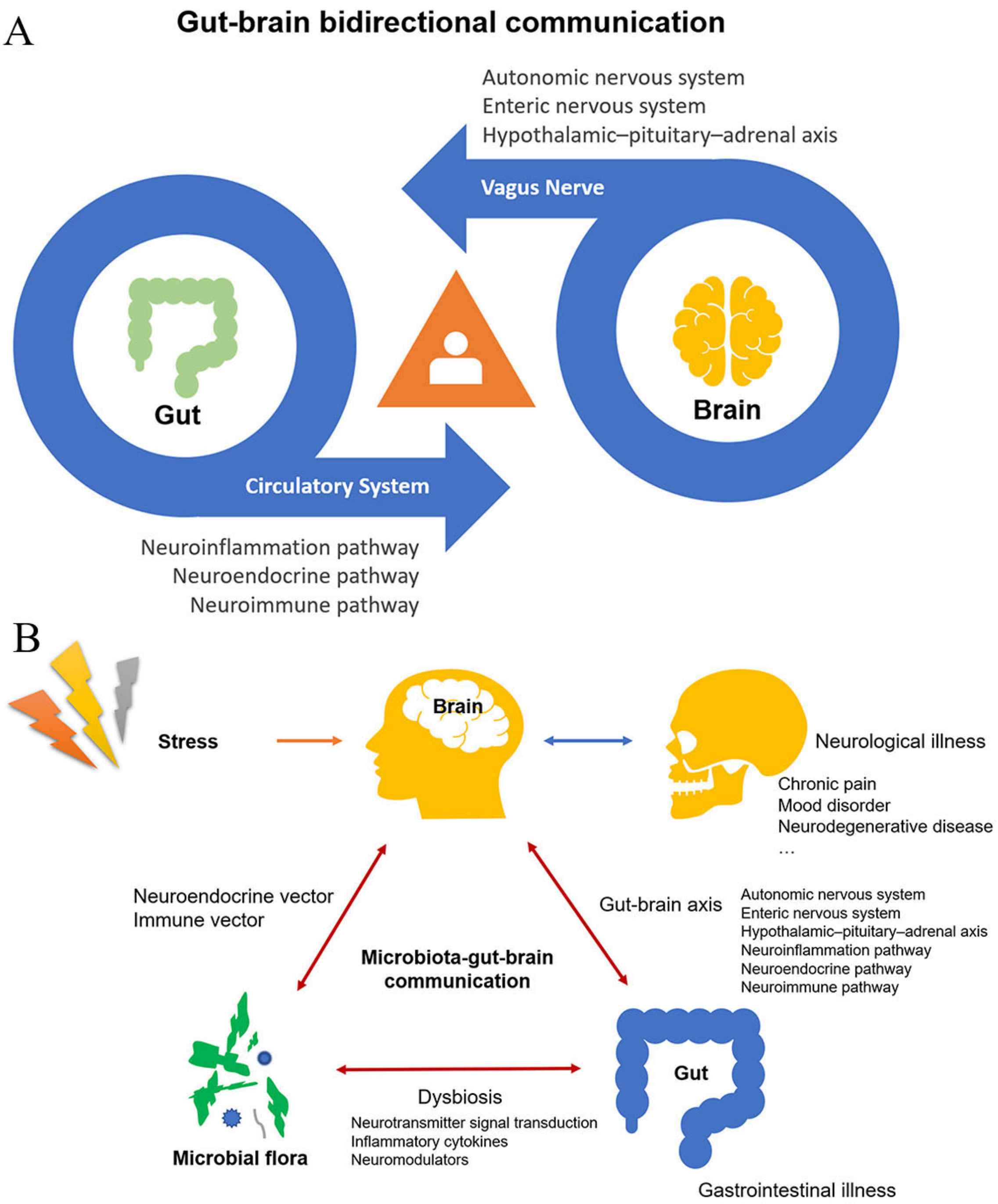

FIGURE 2. Schematic diagram of gut-brain bidirectional communication (A) and microbiota-gut-brain communication (B).

proteins, microRNAs, gene editing machinery like Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR), and anti-sense oligonucleotides (ASO's) are classically utilized to treat those defective genes which contribute to disease development [32–34]. A critical issue in transgene delivery analysis is the immune reactivity to the transgene-encoded protein, and its influence on sustained gene expression. Moreover, literature reported using viral and non-viral vectors to deliver the oligonucleotide precisely and treat glioblastoma multiforme [35, 36].

3. Neurosurgery related topics - basic

3.1 Cellular and molecular neuroscience

Cellular and molecular neuroscience is a section of neuroscience that studies the biological mechanisms of neurons and supporting cells. The communications between neurons and the exploration of physiological functions of neurons are fundamentals in this field. Stem cells for the therapeutics of PD and spinal cord injury (SCI) have been applied in recent years [37, 38]. However, there are still unmet issues which need to be resolved, including ethical concerns and the possibility of malignant transformation of stem cells [39].

3.2 Behavioral and systems neuroscience

Behavioral neuroscience focuses on the use of biological principles to study psychological processes and behaviors. On the other hand, systems neuroscience focuses on the study of the cooperative work of neurons in a network and their relationship between mental and neurological diseases. Resultant developments of new drugs are possible because of the in-depth research conducted in both disciplines.

3.3 Cognitive and computational neuroscience

Cognitive and computational neuroscience describes the relationship between anatomy, thinking, and sensory process through mathematical models to evaluate the cognitive function. Control theory, quantitative psychology, machine learning, artificial intelligence, artificial neural network, and computational learning theory have shown rapid progress and development in recent years [40].

3.4 Biophysics of the brain

This module includes a new diverse spectrum of techniques, such as computational, structural, spectroscopical, or electrophysiological techniques, to investigate the components of the neural systems involved in physiological and pathophysiological conditions. Biophysical networks address a wide range of questions from gating at the channel level, exocytosis, long-term potentiation, to conformational states of proteins involved in problems such as Alzheimer's disease [41].

3.5 Gut-brain connection

Gut-brain axis (GBA) is a complex bidirectional communication network that links the enteric with central nervous system (CNS). The gut communicates with the brain through vagus nerve that innervates the enteric nervous system, which is critical for the function of the gastrointestinal (GI) tract. Dysbiosis of gut microbiota plays a role in a number of neurological conditions, such as chronic pain, mood disorder, and neurodegenerative disease [42].

Recent literature has demonstrated the character of GBA connecting GI tract with CNS using molecular signals, hormone, and nerve transmission. Sangjune Kim *et al.* [43] showed a transneuronal propagation of pathologic α-synuclein in PD GBA. Dong Seok Kim and colleagues even used glucagon-like peptide-1 receptor pathway as a new treatment strategy for PD through the axis [44]. Nevertheless, another report revealed fecal microbiota transplantation to downregulate IL-1β/NF-κB signaling in spinal cord and NF-κB signaling in gut following SCI in a mouse model, which eventually improve locomotion and GI functions of the mice that suffered from SCI [45]. Researchers should pay more attention to this extraordinary disease in future challenges (Fig. 2) [46, 47].

4. Conclusions

Advances in science and technology demonstrate evolutionary progress in neurosurgery and neuroscience [48, 49]. For example, intraoperative navigation and imaging during surgery may gradually replace quite a part of human surgical skills. Neurosurgeon's competency may decline, because less and less experiences can be accumulated due to advanced technology. All neurosurgical procedures will go through a vigorous randomized clinical trial in future, which provides clinical evidence of benefits. For instance, extracranial-intracranial bypass surgery failed to prove its impact in stroke prevention [50]. Today, emerging evidences support the application of detachable coils embolization to treat cerebral aneurysm rather than open microsurgery [51]. Similarly, carotid stent placement is more popular than endarterectomy in our daily clinical practice [52]. Neurosurgical repertoires reduce as ability of neurosurgeon rust away. A second death of neurosurgery will be inevitable if neurosurgeon only rely on machine but not his brain and hand-eye coordination. Neurosurgery and neuroscience are rigorous, complex, and extremely challenging [53]. They are based on large amount of professional knowledge. With the aid of current technological research and development, the evolution of neuroscience will be the cornerstone of neurosurgery, and the boundary between the two will become increasingly blurred. In the future, precision medicine and precise targeting of neural-cancer interactions will be a growing trend to provide new opportunities for neurosurgical and even cancer patients [54].

AUTHOR CONTRIBUTIONS

PCL participated in the study design and wrote the original draft. WMK contributed to the initial concept, in-depth investigation, and supervision. All authors reviewed, edited, and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

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CONFLICT OF INTEREST

The authors declare no conflict of interest. Woon-Man Kung is a member of the Editorial Board of this journal.

DATA AVAILABILITY

The data used to support the findings of this study are included within the article.

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