

Future Directions in Neurosurgery

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Abstract: The neurosurgical field is changing swiftly. In the last 100 years, neurosurgery has achieved success and access that was beyond the imagination of a nineteenth-century surgeon. What is science-fiction now will be fact tomorrow. Open microsurgery has transformed and is transforming into endoscopic/minimally invasive neurosurgery, which is now, in many cases, aided by robotically assisted surgery. In the near future, neurological and neurosurgical diseases will probably be treated by “biological manipulation”. Many researches are defining the future directions of neurosurgery. In this chapter, we will touch on future directions in neurosurgery, i.e., robotics in neurosurgery, neuro stem cell therapy, hydrocephalus research, gene therapy in neurological diseases, and drug addiction surgery.

Abbreviations

ROSA	robotic operating surgical assistant	TBI	traumatic brain injury
MSC	mesenchymal stem cells	NSC	neural stem cells
MAPC	multipotent adult progenitor cells	EPC	endothelial progenitor cells
GBM	glioblastoma multiforme	RNA	ribonucleic acid
GABA	glutamic acid decarboxylase	STN	subthalamic nucleus
ADDC	aromatic amino acid decarboxylase	PD	Parkinson disease
BDNF	brain-derived neurotrophic factor	FGF	fibroblast growth factor
NAC	nucleus accumbens	DBS	deep brain stimulation
CSF	cerebrospinal fluid	NKCC	Na ⁺ /K ⁺ /2Cl ⁻ cotransporter
VP	Ventriculoperitoneal	ETV	endoscopic third ventriculostomy
CPC	choroid plexus cauterization		

1. Introduction

The neurosurgical field and practice are changing very rapidly. In the last 100 years, neurosurgery has achieved success and access that was beyond the imagination of a nineteenth-century surgeon. What is science-fiction now will be real tomorrow. Open mechanical microsurgery has converted and is converting to endoscopic/minimally invasive neurosurgery, which is now, in many instances, aided by robotically assisted surgery. In the near future, neurological and neurosurgical diseases will likely to be treated by “biological manipulation”. Many researches are defining the future directions of neurosurgery.

2. Robotics in Neurosurgery

2.1. Introduction

Robotic surgery is not as prevalent in neurosurgery compared to other field of surgery like gastroenterology, cardiology, and urology. This is mainly because of anatomical challenges in the complexity of very sensitive brain structures (Gui et al. 2015). “Heartthrob” was the world’s first surgical robot, and it was initially utilized in Vancouver, British Columbia, Canada, in 1983. The MKM system, released by Zeiss in 1993, was the first neurosurgery robotic microscope; a robot arm held various instruments, including a microscope head, in the system (Roser et al. 2013; Haegelen et al. 2010).

The first neurosurgical robot commercially available was NeuroMate, which was approved by the FDA. At its most basic level, the neurosurgical robot is made up of the following parts: a robotic arm, controllers that guide the robot (end-effector), feedback sensors, a wireless localization system, and a data processing center (the brain).

Robots can be wholly autonomous, completely reliant, or a hybrid of both autonomous and controlled systems. The most commonly available neuro-robots these days are Neuromate, NeuroArm, SpineAssist, and the Pathfinder (Fomekong et al. 2017; Pak et al. 2015).

2.2. Types of Neuro-Robots

Neurosurgical robots are grossly classified into three categories:

1. Telesurgical robots (master-slave), in which the surgeon remotely controls the activities of the robot.

2. The supervisory surgeon-controlled robot, where the robot assists the surgeon to perform precise tasks.
3. Hand-controlled systems, where the surgeon and the robot both control the instruments utilized to handle and dissect the brain tissue.

2.3. Advantages of Neuro-Robotics

Robotics provides different advantages in surgical tasks (Fomekong et al. 2017; Pak et al. 2015; Kapoor and Rath 2016):

- Helping to improve stereotaxic neurosurgery precision and accuracy;
- In minimally invasive surgery, access to narrow passageways;
- In image-guided surgery, the capability to process enormous amounts of data;
- By stabilizing a surgeon's hand or scaling the surgeon's hand motions;
- The capacity to perform telesurgery, provide a 10-fold reduction in surgeons' physiological tremor, and eliminate surgeons' fatigue.

As compared to modern surgical procedures, robotic surgery provides improved visualization, minimal blood loss, very minimal scarring, a decreased infection rate, less pain, a reduced hospital stay, and early immobilization.

2.3.1. Disadvantages

Despite its many advantages, high costs, the need for high expertise, complicated technical procedure, and time-consuming processes make robotics impractical for many neurosurgeons. At present, robots are utilized primarily as stands, freeing up a neurosurgeon's hand and decreasing muscle fatigue (Vougioukas et al. 2003).

2.4. Applications in Neurosurgery

Common robotic procedures in neurosurgery include stereotaxic procedures, endoscopic procedures, applications in robotized microscopes, telepresence, and tumor resection (Chauvet et al. 2017; Tsai et al. 2002).

2.4.1. In Hematoma Evacuation

Robots in neurosurgery assist in stereotactic procedures as well as endoscopic interventions. Hematoma removal with a hand-held endoscope and with robotic endoscopic evacuation has been studied. The findings imply that robotic assistance, at the cost of a somewhat longer procedure time, increases the safety of the target volume excision by increasing the surgeon's solace and dexterity (Kulkarni et al. 2016; Hoshide et al. 2017).

2.4.2. In Functional Neurosurgery

ROSA (robotic operating surgical assistant) Brain, a robotic tool, helps to perform minimally invasive procedures in the brain. The targets can be on the surface or deep within the brain. ROSA can perform many procedures in the brain, including putting an electrode in an epileptic focus for the treatment of epilepsy, which helps in performing biopsies of brain tumors and cortical dysplasia. It also helps in laser ablation in the treatment of hypothalamic hamartoma and in putting electrodes deep inside the brain for movement disorders as a part of deep brain stimulation. Functional procedures are also performed in the spinal cord. ROSA has also proven beneficial in performing stereotaxic biopsies of pontine glioma, with no surgical complications. ETV procedures for pediatric hydrocephalous have been successfully performed, with no complications (Miller et al. 2017; Carai et al. 2017; De Benedictis et al. 2017; Marcus et al. 2015; Hong et al. 2013).

2.4.3. In Spinal Surgery

Spinal robots help not only in the accuracy of the interventions but also by adding the additional benefits of other factors like radiation dosage, minimal invasiveness, and learning curves. Spine surgeries have been successfully performed without complications. In minimally invasive surgeries, robot-assisted transpedicular screw placement in spinal fixation has been performed without any screw misplacements. Roser et al. found that the ideal accuracy with a pure intrapedicular trajectory was 92% in a set of 46 patients with 244 robotic-assisted pedicle screws, with 5.3% of the screws showing a lateral deviation and 2.5% showing a medial deviation. A surgical revision was performed on the patients who had medial screw abnormalities. A total of 65% (30–46) of

these patients received intervention using a minimally invasive pure percutaneous technique (Fiani et al. 2017; Ettore et al. 2016).

2.5. Conclusions

Although the utilization of robotics in neurosurgery is still in its early stages, we feel that the few neurosurgical robots now in use in operating rooms have already demonstrated high potential for improving surgical results, particularly when precision and low invasiveness are required.

3. Neuro Stem Cell Therapy

3.1. Introduction

Stem cells are pluripotent cells with the ability to divide into a variety of cell types within the body. The divided stem cells have the capability to remain as stem cells or transform into a different type of cell with a more specialized purpose. They have unique characteristics in that they lack tissue-specific features that would enable them to conduct specialized functional activities. These unspecialized stem cells can differentiate into specialized cells such as blood cells, heart muscle cells, and brain cells. They also have the capability to divide and regenerate for long periods of time, as well as replicate multiple times (Lee 2003; Horita et al. 2006). Stem cells for transplantation can be autologous (person's own cells) or allogenic (from donor). Pre-implantation embryos, aborted fetuses, children, adults, embryos, umbilical cord, amniotic fluid, menstrual blood, and the placenta are all possible sources of stem cells.

Pluripotent stem cells can be used to treat a variety of diseases, pathological conditions, and disabilities, including stroke, Parkinson's and Alzheimer's diseases, cerebral palsy spinal cord injury, Batten's disease (a pediatric lysosomal storage disease that causes neuronal loss), chronic pain, epilepsy, amyotrophic lateral sclerosis, vision restoration, and many other neurodegenerative diseases (Horie et al. 2011; Ourednik et al. 2000).

Embryonic stem cells, e.g., human embryonic cells or mouse-derived cells are derived from the inner cell mass of the embryonic blastula. The main drawback of embryonic cell transplantation is the development of teratomas. Adult stem cells could be a source of autologous cells for transplantation, removing immunological risks. A notable example of this is bone marrow transplantation. When implanted into irradiated recipients, bone-marrow-derived hematopoietic or mesenchymal stem cells can move into the brain and develop into astrocytes, microglia, and possibly neurons.

3.2. Applications in Neurosurgery

3.2.1. Spinal Cord Injury

Stem cells in spinal cord injury not only take part in neuron replacement but also foster functional recovery. They influence the post-traumatic cord milieu by secreting a collection of bioactive chemicals that decrease local immune responses, increase angiogenesis, and inhibit scarring and cell death in a paracrine and autocrine manner. They are also in charge of axon remyelination, sprouting, and directing them to their destinations, as well as the development of functional bridges. Possible mechanisms through which stem cells work and their modes of action have been summarized in Table 1 below.

Direct injection to the wounded location, Subarachnoid Stem Cell Implantation by intra-arterial, Lumber Puncture, and intravenous injections are all options for stem cell delivery. Intranasal (i.n.) administration of stem cells after stem cell implantation using brain stereotactic surgery is another option. The best sort of cells to choose for implantation, their dosage, the best delivery route, and the optimal timing for therapy are all important variables to specify in this discipline. Mesenchymal stem cells from adipose tissue and bone marrow, hematopoietic stem cells, olfactory ensheathing, embryonic cord blood stem cells, and neural precursor cells have all been used to treat spinal cord injuries (Iwanami et al. 2005).

Logistics and ethical issues, the utilization of allogeneic cells demanding immunosuppressive therapy, and the possible tumorigenicity of transplanted cells are some of the disadvantages of using neural stem cells. Autologous cells should be used in cellular treatment if they can be easily obtained, processed in vitro, and reinoculated into the same patient. Stem cells have also found potential in the treatment of spinal and cranial bony defects, as well as intervertebral disc degeneration. Careful selection of patients with spinal cord injuries is necessary for the transplantation of neural stem cells, which have the ability to replace lost tissue after nervous system injury.

Table 1. Mechanism of functional recovery in spinal cord injury.

Events	Consequences	Mechanism
After spinal cord injury	Parenchymal damage	Inflammation-induced stimulation of host plastic reactions
	Interference	With autologous neural activity
After neuro stem cell therapy	Make up of biochemical deficiency	Missing transmitter discharge ('minipump')
	Growth factor release	Initiation of plastic responses; improvement in survival and activity of host neurons
	Local reinnervation	Re-establishment of synaptic neurotransmitter release
	Reformation of neural circuitries	Reconstruction of functional efferent and afferent connections

Source: Authors' compilation based on data from Iwanami et al. (2005).

3.2.2. In Peripheral Nerve Injury

The peripheral neural system has a stronger capacity for regeneration than the CNS. Embryonic neural stem cells, adipose tissue, bone marrow cells, and the skin and its accompanying structures are all possible sources for peripheral nerve repair. Stem cell therapy's therapeutic potential for damaged peripheral nerves is unclear. According to some evidence, transplanted, neutrally generated embryonic stem cells develop into myelin-forming cells, suggesting that they could be used to treat severely wounded peripheral nerves. The implantation of embryonic stem cells potentiates nerve repair in peripheral nerves (Walsh and Midha 2009).

3.2.3. In Degenerative Intervertebral DISC

Mesenchymal stem cells have been used to try to repair or regenerate the degenerated intervertebral disc. Stem cells have the ability to develop into nucleus-pulposus-like cells capable of producing the physiological, proteoglycan-rich extracellular matrix found in healthy intervertebral discs (Lee 2003).

3.2.4. Traumatic Brain Injury (TBI)

TBIs include concussion, contusions, diffuse axonal injury, and penetrating injury. In all types of TBI, brain cell death occurs when brain tissues are damaged or when blood supply to crucial parts of the brain is disrupted. When neurons die, they are incapable of regenerating or growing, and the sections of the body that they control become disabled. Exogenous stem cells have been found to move to damaged brain tissue and then assist in brain parenchyma repair by further differentiation into substitute damaged cells while producing anti-inflammatory and growth factors, leading to considerable enhancements in neurological function. In recent studies, a variety of stem cells, including neural stem cells (NSCs), mesenchymal stem cells (MSCs), multipotent adult progenitor cells (MAPCs), and endothelial progenitor cells (EPCs), have been discovered to heal neurological damage following a TBI (Boockvar et al. 2005).

The utility of SB623 bone-marrow-derived modified stem cells has showed promise in neuro-regeneration and repair, as well as preserving functional recovery after various forms of injuries. Twenty-eight endothelial progenitor cells are migratory precursor cells that can convert into vascular endothelial cells and contribute to endothelial healing, particularly in the brain following trauma. Mesenchymal cells, the neuroectoderm, the visceral mesoderm, and the endoderm can all be differentiated from multipotent adult progenitor cells. This has the potential to improve information retention, spatial learning, memory retrieval, and dyskinesia following delayed brain injury as well as maintain the blood-brain barrier's integrity during the acute phase of TBI. Neurons, glial cells, and oligodendrocytes can all be formed from neural stem cells. It could be a long-term treatment for neurological recovery following brain damage (Boockvar et al. 2005; Burns et al. 2009).

3.3. Conclusions

Stem cell transplantation appears to be a viable therapeutic option for patients suffering from a variety of neurosurgical illnesses. The expectation that stem-cell-based therapies can restore and sustain function in the spinal cord and brain has been bolstered by recent developments and progress.

4. Gene Therapy in Neurosurgery

4.1. Introduction

Gene therapy is the transfer of nucleic acid as genetic material into somatic cells to provide a therapeutic effect. Gene transfer into the human body can be performed by *ex vivo* and *in vivo* approaches. *Ex vivo* approaches include the process of cell isolation from the patient and genetic modification exterior to the body in a cultivated area and then re-implantation into the patient, while *in vivo* gene transfer includes transferring a gene by a vector into the subject as a direct target cell transducer. For *in vivo* gene transfer, issues like the selection of appropriate vectors to carry the genetic load, the efficacy of distribution and targeting, the capacity to regulate gene function or expression *in vivo*, and safety concerns, especially when viruses are used as vectors, should be addressed (Weihl et al. 1999; Ourednik et al. 2000).

Germ line gene therapy and somatic gene therapy are the two types of gene therapy that can be used. In somatic gene therapy, therapeutic genes are deployed into a patient's somatic cells, or body. Any changes and effects will be limited to one patient only, and it will not be passed along to the patient's children or future generations. In germ line gene therapy, however, sperm or ovum are transformed through the implantation of functional genes into their genomes. This would make the therapy heritable, allowing it to be handed down to future generations (Chiocca 2003; Helm et al. 2000). Most brain tumors are treated with viral gene transfer as viral vectors are increasingly safe and non-immunogenic. While non-viral vectors are less efficient, they are safer, can be produced more easily, and offer reduced pathogenicity. The issue with non-viral vectors is that they link to blood cells or plasma proteins, causing aggregation and capillary blockage. Recombinant herpes simplex virus, retroviruses/lentiviruses, adeno-associated viruses, and adenoviruses are examples of viral vectors. Cationic polymers and cationic lipids are non-viral delivery techniques whose efficacy is determined by saturation, cationic charge, and linker stability.

The main drawback of gene therapy is that the vector cannot cross the blood-brain barrier. Another problem is that it causes immune-mediated vector toxicity. That is why the delivery of a vector into the brain is achieved by stereotactic inoculation of the vector into the wall of the tumor cavity, direct intrathecal or intraventricular administration, and intravascular application by disruption of the blood-brain barrier using an intracarotid infusion of vasoactive compounds and hyperosmolar solutions (Freese et al. 1997; Alden et al. 1999).

4.2. Applications in Neurosurgery

Some of the conditions of the brain treated with gene therapy include Parkinson disease, Alzheimer's disease, ischemic brain diseases, brain tumors, epilepsy, lysosomal storage disease, amyotrophic lateral sclerosis, motor neuron disease, and Huntington's disease.

4.2.1. For Glioblastoma Multiforme

Gene therapy for brain tumors is used especially for glioma. Among gliomas, most studies on gene therapy strategy have been trialed on glioblastoma multiforme, due to its very low survival rate, inaccessibility to respective surgery due to the anatomical site of the tumor, and infiltration from tumor cells into nearby tissues. A combination of thymidine kinase and ganciclovir, called "suicide" gene therapy, has been studied for GBM. The non-toxic prodrug is transformed into a toxic compound that kills tumor cells in transduced cells. The *Escherichia coli* cytosine deaminase/5-fluorocytosin system, the rat cytochrome P450 2B1/cyclophosphamide system, and the *Escherichia coli* reductase/CB1954 system have all been employed for gene therapies in experimental animal models for the management of gliomas (Weihl et al. 1999; Ourednik et al. 2000; Helm et al. 2000). Other gene therapy strategies include tumor suppressor genes (such as p53, Fas, ras, TNF- α , and caspases); augmentation of extracellular matrix protein expression; inhibition of angiogenesis; immune system modulation; oncolytic virus eradication; and the utilization of ribozymes, small interfering RNA, and antisense oligonucleotides to induce apoptosis in tumor cells.

4.2.2. For Parkinson's Disease (PD)

Two gene therapy clinical studies for Parkinson's disease are currently underway. One method is to use glutamic acid decarboxylase gene transfer and subsequent GABA synthesis in the subthalamic nucleus (STN). The other employs an ADDC intrastriatal gene transfer strategy (aromatic amino acid decarboxylase) (Chiocca 2003; Freese et al. 1997; Alden et al. 1999). The newer therapy with gene transfer for the treatment of various brain conditions has gained new popularity after the rapid progress of viral and non-viral vector systems as an alternative to existing pharmacological treatments. Both vector systems, however, have advantages and limitations, thus the search for the optimum one continues. When medicine fails to control PD symptoms, gene therapy is a better option than DBS or subthalamotomy.

4.2.3. For Epilepsy

Gene therapy has been attempted for focal seizures like temporal-lobe-originated seizures, which are medically refractive. It has anti-epileptogenic, antiseizure, and disease-modifying properties. Gene therapy produces a combination therapy based on the replenishment of fibroblast growth factor 2 (FGF-2) and brain-derived neurotrophic factor (BDNF) to counteract epilepsy (Chiocca 2003; Helm et al. 2000).

4.3. Conclusions

The role of gene therapy in many of brain diseases is very promising. However, more preclinical and clinical research is needed in this field to fully understand the potential side effects and develop truly effective treatments for neurological illnesses.

5. Drug Addiction Surgery

5.1. Introduction

Neurosurgery for addiction is not a futuristic concept. On the contrary, neurosurgery to treat addiction to heroine, alcohol, methamphetamine is happening now in many parts of world. In fact, DBS is the preferred method of treatment for this purpose and is well known for its management of Parkinson's symptoms that cannot be treated with medications. It is considered a last-resort therapy if traditional treatment, such as medication to lessen drug cravings, has failed (Li et al. 2013; Lu et al. 2009; Voges et al. 2013).

5.2. Application

When there is substantial relapse frequency after conservative therapy and the negative effects of persistent alcohol consumption on the mental, physical, and social life of these people persist, deep brain stimulation may be considered. Its exact mechanism is unknown, although it is considered to work by modifying the reward circuit, which is dependent on a chemical messenger called dopamine. Dopamine elevations in the nucleus accumbens (NAc) caused by drugs facilitate reward. The medial forebrain bundle, which links the ventral tegmental region and hypothalamus with the olfactory tubercle, and the NAc make up the reward circuit (Gao et al. 2003; Lamphier 1957; Luigjes et al. 2013). The nucleus accumbens, which is often called the "pleasure center" of the brain, is the main nucleus of the brain's reward circuit, where deep brain stimulation electrodes are placed. The neurotransmitter dopamine stimulates cells of the NAc, which elicit pleasurable sensations after taking heroin, etc. An electrical current is transmitted through the electrodes that destroys the cells of the NAc. By destroying the pleasure center, it is easy to get rid of addictions. Surgery is performed in an awake condition where the patient talks during the procedure, so that surgeons know if the electrodes are too close to actual sites that control various functions.

Resetting of the NAc function, according to evidence, can significantly enhance addictive behavior. However, the findings of DBS in clinical trials are still quite preliminary. As a result, the initial priority of future activities should be to confirm the seen improvement in prospective studies employing DBS stimulation procedures that are randomized, double-blind, or crossover. These studies are restricted by small patient numbers, unpredictable long-term follow-up, probable publication bias, and a lack of blinded stimulation, despite their encouraging results (Pelloux and Baunez 2013; Wang et al. 2018).

5.3. Conclusions

Neurosurgeons have worked hard to develop procedures that are both successful and safe for treating addiction. The surgical management of addiction will continue to pursue a safer and more standardized path as technical approaches and the realization of neurophysiology increase, and as the aggregation of high-level clinical trial data occurs.

6. Hydrocephalus Research

6.1. Introduction

Much of the research focuses on finding better ways to prevent, treat, and ultimately cure hydrocephalus. For many, the future is bright if hydrocephalus is detected early and treated appropriately. Recent research has advanced our understanding and brought us closer to a cure. Technological advancements, as well as improved diagnosis and treatment regimens, are allowing an increasing number of persons with hydrocephalus to live full and active lives. There is currently no effective medical treatment for hydrocephalus. Neurosurgical treatment is the primary choice for accurate management at present.

6.2. Medical Research

The choroid plexus produces nearly half of all cerebrospinal fluid (CSF), according to new research. The $\text{Na}^+/\text{K}^+/\text{2Cl}^-$ cotransporter, or NKCC1, is a protein found in the choroid plexus that is responsible for the majority of CSF production. CSF is primarily created by a process known as osmosis, in which water passively accompanies the movement of salts. However, current studies suggest that KCC1 creates cerebrospinal fluid by moving ions across choroid plexus cell membranes while also conveying water via a mechanism built into this unique protein. Because the fluid conveys both salts and water at the same time, this action is known as “cotransport” of water. This finding is particularly significant because, for a long time, people believed that cerebrospinal fluid was produced by a process called osmosis.

Bumetanide, a well-known diuretic medicine that inhibits NKCC1, could eventually lead to novel nonsurgical hydrocephalus treatments, which would be a huge step forward for patients (Steffensen et al. 2018).

TGF-1 (transforming growth factor-1) and VEGF (vascular endothelial growth factor) are two biomarkers found in high concentration in CSF that govern cell differentiation, proliferation, and other important biological activities. TGF-1 has been demonstrated in studies to be released into CSF following an intraventricular hemorrhage and to upregulate genes involved in the formation of extracellular matrix proteins (e.g., fibronectin and collagen). By focusing on pathways that affect the hydrocephalic brain, researchers revealed that certain medical therapies can reduce the rate at which hydrocephalus develops in animal models. Decorin, a growth factor antagonist, has been shown in an animal model to be effective in preventing the development of juvenile communicative hydrocephalus (Merhar 2012; Botfield et al. 2013).

6.3. Surgical Research

The current surgical treatments used are mainly ventriculoperitoneal shunt, endoscopic third ventriculostomy, and combined endoscopic third ventriculostomy (ETV) and choroid plexus cauterization (CPC). Ventriculoperitoneal shunt is the commonly performed procedure for hydrocephalus. The only advances in VP shunt treatment to date include the development of newer types of shunt valves to prevent the complications of over-drainage. Some of the valves available are antisiphon devices, siphon control devices, delta valves, and Orbis-Sigma valves. Hydrocephalus programmable valves are devices that have several differential pressure valves, all of which are differential pressure valves. It is still unclear how much these new advanced technological devices have contributed to patient therapy (Rekate 1997). The use of combination ETV and CPC for hydrocephalus management is also gaining popularity. In research in East Africa, ETV/CPC treatments were shown to be safer, with minimal mortality and morbidity; infection and long-term ETV/CPC failure rates were lower than shunts, along with success rates ranging from 62–82% (Warf et al. 2012).

Researchers have also worked on new protocols to minimize postoperative shunt infections as this is vital in controlling the morbidity and mortality of patients, even though the old protocols to minimize infections are also followed these days. In pediatric neurosurgery, the utilization of standardized protocols to minimize infection is not recent. To prevent infections, a series of steps are taken in the preoperative, peroperative, and postoperative

periods, including using a no-touch technique protocol in which the neurosurgeons' hands do not touch the shunt equipment, limiting implant and skin-edge manipulation, and using educated assistants; the operative field has two drapes, neurosurgeons wear double gloves, meticulous surgical techniques are used, antibiotic prophylaxis is initiated, and total shunt revision occurs. Researchers have found that silver or antibiotic-impregnated catheters have the capability to decrease shunt infections and reduce the necessity for shunt replacement. Initial outcomes are promising and a 63% decrease in the relative risk of infections related to shunts for pediatric patients has been demonstrated (Parker et al. 2015; Jenkinson et al. 2014). Even after sticking to a strict protocol to prevent shunt infections, following modern medical and surgical management of hydrocephalus, the results are not promising. Still more research is needed for better results and outcomes.

6.4. Conclusions

Research in the field of the overall management of hydrocephalus patients is promising. More research is needed to better understand the genetics of hydrocephalus, develop models to better understand the condition, employ multidisciplinary opportunities and standardized protocols, emphasize novel bioengineering concepts, improve surgical trials, and produce validated outcome metrics.

7. Culminating Remark

At the conclusion of this chapter, we can say that what we cannot dream of today could become fact in the near future. Investigation and research in neurosurgery and other branches of medicine are growing so fast that it is even possible that the scalpel will no longer be required for treating nervous system diseases in the near future (bad news for neurosurgeons)!

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References

- Alden, Tord D., Debra D. Pittman, Elisa J. Beres, Gerald R. Hankins, David F. Kallmes, Benjamin M. Wisotsky, Kelvin M. Kerns, and Gregory A. Helm. 1999. Percutaneous spinal fusion using bone morphogenetic protein-2 gene therapy. *Journal of Neurosurgery: Spine* 90: 109–14. [CrossRef] [PubMed]
- Boockvar, John A., Joost Schouten, Nicolas Royo, Marie Millard, Zak Spangler, Debbie Castelbuono, Evan Snyder, Donald O'Rourke, and Tracy McIntosh. 2005. Experimental traumatic brain injury modulates the survival, migration, and terminal phenotype of transplanted epidermal growth factor receptor-activated neural stem cells. *Neurosurgery* 56: 163–71. [CrossRef] [PubMed]
- Botfield, Hannah, Ana Maria Gonzalez, Osama Abdullah, Anders Dæhli Skjolding, Martin Berry, James Pat McAllister, and Ann Logan. 2013. Decorin prevents the development of juvenile communicating hydrocephalus. *Brain* 9: 2842–858. [CrossRef] [PubMed]
- Burns, Terry C., Catherine M. Verfaillie, and Walter C. Low. 2009. Stem cells for ischemic brain injury: A critical review. *Journal of Comparative Neurology* 515: 125–44. [CrossRef]
- Carai, Andrea, Angela Mastronuzzi, Alessandro De Benedictis, Raffaella Messina, Antonella Cacchione, Evelina Miele, Franco Randi, Giacomo Esposito, Andrea Trezza, Giovanna Stefania Colafati, and et al. 2017. Robot-assisted stereotactic biopsy of diffuse intrinsic pontine glioma: A single-center experience. *World Neurosurgery* 101: 584–88. [CrossRef]
- Chauvet, Dorian, Stéphane Hans, Antoine Missistrano, Celeste Rebours, Wissame El Bakkouri, and Guillaume Lot. 2017. Transoral robotic surgery for sellar tumors: First clinical study. *Journal of Neurosurgery* 127: 941–48. [CrossRef]
- Chiocca, E. Antonio. 2003. Gene therapy: A primer for neurosurgeons. *Neurosurgery* 53: 364–73. [CrossRef]
- De Benedictis, Alessandro, Andrea Trezza, Andrea Carai, Elisabetta Genovese, Emidio Procaccini, Raffaella Messina, Franco Randi, Silvia Cossu, Giacomo Esposito, Paolo Palma, and et al. 2017. Robot assisted procedures in pediatric neurosurgery. *Neurosurgical Focus* 42: E7. [CrossRef]
- Ettore, Éric, Emeline Wyckaert, Renaud David, Philippe Robert, Olivier Guérin, and Frédéric Prate. 2016. Robotics and improvement of the quality of geriatric care. *Soins. Gerontologie* 21: 15–17. [CrossRef]

- Fiani, Brian, Syed A. Quadri, Vivek Ramakrishnan, Blake Berman, Yasir Khan, and Javed Siddiqi. 2017. Retrospective review on accuracy: A pilot study of robotically guided thoracolumbar/sacral pedicle screws versus fluoroscopy-guided and computerized tomography stealth-guided screws. *Cureus* 9: e1437. [CrossRef]
- Fomekong, Edward, Salah Edine Safi, and Christian Raftopoulos. 2017. Spine navigation based on 3-dimensional robotic fluoroscopy for accurate percutaneous pedicle screw placement: A prospective study of 66 consecutive cases. *World Neurosurgery* 108: 76–83. [CrossRef] [PubMed]
- Freese, Andrew, Michael G. Kaplitt, William M. O'Connor, Maureen Abbey, David Langer, Paola Leone, Michael J. O'Connor, and Matthew J. During. 1997. Direct Gene Transfer into Human Epileptogenic Hippocampal Tissue with an Adeno-Associated Virus Vector: Implications for a Gene Therapy Approach to Epilepsy. *Epilepsia* 38: 759–66. [CrossRef] [PubMed]
- Gao, Guodong, Xuelian Wang, Shiming He, Weixin Li, Qingfeng Wang, Qinchuan Liang, Yaqun Zhao, Fang Hou, Ling Chen, and Aining Li. 2003. Clinical study for alleviating opiate drug psychological dependence by a method of ablating the nucleus accumbens with stereotactic surgery. *Stereotactic and Functional Neurosurgery* 81: 96–104. [CrossRef]
- Gui, Haijun, Shilei Zhang, Nan Luan, Yanping Lin, Steve G. F. Shen, and Joy S. Bautista. 2015. Novel system for navigation-and robot-assisted craniofacial surgery: Establishment of the principle prototype. *Journal of Craniofacial Surgery* 26: 746–49. [CrossRef]
- Haegelen, Claire, Gustavo Touzet, Nicolas Reyns, Claude-Alain Maurice, Mohamed Ayachi, and Serge Blond. 2010. Stereotactic robot-guided biopsies of brain stem lesions: Experience with 15 cases. *Neurochirurgie* 56: 363–67. [CrossRef]
- Helm, Gregory A., Tord D. Alden, Jason P. Sheehan, and David Kallmes. 2000. Bone morphogenetic proteins and bone morphogenetic protein gene therapy in neurological surgery: A review. *Neurosurgery* 46: 1213–22. [CrossRef] [PubMed]
- Hong, Wei-Chen, Jui-Chang Tsai, Steven D. Chang, and Jonathan M. Sorger. 2013. Robotic skull base surgery via supraorbital keyhole approach: A cadaveric study. *Neurosurgery* 72: 33–38. [CrossRef]
- Horie, Nobutaka, Marta P. Pereira, Kuniyasu Niizuma, Guohua Sun, Hadar Keren-Gill, Angelo Encarnacion, Mehrdad Shamloo, Scott A. Hamilton, Kewen Jiang, Stephen Huhn, and et al. 2011. Transplanted stem cell-secreted vascular endothelial growth factor effects poststroke recovery, inflammation, and vascular repair. *Stem Cells* 29: 274–85. [CrossRef]
- Horita, Yoshifumi, Osamu Honmou, Kuniaki Harada, Kiyohiro Houkin, Hirofumi Hamada, and Jeffery D. Kocsis. 2006. Intravenous administration of glial cell line-derived neurotrophic factor gene-modified human mesenchymal stem cells protects against injury in a cerebral ischemia model in the adult rat. *Journal of Neuroscience Research* 84: 1495–504. [CrossRef]
- Hoshide, Reid, Mark Calayag, Hal Meltzer, Michael L. Levy, and David Gonda. 2017. Robot-assisted endoscopic third ventriculostomy: Institutional experience in 9 patients. *Journal of Neurosurgery: Pediatrics* 20: 125–33. [CrossRef]
- Iwanami, A., S. Kaneko, M. Nakamura, Y. Kanemura, H. Mori, S. Kobayashi, M. Yamasaki, S. Momoshima, H. Ishii, K. Ando, and et al. 2005. Transplantation of human neural stem cells for spinal cord injury in primates. *Journal of Neuroscience Research* 80: 182–90. [CrossRef] [PubMed]
- Jenkinson, Michael D., Carrol Gamble, John C. Hartley, Helen Hickey, Dyfrig Hughes, Michaela Blundell, Michael J. Griffiths, Tom Solomon, and Conor L. Mallucci. 2014. The British Antibiotic and Silver-Impregnated Catheters for ventriculoperitoneal shunts multi-centre randomised controlled trial (the BASICS trial): Study protocol. *Trials* 15: 4. [CrossRef] [PubMed]
- Kapoor, Indu, and Girija P. Rath. 2016. Robotized surgical assistant in neurosurgery. Anaesthetic implication! *Journal of Neuroanaesthesiology and Critical Care* 3: 151–52. [CrossRef]
- Kulkarni, Abhaya V., Jay Riva-Cambrin, Richard Holubkov, Samuel R. Browd, D. Douglas Cochrane, James M. Drake, David D. Limbrick, Curtis J. Rozzelle, Tamara D. Simon, Mandeep S. Tamber, and et al. 2016. Endoscopic third ventriculostomy in children: Prospective TD, multicenter results from the Hydrocephalus Clinical Research Network. *Journal of Neurosurgery: Pediatrics* 18: 423–29. [CrossRef]
- Lamphier, Timothy A. 1957. Drug addiction. *Journal of the American Medical Association* 163: 68. [CrossRef]
- Lee, Il Woo. 2003. Stem cells and neurosurgery. *Journal of Korean Neurosurgical Society* 33: 1.
- Li, Nan, Jing Wang, Xue-lian Wang, Chong-wang Chang, Shun-nan Ge, Li Gao, He-ming Wu, Hai-kang Zhao, Ning Geng, and Guo-dong Gao. 2013. Nucleus accumbens surgery for addiction. *World Neurosurgery* 80: S28.e9–S28.e19. [CrossRef]

- Lu, Lin, Xi Wang, and Thomas R. Kosten. 2009. Stereotactic neurosurgical treatment of drug addiction. *The American Journal of Drug and Alcohol Abuse* 35: 391–93. [CrossRef]
- Luigjes, Judy, Bart P. de Kwaasteniet, Pelle P. de Koning, Marloes S. Oudijn, Pepijn van den Munckhof, P. Richard Schuurman, and Damiaan Denys. 2013. Surgery for psychiatric disorders. *World Neurosurgery* 80: S31.e17–S31.e28. [CrossRef]
- Marcus, Hani J., Archie Hughes-Hallett, Thomas P. Cundy, Guang-Zhong Yang, Ara Darzi, and Dipankar Nandi. 2015. da Vinci robot-assisted keyhole neurosurgery: A cadaver study on feasibility and safety. *Neurosurgical Review* 38: 367–71. [CrossRef]
- Merhar, Stephanie. 2012. Biomarkers in neonatal posthemorrhagic hydrocephalus. *Neonatology* 101: 1–7. [CrossRef]
- Miller, Brandon A., Afshin Salehi, David D. Limbrick, and Matthew D. Smyth. 2017. Applications of a robotic stereotactic arm for pediatric epilepsy and neurooncology surgery. *Journal of Neurosurgery: Pediatrics* 20: 364–70. [CrossRef] [PubMed]
- Ourednik, Vaclav, Jitka Ourednik, Kook I. Park, Y. D. Teng, Karen A. Aboody, Kurtis I. Auguste, Rosanne M. Taylor, Barbara A. Tate, and Evan Y. Snyder. 2000. Neural stem cells are uniquely suited for cell replacement and gene therapy in the CNS. In *Neural Transplantation in Neurodegenerative Disease: Current Status and New Directions: Novartis Foundation Symposium 231*. Edited by Derek J. Chadwick and Jamie A. Goode. Chichester: John Wiley & Sons, Ltd., pp. 242–69. [CrossRef]
- Pak, Nikita, Joshua H. Siegle, Justin P. Kinney, Daniel J. Denman, Timothy J. Blanche, and Edward S. Boyden. 2015. Closed-loop, ultraprecise, automated craniotomies. *Journal of Neurophysiology* 113: 3943–53. [CrossRef] [PubMed]
- Parker, Scott L., Matthew J. McGirt, Jeffrey A. Murphy, J. Thomas Megerian, Michael Stout, and Luella Engelhart. 2015. Comparative effectiveness of antibiotic-impregnated shunt catheters in the treatment of adult and pediatric hydrocephalus: Analysis of 12,589 consecutive cases from 287 US hospital systems. *Journal of Neurosurgery* 122: 443–48. [CrossRef]
- Pelloux, Yann, and Christelle Baunez. 2013. Deep brain stimulation for addiction: Why the subthalamic nucleus should be favored. *Current Opinion in Neurobiology* 23: 713–20. [CrossRef]
- Rekate, Harold L. 1997. Recent advances in the understanding and treatment of hydrocephalus. *Seminars in Pediatric Neurology* 4: 167–78. [CrossRef]
- Roser, Florian, Marcos Tatagiba, and Gottlieb Maier. 2013. Spinal robotics: Current applications and future perspectives. *Neurosurgery* 72: 12–18. [CrossRef]
- Steffensen, Annette B., Eva K. Oernbo, Anca Stoica, Niklas J. Gerkau, Dagne Barbuskaite, Katerina Tritsaridis, Christine R. Rose, and Nanna MacAulay. 2018. Cotransporter-mediated water transport underlying cerebrospinal fluid formation. *Nature Communications* 9: 1–3. [CrossRef] [PubMed]
- Tsai, Eve C., Stephen Santoreneos, and James T. Rutka. 2002. Tumors of the skull base in children: Review of tumor types and management strategies. *Neurosurgical Focus* 12: e1. [CrossRef]
- Voges, Juergen, Ulf Müller, Bernhard Bogerts, Thomas Münte, and Hans-Jochen Heinze. 2013. Deep brain stimulation surgery for alcohol addiction. *World Neurosurgery* 80: S28.e21–S28.e31. [CrossRef]
- Vougioukas, Vassilios I., Ulrich Hubbe, Albrecht Hochmuth, Nils C. Gellrich, and Vera van Velthoven. 2003. Perspectives and limitations of image-guided neurosurgery in pediatric patients. *Child's Nervous System* 19: 783–91. [CrossRef] [PubMed]
- Walsh, Sarah, and Rajiv Midha. 2009. Use of stem cells to augment nerve injury repair. *Neurosurgery* 65: A80–A86. [CrossRef] [PubMed]
- Wang, Tony R., Shayan Moosa, Robert F. Dallapiazza, W. Jeffrey Elias, and Wendy J. Lynch. 2018. Deep brain stimulation for the treatment of drug addiction. *Neurosurgical Focus* 45: E11. [CrossRef] [PubMed]
- Warf, Benjamin C., Sarah Tracy, and John Mugamba. 2012. Long-term outcome for endoscopic third ventriculostomy alone or in combination with choroid plexus cauterization for congenital aqueductal stenosis in African infants. *Journal of Neurosurgery: Pediatrics* 10: 108–11. [CrossRef]
- Weihl, Chris, R. Loch Macdonald, Marcus Stoodley, Jürgen Lüders, and George Lin. 1999. Gene therapy for cerebrovascular disease. *Neurosurgery* 44: 239–52. [CrossRef]

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