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Neuroregenetic Neurosurgery - a possible Subspecialty in Neurosurgery?

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Abstract: Neurosurgery in the past Century has witnessed massive development in terms of technique and specialization. There was a period when the skull was simply opened to remove or correct lesions as a separate ill-defined territory in the Surgical department, now Neurosurgery has moved on to advanced procedures carried out in different sub-specialties, making Neurosurgery one of the most advanced specializations in Medicine.

Neurogenetic Neurosurgery would be a branch of Neurosurgery that specializes in the Surgical treatment of Neurological diseases utilizing genetic manipulations like: stem cell implants and stimulation of differentiation of glial cells to functional Neurons. The need for this special branch arises on the background of current advances in genetics as applied in Neuroscience.

Keywords: Neurosurgery, Neuroregeneration, Neurogenetics, Neurodegenerative diseases, brain injury

1. Introduction

Neurosurgery has come a long way, in a sense, it has been around for millennia. The oldest evidence of purposeful "surgery" on the skull is over 10,000 years old [1]. In fact, we know from the Edwin Smith Papyrus [2] that the Egyptians practiced rather sophisticated neurosurgery 2000 years before the birth of Christ. The 1913 expedition of Dr. Ales Hrdlicka [3] in Peru provided proof of pre-Columbian neurosurgery in the New World. Subsequently, archeologists have found signs of neurosurgery at digs throughout most of the world. [4] Neurosurgery performed during the 19th century was done only as a last resort and most often with disastrous consequences. During the 20th century, however, Neurosurgeons have achieved important improvements to both technique and diagnosis.

Early advances in Neurosurgery, during the first part of the 20th Century, was based on technique, this was followed by technology – methods of detection/diagnosis and the use of advanced technologies in treatment with most attributed to Walter Dandy MD. Although Harvey Cushing is credited as the Father of Modern Neurosurgery due to his firm role in delineating Neurosurgery as a subspecialty in Surgery, Walter Dandy is arguably the one that made Neurosurgery what it is today, of course other Neurosurgeons contributed and are contributing to this ever expanding and advancing Specialty. The interplay between technique and technology saw the development of various subspecialties in the field of Neurosurgery: Trauma, Neuro-oncology, Neurovascular Neurosurgery, Spinal surgery, Functional Neurosurgery and Paediatric Neurosurgery.

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2. History

The quest for understanding and isolating pluripotential stem cells have been on for decades. In 1964, some Researchers isolated a type of cell from a teratocarcinoma, a tumor currently described as being from a germ cell. These cells from the teratocarcinoma were replicated in cell culture as a stem cell and are now known as Embryonal carcinoma cells. [5] Some issues arose due to the fact that these Embryonic Carcinoma cells possessed genetic mutations and abnormal karyotypes that accumulated during the development of the teratocarcinoma. Despite that, it formed the template for early mouse development [6] and emphasized the need to culture pluripotent cells directly from a normal tissue like an embryo.

The first true embryonic stem cells were independently isolated from Mouse embryos by two groups in 1981: Martin Evans and Matthew Kaufman from the Department of Genetics, University of Cambridge, and Gail Martin from the Department of Anatomy, University of California. Martin Evans and Matthew Kaufman published first in July of the same year creating a novel technique in culturing the Mouse embryos to allow for an increase in cell number and derivation of Embryonic Stem cells from these embryos [7]. It was Gail Martin who first coined the term 'Embryonic Stem Cell' [8]. She published in December showing that embryos could be cultured in vitro and that Embryonal Stem Cells could be derived from these embryos.

Human Embryonic stem cells were first derived in 1998 by a team of Researchers at the University of Wisconsin-Madison led by James Thomson. They developed a new technique to isolate and grow human embryonic stem cells in cell culture. [9]

Ethical issues arose about the new technique of isolating Embryonal Stem Cells from human embryos as these embryos would be destroyed in the process. Two groups working independently came up with their methods of dealing with the dilemma. Shinya Yamanaka and his team developed a reprogramming technique that could produce stem cells from adult cells utilizing four factors. His work was done in 2006 but published in 2007. [10] For this, he won the Nobel Prize in Science in 2012 which he shared with John Gurdon of the University of Cambridge. In the same year, 2006, Dr. Robert Lanza, medical director of Advanced Cell Technology in Worcester, MA, and his team came up with a novel approach of deriving Embryonal Stem Cells from human embryos without damaging the Embryo. His work was published in the Nature journal. [11]

Researchers began looking beyond the derivation of stem cells to the application of the technology. On January 23, 2009, Phase I clinical trials for transplantation of oligodendrocytes (a cell type of the brain and spinal cord) derived from human ES cells into spinal cord-injured individuals received approval from the U.S. Food and Drug Administration (FDA), making it the world's first human ES cell human trial. [12] The study leading to this scientific advancement was conducted by Hans Keirstead and colleagues at the University of California, Irvine and supported by Geron Corporation of Menlo Park, CA, founded by Michael D. West, PhD. A previous experiment had shown an improvement in locomotor recovery in spinal cord-injured rats after a 7-day delayed transplantation of human ES cells that had been pushed into an oligodendrocytic lineage. [13] The phase I clinical study was designed to enroll about eight to ten paraplegics who have had their injuries no longer than two weeks before the trial begins, since the cells must be injected before scar tissue is able to form. The researchers emphasized that the injections were not expected to fully cure the patients and restore all mobility. Based on the results of the rodent trials, researchers speculated that restoration of myelin sheathes and an increase in mobility might occur. [14]

Professor Gong Chen and his team utilized a new technique of stimulating differentiation of glial cells to functional neurons in the brain using a factor called NeuroD1 [15] opening doors to potential treatment of deficit from stroke, Alzheimer's disease and other neurological lesions.

3. Discussion

The Theoretical possibilities are immense: treatment of Alzheimer's disease, Cerebral palsy, Amylotrophic lateral sclerosis, neurologic deficit from stroke and other brain injuries… the list continues. Few human trials have been recorded with some being successful. The Safety of this procedure in humans in the long run has been the bane of the limited application in humans, but with increasing evidence of safety in laboratories and the few clinical trials, the future looks promising just as Functional Neurosurgery got approved and has since provided long term treatment for certain neurological lesions.

Different surgical methods of the application of this technique in humans have been proposed and implemented with varying levels of success. The need arises for a special unit in Neurosurgery dedicated to the study of the genetic basis of the current and future genetic technologies and surgical techniques for the implementation in humans in treatment of neurological lesions. I propose Neurogenetic Neurosurgery as the subspecialty to unify all neurosurgical procedures carried out on the basis of genetic technology. I believe it would help fast track the current progress in the translation of the successes recorded in the laboratories to clinical breakthrough in humans, thus providing an alternative treatment to certain neurological diseases.

4. Conclusion

With the advances in genetic technologies and successes recorded in the laboratories and trials, a new specialty in Neurosurgery is in the offing.

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