Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/13445
DOI URL: http://dx.doi.org/10.21474/IJAR01/13445

ISSN NO. 2320-5407

RESEARCH ARTICLE

HEAD TRANSPLANTS: FROM REVERIE TO REALITY

Dr. Mrinalini Mathur[1], Dr. Jitender Kumar Aurora[2] and Dr. Priyatam Mishra[3]

1. Post Graduate Student, Department of Oral and Maxillofacial Surgery, Saraswati Dental College.
2. Professor and Head, Department of Oral and Maxillofacial Surgery,SaraswatiDental College.
3. Post Graduate Student, Department of Oral and Maxillofacial Surgery, Saraswati Dental College.

……………………………………………………………………………………………………....

Manuscript Info

……………………….

Manuscript History
Received: 25 July 2021
Final Accepted: 29 August 2021
Published: September 2021

Key words: -
Human Cephalic Anastomosis, Head Transplant, Project HEAVEN, Sergio Canavero

Abstract

………………………………………………………………….

In the past, head transplantation used to be an imagination mostly narrated in folklore. However, nowadays with the advancement in science it is possible that soon head transplant might be feasible. It promises to be a boon to individuals who suffer from a terminal disease but have a healthy brain. Fear and skepticism over surgical, ethical and psychosocial issues do exist in the community over it but recently, the first cephalosomatic anastomosisperformed in a human model confirms the possibility of such a procedure in near future. What remains unanswered though is the outcome of such a crazy procedure.

……………………………………………………………………………………………………....

Introduction:-

Over the past 150 years, medicine has revolutionised patient care and cure beyond imagination and is continuing its progress to improve the quality of life. The idea of head transplantation (cephalosomatic anastomosis) has long been an attractive fantasy.[1] The history of headtransplant dates back to the early Hindu mythology where the almighty lord Shiva is said to have 'transplanted' an elephant's head on Lord Ganesha, in what is the first recorded instance of a feat that has thus far failed to break out of the realms of science friction.From the myths of such procedure to the current human cadaver trial there has been a major leap in medicine.

History of The Head Anastomosis

One of the unrealized plans of transplantology is a futuristic vision of a head transplant, in patients with progressive genetic, metabolic diseases, and muscular dystrophies.
The first attempt on head transplant started in the beginning of 20th century. Alexis Carrel was one of the pioneers in transplantation due to invention of a modern method of triangular anastomosis, called the 'Carrel maneuver' which enables fast and stable stitching.

He also invented the perfusion pump, which allowed further research on the development of heart-lung machine.[2]
In 1908, Carrel and American physiologist, Dr. Charles Guthrie, performed the first dog head transplantation. They attached one dog's head onto another dog's neck, and while the dog demonstrated aural, visual, and cutaneous reflex movements early after the procedure, its condition soon deteriorated, and it was euthanized after a few hours.[3]

In1954,Demikhovalsoattemptedacanineheadtransplant. Demikhov's dogs demonstrated more functional capacity than Guthrie and Carrel's dogs and were able to move, see, and lap up water.[4]In1970Whiteperformedthefirstcephalicexchangetransplantation in primates.

Corresponding Author:- Dr. Mrinalini Mathur
Address:- Post Graduate Student, Department of Oral and Maxillofacial Surgery, Saraswati Dental College.

He performed four cephalosomatic associations between isolated monkey heads and isolated monkey bodies, employing direct suture of the carotid and jugular veins.

XiaoPing Renin 2015,utilized a method in which only one carotid arteryandthecontralateraljugularveinwerecut,allowing the intact carotid artery and jugular vein to continuously perfuse the donor head throughout the procedure.Over half of his mice survived for periods longer than 24 h, with the longest survival being 6 months.

While White's dog and primate head transplants had demonstrated short-term success, in part due to complications related to clotting, heparinization, and ischemia, Ren's revascularization protocol allowed for longerterm survival in mice.

Starting from 2013, whole world is also observing with simultaneous fright and admiration plans of the project HEAVEN, started by an Italian neurosurgeon Sergio Canavero from Turin Neuromodulation Group, and Chinese transplantation specialist, Xiao Ping Ren.

It has been 7 years since the research project plan has been revealed to the world, and every now and then, new pieces of information have been published on the procedure.

The Proposed Procedure

The head transplant project consists of two procedures: **HEAVEN**- the Head Anastomosis VENture- the transplant procedure of the deceased donor's body to the living recipient's head combined with **GEMINI**-subsequent spinal cord fusion.

Several conditions would qualify for HEAVEN surgery.Whitepointed to tetraplegics, who show a tendency to multi-organ failure. The patient should be someone, probably young, suffering from a condition leaving the brain and mind intact while devastating the body, for instance, but by no means exclusively, progressive muscular dystrophies or even several genetic and metabolic disorders of youth.Donor will be a brain-dead patient, matched for height and build, immunotype and screened for absence of active systemic and brain disorders.[5]

Before profound hypothermia, barbiturate or propofol loading will be carried out in therecipient to obtain burst suppression pattern. Recipient's head will be subjected to profound hypothermia (low temperatures of around 10-14°C), while donor's body will only receive spinal hypothermia; this does not alter body temperature and also avoids any ischemic damage to donor's major organs.

Three surgical phases can be recognized; the anterior and the posterior approach both in the recipient and the donor, and the chimera anastomosis.

Beginning with the anterior approach, both the patients will be positioned supine and the two teams, working in concert, will make deep incisions around each patient's neck, carefully separating all the anatomical structures (at C5/6 level forward below the cricoid) to expose the carotid and vertebral arteries, jugular veins and spine. All muscles in both recipient and donor would be color-coded with markers to facilitate later linkage. Besides the axial incisions, three other cuts are envisioned, both for later spinal stabilization and access to the carotids, trachea and esophagus. Two along the anterior margin of the sternocleidomastoids plus one standard midline cervical incision. The recurrent laryngeal nerves will be recognized and preserved intact.

In the posterior approach both the donor and recipient will be placed in the prone position, the laminectomies will be performed, the vertebral bodies or the intervertebral spaces transected, and the dura will be cut to expose the spinal cord. Under the operating microscope, the cords in both subjects will be cut clean simultaneously as the last step before separation.

Once recipient's head is separated, it will be transferred onto donor's body to the tubes that would connect it to donor's circulation, whose head had been removed. The two cord stumps will be accosted, length-adjusted and fused within 1-2 minutes.

A chitosan-polyethylene glycol glue(fusogens),will affect the fusion.The vascular anastomosis for the cephalosomatic preparation will be easily accomplished by employing the carotid and jugular silastic loop cannula.

Subsequently, the vessel tubes will be removed one by one, and the surgeons will sew the arteries and veins of the transplanted head together with those of the new body.Upon linkage, donor's flow will immediately start to rewarm recipient's head. The dura will be sewn and a spinal cord stimulator will be secured to the dura. Trachea, esophagus, vagus and phrenic nerves will be reconnected. Finally, all the muscles will be linked and the skin will be sewn.[6]

Recipientwill then be transferred to the intensive care unitwhere he/she will be kept sedated for 3 days, with a cervical collar in place. Appropriate physiotherapy will be instituted during follow-up until maximal recovery is achieved.

Keys to Success

Profound - Hypothermia

During Cephalosomatic Anastomosis (CSA),the brain of the recipient will be detached from its vascular supply for a limited time before being positioned to allow revascularization by the blood supply of the donor body.The brain needs to be protected during this ischemic period (i.e., time of transfer and time of revascularization, total time about 30 minutes) to avoid massive stroke and death.

The relationship between brain temperature, cerebral metabolic rate, and blood flow is well established.A drop of 18°C in body temperature decreases cerebral metabolic rate by about 6–7%.In the absence of cerebral blood flow, hypothermia decreases oxygen demand, preserves energy stores, and prevents lactate production and the development of acidosis by decreasing metabolic rate and stimulating brain utilization of glucose.

One of the several techniques to obtain deep hypothermia is autocerebral hypothermic perfusion. In this approach, the leftfemoral artery and both common carotid arteriesare cannulated with small metal cannulas connected to each other via a high-efficiency heat exchanger.

Fluids of varying temperatures are circulated into the external cylinder chamber that surrounds the tube containing the perfusing blood. In <1 hour, the intracerebral temperature of 11.4°C can be achieved.[7]

Spinal Cord Anastomosis

Fusogens and sealants are substances that can reconstitute theintegrity of the neural membranes and restore electrophysiologic conduction acutely when applied shortly after damage or severance ofneuronal bodies and branches. The most widelystudied fusogens are polyethylene glycol (PEG)and chitosan.

Time plays a very important role here as the ends of the transected spinal axons remain stable for only about 10-20 minutes before they undergo fragmentation at both the cut ends. Thus, the fusogens must be brought to the site of anastomosis within less than 10 minutes. A final step in ensuring a rapid spinal cord fusion is electrical stimulation which has experimentally been found to accelerate nerve growth.

In GEMINI,there will be no gap, and as a result, after sharp severance and application of PEG with electrophysiologictransmission within days to weeks will lead to excellent behavioral recovery.[8]

Axon Nanoknife

Nanoknives are simple microfabricated devices that cut, electrostatically translocate, and splice together individual axons.

They consist of a thin layer of silicon nitride with a nanometer sharp cutting edge.

By using the nanoknife mounted on a micromanipulator in conjunction with a simple, custom-assembled micro-platform to hold and isolate an individual nerve, it is possible to precisely manipulate this surgical microdevice in the operating field and tomake targeted, effective cuts in the nerve while simultaneously monitoring the entire process visually. This leaves minimum gap in between the transected nerves which gets easily sealed by fusogens thus ensuring early return to nerve conduction.[9]

Immunosuppressants

Sirolimus, with its minimal neurotoxicity and pro-neuroregenerative properties is especially indicated in HEAVEN to decrease the chances of rejection. However long- term administration of these medications results in significant morbidity and mortality, including nephrotoxicity, infections, neoplasm, and cardiovascular diseases. Equally important, chronic rejection (graft-versus-host-disease [GVHD]) is not prevented, even with maximal immunosuppression. Therefore, induction of allograft tolerance-so that no drug is required- is a sine-qua-non.[10]

Preoperative Training in Virtual Reality

Once the recipient is able to perform movements in the transplanted body, there is the possibility of being psychologically overwhelmed by the sense of bodily freedom. This might trigger hypomania, that can transit into depression, mania, psychosis and symptoms such as detachment from one’s sense of self and experiencing objects, people, and/or surroundings as unreal.

These psychological conditions can potentially influence the recipient into making decisions that are harmful to their well-being. Replicating natural body movements through VR experiences will serve as training against unexpected psychological reactions. Commercially available immersive VR hardware such as HTC's Vive®and Oculus' Rift®facilitate interactivity by immersing the user in a three-dimensional, computer-generated world enabling them to naturally interact with virtual objects.

These technologies allow the user to experience the virtual world through the first-person viewpoint of the avatar that represents them in VR. Interaction with objects in VR is a multisensory experience in which augmented feedback (visual, auditory, proprioceptive, etc.) is experienced by the user enabling a sense of realism. For the recipient of HEAVEN, VR is an essential tool for improving motivation, alleviating stress, and distracting from pain. These effects will result in more time spent performing rehabilitation activities, which would increase the preparedness of the recipient for life in a new body.[11]

First Cephalosomatic Anastomosis in A Human Model

Full rehersal of a cephalosomatic anastomosis on a two recently deceased human cadavers was performed at Harbin Medical University, Harbin, China by Ren et al.The surgery took 18 hours to completebeginning from first skin incision in both donor and recipient to final skin closure in the chimera. This rehersal confirmed the surgical feasibility of human CSA and further validated the surgical plan.

Several advances resulted from this rehersal, including optimization of the surgical steps, sparing of the phrenic and recurrent laryngeal nerves for phonetics and assessment of vertebral stabilization.

Even though Sergio Canavero had claimed that he would have performed a head transplant by 2017; this procedure has not yet been performed on a living human till now.

Obstacles In the Way

Postoperative Complications

Long term ventilatory and circulatory support, neurogenic shock, paralytic ileus, neurogenic bladder, infections,vocal cord dysfunction and pain are the major issues that need to be dealt with postoperatively. The head and spinal column needs to be kept stable at all times to ensure spinal cord fusion. After the initial phase, spinal cord injury rehabilitation protocol and intensive rehabilitation for quadriplegia should be started.[6]

Psychosocial Considerations

Head transplant may create confusion about the relationship between body and identity.

Firstly, the percentage of the body that is now from "another"creates a scale of adaptation not previously encountered. Consequently, patients may thinkdifferently about receiving a full body than patients getting individual body parts.

Forexample, previous actions by "the body," such as having committed a crime or terminated apregnancy, or getting body art, may lead to questions concerning the level of responsibilityand ownership a person may feel for the actions of a body that previously was not their own.

Secondly,it is reasonable to assume that the probability of death due tocatastrophic failure is high. Patients and their family will require psychological preparationfor the possibility of not surviving the surgery.

Thirdly, surviving recipients without successful spinal cord reconnection will face a comprehensive quality of life and psychological well-being problems.

It is likely thatinitial candidates will already be more than quadriplegic.Patients who survive will express relief that their life-threatening illness has ended; however, in time they may experience the psychosocial consequences, such as low quality of life and depression, that quadriplegia poses.[12]

Ethics

From the historic axiom of bioethics, 'first do no harm' the principle of nonmaleficence may be the most applicable principle of medical ethics to human head transplantation in addition to the principles of beneficence, justice, and autonomy. There is a huge waiting list for organ transplantation. Head transplant has no clinical success yet and it requires a body in its entirety. If it fails quiet a number of individuals may die with one less donor to provide them with heart, lung,kidney etc. So, before the procedure the ethics of human head transplantation need to be formally addressed.[13]

Reproductive Implications

The recipient of head transplant can never truly reproduce; rather, the donor body will reproduce upon the recipient's will to do so. Also, it will be difficult to decide who will be the parent of the child the donor or the recipient?

So, if human head transplant is to be deemed as ethical then the medical community ought to comprehensively decide on the familial ramifications of the recipient's 'reproduction'.[13]

Are we ready?

When English author Mary Shelley penned Frankenstein in 1818, little did she know that her version might come true, albeit in a slightly different way and as a boon to mankind. Shelley's Frankenstein created monsters by sewing together body parts from human corpses. In a way, Frankenstein created life. Today lives are saved by transplanting organs, bones, skin, nerves and veins. To date there has been a transplant of almost every major organ of the body like heart, liver, lungs, kidneys, pancreas and intestine but not the head. This is about to change.Everygreat scientific breakthrough sounds incredulous at first.

The idea of a head transplant in humans may sound fantastic, dreadful or ridiculous but the current times have scope for it. Potential benefits for certain patients are obvious.

Irrespective of the value, good intentions and even the technological feasibility of a head transplant, there is a gut factor in all of us that makes us reject somethings because they cause disgust. And this 'yuck factor' associated with having someone else's body has been a moral hurdle in further exploring the unknown realms. So, the question remains, are we ready to take a step forward?

References:-

1.Harikrishnan P. Head Transplant: Surprising and interesting facts from the hindu mythology. The Journal of Craniofacial Surgery 2019;30(5):1329-1330.

2.Golębiowska M, Golębiowska B. Head transplant-the latest reports and concerns on planned procedure. World Scientific News 2018; 105:212-217.

3. Guthrie CC. Blood vessel surgery and its applications. Edward Arnold, London 1912.

4. Erika E. Human head transplant proposed-how did we get here? http://phenomena.nationalgeographic.com/2015/05/05/human-head-transplant-proposed-how-did-we-get-here.

5. Canavero S. HEAVEN: The head anastomosis venture project outline for the first human head transplantation with spinal linkage(GEMINI). Surg Neurol Int. 2013; 4(Suppl 1): S335-S342.

6. Gkasdaris G, Birbilis T. First human head transplantation: Surgically challenging, ethically controversial and historically tempting- an experimental endeavor or a scientific landmark. Maedica- a Journal of Clinical Medicine 2019; 14(1):5-11.

7. Ren XP, Orlova EV, Maevsky EI, Bonicalzi V, Canavero S. Brain protection during cephalosomatic anastomosis. Surgery 2016; 160(1):5-10.

8. Canavero S, Ren XP, Kim CY, Rosati E. Neurologic foundations of spinal cord fusion (GEMINI). Surgery 2016; 160(1):11-19.

9. Chang WC, Hawkes EA, Kliot M, Sretavan DW. In vivo use of a nanoknife for axon microsurgery. Neurosurgery 2007; 61(4):683-91.

10. Canavero S, Ren XP. Advancing the technology for head transplants: From immunology to peripheral nerve fusion. Surgical Neurology International 2019; 10(240):1-3.

11. Iamsakul K, Pavlovcik AV, Calderon JI, Sanderson LM. Project HEAVEN: Preoperative training in virtual reality. Surgical Neurology International 2017; 8:59.

12. Furr A, Hardy MA, Barret JP, Barker JH. Surgical, ethical, and psychosocial considerations in human head transplantation. Int J Surg 2017; 41:190-195.

13. Cuoco JA, Davy JR. Operation Frankenstein: Ethical reflections of human head transplantation. Neurosurg. 2016; 1:2.