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### **EDITORIAL COMMENTARY**



# The Age of Head Transplants

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If we disregard religious myths, the first reference to a body swap is found in the work of Pu Song Ling, a Chinese poet who died in 1715 but only became famous later on when his collection Strange Tales from a Chinese Studio was published. In one tale, a demon, Judge Lu, after some vicissitudes, falls in with Mr Zhu and humors his request of giving his wife, who "is not at all a bad figure, but she is very ugly," a new face, actually the head of a nice-looking young girl. What happened is that:

Zhu then led (Judge Lu) to the bed where his life was lying asleep on her side; and the Judge, giving Zhu the head to hold, drew from his boot a steel blade shaped like the handle of a spoon. He laid this across the lady's neck, which he cut through as if it had been a melon, and the head fell over the back of the pillow. Seizing the head he had brought with him, he now fitted it on carefully and accurately, and pressing it now to make it stick, bolstered the lady up with pillows placed on either side. When all was finished, he bade Zhu put his wife's old head away, and then took his leave. Soon after Mrs Zhu waked up, and perceived a curious sensation about her neck...Mrs Zhu took a mirror to look at herself...and when he came to look at her neck, he found a red seam all around, with the parts above and below of a different coloured flesh.

At the time, the heart was considered the site of human personality, so Mr Zhu still had his wife, only "upgraded." But it was only with Mary Shelley's Frankenstein novel of 1818 that body swap took up a new meaning. In the words of Viktor Frankenstein,

...when I was fifteen years old...we witnessed a most violent and terrible thunderstorm...before this I was not unacquainted with the more obvious laws of electricity. On this occasion a man of great research...entered on the explanation of a theory which he had formed on the subject of electricity and galvanism, which was at once new and astonishing to me...(p33)

The "man of great research" Mary Shelley is referring to is Luigi Galvani (1737-1798)'s nephew, Giovanni Aldini (1762-1834), the Italian scientist that rocked his times by proving the effects of electrical stimulation on human cadavers! Using Alessandro Volta's pila, he shocked Europe. Here is the account of London's TIMES of January 22, 1803.

The body of Forster, who was executed on Monday last for murder, was conveyed to a house not far distant, where it was subjected to the Galvanic Process, by Professor Aldini, under the inspection of Mr. Keate, Mr. Carpue, and several other Professional Gentlemen. M. Aldini, who is the nephew of the discoverer of this most interesting science, showed the eminent and superior powers of Galvanism to be far beyond any other stimulant in nature. On the first application of the process to the face, the jaw of the deceased criminal began to quiver, and the adjoining muscles were horribly contorted, and one eye was actually opened. In the subsequent part of the process, the right hand was raised and clenched, and the legs and thighs were set in motion. It appeared to the uninformed part of the by-standers as if the wretched man was on the eve of being restored to life. This, however, was impossible, as several of his friends who were under the scaffold had violently pulled his legs, in order to put a more speedy termination to his sufferings. The experiment, in fact, was of a better use and tendency. Its object was to show the excitability of the human frame, when this animal electricity is duly applied. In cases of drowning or suffocation, it promises to be of the utmost use, by reviving the action of the lungs, and thereby rekindling the expiring spark of vitality. In cases of apoplexy, or disorders of the head, it offers also most encouraging prospects for the benefit of mankind. The Professor, we understand, has made use of Galvanism also in several cases of insanity, and with complete success. It is the opinion of the first medical men, that this discovery, if rightly

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managed and duly prosecuted, cannot fail to be of great, and perhaps, as yet, unforeseen utility

Actually, this "unforeseen utility" soon left its mark. From the TIMES of September 28, 1838

Last week a little girl named Hannah Sheets fell headforemost into a butt of rain water which stood open in the back-yard of the house where her parents resided, in Castle-street, Golden-square. It is not exactly known how long she lay there, for she was not immediately missed, and even then an anxious search of many minutes was made through the house and streets adjacent ere the water-butt was thought of. When dragged out she was quite cold, and all the usual remedies were tried for a length of time by Mr. W. B. Parkes, surgeon, of Carnaby-street, without success. Amongst the rest, attempts to inflate the lungs were unremittingly persevered in for a considerable time. As a last resource, Mr. Parkes applied the stimulus of electricity. He first passed shocks gently through the head and chest, along the course of the spine, gradually increasing their power, and persevering during the whole time (by means of other assistance) in the inflation of the lungs. After these means had been employed conjointly for about 10 min, faint traces of respiration were observed, and in three-quarters of an hour he had the pleasure to behold his patient in a fair way of recovery. The child is now in the enjoyment of perfect health.

Anyway.

Not only the Frankenstein myth became common lore, but for two centuries, the story of Viktor Frankenstein and his monster (actually two, as there was also a female Frankenstein creature) wormed its way into the collective unconscious of mankind. Films, comics, similarly conceived novels, and much more gushed out. A horror story, actually. Gothic. But...

Gothic finally became reality: on May 21, 1908, Charles Guthrie in the USA succeeded in grafting one dog's head onto the side of another's neck, creating the world's first artificially two-headed dog (although the grafted head was without neural function due to ischemic damage). Fast forward to February 24, 1954: Vladimir Demikhov in the Soviet Union succeeded in producing dogs with two viable heads, and in 1959, Zhao in China followed suit with dogs [1,2]. Similar procedures were reported by other groups [3–5]. It was only a matter of time before Robert White in Cleveland beheaded a monkey and attached the head of another monkey, with full brain preservation. The year: 1970 [1,2]. These experiments were met with horror and disbelief by scientists and society alike, but the fact is that they helped test neural preservation techniques, above all hypothermia, in the absence of blood flow to the brain. Their goal was NOT long-term survival. At the time, there was no effective antiimmune rejection protocol. Even so, Prof White specifically wrote that histology showed "no evidence of cellular changes compatible with a hyper-rejection reaction in cerebral tissue"

Clearly, a Frankenstein-like procedure in man was on nobody's agenda. A full head transplant—which is understood nowadays as a composite tissue allotransplantation (CTAs)—was simply considered impossible until the real stumbling block—the spinal cord could be successfully dealt with, that is, reconnected with restoration of function. For decades, scientists had sought the holy grail of spinal cord regeneration and failed. In the meantime, transplant surgery made great strides, and in the 21st century, other CTAs have been successfully carried out, including hands, limbs, and faces [1,2]. Antirejection protocols have greatly improved with the introduction of new strategies. A head transplant has become feasible but yet the last obstacle had to be overcome.

In 2013, Canavero introduced the GEMINI protocol [6-8], which promises to achieve spinal cord reconstruction after a sharp severance, thus opening the way to a full human head transplant (code named by us HEAVEN/AHBR). In 2014, Ren announced the first successful head transplants in mice [9–11]. The high point of the renewed efforts in this field came in June 2015, when this editor and Canavero delivered their combined talks to the AANOS/ICS annual meeting in Annapolis, Maryland. On August 27, 2015, XinHua, China's official news-agency, announced the start of the cooperation between Canavero and this author toward the first human head transplantation. A plan has been laid down that involves experimentation with brain-dead organ donors. The manufacturing of the GEMINotome, an ultra-sharp nanometergrade blade, and of a negative pressure microconnector for PEG circulation are part of this endeavor. In the meantime, scientists from the Institute of Theoretical and Experimental Physics in Moscow (Prof. Maevsky and Orlova) have volunteered their know-how to boost the HEAVEN neuroprotection protocol. Health professionals from all around the world, including the USA, have offered to be part of the transplant team. Dr. Kim in South Korea has performed plenty of GEMINI-related work that complements our work with fusogen-assisted reconstruction of the cord.

It is thus my pleasure then that two mini-symposia delineating the science behind HEAVEN/AHBR are now being published and brought to the scientific arena: one in this journal and a twin one in SURGERY at the hands of chief editors Prof. Sarr and Prof. Behrns in the US. Both interested parties and critics will find answers to their doubts. In particular, the preliminary experiments on animals bear out GEMINI, namely, that a sharp section of the cord can be mended with the use of fusogens.

Yet there is a point that must be tackled. And that is as follows: Why HEAVEN/AHBR met with so much skepticism. Why so much acrimony for a life-saving procedure?

The reason is psychological: HEAVEN/AHBR opens the Pandora's Box of medical failures.

Biochemical/Genetic Medicine at large has failed for chronic conditions, insomuch as no quick, definitive cure is available for any condition. And of course, bioengineering advances cannot be conflated with biochemical medicine.

Had medicine succeeded in rooting out the genetic and biochemical causes of chronic degenerative conditions, but also cancer, we would be free—or on the way to—of the major killers that affect mankind. There would be no need for a full body exchange. HEAVEN/AHBR bears brutal testimony to this simple fact. When you have to change a body, because you cannot fix it, that is a sign of failure. Actually, the whole field of transplantology attests to the fact that our biochemical insights have led nowhere, despite vast amounts of money spent over the past 50 years! As we cannot reverse a biological process gone awry, we are left with little else than replacing this or that organ.

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Unfortunately, humility is not part of the medical lore.

HEAVEN/AHBR is growing into a major international collaboration. In the meantime, people are dving because we doctors failed. This is a time for humility. But also a time to act. Doctors, patients, and funding bodies (including well-meaning billionaires), together.

It is my hope these mini-symposia will make it clear why we have to act.

Now [12].

In this mini-symposium, Minassian and his Hofstoetter, worldclass experts in the field of spinal cord stimulation for spinal cord injury rehabilitation, illustrate what is Axis 2 of the spinal cord fusion protocol—Axis 1 being the use of special substances called fusogens, dealt with in the twin symposium in SURGERY. Spinal cord stimulation targets the propriospinal system that is responsible for motor and sensory transmission, along with long-fiber tracts in the white matter. Alone it can make paralyzed patients recover function. In GEMINI, it will also speed up neurological recovery by enhancing the sprouting process in the reconnected spinal cord.

Next, Canavero and Bonicalzi describe what is arguably one of the two main obstacles on the road to HEAVEN/AHBR, that is, the dreaded complication of central pain. No one is planning on achieving a successful head graft with the patient going on to suffer horrible pains for the rest of his or her life. Happily, Canavero's work in the field for the past 25 years led to an effective although still experimental—cure. Incredibly, none of the critics flagged this condition as a no-no for the whole initiative, which goes some way in confirming how there are truly no "experts" in

Finally, Prof. Mori, a professional philosopher, explains how the concept of identity is rather fluid both in the literature and philosophy and that actually nothing can be said at this point about this important problem. Certainly, the first head transplantation will rewrite the concept of Self and other aspects of what it means to be "human."

Further details are to be found in the parallel symposium in SURGERY

In the end, it should be clear how the most daring medical endeavor ever has left science fiction behind to enter the scientific arena. The question remains though: Is the world ready? No matter what the answer is, science is about to break the final frontier.

## **Conflict of Interest**

The authors declare no conflict of interest.

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