

Editorial

# Is it time to perform the first human head transplant? Comment on the CSA (CephaloSomatic Ansatomisis) paper by Ren, Canavero, and colleagues 对任及卡纳维罗头身吻合术论文的评论

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对任晓平、卡纳维罗以及他们同事的头身接合术论文的评论

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In November 2017, SNI published another in the series of scientific papers on basic science studies leading to the first transplant of a Human Head to a donor body (CSA) by an international team of scientists led by Ren and Canavero. The latest paper was on the trial using cadavers to perfect the details of the complex surgical transplant procedure to be performed in the future.<sup>[22]</sup>

2017年11月，《国际外科神经学》发布了一系列关于首例人类遗体换头手术（头身接合术）基础科学研究的科研论文，这个手术是由任晓平以及卡纳维罗领导的国际团队执行。最新的这篇论文是从外科学和解剖学方面为将来的异体头身重建术提出了详细的外科手术设计方案和步骤。

The reasons to perform such a healthy head transplant to a healthy body was well described by Ren *et al.*<sup>[22]</sup>

Composite tissue allo-transplantation (CTA) involves the grafting of limbs or other complex tissues from an unrelated donor and recipient. In the 1990s, animal studies helped to pave the way for the first successful human hand transplantation in United States, which was performed at the University of Louisville and Christine M. Kleinert Institute for Hand and Microsurgery in 1999. This patient recovered fully, and continues to work and lead a normal social life. Studies in small animals and a porcine model allowed for optimization of the immunosuppressive regimen,

as well as a system for characterizing the degree of immune rejection of transplanted tissues. Facial tissue transplantation has also become a clinical reality, and worldwide there have been more than 100 completed cases of the CTA operation. However, there is no effective way in which to save a survival healthy mind when there is critical organ failure in the body, such as complete cervical spinal cord injury with paraplegia, tumors metastatic disease, hereditary body muscle atrophy, and others.<sup>[22]</sup>

对于执行这种将健康的头颅移植到健康的身体上的手术的理由，任晓平以及他的同事是这样描述的：

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异体复合组织移植涉及从其供体那移植四肢或者其他复杂组织到受者身上。在20世纪90年代的美国，动物实验为第一人移植铺平了道路，这例手术由路易斯维尔大学以及克里斯汀M克莱纳特研究所在1999年实施。那名患者基本痊愈，可以继续工作，社交生活也正常。对小型动物和猪的研究可以使免疫抑制方案以及移植组织的免疫排斥程度的系统达到最优化。面部组织的移植也在临床上实现了，而且在世界范围内有超过100例异体复合组织移植的成功案例。**然而，现在并没有办法来拯救一个身体重要器官衰竭的存活的健全大脑，如带截瘫的完全性颈椎脊髓损伤，肿瘤转移性疾病，遗传性肌肉萎缩等。**

There are three major parts of this CTA, head to body transplant, that represent the significant components of this transplantation of a human head from one person to the body of a second person: 1) Reconnection of a severed spinal cord to produce a functional outcome; 2) The actual steps in a complex surgical procedure to complete the transplantation; 3) The potential transplant rejection. The work on these steps will be discussed in the following paragraphs.

该头身接合的异体复合组织移植存在三个主要问题：1) 重新连接切断的脊髓以产生功能性结果；2) 完成复杂的移植手术过程中所需要执行的实际步骤；3) 潜在的移植排斥反应。 这些问题将在下面的段落中讨论。

### Reconnection of a severed spinal cord

#### 1) 断裂脊髓的重连

It is generally believed by almost all neuroscientists that a severed spinal cord cannot be reconnected to yield a functional recovery below the severed level.<sup>[2,5,7]</sup> Many attempts using various biological combinations have been tried without success.<sup>[5,7]</sup> However, this long held viewpoint has been found not to be true based on historical observations and the experimental work of Canavero, Ren, and their colleagues worldwide and the observations of others.<sup>[3,5,7]</sup>

几乎所有的神经学家都普遍相信，切断的脊髓无法通过再连接来恢复切断平面以下的机能。许多各种各样的通过生物组合的尝试都以失败告终。然而，这种长期以来的观点被卡纳维罗、任晓平以及他们来自世界各地的同事发现是不正确的，他们是基于历史考察和实验工作以及其他人的观察成果得出了这个结论。

### Early evidence for spinal cord repair in humans and animals

#### 1a) 人类与动物的脊髓修复的早期证据

In their in-depth review of the literature on spinal cord repair, Canavero and Ren describe two case reports in the literature from 2005 and 2014 respectively.

在他们全面地回顾了关于脊髓修复的文献后，卡纳维罗和任晓平在文献里发现了两个分别来自2005年和2014年的案例报告。

In the first case observation, a 24-year-old woman sustained a traumatic spinal cord injury and

transection at T6-T7. After thirty-nine (39) months as a paraplegic with no motor or sensory activity below the level of the injury, Goldsmith removed the scarred portion of the spinal cords proximally and distally leaving a 4-cm gap. He then placed a collagen bridge between the two spinal cord segments and placed an omentum pedicle to cover the operative site of the severed spinal cord and collagen bridge. At 6 months, the patient could move her legs on command and in 4 years she was able to walk long distances. There was no detailed independent neurological examination of her status at 4 years to evaluate the extent of the patient's recovery. (But the fact that she regained function after being paraplegic for 39 months is remarkable. I know Dr. Goldsmith personally and believe he is a credible surgeon and observer-Ed).<sup>[5]</sup>

在第一个案例的观察报告中，一名24岁的女性患有创伤性脊髓损伤，横截面积为T6到T7。在39个月之后，她的损伤平面以下失去了肌肉运动能力和知觉，成为了截瘫患者。戈德史密斯去除脊髓的伤痕部分，近端和远端间隔着4厘米。然后，他在两个脊髓节段之间放置一个胶原蛋白桥，并放置一个带蒂大网膜以覆盖切断的脊髓和胶原蛋白桥的手术部位。6个月后病人已经可以控制移动自己的腿，4年后她已经可以进行长距离行走了。在第4年时没有详细的神经检查来评估患者康复的程度。但是她在截瘫三十九个月后恢复了功能的事实是值得注意的。我私底下认识戈德史密斯博士，并相信他是一位可信的外科医生和观察者。

In a second case, a 38-year-old man sustained a traumatic transection of his spinal cord at T9. "Using one of the patient's olfactory bulbs, a cell culture containing olfactory ensheathing cells and olfactory nerve fibroblasts was developed. After operative resection of the glial scar in the patient's spinal cord, the cultured cells were transplanted into the spinal cord stumps above and below the site of injury, and the 10-mm gap between the stumps of the spinal cord was bridged with 4 strips of autologous sural nerve." After 19 months of rehabilitation the patient had partial recovery of voluntary movements and superficial and deep sensation below the level of the spinal cord transection.<sup>[5]</sup>

在第二个案例中，一名38岁的男性的脊髓损伤横截面达到T9。“通过使用患者的嗅球，开发了含有嗅鞘细胞和嗅觉神经成纤维细胞的细胞培养物。通过手术切除患者脊髓中的胶质瘢痕后，将培养的细胞移植到损伤部位上方和下方的脊髓残端中，脊髓残端之间10mm的间隙通过4条自体腓肠神经桥接。”经过19个月的康复治疗，病人部分恢复了自主运动能力以及脊髓横断面以下的浅表和深层感觉。

Canavero and Ren describe the work of Freeman who in the 1950s and 60s sharply transected the spinal cords of rats and dogs and then re-approximating

them. The animals re-established function below the transection site, which could be seen in 7-14 months after the operation. Electrical activity and nerve growth across the repaired site was seen and recorded.<sup>[5]</sup>

卡纳维罗和任晓平还描述了弗里曼的实验，他在20世纪50年代和60年代快速切断大鼠和狗的脊髓，然后将两端离断的脊髓重新对接。动物在切断部位之下的重建功能在术后7到14个月可见。他观察并记录下了整个修复部位的电活动和神经生长。

## Two neuronal systems that regulate sensory and motor behavior

1b) 调节感觉和运动行为的两个神经系统

### The pyramidal tract and the Cortico-trunco-reticulo-propriospinal pathway (CTRPS)

锥体束和脊髓固有的皮层网状通路

How could this spinal cord recovery in man and animals be explained in view of the belief in the scientific community that the long fiber tracts, which course from the brain's cortex to the spinal cord, cannot re-grow across a severed cord?

鉴于科学界相信从大脑皮层到脊髓的长纤维束不能在断裂的脊髓上重新生长，人类和动物的脊髓如何恢复呢？

In a detailed explanation, Canavero cites known evidence that there are two sets of fiber tracts from the brain to the spinal cord that regulate voluntary function of the extremities. The first system is a multi-synaptic pathway from the brain to the spinal cord that connects many neurons in sequence over short segments from the brain cortex to the spinal cord to provide movement to the extremities. This is the remnant of the primitive spinal cord system in lower species, as worms or centipedes, which have a segmental nervous system. However, as the species evolved, a faster conducting system, consisting of long fast signal transmitting neurons connecting the brain cortex nerve cells to the spinal cord nerve cells allowed for rapid transmission of volitional signals. This long fiber tract is called the Pyramidal Tract. When the spinal cord is transected, the long neuron tracts, which are cut, are slow to recover because the re-growth of the nerve must be from the brain to the spinal cord. However, with the short multi-neuron pathway that travels short segments from the brain to the spinal cord, the short neurons can quickly re-grow and establish connections to the spinal segment below the transection re-establishing the multi-neuronal pathway that controls movement and sensation. This multi-synaptic motor system, called the Cortico-trunco-reticulo-propriospinal pathway (CTRPS), re-establishes the integrity of this duplicate motor system to allow voluntary movement of the extremities to occur.<sup>[3,5,20]</sup>

在详细的解释中，卡纳维罗引用了已知的证据，即从脑到脊髓有两组纤维束用以调节四肢的自主功

能。第一个系统是从大脑到脊髓的多突触通路，这条通路通过大脑皮层到脊髓的短节段依次连接神经元来让四肢运动。这是像蠕虫和蜈蚣这样拥有阶段性神经系统的低级生物的原始脊髓残余。然而，随着物种的进化，一个更快的传导系统产生了，它由连接大脑皮质神经细胞和脊髓神经细胞的长的快速信号传输神经元组成，允许快速地传输意志信号。这种长纤维束被称作锥体束。但脊髓被切断后，这个被切断长神经束恢复得很缓慢，因为神经的再生必须经由大脑到脊髓才能完成。然而，有这种从大脑到脊髓之间短节段传播神经元的多神经元通路，短的神经元就可以快速地重新生长并建立与横断面下的脊髓节段的连接，重新建立控制肌肉运动的多神经元通路和感觉。这种多突触运动系统称为脊髓固有的皮层网状通路，重新建立这两种运动系统的完整性，才能使肢体随意运动。

### How to get neurons to grow across the severed cord ends

*Fusogens/sealants*

1c) 如何让神经元穿越切断的脊髓端部生长

促融剂/密封剂

With the evidence from animals and humans that the spinal cord could indeed be repaired, Canavero and Ren believed it was important to speed up the repair process in the severed spinal cord. It was important to improve the rate of growth of the short nerves across the sectioned spinal cord so that motor and sensory function can occur more quickly. A number of molecular agents have been tested in different models of Acute and Chronic spinal cord injury. They include Chitosan nanospheres,<sup>[8]</sup> PEG-polyethylene glycol biopolymer matrix,<sup>[3,5,9,12,15,16,20]</sup> IKVAV membrane spanning peptide,<sup>[12]</sup> and Olfactory Mucosa Autograft.<sup>[11]</sup> All were used in different chronic cord injury models and neuronal growth occurred with all. PEG was used more commonly and allowed nerve growth to occur before scar formation. None have been compared with each other. Canavero and Ren used the PEG fusogens to accomplish the goal of fusion of sharply cut spinal cord ends that would have less tissue damage.<sup>[3,5,7]</sup>

这些来自动物和人类身上的证据证明脊髓的确能够被修复，卡纳维罗和任晓平相信加速断裂脊髓的修复进程是非常重要的。提高穿过切断的脊髓的短神经的生长速度是很重要的，这样肌肉运动功能和知觉功能可以更快地恢复。一些分子试剂已经在不同的急性和慢性脊髓损伤模型中被测试过了。它们包括壳聚糖纳米球、聚乙二醇生物高聚物基体、IKVAV跨膜肽以及嗅黏膜自体移植。这些都在不同的慢性脊髓损伤模型中用过，并且神经元的生长都有出现。聚乙二醇更常用，并且能在瘢痕出现前让神经生长。它们都没有相互比较过。卡纳维罗和任晓平用聚乙二醇促融剂来实现融合两个尖锐切割的脊髓末端，这样组织的损伤较小。

### Properties of fusogens 促融剂的特性

“Fusogens/sealants, are molecules that can reconstitute the integrity of the neural membranes and nerve fibers and restore electrophysiologic conduction when applied to the cut spinal cord ends shortly after severance. Fusogens were discovered in 1986 but were not used in medicine until these spinal cord fusion experiments. “Fusogens allowed nerve axon growth to occur at 1 week post treatment. This growth increased steadily over time, and was long lasting.”<sup>[7]</sup> Polyethylene glycol (PEG) is a glycoprotein fusogen that facilitates this fusion of cell to cell and neuronal membranes.<sup>[5]</sup> It has been characterized as a Biopolymer-Matrix.<sup>[9]</sup>

促融剂/密封剂是一种当施加在切断不久的脊髓上时，能够重建神经膜和神经纤维的完整性，并且使脊髓末端恢复电生理传导的分子。促融剂在1986年就被发现了，但在这些脊髓融合实验之前都没有用在医学领域。“促融剂可以让神经轴突在治疗的一周后开始生长，这种生长随着时间推移会越来越稳定并且是长期性的。”聚乙二醇是促进细胞与细胞和神经元膜融合的糖蛋白促融剂。它被描述为生物高聚物基体。

Sikkema *et al.* described physical and electrical characterization of Texas PEG, the PEG fusogen combined with Graphene Nanoribbons (GNR) they developed.<sup>[25]</sup> By adding conductive graphene nanoribbons (GNR) to the fusogen solution, the PEG-GNR mixture is believed to first act as an electrical conduit and then as an electrically active scaffold upon which the neurons will grow, directing their processes across the spinal cord gap.<sup>[20]</sup> Kim and his colleagues used PEG alone in their mouse experiment and PEG-GNR in their rat experiment. The PEG-GNR allowed a faster recovery of spinal cord function.<sup>[3,7,16,25]</sup>

西克马等人描述了德克萨斯聚乙二醇的物理特性和电特性，这是一种将聚乙二醇促融剂与他们开发的石墨烯纳米带结合的产物。通过在促融剂溶液中加入可导电的石墨烯纳米带，他们相信这种聚乙二醇-石墨烯纳米带混合物首先会起到电导管的作用，然后作为一个电活性支架让神经元在其上生长，引导神经元越过脊髓的缺口。金和他的同事分别用聚乙二醇和聚乙二醇-石墨烯纳米带在小鼠和大鼠上进行了实验。结果表明聚乙二醇-石墨烯纳米带能让脊髓更快地恢复功能。

### Critical time for fusogens to act 促融剂施用的临界时间

However time is critical in allowing this fusion to happen. As Canavero and Ren state, “The ends of the transected spinal axons remain stable for only about 10–20 minutes before they undergo fragmentation (the first step before classic Wallerian degeneration, or dieback) at both cut ends of the spinal cord or nerve. These cut

cells and neurons span 0.3 mm, only to stabilize and persist for 3–7 days; about 30% of proximal axons then start regrowing within 6–24 hours. Thus, the fusogens must be brought into the site of anastomosis within minutes (certainly <10 minutes). As for the axons that do not get re-fused, dieback is on average 0.5–2.5 mm in rat models and is short-lived (1 month). Considering about a 1 mm/day regrowth rate, even these axons would reach the point of section within 3 days (with the minority, within 3 weeks).”<sup>[3,5,7]</sup>

时间对这种融合的发生至关重要。就像卡纳维罗和任晓平所说的，“切断的脊髓轴突的末端在脊髓或神经的两个切割末端经历断裂（经典瓦勒变性或枯死前的第一步）之前仅保持稳定约10–20分钟。”这些被切断的细胞和神经元只有0.3毫米，并且只稳定存活3到7天，大约30%的近端轴突会在6到24小时内开始再生。因此促融剂必须在几分钟内（一定小于10分钟）施加到接合点。至于那些没有再融合的轴突，枯死的长度在大鼠模型中平均是0.5到2.5毫米并且是短期的（一个月）。考虑到大约每天1毫米的再生速度，就算是这些轴突也能在3天内（少数情况在3周内）到达断面。

### Electrical stimulation to accelerate nerve growth

#### 1d) 加速神经生长的电刺激

A final step in promoting a faster spinal cord fusion process is the use of electrical stimulation of the spinal cord.

促进脊髓更快地融合的最后一步是使用电刺激来刺激脊髓。

Electrical stimulation of the spinal cord and peripheral nerves has been found to accelerate nerve growth in animals and is used in the fusion process.<sup>[3,4,7]</sup>

已经发现对脊髓和周围神经的电刺激可以加速动物的神经生长，并已在这个融合过程中应用。

Now the stage was set for the judicious use of animals to prove that spinal cord repair can be achieved before its use in humans.

现在已经准备好明智地使用动物来证明在其用于人类之前可以实现脊髓修复。

### Experiments reconnecting the sharply severed spinal cords of animals—acute spinal cord injury

#### 1e) 动物急性脊髓损伤的切断脊髓的重连实验

In a series of experiments in mice,<sup>[15]</sup> rats,<sup>[16]</sup> and a dog,<sup>[13]</sup> first reported in SNI, the spinal cords of these animals were sharply transected in the cervical region and then re-approximated with the fusogen, PEG, in the interface between the transected upper and lower cords. The animals regained their function within 24 hours and improved over 4 weeks of observation. The videos accompanying these papers show the animals regaining function.<sup>[13,15,16]</sup>

在《国际外科神经学》首先报道的一系列小鼠、大鼠以及狗的实验中，这些动物的脊髓在颈部被快速地切断，然后在脊髓断口的两端施用促融剂和聚乙二醇并重新逼近。这些动物在24小时内重获机能，并4周的观察中获得了改善。这些论文中附上的视频显示了这些动物们重获了机能。

In the mouse experiment performed by Kim *et al.* in Korea, fusogens (PEG) were not used in the control animals but were used in the treated group. In the 5 control animals there was some recovery of function after two weeks. The PEG-fusogen treated mice recovered some function in 24 hours and moved all four limbs in 4 weeks after the surgery indicating that the fusogens allowed faster recovery and likely growth of neurons.<sup>[15]</sup>

由金等人在韩国进行的小鼠实验中，聚乙二醇促融剂没有用在对照组而是用在治疗组。这5只对照组动物中有一些在两周后恢复了机能。那些施用过聚乙二醇促融剂的小鼠在24小时内恢复了部分机能并在术后的4周可以移动四肢，这说明了促融剂可以让神经元更快地恢复和生长。

In another experiment by Kim *et al.* using rats, PEG-GNR was used as the fusogen scaffolding for nerve fiber growth. Somato Sensory Evoked Potentials (SSEP) were recorded from the scalp after stimulation of the sciatic nerve as a measure of electrical transmission across the severed spinal cord. In all 5 of the PEG-GNR treated rats the SSEPs were recorded 24 hours after the surgery indicating a transmission of electrical stimulus from the sciatic nerve to the rat cortex. None of the 5 control animals, which had saline instead of a fusogen at the site of spinal cord section, showed any SSEPs. Because 4 of the treated rats died in an unexpected laboratory flooding, long-term assessment of recovery of function was only possible in one rat. In that animal, there were steady signs of functional recovery after 24 hours with the rat being able to stand and walk in two weeks. This was a remarkable achievement in spinal cord injury research.<sup>[16]</sup>

在金等人的另一项大鼠实验中，聚乙二醇-石墨烯纳米带被用作神经纤维生长的促融支架。在刺激坐骨神经之后，从头皮处记录躯体知觉诱发电位，作为穿过切断的脊髓的电传递的量度。在所有的5只聚乙二醇-石墨烯纳米带处理的大鼠中，都在手术后24小时记录到了躯体知觉诱发电位，表明在坐骨神经和大鼠皮质之间进行了电刺激的传递。而在那5只用盐水替代促融剂施加在脊髓断裂面的对照组动物中，没有记录到躯体知觉诱发电位。因为有4只治疗组大鼠死于意外的出血，所以只有一只大鼠可以长期评定其机能恢复情况。这只大鼠在24小时后有了稳定的机能恢复信号，并在2周后可以站立和行走。这在脊髓损伤研究上是一个非凡的成就。

Kim also reported recovery of function from spinal cord transection in 7 more rats using PEG in 2016.<sup>[14]</sup>

金还在2016年报告了7只以上的大鼠施用聚乙二醇后从脊髓断裂中恢复了机能。

Kim *et al.* sectioned the spinal cord of a dog nearly completely and re-approximated the cut ends in a PEG solution so that the ends were touching. The animal was followed with videos of its function twice a week. The dog recovered at least 90% of his normal function by three weeks post surgery. No further experiments were conducted on the dog.<sup>[13]</sup>

金等人几乎完全地切断了一只狗的脊髓，然后在聚乙二醇溶液中将断口重新逼近以让断口彼此接触。每周两次对该动物进行视频跟踪以记录其机能。

S.Ren and colleagues reported on a more detailed experiment in another set of rats in China.

任晓平和他的同事在中国报告了一份更详细的另一组大鼠实验。

Using 15 rats with 6 as controls, the scientists used a specially designed sapphire knife to make a sharp cut at the T10 spinal cord level that produced a minimum of cell and fiber damage. The control animals had saline placed in the cut area while the 9 treated animals were given a PEG fusogen mixture between the cut ends of the spinal cord. "After 4 weeks, the treated group had recovered ambulation vs. none in the control group... All animals were studied with somato-sensory-evoked potentials (SSEP) [measuring an electrical impulse that travelled from the leg though the sectioned spinal cord level to the sensory cortex recorded from the scalp of the rat-Ed]..." The SSEP recovered postoperatively only in the PEG-treated rats, [indicating the recovery of electric conduction across the treated spinal cords. Using an Magnetic Resonance imaging technique which demonstrates nerve fiber tracts, called Diffusion Tensor Imaging (DTI)], the DTIs showed disappearance of the transection gap in the treated animals vs. an enduring gap in the controls... On qualitative visual inspection, the extent of re-growth of the imaged nerve fibers correlated with behavioral recovery, with near-normal rats with a more normal fiber pattern vs. no or little change in controls."<sup>[20]</sup>

使用了15只大鼠，其中6只作为对照组，这些科学家们使用了一把特别设计的蓝宝石刀来在T10节段进行快速切断，这样可以最小化细胞和纤维的损伤。对照组的大鼠在脊髓断面施加了盐水，而治疗组的9只大鼠施用的是聚乙二醇促融剂混合物。4周后治疗组已经恢复到可以行走而对照组还没有一例可以行走。所有的动物都进行了躯体知觉诱发电位研究，“[测量从腿部通过脊髓断裂处到达感觉皮层的电脉冲，并在大鼠的头皮处记录下来]”，躯体知觉诱发电位只有在被聚乙二醇处理过的大鼠身上恢复了，[表明被处理的脊髓恢复了导电的能力。运用了显示神经纤维束的，被称为扩散张量成像的磁共振成像技术]，扩散张量成像显示治疗组大鼠的断面切

口已经消失，而对照组的依然存在。在定性视觉检查中，神经纤维的再生长程度与行为恢复相关，接近正常的大鼠具有更正常的纤维图像，而对照没有或几乎没有变化。

In the Discussion of the paper the authors continue, “The minimally disruptive (nanometers) severance of the cord [by the sapphire knife] damages a very thin layer of these inter-neurons: PEG reseals their membranes and curbs cell death. These same cells, along with others in proximity, which were not damaged by the extra-sharp blade, can immediately re-grow (sprout) their appendages and reestablish contact between the apposed interfaces. Consequently, the gray matter neuropil is restored by spontaneous re-growth of the severed axons/dendrites over very short distances at the point of contact between the apposed cords” [These conclusions-Ed] “were recently suggested by an immuno-histochemical study of PEG-treated mice submitted to 100% cervical transection” by Kim *et al.* on their mouse experiment tested groups which showed axonal growth across the severed part of the cord.<sup>[17]</sup>

在论文的谈论部分作者继续写道，“[由蓝宝石刀造成的]最小化的脊髓断面损伤（纳米级）只伤害了这些中间神经元非常薄的一层：聚乙二醇重新封好了它们的细胞膜并且抑制了细胞坏死。这些近端的、没有被那把锋利的刀所伤害的细胞，可以立即重新生长（萌发）他们的附器，并重新建立接口之间的联系。因此，灰质神经毡通过被切断的轴突/树突在断裂的脊髓接触点之间非常短的距离内发生自发再生成来进行恢复。[这些结论]最近由一项对受过聚乙二醇处理的、颈部脊髓完全切断的小鼠的免疫组织化学的研究提出。金等人的小鼠实验的实验组显示了横跨脊髓切断部分的轴突生长。

In communication with Canavero, he reports that the same observations that are described above in the mouse, rat and dog using PEG, have been duplicated in the primate. Ren and colleagues will report in the journal, *Surgery*, a recent randomized controlled study in dogs comparing control animals with T10 sectioned spinal cords with dogs having PEG treated T10 sectioned spinal cords. Most of the motor recovery occurred in the PEG treated dogs after 60 days compared with no recovery in the control dogs. The work was further enhanced with evidence of electrical conduction across the severed cord in the treated dogs and DTI evidence of nerve fiber growth across the severed cords compared with none in the control animals Liu, *et al* (2017). These observations will expand the success of spinal cord fusion to higher order mammals. We await the publication of the primate studies in this singularly important landmark research. For information, the observations of spinal cord repair recorded in humans case reports are not as thoroughly investigated as the animal models.

在与Canavero的交流中，他报告说，使用聚乙二醇的上述小鼠，大鼠和狗中观察到的相同结果已经在灵长类

动物实验中复制。任晓平和他的同事们会在外科期刊上发表报告。最近的一项关于狗的随机对照研究，对比了T10节段脊髓切断的对照组和T10节段脊髓切断并施用了聚乙二醇的治疗组。在60天后大多数的治疗组动物都恢复了运动机能，而对照组则没有一例恢复了。这个成果被治疗组的狗的脊髓断部可以进电传导这一证据，以及扩散张量成像显示的治疗组的狗的跨越脊髓断部的神经纤维的生长对比对照组完全没有这样的生长这一证据所进一步证实。这些观察结果将增加高阶哺乳动物脊髓融合的成功率。我们静待这一重要的、里程碑式的灵长类研究的发表。记录在人类病例报告中的脊髓修复观察结果并不像动物模型那样彻底调查过。

Finally, In this superbly conceived and executed experiment in rats (and now dogs) the authors concluded, “We show for the first time, in an adequately powered study, that the paralysis attendant to an acute complete transection of the spinal cord can be reversed. This opens the path to a severance-reapposition cure of spinal paralysis...”<sup>[20]</sup>

最后，通过这个壮丽的构想以及在大鼠（现在还有狗）身上做的实验，作者总结道，“我们第一次在充分的研究中表明，伴随脊髓急性完全切断的麻痹是可以逆转的。这为脊髓麻痹的切断 - 再治疗开辟了道路。”

## Perfection of the surgical transplant procedure

### 2) 完善手术移植程序

As the next step toward CSA, Ren and Canavero wanted to perfect the technical aspects of the CSA in cadavers before the actual human trial. This concept is the substance of their most recent paper published in *SNI*.<sup>[21]</sup> The appropriate consents were obtained in the country of China, and the deceased patients families. Working at Harbin University in China, Ren and Canavero assembled a team of scientists and surgeons who worked to develop the plan for the transfer of a cadaver head to a second cadaver patient's body in a trial run of the actual live human operation. This report by Ren and colleagues and Canavero is the first publication of that work of a human CSA.<sup>[21]</sup> The experiment was a trial for the perfection of the techniques that will be used in an actual human CSA in the future.

作为头身接合术的下一步，任晓平和卡纳维罗想要在未来实际的人体实验之前，在尸体上完善头身接合术的技术方面的问题。这个理念是他们最近在《国际外科神经学》上发表的论文的主旨。他们获得了中国的和死者家属的批准和同意。在中国的哈尔滨医科大学，任晓平带领一个由科学家和外科医生组成的队伍，他们致力于制定一个将一名死者的头颅转移到另一名死者的身体上的解剖学实验研究计划，这是为了进行实际的人体手术前的试验操作。这个由任晓平、卡纳维罗以及他们的同事一起发表的报告是第一份关于人类头身接合术的出版物。这次实验是为了完善将来运用在活人身上的头身接合术技术的试验。

The paper on CephaloSomatic Anastomosis (CSA)<sup>[21]</sup> was the product of a combined team effort of many specialists and others. Many experiments were unreported and were conducted in animals and in cadavers to answer all the technical questions posed by this huge experimental project before the first cadaver surgical CSA was performed. Most of these experiments dealt with choosing the proper routes to the various surgical targets in the transplant, which were to be carried out simultaneously in two cadavers by multiple teams of surgeons.

这个头身接合术的论文是许多专家组成的团队的努力的成果。许多实验未被报告，并且在动物和尸体上进行，就是为了在第一次尸体头身接合术进行之前解决这个巨大的实验项目所提出的所有技术问题。这些实验中的大部分都是为了解决在移植过程中为各种手术目标选择适当路线的问题，而这将由多个外科医生团队在两个尸体中同时进行。

I will not detail the various aspects of the procedure but will highlight some. For a complete understanding of how the investigators have planned and performed this operation, I refer the reader to the actual paper.

我不会详细讲述所有的步骤，但我会重点说几个。为了完全理解调查人员如何计划和执行这项手术，我建议读者参考实际的论文。

In an operative approach that included many standard operations that are done around the world from spine surgery, to trachea<sup>[19,27]</sup> and esophagus repair, and including vascular reanastomosis, the surgeons developed an extremely clever operative plan to achieve the removal of the head from the first cadaver and then to attach the recipient cadaver's head to the donor cadaver's body in a complex operation using multiple teams of surgeons. According to the authors, more steps will be necessary to perfect the procedures in CSA in cadavers before the first CSA can be performed in the live patient. This undertaking has all the aspects of a well-planned surgical approach.

一个行之有效的手术方法包含着许多标准操作，这些操作由世界各地的外科医生开发，从脊柱外科手术到气管和食道修复手术，以及血管再吻合术，外科医生们开发出了极其聪明的手术计划来实现第一具尸体的头颅摘除，然后将受体的头颅安到供体的躯体上，这是需要几个外科医生团队的复杂手术。作者认为，在第一次头身接合术在活体患者身上进行之前，需要在尸体进行更多的试验来完善手术的程序。这项工作就是一个精心策划的手术方法。

In order to ensure that the patient will be able to talk after the head transplant, his head and cervical spine to C3 will be removed from his diseased body. However, the entire trachea and its recurrent laryngeal nerve supply will be transplanted with the patient's head so that the patient's speech, or phonations, can be obtained after the procedure. Hopefully, the scientists will be able to

communicate with the patient as he experiences recovery from the transplantation.

为了确保患者在进行了换头手术后可以说话，他的头和C3节段的颈椎会从他患病的身體上移除。然而整个气管及喉返神经分布都会随患者的脑袋移植，这样患者的声音可以在术后保留下来。希望科学家们可以在患者康复后与他进行交流。

The patient's head will be cooled by hypothermia during the surgery to preserve brain function at the time of transfer. The circulation between the donor body and the recipient head will be established initially along with external carotid vertebral anastomoses to limit the cooling process to one hour. This work has also been done in the literature and modified by Dr. Ren and his colleagues.<sup>[23,24]</sup>

在手术过程中，患者的头部将被低温冷却，以在转移时保持脑功能。供体的身体和接受者的头部之间的循环最初将与外部颈动脉椎体切断术一起建立，以将冷却过程限制到一小时之内。这项工作也在文献中完成了，并由任晓平教授及其同事进行了改进。

The crucial step, taken from the experimental work outlined previously above, will be the re-fusion of the two spinal cords. The donor and recipient bodies will be in the sitting positions. The donor body's spine will be fused with instrumentation from in front early on in the procedure on the donor body. Posteriorly, lateral mass screws will be placed in the donor cervical and recipient cervical laminae so that an immediate posterior instrumented fusion will be ready for fusion of the recipient head and donor body cervical vertebrae. A specially designed lift that will take the recipient head and move it to the donor body for the fusion of the cervical vertebrae and spinal cords has been developed. The next immediate need will be to sharply cut and fuse the spinal cords in bath of PEG achieving a time limit of less than 20 minutes for the fusion of the spinal cords to be achieved from the time the recipient head was detached from its body and transferred to the donor body.<sup>[3]</sup> The fusion site will be encased in a vacuum apparatus containing the PEG. The negative pressure will keep the cord ends apposed. This work has been validated in animal models.<sup>[5]</sup> An electrical grid will be placed across the fusion site to provide the electrical current to promote the nerve growth also, another aspect of the procedure that was worked out in animals. The goal is to provide maximum stability without motion to the fusion site so that a successful fusion can proceed. The vagus nerve end will be anastomosed to the donor vagus using the fusogen techniques described above and in the literature.<sup>[1,7]</sup> Transplantation of tracheal parts between the donor and recipient has already been reported in the literature during tracheal repair surgery.<sup>[19,27]</sup> The remaining closure of the incisions and surgical sites

will complete the procedure. Many more aspects of this challenging feat are presented in the Discussion of the paper.<sup>[21]</sup>

从前面概述的实验工作中提取的决定性步骤将是两条脊髓的再融合。供体和受体的身体都会呈坐姿。供体躯体的脊柱将在早期处理受体躯体时与仪器融合。将在供体颈部和受体颈椎板上放置侧块螺钉，以便立即进行后部器械融合，以准备融合受体头部和供体颈椎。已经开发出一种专门设计的升降机来将受体头部移动到供体，以便融合颈椎和脊髓。下一个迫切的需要是快速切割然后在PEG溶液中融合脊髓，以便在20分钟的脊髓融合时限内，将受体头部从其身体分离并转移到供体身上。融合场所将在一个装有聚乙二醇的真空装置中进行。负压可以让脊髓保持并列。这项工作已经在动物模型中得到验证。电网将被放置在融合部位上以提供电流以促进神经生长，这也是在动物实验中得到过验证的。目标是为脊髓的融合提供最大的稳定性，不要有丝毫的移动，这样才能进行成功地融合。迷走神经末端将通过上文和文献中所述的融合技术与供体迷走神经吻合。在文献中已经提到了供体和受体之间的气管部分的移植将会在气管修复手术期间完成。完成剩下的切口和手术创口的缝合之后，手术就完成了。更多挑战性的内容将在论文的讨论部分中进行介绍。

## Composite tissue allo-transplantation experience

### Relating to the allo-head and body transplantation

#### 3) 与异体头身重建术相关的复合组织异体移植的经验

Ren has stated, “There is still no effective way to save a surviving healthy mind when there is critical organ failure in the body. The next frontier in CTA (composite tissue allo-transplantation) is allo-head and body reconstruction (AHBR), and just as animal models were key in the development of CTA, they will be crucial in establishing the procedures of AHBR for clinical translation.”<sup>[22]</sup>

任晓平说过，“当身体出现严重的器官衰竭时，没有有效的办法能够拯救健康的心灵。异体复合组织移植中的另一个前沿技术是异体头身重建术，正如动物模型是头身接合术发展的关键，它们对于建立临床转化为异体头身重建术的过程至关重要。”

Transplantation of organs, or solid organ transplantation (SOT), is practiced around the world. Kidney, heart, pancreas, intestine, lung, and liver transplantation are well known SOT and practiced successfully. SOT is performed when organ failure threatens survival. SOT success is based on the functioning of the organ transplanted.<sup>[10]</sup>

器官的移植，或者实体器官的移植，在世界范围内已经成熟了。肾脏、心脏、胰腺、肠、肺以及肝脏的移植都被称为实体器官移植，这些都是可以成功运用的技术。实体器官移植术会在器官衰竭威胁到生命时进行。实体器官移植术的成功是基于移植器官的功能。

In almost two decades we have seen transplantation of hands and facial tissue. This Reconstructive Transplantation (RT) is performed in physically healthy individual except for the defect in the body part that is affected. The reasons for the RT become complicated with psychological and other factors and may not be life threatening but are related to quality of life. According to Hautz *et al.*<sup>[10]</sup> an in-depth psychological assessment including the patient's coping mechanisms need to be explored. Side effects of immuno-suppressants, metabolic complications, infections, and tissue rejections occur with RT. “The question whether risks associated with indefinite immuno-suppressive treatment are justified for a non-lifesaving procedure in an otherwise physically uncompromised patient still remains unanswered. [The body of the recipient head in this case is significantly compromised-Ed]. While the risks must be weighed against psychological and social benefits, individual outcomes differ significantly and make conclusions and generalizations difficult. In contrast to SOT, decision making in RT, therefore, remains more on an individual basis, and careful patient selection, comprehensive patient information, and an individualized approach seem most suitable currently.”<sup>[10]</sup> The subject of personality change in accepting a new body<sup>[18]</sup> and in treating central pain if it should occur have also been addressed by the authors.<sup>[6]</sup> The literature indicates that the SOT transplantations are successful in greater than 50% of cases depending upon the organ and recipient. The results are improving with knowledge of the immunologic resistance. Hands have been successfully transplanted for 20 years but still with RT there is a 60% success rate on a smaller total number of cases than have undergone Solid Organ Transplantation.

在过去的20年里，我们看到了手部和面部组织的移植。这种重建性移植是在除了某些受影响的身体部位有缺陷之外的健康的个体中进行的。进行重建性移植的原因与心理因素等因素有关，它可能不会危及生命，但关系着生活质量。根据豪兹等人的深入的心理评估，包括患者需要被探索的应对机制。免疫抑制剂的副作用，代谢性并发症，感染和组织排斥会随着重建性移植出现。冒着不确定的免疫抑制治疗的相关风险，在不缺乏抵抗力的患者身上进行非挽救手术是否合理的问题仍然没有得到解答。在我们的情况里，受体的身体显然是缺乏抵抗力的。虽然必须将风险与心理利益和社会效益进行权衡，但个人情况的不同使得难以得出结论。与实体器官移植相比，重建性移植的决定更多地取决于个人情况，目前通过患者认真的选择，全面的患者信息以及个性化的方法来决定似乎是最合适的。接收新身体后个性的变化以及可能出现的中枢性疼痛的问题也被作者解决了。文献表明，取决于器官和受体，实体器官移植在50%以上的病例中获得成功。这一结果还随着免疫抵抗力的知识的增加而不断改善。手部的成功移植已经有20年的历史了，重建性移植的成功率有60%，但案例总数要少于实体器官移植。

Harbin Medical University (HMU) in Harbin China, where the CSA will be done by Ren and Canavero and the team of doctors, according to Wikipedia, is known for its excellence in allogeneic organ transplantation. “Allogeneic organ trans-plantation is a specialty of HMU. Allogeneic spleen transplantation, allogeneic both-hands transplantation, and allogeneic single-forearm transplantation have reached international renown. Patients who receive allogeneic heart transplantation go on to enjoy the best life quality in Asia.<sup>[26]</sup> At Harbin Medical University there exists a team of people apparently well qualified to do CSA transplantation.<sup>[26]</sup>”

哈尔滨医科大学位于中国的哈尔滨市，任晓平以及他们的医生团队在那里进行异体头身重建术实验解剖学研究，根据维基百科所述，哈尔滨医科大学以其优秀的同种异体器官移植历史著称。“同种异体器官移植是哈尔滨医科大学的专长，同种异体脾脏移植、同种异体双手移植以及同种异体单前臂移植在国内外享有盛誉。接收了同种异体心脏移植手术的患者依然可以享受亚洲地区最好的生活质量。显然在哈尔滨医科大学有一个优秀的同种异体移植团队。”

## CONCLUSION

### 结论

It appears to me after reviewing the extensive literature surrounding the fusion of the spinal cords, the transplant of the recipient head to a donor body, and the problems faced with transplant rejection, that the authors and their multinational team of basic and clinical scientists have done a superb job of establishing the foundation for this operation to proceed. It would be important to the worldwide audience to read the reports of the primate work they and others have done to complete the scope of the project. It would also be important for scientists to read the literature quoted in this review and the CSA paper<sup>[21]</sup> to gain a personal understanding of this important work.

在阅读了大量关于脊髓融合治疗，受体头部移植到供体身体，以及面临的移植排斥的问题的文献后，我认为，作者们和由各国的基础与临床科学家们组成的团队已经为这一事业的发展奠定了良好的基础。对全世界的读者来说，阅读他们为完成这个项目所做的工作的报告是非常重要的。对于科学家而言，阅读本评论和头身接合术论文中引用的文献以获得对这一重要工作的个人理解也是很重要的。

In my opinion, this body of work represents a quantum leap in Medical Science in which many hypotheses in regard to spinal cord repair, including the use of fusogens to enable faster spinal cord recovery, the chance to offer paralyzed patients hope that they can regain recovery of their inactive limbs, the ability to grant a patient suffering from a terrible disability of the body to have a new body that hopefully should function, to maintain a functioning human brain under hypothermia, and other

hypotheses can be proven. Without the observations of many in Medical History and the ability to test these hypotheses thoughtfully in animals, none of these advances with potential benefit to thousands of people worldwide would have been possible. Also, I would expect challenging issues to be uncovered that will take more creativity to resolve.

在我看来，这些工作代表了医学上的一个飞跃，其中有许多关于脊髓修复的假设，包括使用促融剂使脊髓快速恢复，给予瘫痪患者可以恢复瘫痪肢体的能力的希望，使患有严重身体残疾的病人一个拥有正常机能的新身体，在低温下使一个大脑保持正常，以及其他可以被证明的假设。如果没有对以往案例那么多的观察，也没有在动物身上仔细地检验这些假设，那么这些对全世界的人们来说有许多潜在益处的假设都没有任何实现的可能。另外，我也希望能够发现新的，具有挑战性的，需要更多的创造力去解决的问题。

As Ren and Canavero have stated:

就如任晓平和卡纳维罗所说：

“There is no effective way in which to save a survival healthy mind when there is critical organ failure in the body, such as complete cervical spinal cord injury with paraplegia, tumors and metastatic disease, hereditary body muscle atrophy, and others...The next frontier in CTA is allo-head and body reconstruction (AHBR), and just as animal models were key in the development of CTA, they will be crucial in establishing the procedures of AHBR for clinical translation.”<sup>[22]</sup>

“当身体出现严重器官衰竭，如截瘫，肿瘤和转移性疾病，遗传性全身肌肉萎缩和其他疾病的完全性颈脊髓损伤时，没有有效的方法能够拯救健康的心灵。异体复合组织移植中的另一个前沿技术是异体头身重建术，正如动物模型是头身接合术发展的关键，它们对于建立临床转化为异体头身重建术的过程至关重要。”

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