УДК 616.832-001.5-053.2-06:616.98
DOI: https://doi.org/10.17816/PTORS191378

Научный обзор

Электростимуляция как метод коррекции респираторных расстройств у пациентов с травмой шейного отдела спинного мозга (обзор литературы)

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Обоснование. У пациентов с травмой шейного отдела спинного мозга наибольший риск развития дыхательной дисфункции и сопутствующих осложнений, таких как пневмония, ателектаз и дыхательная недостаточность. Дыхательные расстройства — ведущая причина развития сопутствующей соматической, инфекционной патологии и смертности после травматического повреждения шейного отдела спинного мозга. Механическая вентиляция легких является спасительным стандартом лечения таких больных и ассоциирована с атрофией и дисфункцией диафрагмы.

Цель — проанализировать литературные данные, содержащие информацию о методиках электростимуляции спинного мозга, нервов и мышц для коррекции респираторных расстройств у пациентов с травмой шейного отдела спинного мозга.

Материалы и методы. В статье представлены результаты поиска и анализа рецензируемых статей, в которых изучали влияние различных методик электростимуляции на дыхательную функцию у пациентов с травмой шейного отдела спинного мозга. Поиск выполнен на платформах ScienceDirect, Google Scholar, PubMed за период с 2000 по 2022 г.

Результаты. В настоящее время разработаны новые варианты лечения пациентов с тетраплегией, со сниженной вентиляционной функцией легких. Множество исследований показывают положительное воздействие методик электростимуляции на вентиляционную функцию легочной ткани в виде уменьшения сроков нахождения на искусственной вентиляции легких, количества инфекционных и других осложнений со стороны легких.

Заключение. Электростимуляция способствует нервно-мышечной пластичности и улучшению спонтанной активации диафрагмы и дыхательных мышц. Включение электростимуляции в комплексную программу восстановительного лечения больных с травматическими повреждениями спинного мозга на шейном уровне — стратегия, используемая в настоящее время для содействия отмене искусственной вентиляции легких и борьбе с сопутствующими негативными эффектами, такими как дыхательная недостаточность, пневмония, ателектаз. Помимо инвазивной электростимуляции диафрагмального нерва и/или спинного мозга, существуют менее инвазивные методы электростимуляции, которые необходимо изучать для применения у пациентов с нарушением функции дыхании при травме спинного мозга.

Ключевые слова: транскутанная стимуляция спинного мозга; стимуляция спинного мозга; эпидуральная стимуляция спинного мозга; нейромодуляция; нейропротезирование; электростимуляция; функциональная электростимуляция; стимуляция мышц; дыхание; кашель; инспираторный; экспираторный.

Как цитировать:
Тория В.Г., Виссарионов С.В., Савина М.В., Баиндурашвили А.Г. Электростимуляция как метод коррекции респираторных расстройств у пациентов с травмой шейного отдела спинного мозга (обзор литературы) // Ортопедия, травматология и восстановительная хирургия детского возраста. 2023. Т. 11. № 2. С. 239–251. DOI: https://doi.org/10.17816/PTORS191378

Рукопись получена: 04.02.2023 **Рукопись одобрена:** 20.04.2023 **Опубликована:** 30.06.2023

DOI: https://doi.org/10.17816/PTORS191378

Review

Electrostimulation as a method of correction of respiratory disorders in patients with cervical spinal cord injury: A review

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BACKGROUND: Patients with cervical spinal cord injury have the highest risk of developing respiratory dysfunction and associated complications such as pneumonia, atelectasis, and respiratory failure. Respiratory dysfunction is the leading cause of comorbid, somatic, and infectious pathology, and mortality following traumatic cervical spinal cord injuries. Mechanical ventilation of the lungs is the standard treatment for such patients; however, it is associated with atrophy and diaphragm dysfunction.

AIM: To analyze literature data on the use of electrical stimulation techniques of the spinal cord, nerves, and muscles for the correction of respiratory disorders in patients with cervical spinal cord trauma.

MATERIALS AND METHODS: This study presented the results of the search and analysis of peer-reviewed articles that examined the effects of various electrical stimulation techniques on respiratory function in patients with cervical spinal cord injury. ScienceDirect, Google Scholar, and PubMed were searched from 2000 to 2022.

RESULTS: Currently, new treatment options are available for patients with tetraplegia, with reduced ventilatory function. Many studies have shown the positive effect of electrostimulation techniques on ventilatory function such as reduced time spent on mechanical ventilation and reduced incidence of infections and other lung complications.

CONCLUSIONS: Electrical stimulation promotes neuromuscular plasticity and results in improved spontaneous activation of the diaphragm and respiratory muscles. Electrostimulation in a comprehensive rehabilitation program of patients with traumatic spinal cord injuries at the cervical level is currently employed to promote weaning from mechanical ventilation and prevent accompanying complications such as respiratory failure, pneumonia, and atelectasis. In addition to invasive electrical stimulation of the diaphragmatic nerve and/or spinal cord, existing less invasive electrostimulation techniques require further investigation in patients with spinal cord injury and respiratory dysfunction.

Keywords: transcutaneous spinal cord stimulation; spinal cord stimulation; epidural spinal cord stimulation; neuromodulation; neuroprosthesis; electrical stimulation; functional electrical stimulation; muscle stimulation; respiration; cough; inspiratory; expiratory.

To cite this article:
Toriya VG, Vissarionov SV, Savina MV, Baindurashvili AG. Electrostimulation as a method of correction of respiratory disorders in patients with cervical spinal cord injury: A review. *Pediatric Traumatology, Orthopaedics and Reconstructive Surgery.* 2023;11(2):239–251. DOI: https://doi.org/10.17816/PTORS191378

Received: 04.02.2023 **Accepted:** 20.04.2023 **Published:** 30.06.2023

DOI: https://doi.org/10.17816/PTORS191378

科学审查

电刺激作为矫正颈脊髓损伤患者呼吸障碍的一种方法（文献综述）

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论证。颈脊髓损伤患者有可能出现呼吸功能障碍和相关并发症，如肺炎、肺不张和呼吸衰竭。呼吸障碍是外伤性颈脊髓损伤后合并躯体和感染性病症以及死亡的主要原因。机械通气是这些患者的救生标准，与膈肌萎缩和功能障碍有关。

本研究旨在分析有关脊髓、神经和肌肉电刺激技术来矫正颈髓损伤患者呼吸障碍的文献资料。

材料与方法。本文介绍了对同行评议文章的检索和分析结果，这些文章研究了各种电刺激技术对颈脊髓损伤患者呼吸功能的影响。搜索在ScienceDirect、Google Scholar和PubMed上进行，时间跨度为2000年至2022年。

结果。目前，针对肺通气功能减退的四肢瘫痪病人开发出了新的治疗方案。许多研究表明，电刺激技术对肺组织的通气功能有积极作用，可以缩短人工通气时间，减少肺部感染和其他并发症的数量。

结论。电刺激可促进神经肌肉的可塑性，改善膈肌和呼吸肌的自发激活。将电刺激纳入创伤性颈椎损伤患者的综合康复计划中，是一种有助于避免人工通气和消除相关不良影响（如呼吸衰竭、肺炎和肺不张）的策略。除了对横膈膜神经和/或脊髓进行有创性电刺激外，还应该探索对脊髓损伤呼吸功能障碍患者使用创伤较小的电刺激技术。

关键词：经皮脊髓刺激；脊髓刺激；硬膜外脊髓刺激；神经调节；神经义肢；电刺激；功能性电刺激；肌肉刺激；呼吸；咳嗽；吸气；呼气。

引用本文：
Toriya VG, Vissarionov SV, Savina MV, Baindurashvili AG. 电刺激作为矫正颈脊髓损伤患者呼吸障碍的一种方法（文献综述）. *Pediatric Traumatology, Orthopaedics and Reconstructive Surgery.* 2023;11(2):239–251. DOI: https://doi.org/10.17816/PTORS191378

收到： 04.02.2023 **接受：** 20.04.2023 **发布日期：** 30.06.2023

论证

根据治疗急性不稳定型脊髓损伤的临床指南，脊柱骨折在肌肉骨骼损伤中所占比例为从5.5%到17.8%不等。急性复杂性脊髓损伤患者占神经外科住院患者总数的2-3%[1]。

颈部脊髓损伤会导致呼吸肌瘫痪和呼吸能力下降从而危及生命。该脊髓节段的所有受伤患者中约有40%需要一定程度的机械通气，其中5%的患者必须在人工肺通气装置（artificial lung ventilation,人工肺通气装置）的帮助下长期进行人工肺通气[2]。

颈部脊髓损伤患者出现呼吸功能障碍，如肺炎、肺不张和呼吸衰竭等及相关并发症的风险最高[3，4]。

呼吸紊乱是外伤性颈脊髓损伤后伴随躯体和感染性病变以及死亡的主要原因[5，6]。

得益于医疗救助的进步，脊髓损伤患者的平均寿命在过去50年里有所延长。与此同时，依赖人工肺通气装置人工肺通气装置出院的患者人数也在增加[7，8]。

机械通气是这些患者的救生标准治疗方法。它与膈肌萎缩和功能障碍有关，导致限制性通气障碍的发展。许多研究表明，这类患者存在基线支气管收缩，这是因为肺交感神经支配的中断所致[9]。将电刺激纳入颈部脊髓创伤性损伤患者的综合康复治疗计划是目前用于促进人工肺通气装置人工肺通气装置戒断和消除相关不良反应的一种策略。大量研究表明，电刺激可促进神经肌肉的可塑性，改善膈肌和呼吸肌的自发激活[10-15]。

这些研究结果表明，需要重新评估呼吸康复在颈椎脊髓损伤患者中的作用，并考虑采用新的模式来满足他们的康复和护理需求。

目的。本研究旨在分析有关脊髓、神经和肌肉电刺激技术的文献资料，以矫正颈椎脊髓损伤患者的呼吸障碍。

材料和方法

本文介绍了对同行评议文章的搜索和分析结果，这些文章研究了各种电刺激技术对颈椎脊髓损伤患者呼吸功能的影响。

本检索在ScienceDirect、Google Scholar和PubMed平台上进行，时间跨度为2000年至2022年。搜索时使用了以下关键词：transcutaneous spinal cord stimulation, diaphragm pacing, spinal cord stimulation, epidural spinal cord stimulation, neuromodulation, neuroprothesys, stimulation, electrical stimulation, functional electrical stimulation, muscle stimulation, respiration, cough, spirometry, tidal volume, inspiratory, expiratory.

如果文章对电刺激进行了描述，并对治疗背景下患者的呼吸功能进行了评估，则这些文章被纳入分析。重复的文章（或研究参与者并非独立于之前发表的文章）和编辑论文均被排除在外。

首先，根据预先确定的纳入标准对所有摘要进行审查和排序。然后对符合这些标准的研究报告全文进行审阅，并再次根据预定的纳入标准进行筛选。总共分析了68个资料来源。

结果与讨论

脊髓损伤前后的呼吸生理机能

呼吸的时间和协调特性非常复杂，涉及控制着多个肌肉群的多个神经群（图1）。随着感觉反馈的整合，呼吸节奏的自动中枢控制发生在脑干呼吸中枢。然后，球脊髓输入会突触到颈脊髓（C_{III}-C_{V}节段）中膈神经的前运动神经元和运动神经元。双侧膈神经支配主要的吸气肌，即收缩的横膈膜。这样可以扩大胸腔，增加肺容量，促进吸入气体的机械交换。脑干的节律性呼吸中枢还与胸脊髓运动神经元有突触，最终支配在吸气时负责胸廓扩张的肋间外肌（主要由T_{I}-T_{III}节段做出贡献，更多的尾部胸脊髓运动神经元在不同程度上补充其工作）。用于主动呼吸和受伤后的辅助呼吸肌包括胸锁乳突肌、斜角肌、腹斜肌、腹直肌、胸大肌和肋间内肌。

横膈膜可以通过意志力收缩。基本调节是根据大脑呼吸中枢监测到的二氧化碳水平自动进行的。当横膈膜放松时，空气通过肺部

DOI: https://doi.org/10.17816/PTORS191378

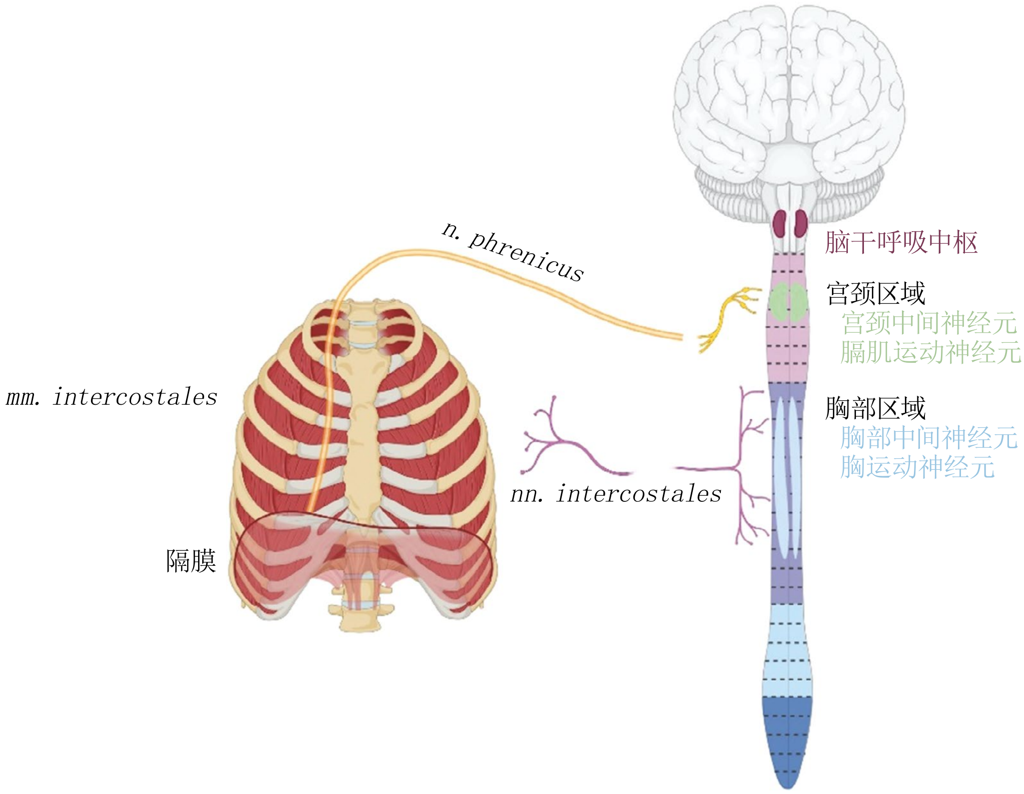

图1. 呼吸神经控制的中枢组织

和胸膜腔的弹性反冲力呼出。在用力呼气时，如咳嗽时，肋间内肌和腹壁肌的作用与横膈膜相反。

颈脊髓损伤会导致呼吸肌麻痹或瘫痪，呼吸功能和气道通畅性下降，这是由于从脑干通气中枢到颈脊髓（膈神经）和胸脊髓（如肋间神经）呼吸肌运动神经元的通路受损所致[16，17]。

在高位颈椎损伤时（脊髓C_{III}节段以上），直接属于膈肌神经并支配膈肌的脊神经根保持完整。但是，从延髓的呼吸中枢到脊髓的轴突会中断。这类患者将来肯定需要外源通气[18]。

由此导致的呼吸衰竭是脊髓损伤急性期和慢性期最常见的并发症和死亡原因[3，19，20]。

在这些脊髓损伤患者中，即使不需要机械通气，白天睡眠时呼吸也可能受到干扰[3，21]，并导致咳嗽以保护气道的能力下降。这大大增加了发生诸如肺不张和肺炎等危及生命的情况的风险[3，22]。在某些情况下可以断开人工肺通气装置连接[23]，但对呼吸应激的耐受性通常仍会显著降低[24]。

在受伤后的最初几周，颈脊髓损伤患者有呼吸停止的风险。有时这种情况与同时发生的胸部创伤有关。肋间肌麻痹会导致肺活量丧失40%，交感神经介导的支气管扩张功能丧失可能会进一步增加呼吸衰竭的风险。在脊髓损伤后的急性期，通常使用吸入式支气管扩张剂。尽管使用了这种治疗方法，但仍会出现粘液分泌过多和分泌物淤积的现象。这种情况下的自主神经系统失衡可能会危及生命，因为容易缺氧的颈部脊髓损伤患者可能会在气管清创期间出现严重的心动过缓或心跳骤停。即使对于健康人来说，气管受到刺激也会强烈刺激迷走神经反射。脊髓损伤患者由于失去了脊髓上交感神经系统的控制，反应会更加强烈。

通过呼吸装置进行外源性通气会对患者产生长期的负面影响。身体自身的肌肉组织没有受到刺激，而是被动地运动起来。该研究比较了14名已确认脑死亡并接受机械通气的器官捐献者和8名未接受机械通气的对照组患者的膈肌活检标本[25]。器官捐献者接受了18至69小时的机械通气。在正压通气18小时后，膈肌纤维已出现

明显萎缩，I型缓慢收缩纤维的体积减少了57%，快速收缩纤维的体积减少了53%。活跃的肌肉区域萎缩得更快，这导致了氧化应激和蛋白水解增加[25]。

在急性或慢性呼吸衰竭的情况下，正压机械通气可维持生命。有些患者可以耐受侵入性较小的机械通气模式。不过，大多数患者最初都需要通过气管插管进行正压通气[26]。

一项对20岁健全人和脊髓损伤患者预期寿命的比较分析表明，长期机械通气的预期寿命会从58.6岁明显缩短到17.1岁。根据2002年美国国家脊髓损伤数据库的数据，不通气患者的存活率为84%，而通气患者的存活率仅为33%[27]。

此外，机械通气对因外伤导致肢体运动障碍的患者的行动能力和独立性造成了额外的障碍，导致不同程度的身体不适以及语言和嗅觉障碍[28]。

完全机械通气可能会使患者无法在家生活，这时大部分护理责任就落在了长期护理机构身上。对通气病人的护理包括由训练有素的工作人员进行24小时监督。护理人员应能够操作设置人工肺通气装置，以优化呼吸功能并适应氧合的周期性变化。此外，还必须通过胸部叩击（促进分泌物排出）或经常清创等方法确保肺部充分排气[29]。

校正方法

设置呼吸起搏器（pacemaker）

呼吸起搏器是指患者佩戴一种利用电脉冲实现特定功能的装置。

该设备由外部发射器和接收器组成。接收器与电极相连，这些电极在颈部前表面或沿着胸腔神经缝合到膈神经。另一种方法是腹腔镜植入。该方法包括通过腹腔镜对膈肌腹部表面进行可视化，绘制肌肉电生理图以确定主要运动点和最佳收缩点，并在该位置通过手术植入刺激电极。

目前，脊髓损伤患者植入起搏器最常见的适应症是C_{III}级以上的四肢瘫痪，根据ASIA分类为A型和B型[30-32]。四肢瘫痪患者必须有需要机械通气的呼吸麻痹、可运行的膈神经、无肺部疾病和意识保持清醒。

根据临床研究，对横膈膜进行电刺激不仅可以减少或消除对机械通气的需求[18，33]，还能促进独立呼吸的逐渐恢复[34，35]。研究认为，横膈膜刺激可能会诱发呼吸系统的神经可塑性变化，并促进脊髓损伤患者的恢复[36]，但相关机制仍不清楚。

避免外源性通气的好处包括降低气道压力、增加后肺的通气量以及维持胸部负压[29]。横膈膜神经刺激更接近自然呼吸行为，因为吸气是通过内在肌肉纤维收缩产生负压而不是外源性充气完成的。言语质量和嗅觉都会得到改善，进而提高整体健康水平[28]。不被人工肺通气装置束缚显然也使患者在家庭和社区中的行动能力更强，因此可能会使患者更容易重新融入社会。

在一些呼吸机依赖型四肢瘫痪患者中，只有一侧的膈神经功能得以保留。因此，这些患者不适合安置起搏器。对4名患者进行了单侧联合刺激膈神经和肋间肌的评估。联合刺激使最大吸气量从600毫升增加到1300毫升。4名患者中有2名能够完全脱离人工肺通气装置，而其他患者在每天不使用机械通气12到16小时的情况下也能感到舒适。

尽管安装膈肌起搏器具有诸多积极意义，但该技术只能使四肢瘫痪患者实现完全通气，而这些患者仅在约50%的病例中依赖呼吸机[37-39]。

这种方法之所以没有取得更大的成功，有几种可能的解释。首先，这种方法不能激活肋间肌，而肋间肌约占肺活量的40%[39-42]。

此外，随着时间的推移，慢性刺激膈肌神经会改变I型和II型肌纤维的比例，使其从均匀分布变为更多分布I型肌纤维，而I型肌纤维的特点是耐力高但强度低，从而导致吸入空气量降低。最后，这种电极技术不能完全激活横膈膜，也会减少吸入量[43-47]。

植入任何异物都有潜在的手术风险，特别是考虑到这类患者的脆弱性。此外，呼吸起搏器的

操作中可能会出现技术故障，如电池或接收器故障以及天线断线。系统通常配有低电量警报器，以防止此类情况发生。

儿科患者使用起搏器时，可能会出现一种特有的并发症。由于15岁以下患者的肺顺应性较高，在负压呼吸时可能会出现胸壁向内的反常运动，从而显著减少吸入的空气量。随着15岁以后顺应性的降低，以及脊髓损伤时间的延长，胸壁运动会趋于正常[18]。

电刺激腹部肌肉

对腹部肌肉进行经皮（浅表）电刺激，即腹部功能性电刺激（functional electrical stimulation，FES），即使腹部肌肉因脊髓损伤而瘫痪，也能诱发腹部肌肉收缩[48]。

正常情况下，由于胸壁和肺部的弹性，呼气是被动的。用力呼气和咳嗽需要激活下肋间肌和腹肌，以产生正常的咳嗽。由于四肢瘫痪患者的腹肌通常会部分或完全瘫痪，这就导致脊髓损伤患者无法通过咳嗽清理气道，往往会引发呼吸系统并发症，如肺不张、肺炎和呼吸衰竭[9]。

腹部FES是改善这类患者呼吸功能的有效方法。

该技术是用电流刺激腹斜肌（图2），较少使用腹直肌（图2）。根据各种数据，平均最大振幅为100mA，平均脉冲宽度（脉冲持续时间）为250μs，平均刺激频率为50Hz[49]。

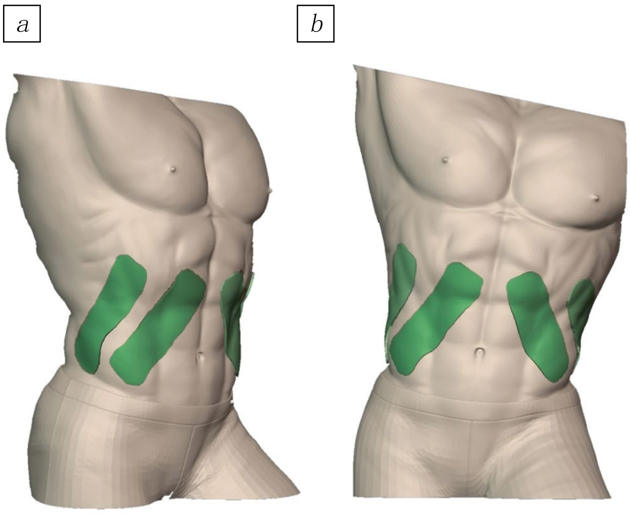

图2：腹部功能性电刺激时后侧电极放置示意图：*a* – 45° 角的腹部；*b* – 从正面看的腹部（电极放置区域已标记）

咳嗽是防止呼吸道并发症的关键气道防御机制。咳嗽峰值流量大于4.5升/秒的患者出现并发症的风险较低。使用皮肤上的电极对腹部肌肉进行电刺激产生的咳嗽效果与手法治疗产生的效果相当[50]。根据一项对四项研究的补充分析，腹部FES可显著提高脊髓损伤患者的咳嗽峰值流量[标准化平均差异为2.43升/秒，95%置信区间（CI）为0.32–4.54][49]。咳嗽流量峰值的即时改善应能减少四肢瘫痪患者的呼吸道并发症。腹部FES是一种直接作用的临床工具，可与人工咳嗽辅助、器械机械充气–排气、气管支气管卫生和体位引流等常用技术相结合[49]。

因此，腹部FES是实现咳嗽和呼吸功能改善的一种经济实惠的非侵入性方法，可为四肢瘫痪患者提供立竿见影的咳嗽效果。持续6周的每日腹部FES疗程可改善患者的自主呼吸功能。此外，反复使用这种技术还可以缩短有创通气的时间和佩戴气管造口的时间。研究表明，腹部FES对急性和慢性脊髓损伤患者有效[51]。

要有效使用腹部FES，需要完整的运动神经元。运动神经元受损的患者会出现弛缓性麻痹。受伤后，肌肉会迅速萎缩，因此，对这些患者进行腹部FES治疗可能收效甚微。

硬膜外刺激

即使在临床上脊髓完全断裂的情况下，对创伤性病变水平以下的脊髓进行硬膜外刺激，也能恢复自主和意志感觉运动功能[2，10–14，52–55]。

通过在Th_{II}水平的腹侧硬膜外表面放置单个电极来激活吸气肋间肌。在一项针对依赖呼吸机的四肢瘫痪患者的临床研究中，仅激活肋间肌就可将5名患者中4名的吸气量从470毫升增加到850毫升。然而，维持通气的最长时间从20分钟到165分钟不等[56]。尽管肋间肌刺激可显著增加吸入空气量，但仅靠这种技术并不能提供足够的容量来长时间维持足够的通气量。

后来，提出了高频硬膜外刺激的概念，以激活吸气肌[57，58]。

通过位于第二胸椎（Th_{II}）水平的单个硬膜外电极进行高频（300Hz）脊髓刺激，能够在脊髓损伤模型的实验动物中诱导吸气肌的生理激活模式[58]。

在这种情况下，肌电图期间记录到的诱发电位与自发生理呼吸相似[58]。

对于有呼吸起搏器置入禁忌症的患者，即C_{III}–C_V节段的膈肌运动神经元和/或膈肌神经受损时，脊髓高频刺激也可能有助于恢复人工肺通气装置的独立性[58，59]。颞叶干扰刺激也被用于类似的呼吸肌激活[60]。之前获得的结果已应用于此类患者[52，61]。所提供的数据证明了硬膜外刺激作为脊髓接口的可能性，能够对呼吸肌和/或神经调节进行功能性激活。

为了激活呼气肌，通过刺激胸椎下段和腰椎上段的脊髓建立了有效的咳嗽机制。硬膜外电极放置在椎体Th_{IX}、Th_{XI}和L_I水平。在高频刺激的背景下，主要呼气肌肉收缩，气道压力分别达到90厘米水柱和82厘米水柱，最大呼气流速分别为6.4升/秒5.0升/秒。联合刺激Th_{IX}和L_I时，气道压力和呼气流速分别增加到132厘米水柱和7.4升/秒[52]。

因此，硬膜外脊髓刺激是促进呼吸神经可塑性以实现长期呼吸康复的一种有前景的途径。鉴于所描述的生理效应，硬膜外脊髓刺激在恢复膈肌功能方面具有巨大潜力，可纳入现代康复策略中，以恢复脊髓损伤后独立呼吸患者的呼吸独立性并改善其呼吸功能。

经皮脊髓刺激

经皮脊髓刺激（transcutaneous spinal cord stimulation，tSCS）是一种使用经皮电极在椎骨上刺激脊髓并提供运动控制的技术[62]。经皮脊髓刺激可能是硬膜外刺激的一种可行替代方法，因为它能使临床上脊髓完全损伤的患者重新参与脊髓运动网络，甚至有助于自主控制所产生的迈步运动[63]。

计算模型表明，经皮脊髓刺激可以激活类似的脊柱结构，从而根据特定参数调节脊髓兴奋性[64]。

这项技术的研究相当深入，其在矫正运动功能、增强四肢肌肉力量和意志控制方面的有效性已得到证实[65-67]。遗憾的是，目前还没有针对大型患者群体和使用经皮脊髓刺激矫正呼吸障碍的研究。不过，颈脊髓经皮脊髓刺激在慢性脊髓损伤患者的呼吸功能和咳嗽方面已显示出良好的效果[68]。

研究了10名年轻男性在刺激Th_{XI}–Th_{XII}区域时肺通气参数和气体交换的动态变化。结果发现，经皮脊髓刺激诱导的阶跃运动会导致呼吸频率增加[69]。

因此，鉴于经皮刺激脊髓各部分的积极经验，以及少量描述慢性创伤患者呼吸功能改善的病例，这种技术可能是促进呼吸神经可塑性的可行方法。值得进一步研究，通过对获得的数据的解释和侵入性刺激方法的经验来选择最有效的刺激方案。

结论

目前，针对四肢瘫痪和肺通气功能减退的患者，已经开发出了新的治疗方案。许多研究表明，电刺激技术对通气功能有积极影响，表现为减少机械通气时间、减少肺部感染和其他并发症的数量。目前已有不同的治疗策略来改善脊髓损伤后的呼吸功能。长期的电刺激疗程可促进神经可塑性、神经回路重组、呼吸功能改善以及这类患者独立呼吸能力的恢复。与人工通气和被动咳嗽方法相比，使用电刺激更为可取。除了对膈神经和/或脊髓进行侵入性电刺激外，还应该探索一些侵入性较小的电刺激技术，以用于脊髓损伤呼吸功能障碍患者。

其他信息

资金来源。没有资金来源。

利益冲突。作者声明，他们与本出版物没有明显或潜在的利益冲突。

作者的贡献。*V.G. Toriya*，撰写文章的所有部分、数据收集与分析、文献分析、插图创作；*S.V. Vissarionov*，文章文本的阶段和最终编辑；*M.V. Savina*和*A.G. Baindurashvili*，文章文本的阶段编辑。

所有作者都对研究和文章做出了重要贡献，并在发表前阅读和批准了最终版本。

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DOI: https://doi.org/10.17816/PTORS191378

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