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Historical Article

Adaptation to Neural Damage due to Discopathy throughout the History of Medicine

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Abstract

Evidence from medical literature implies that back radiculopathy pain is primarily caused by inflammation and disc herniation. Based on our examined sources, this theory was initially put forward in 1934 by two American surgeons, William J. Mixter and Joseph S. Barr. The theory proposes that the intervertebral disc changes shape for various reasons, leading to the compression of nerve fibers in the epidural canal. This compression can result in inflammation, pain, and restrictions in movement. Today, this theory is perceived to be increasingly inconsistent with clinical experiences. Hubert L. Rosomoff was the first to publish the article "Do Herniated Disks Produce Pain?" in 1984. In The Clinical Journal of Pain, he rejected Mixter and Joseph S. Barr's theory, but did not introduce a mechanism for how patients with discopathy do not experience pain. Recent studies indicate that the human body can adapt to various types of deformities and alleviate the symptoms of a wide range of complications without any measurable change in the pressure or shape of the disc. This study proposes a hypothesis to understand the body's ability to achieve balance and adapt to a deformed disc and radiculopathic pain.

Keywords: Integrative medicine; Discopathy; Neuroplasticity; Low back pain; History of medicine

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Introduction

Low back pain (LBP) is the first cause of hospitalization in the United States [1]. Research further reveals that its prevalence is increasing due to urban sedentary lifestyles [2]. Despite the increasing prevalence of chronic LBP in adults over the past decade, the leading cause of many cases of LBP remains elusive, resulting in reduced functional capacities and occupational performance [3]. Throughout history, various theories have been proposed for the probable cause of chronic low-back pains, ranging from those that attributed back radiculopathy pain to the disruption of the balance of body fluids [4,5] to the Mixter-Barr theory, which focused on the deformation of the intervertebral discs and the pressure on the nerves tasked with controlling the lower limbs [6]. William Jason Mixter was born in 1880 and graduated from Harvard Medical School in 1906. After various occupational roles, he was appointed the first head of neurosurgery at Massachusetts General Hospital and developed his research on referred back pain [7]. In 1934, Mixter and his colleague Barr, a noted orthopedist published a revolutionary article on intervertebral disc lesions in the Journal of New England Surgical Society.

The article resulted in several profound changes in the public understanding of sciatica at the time. The picture depicted by the Mixter-Barr theory is staggeringly close to what is now called reflective back pain. This article had a tremendous solidifying impact in favor of surgical interventions for sciatica treatment. Over the next few decades, the popularity of discectomy surgery increased, and some refer to that period as the “dynasty of the disc” [8]. The applicability of this theory in describing and predicting many complications was impressive. Even to this very day, this theory, although with some slight developments, is still the prevailing practical theory in various treatment fields. However, new findings indicate that this theory needs to be revised. This study proposes a hypothesis to understand the body's ability to achieve balance and adapt to a deformed disc and radiculopathic pain.

Methods

This study presents a narrative review of investigations focusing on features for adapting to neural damage caused by disc pathology.

In this regard, our main source was scientific electronic databases, including Web of Science, Medline, and Scopus, which were searched for related information and articles on the nervous system's adaptation in discopathies throughout medicine's history.

Hence, "discopathy," "neural system," "adaptation," "history of medicine," and "Neuroplasticity in the spinal cord" were searched as keywords.

After collecting the documents, we reviewed the texts and collected relevant data for this study. We then organized the information in a categorized file in historical order. Then, we composed the primary narrative of the manuscript using the initial data and subsequent information obtained from our work. Finally, we analyzed the data and extracted a comprehensive conclusion.

Findings

Discopathy comprises two words, disc, and pathy, a suffix denoting disorder. It is a medical term that describes the deformation of the intervertebral discs that separate the spinal cord bones. The discs create a cushion-like space between the vertebrae, allowing the spine to have the necessary flexibility. In light of the available data, disc degeneration is often associated with disc herniation. As intervertebral disc fibrochondrocytes age, they undergo senescence, decreasing proteoglycan production. Repeated mechanical stress on the disc can cause dehydration, leading to disc collapse and increased pressure on the annulus fibrosus. This increased pressure can result in ruptures, facilitating the herniation of the nucleus pulposus. Consequently, repetitive mechanical stresses often lead to a gradual onset of symptoms that become chronic over time.

On the other hand, axial overload exerts a large biomechanical force on the healthy disc, which may result in the extrusion of the disc material through a ruptured annulus fibrosus, subsequently putting pressure on the adjacent nerve roots. These complications generally lead to more severe acute symptoms where the patient feels pain and inflammation along the nerve root compressed by the degenerated disc [9]. In such scenarios, the prospects of surgery for lifting the pressure from the nerve roots are discussed (Figure 1).

Although surgical procedures have proved to be hugely successful in treating back pain, non-surgical methods also garnered a significant share of interest in alleviating the symptoms of the disease. Research on non-invasive treatments for LBP indicates that some non-surgical methods, such as massage and acupuncture for radiculop-

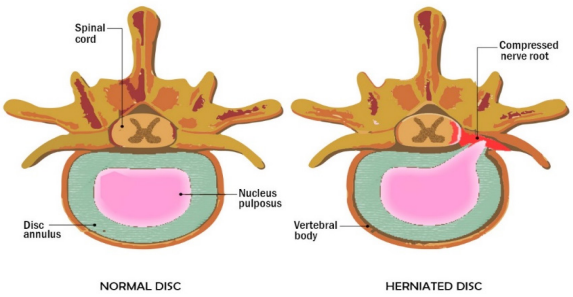

Figure 1. Spinal disc herniation

athy pain [10], are effective in controlling the symptoms of the disease. The efficiency of non-invasive treatment has raised the question of how interventions, such as massage, can affect spinal stenosis and alleviate the disease symptoms without treating the herniation disc or the degenerate disc, putting pressure on the nerve. As such, most researchers failed to analyze the clinical findings regarding this theory. The initial assumption was that the soon-to-be-herniated disc occupies a larger volume along the spinal canal in the early stages of inflammation. Following the period of inflammation, the volume of the occupying material is reduced, thus partially relieving pressure on the nerve root. Nevertheless, this assumption lacked prognostic capacity; hence, many endeavors were piloted to explain this feature better, some of which dated back to the 1960s. One of the earliest studies in this field was conducted by Dr. Splithoff, a radiologist, in 1953. The results were later published in the Journal of the American Medical Association [11]. He examined nine defects in the lower back area and the tail-end of the spine between two random groups of patients and healthy individuals. He reported that there is no statistical difference between these two groups except for the spondylolisthesis disease, concluding in the aftermath that back pains cannot be generally attributed to defects in the spine. This line of research was continued from 1976 to 1980 by two experts, Dr. Magora and Dr. Schwartz. They published four articles in the Scandinavian Journal of Rehabilitation Medicine to address whether specific spine defects can lead to LBP [12]. Their research method was to compare the images of patients with those of healthy people who had voluntarily allowed their backs to be scanned. If these defects were more common in patients with back pain, they could have concluded that these defects could be the cause of back pain. However, they did not find any significant difference between the data about the two groups of healthy individuals and those with back pain regarding the number of cases of osteoarthritis, extra vertebra, and spina bifida. There was only a very slight difference in the number of cases of spondylolisthesis. This research implied that the factors causing LBP could not be readily identified in radiological images; hence, the images are inadmissible for modeling the interpretations of the Mixter-Barr theory. On the other hand, one of the principles of this theory is that radiculopathy pain occurs due to nerve compression. However, in 1985, Hubert Rosomoff published “Do Herniated Discs Produce Pain” in The Clinical Journal of Pain [13], which directly addressed the reservations regarding the Mixter-Barr theory. This article reviewed experimental evidence and physiological arguments to reveal that intervertebral disc herniation, nerve root compression, cannot cause radiculopathy pain, as the pain stemming from nerve root compression is often perceived less after a while, allowing for coexistence. Nevertheless, patients with intervertebral disc herniation mostly reported sustained periods of acute pain. Rosomoff concluded that nerve root compression is probably not the cause of pain and that some other complication is responsible for the pain, the search for which did not yield any clear conclusion. A major limitation that plagued the works of Rosomoff and others was that they could not simply dismiss the evidence of the effects of disc deformity on radiculopathy pain because the underlying theory was highly consistent in explaining the complication at the time. Nevertheless, they had evidence indicating that the pain goes away in many patients without the disc having priorly returned to its normal state. Over time, with the development of complementary and alternative medicine (CAM), researchers have become more interested in non-surgical treatments. Mazanec and colleagues were among many researchers who conducted studies on non-surgical methods and confirmed their efficacy [14]. These studies popularized methods such as physical therapy [15], moxibustion [16], acupuncture [17], cupping [18], wet cupping [19], and Kermanshahi massage therapy [20], among others, all of which claimed to alleviate radiculopathy pain without serious disc manipulation. Nevertheless, none of the studies have resolved the ambiguity regarding whether a patient with damaged discs can experience reduced pain without first correcting the disc. To this end, the current research sought to explore various sources to explain the healing mechanism of the damage caused by discopathy or coexistence. In the meantime, the neuroplasticity theory was able to explain the underlying causes. *Neuroplasticity* is a term that refers to both synaptic and non-synaptic plasticity and is related to changes in neural pathways and synapses that result from behavioral changes and environmental and neural processes like those caused by physical trauma [21].

Neuroscientists used to think that neuroplasticity occurs only in childhood. However, evidence from the latter half of the 20th century established that many aspects of the nervous system remain plastic even into adulthood [22]. The term “plasticity” was first applied to behavior in 1890 by William James in his book “The Principles of Psychology.” The first person who used the term neural plasticity was the Polish neuroscientist Jerzy Konorski.

Neuroplasticity occurs at different levels, ranging from learning-induced cellular changes to large-scale alterations, such as the remapping or repairing damaged nerves in response to physical injuries. The human body employs different plasticity pathways against damage to its nervous system, some of which are mentioned below.

1. Restoration of synaptic efficiency
2. Increasing synaptic efficiency
3. Increased sensitivity after nerve damage
4. Maintaining and increasing neurogenesis
5. Using silent synapses

6. Repairs and collateral
7. Substitution of nerve
8. Behavioral change of the patient

Up until two decades ago, these studies were primarily based on the paradigm of brain damage, but over time, neuroplasticity in the spinal cord and even neuroplasticity in the peripheral nerves garnered a great deal of academic interest, as they provided the evidence to explain the adaptation mechanism of the spine with discopathy.

Adaptation mechanism of the spine to discopathy

Pain symptoms decrease in over 80% of disc herniation patients within 6 to 12 weeks without any treatment [23]. Patients without radiculopathy are recovered in even less time [23]. These observations illustrate that the spine can adapt to discopathy and spinal canal stenosis. In other words, the spinal cord can be flexible physiologically and anatomically, allowing it to coexist with limited lesions, such as discopathy, more extensively than previously thought. This necessitates further in-depth examinations. This capacity includes long-term changes in synaptic and non-synaptic efficacy and functions such as learning and memory that are pivotal to motor learning. There is also evidence for different forms of morphological plasticities, such as alterations of dendritic configuration and axonal growth. An essential point among these is that damage to the nervous system can cause collateral sprouting of healthy axons to take over empty postsynaptic sites. This capacity represents how a patient with spinal canal stenosis from lumbar disc deformity can lead an everyday life with this level of plasticity after a while without prior mitigation of the compression on the spinal canal.

It should be noted that this level of plasticity is limited to minor lesions exhibiting deformed disc pressure in the spinal canal. As a result, it is not highly regarded in SCI, as repairing damaged axons is anatomically challenging. Treatments that increase the collateral sprouting of axons in the cortico-spinal pathway are perceived to restore the pathway only partially. As such, there is a significant difference between the underlying mechanisms of collateral sprouting and regeneration. Collateral methods rely on reserves of cells, and in case of severe spinal cord injuries, the reserve may not be sufficient.

Collateral sprouting

Long-standing evidence indicates that the damage of some motor axons in the peripheral nervous system causes the sprouting of the adjacent undamaged axons following the loss of nerve stimulation of the muscle fibers (Figure 2), which in turn reinnervates the denervated muscle fibers [25- 27].

Dendritic remodeling

This hypothesis builds upon the notion of the possible remodeling of dendrites owing to sustained levels of physical activity by the patient. Notably, dendritic trees of neurons react to the set of activities that occur in pre-synaptic inputs. This feature makes the accessibility of post-synaptic sites match the intensity of pre-synaptic input. Collateral sprouting, formed from the septum degressive entorhinal cortex, can regenerate a significant share of synaptic contacts [28,29]. However, it must be accepted that some longitudinal dendritic loss is permanent and cannot be completely restored. The underlying mechanisms of dendritic remodeling are not known. However, changes in the number of intracellular calcium ions may be involved in its formation [30], which can regulate the protein synthesis mediated by poly-ribosomes connected to cisternae at the base of dendritic spines [31]. As such, the local protein synthesis regulated by the local synaptic activity can cause changes in the size, shape, and function of the dendritic tree, ultimately making dendritic regeneration possible.

The literature on the functions of dendritic regeneration in the spinal cord is less extensive than that on the brain. However, some general rules that apply to the brain can be used to understand regeneration in the spinal cord.

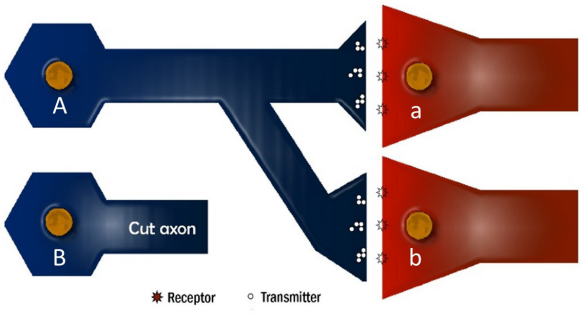

Figure 2. Lateral sprouting of uninjured axons in response to the lesion of adjacent axons. Here, neuron A should have typically synapsed on neuron a, while the adjacent neuron B should have typically synapsed on neuron b. In response to the axon of neuron B being cut, the intact axon of neuron A sprouts collaterally and leans towards neuron B, forming a synaptic contact that replaces the previous contact between B and b. The hypothetic illustration depicts a mechanism that can partially compensate for functional disability stemming from nerve

The functional significance of collateral sprouting is yet to be clarified, but sprouting in the spinal cord may compensate for minor breaks in long axonal pathways.

It is assumed that continuous use of a synaptic path causes physiological changes in synaptic function and leads to changes in the number of synaptic contacts between axon and dendrite and even the length and shape of the dendrites themselves. This behavior significantly affects physical therapy and sustained organ functioning. Along with collateral sprouting, this mechanism can cause anatomical changes on a limited scale of a few hundred micrometers. However, prolonged stimulation for a sustained period may lead to changes on a larger scale of several millimeters [32-35], properly sufficient to compensate for the damage caused by disc deformity (Figure 3).

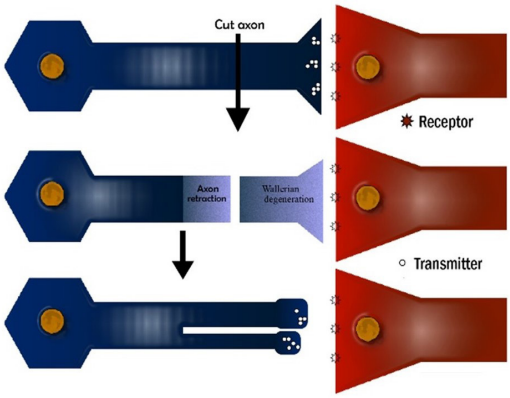

Figure 3. Regeneration of axons after an axon is cut; here, the distal stump is destroyed, and the proximal stump shrinks. Consequently, the axon tries to organize connections with postsynaptic sites for regeneration.

Evidence of inducible events in the nerve cell and plasticity in peripheral nerves

Some researchers ought to develop other theories. An experimental study in 1981 revealed that adult rats could regenerate their peripheral nerves after damage to their nervous system. This study indicated that plasticity in the glial environment of the central nervous system can be extended to the peripheral nervous system [36]. A part of the regeneration occurs along the pathway of the peripheral nerves, which researchers have not previously explored. Richardson revealed that sensory neurons could increase their sensory perception after injury, demonstrating the influence of inducible events in the nerve cell [37]. Schwab complied with his previous findings on spinal cord regeneration and proposed molecules inhibiting neurite growth [38], thereby seeking to outline a mechanism in his future works [39]. Ramer et al. employed this model to discuss the remodeling by neurotrophic factors [40]. The following line of work was dedicated to elucidating a suitable explanation for methods and pathways of developing plasticity in peripheral nerves [41], which is still in its early stages.

Discussion

The terms “neuroplasticity” and “spinal adaptation,” although often used interchangeably, are not the same notions when it comes to discopathy, as the former is one of the many mechanisms for the adaptation of the spinal cord (CSC). These changes can improve motor control or alleviate pain, while others can establish the pre-cursors for chronic pain. Nonetheless, it should be noted that the spinal cord's ability to adapt is limited to neuroplasticity. The more recent literature has proposed numerous functioning mechanisms for CSC, among which the Gate Control Theory of Pain [42] and Neuromatrix Theory of Pain [43] have garnered more academic attention, allowing for a more comprehensive look at the issue of reducing pain symptoms and neuropathies caused by discopathy.

Conclusion

Mixter-Barr’s theory was groundbreaking in explaining the onset of spinal radiculopathy pains and has been relied upon in the world's scientific communities. Nevertheless, more recent studies have revealed that many patients with acute disc deformities do not exhibit symptoms of this disease, indicating that the aforementioned requires revision. Studies demonstrate a limited possibility of retaining the neuroplasticity in the spinal cord. These findings can be used to study how a person with discopathy who has not had a significant modification in his/her vertebral disc degeneration could experience alleviated symptoms, thereby indicating the adaptation of the spine with discopathy.

Although there is no denying that pains of such caliber are unrelated to disc deformations, some patients can achieve this adaptation while others cannot. An in-depth understanding of the adaptation mechanism can be a positive step towards finding the methods that can increase the probability of striking this coexistence, which, in turn, can lead to a better understanding of the function of the spine and the nerves and the complex relationships therebetween. A more precise, applicable definition for root syndrome can be proposed using the underlying notion that revolves around the adaptation mechanism. Prospective studies in line with the current work can provide reliable foundations for conservative treatment methods. The development of the concept of adaptation can even be included in the compilation of physiology studies as an educational course. Nevertheless, more studies are required regarding the adaptation capacity of the spine to be able to identify the exact function of this capacity. This mechanism can even offer novel academic avenues for repairing spinal cord injuries.

Realizing that the body can coexist with discopathy can direct experts' studies toward optimizing this capacity to obtain health through adaptation. This can, in turn, boost

our understanding of patients' capacity to coexist with spine-related complications. The findings of this work can also help future researchers better identify the elements that increase or decrease the probability of achieving coexistence. The implications of this can pave the way for more efficacy in treatment methods, from surgery to physical therapy.

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Conflict of Interests
The authors declare no conflict of interest.

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