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LITERATURE REVIEW

Mechanical Aspects of Intervertebral Disc Injury and Implications on Biomechanics

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Study Design. This article comprises a review of the literature.
Objective. The purpose of this study was to elucidate the different types of structural failures exhibited in intervertebral discs (IVDs), summarize their potential causes with respect to mechanical loading conditions and the consequences on cell homeostasis and biomechanics.
Summary of Background Data. Many studies have been performed to gain insight into how discogenic back pain progresses in humans both *in vitro* and *in vivo* as well as in animal disc models. However, there is a major need to summarize the common factors which initiate the structural failures observed in IVDs and the typical biomechanical changes. This work could help in developing mechanisms aiming to restore the biochemical and biomechanical balance of IVDs.
Methods. The different types of structural failures encountered in IVDs were reviewed from published literature. The types of mechanical loading causing these injuries and their physiological and biomechanical consequences were then summarized and linked to ongoing research in this area.
Results. The most prominent structural failures associated with IVDs are annulus tears, disc prolapse, endplate damage, disc narrowing, radial bulging, and osteophyte formation in the vertebrae. IVDs were found to be vulnerable to compression, flexion, axial rotation, and complex loading mechanisms through single impact, cyclical, and continuous loading. However, chronic loadings had a more damaging impact on the spine. Significant consequences include imbalance of metabolic enzymes and growth factors, alteration in stress profiles of IVDs and a decrease in mechanical stiffness resulting in impaired biomechanics of the spine.
Conclusion. The mode of loading has an important impact on the severity and nature of failures seen in IVDs and the resulting consequences to biomechanics. However, further research is necessary to better understand to the mechanisms that link injury to degeneration and regeneration of IVD tissues.
Key words: biomechanics, discogenic, intervertebral discs, *in vitro*, *in vivo*, mechanical loading, metabolism.
Level of Evidence: 3
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The skeletal system, specifically the spine, is subjected to a wide range of impact and repetitive loading during daily activities such as walking, jumping, lifting, and other occupational activities. The spine can handle the high demands of routine loading due to the robustness of both the vertebrae and intervertebral disc (IVD). IVDs are essential in separating and evenly spreading the load between vertebral bodies. They are composed of three main components as shown in Figure 1: (a) the nucleus pulposus (NP), which is circumferentially enclosed by (b) the annulus fibrosus (AF), both of which are contained inferiorly and superiorly by (c) cartilaginous endplates (CEPs), which attach to the corresponding vertebrae. The NP consists largely of gelatinous proteoglycans that maintain the hydrostatic pressure necessary to resist compression and maintain separation of the vertebrae, as well as collagen and other proteins. The AF is made of highly oriented collagen fibers that surround the NP. The AF consists of 15 to 25 concentric lamellae, which are composed of alternatingly aligned oblique collagen fiber bundles interspersed with proteoglycans. Sheaths of elastic fibers, formed by elastin, fibrillin, and other proteins, enclose these collagen fibril bundles and contribute to the elasticity of the lamellae. The outer lamellae are more fibrous than the inner lamellae, consisting principally of collagen-I, whereas the inner lamellae are less cartilaginous, containing mostly collagen-II and aggrecan. The collagen-I content increases from the inner lamellae to the outer lamellae, whereas the collagen-II and aggrecan content increases toward the NP. AF collagen fibers are tensioned by radial pressure from the NP and

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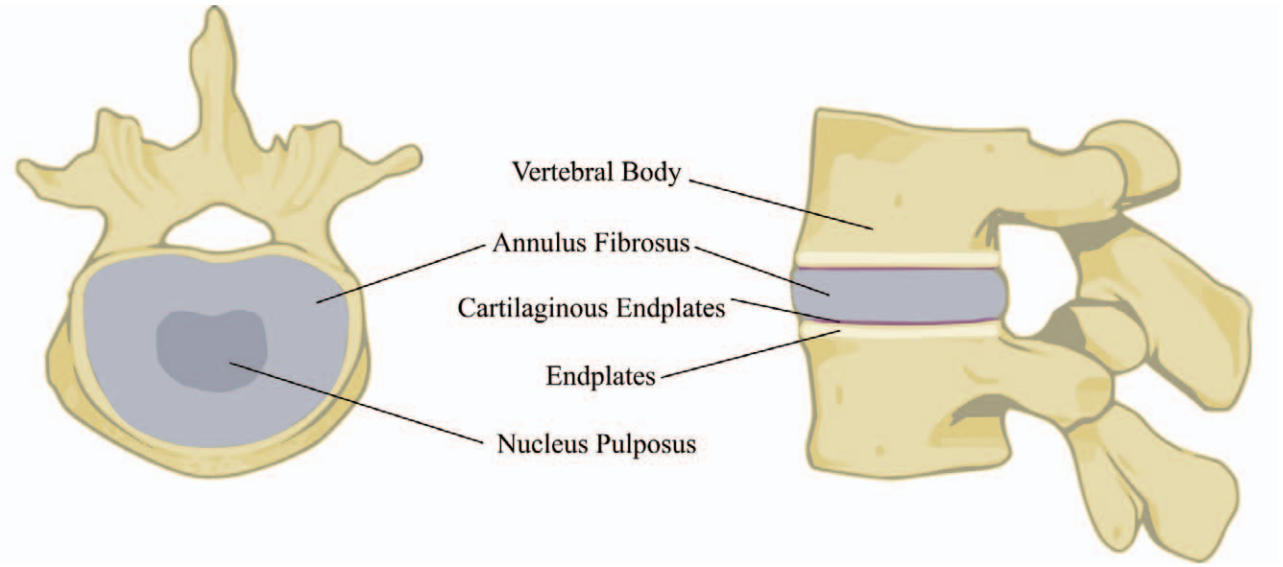

Figure 1. Relevant structures of the spine.

cranial-caudal stretch from the separation of the inferior and superior CEPs. The greater collagen-I content of the outer lamellae makes them stiffer than the inner lamellae such that the elastic modulus of the AF more than doubles from the inner region to the outer region. Sudden and abrupt loading can cause acute injury to one or more of these structures. Forces and torques applied to the spine during lifting, twisting or sudden impact can cause abnormal shear and compressive strain on the IVD leading to injury, physiological changes that alter IVD cell homeostasis and degeneration of the disc.[1] With age IVDs degenerate and become more susceptible to injury. This article will review various types of IVD injury associated with structural failure of the IVD, discuss the potential causes of structural failure and the ensuing physiological and biomechanical consequences.

TYPES OF STRUCTURAL FAILURES

IVD can be damaged in a number of ways. This section aims to outline the mechanisms that have been identified in the literature. Table 1 summarizes the different types of IVD failure that will be discussed in this review.

Annulus Tears

The three most distinguishable types of AF tears are circumferential tears (also known as delaminations), peripheral rim tears and radial fissures, as shown in Figure 2.

An analysis of the response of a three-dimensional nonlinear finite element model of an intact L3-L4 lumbar motion segment to axial compressive loads ranging from 200 to 2000 N showed that circumferential tears occur from shear stresses due to compressive stress concentrations in the laminae of aged discs.[2] The interlaminar shear stresses, together with disc bulging and displacement, were found to be higher in the posterolateral portion of the intact disc, which was hypothesized as the origin for these circumferential tears.

Peripheral rim tears are discrete tears in the outer layers of the AF that run parallel to one or both CEPs and promote vascular granulation tissue ingrowth that can reach the middle layers of the AF. These tears frequently originate in the anterior portion of the AF and appear to have a traumatic etiology.[3] Radiography of cadaveric dorsolumbar spines also revealed lesions of the bony vertebral rim which were associated with avulsion of the AF or AF tears. The lesions occurred predominantly in the anterior portion of

TABLE 1. Summary of Failure Types

Failure Type	Description
Annulus tears	A rupture or tear of the annulus fibrosus.
Disc prolapse	Involves a tear in the annulus fibrosus which allows the nucleus pulposus to bulge out beyond the damaged outer rings.
Endplate damage	Damage to the vertebral interface with the disc.
Schmorl nodes	An upward or downward protrusion of the disc soft tissue into an adjacent vertebral body.
Internal disc disruption	Biochemical loss of integrity of the annulus fibrosus generally focused on the inner rings.
Disc narrowing	A thinning of the disc, reducing the distance between vertebral bodies.
Radial disc bulging	Involves the disc moving off center from the vertebral body, effectively being pushed out to the side.
Vertebral osteophytes	Small bony growths that develop near the edges of the endplates

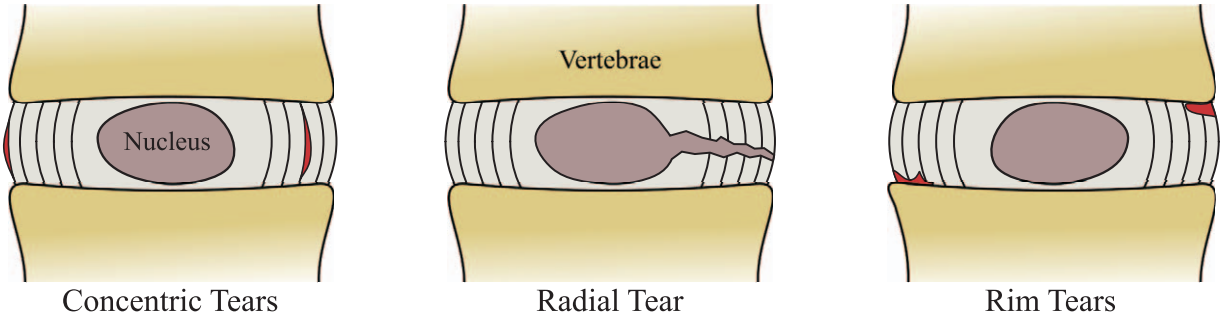

Figure 2. Types of annular tears in intervertebral discs (IVDs).

the upper vertebrae, and were rare below 30 years but increased in frequency with age.[4]

Radial fissures have the capacity to proceed in the posterior or posterolateral directions away from the NP[3] and subsequently propel the NP out of the IVD in a process that can be replicated through the simulated subjection of cadaveric discs to cyclic loading in bending and compression.[5] A radial tear in the AF leads to shrinkage and disorganization of fibrocartilage in the NP and replacement of the disc by dense fibrous tissue and cystic spaces.[6]

Disc Prolapse

Migration of the NP toward the periphery of the disc can result in gradual progression from radial fissures to a prolapsed or herniated disc, as shown in Figure 3. Depending on the extent of nuclear migration, disc prolapse can lead to annular protrusions, nuclear extrusions, or sequestrations of the nuclear content. A study investigating disc prolapse was able to induce prolapse by nuclear extrusion or annular protrusion in 26 of 61 cadaveric intervertebral lumbar joints which were laterally flexed by about 15° and forward flexed at gradually increasing angles until the physiological limit was reached while cyclically compressing the joint.[7]

Nuclear extrusion was observed on the posterolateral edge of the vertebral body and neural canal. The posterior AF was found to protrude into the nuclear canal with damage to the annular rings at the point of bulging and a degenerated NP displaced posteriorly. It was shown that repetitive loading of vertebral motion segments under physiological conditions (7° flexion, <3° rotation, and cyclic compression of 1334 N for 3 to 13 h at a frequency of 1.5 Hz) resulted in disc prolapse comprising primarily annular protrusions and less frequently, nuclear extrusion through annular tears. The AF was the primary site for pathological change, supporting the hypothesis that disc prolapse is primarily the result of peripheral injury.[8]

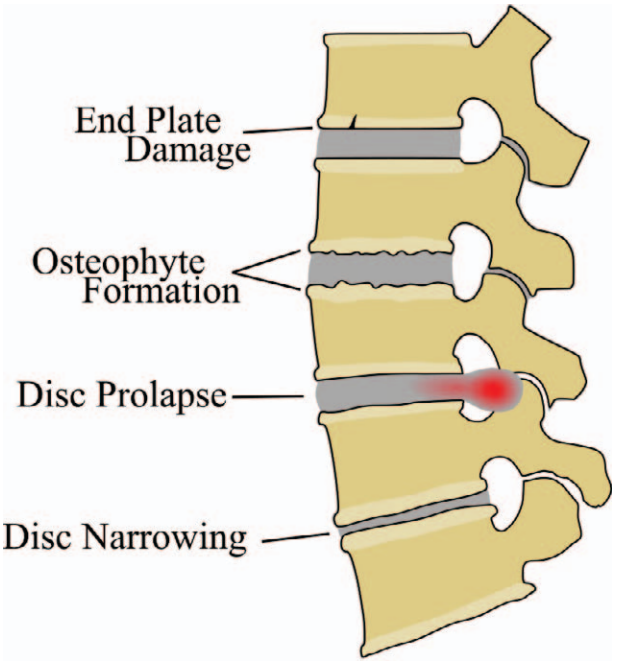

Figure 3. Other forms of structural failures in intervertebral discs (IVDs).

Endplate Damage and Schmorl Nodes

Endplates are most susceptible to trabecular microdamage in compression, as shown in Figure 3, and may explain the increased bulging of the NP in the vertebral bodies over the lifespan. In a post-mortem study, which examined the lumbar spines of 22 middle aged and elderly subjects,[9] the number of vertical endplate trabecular lesions increased from lumbar vertebra L1 to L4 and was positively correlated with age. These lesions were more numerous in regions of the cancellous bone of the CEP that had marked osteoporosis as compared to the surrounding regions. In some subjects with numerous lesions, they were grouped around the margins of Schmorl nodes in a chain-like manner, the nodes being formed from calcification subsequent to herniation of disc tissue through the CEP.

Internal Disc Disruption

There is a possibility of the inner annulus collapsing into the NP due to loss of pressure in the NP after fracturing of the CEP, with the anterior portion damaged more than the posterior. There could be a separation of the cartilage-rich CEP from the underlying bone due to a loss of hydrostatic pressure that keeps the two entities intact and connected. There is radiological and histopathological evidence from L4–5 lumbar discs of autopsy specimens for this separation of the endplate and vertebral body, which was found in 45 out of 88 cadavers ranging in age from 50 to 101 years.[10]

Disc Narrowing, Radial Bulging, and Vertebral Osteophytes

There is a tendency for the NP to bulge into the vertebral bodies with increasing age. This can lead to loss of nuclear pressure and an increase in the vertical load exerted on the AF that subsequently causes it to bulge radially outwards and occasionally inwards, resulting in narrowing of the disc, as illustrated in Figure 3. A magnetic resonance imaging investigation in 232 male adults found that disc narrowing with age was greater in the lower lumbar and lower thoracic spine than in the upper lumbar and upper thoracic spine, respectively.[11] Osteophyte formation has also been linked to disc bulging, although not in the low back region. Formation of osteophytes in the lower lumbar spine was most frequently associated with endplate irregularities whereas osteophytes in the upper lumbar and lower thoracic regions were associated with disc bulging. Nuclear pressure loss and reduction of annular thickness can then lead to the transfer of more than 50% of the compressive forces on the spine to the neural arch. This has been verified through an experiment involving an application of 2000 N compressive creep load on cadaveric lumbar motion segments and measurement of the generated compressive stress in the neural arch.[12]

CAUSES OF STRUCTURAL FAILURES

IVD failures have been shown to occur with different types of repetitive loading. Table 2 associates various repetitive types of loading with their potential consequences.

Compression

Brinkman[13] investigated the deformation of discs in human lumbar motion segments under compressive loading before and after the vertically oriented fibers of the AF had been internally divided to simulate disc degeneration. Twenty-five spinal motion segments were subjected to loads of 1000, 2000, and 300 N, simulating naturally occurring physiological compressive loading of the human spine during standing, during standing with an added load, and in the supine position, respectively. Following radial annular division, the radial bulge increased by 0.31 mm under the 1000 N load and by up to 0.7 mm if the AF was divided both radially and tangentially. For radial annular division the bulge increased an additional 0.17 mm on an average when the load increased from 1000 to 2000 N, whereas it decreased by 0.27 mm when the load was reduced from 1000 to 300 N, suggesting that radial bulging is sensitive to the loading condition. A subset of 15 specimens was treated at an increasing loading rate of 100 N/s up to the limit of fracture, which resulted in failure of vertebral bodies but no peripheral tears in the AF or observable disc protrusions beyond a fraction of a millimeter more than was otherwise observed *in vivo*. This suggests that the radial stress generated within the disc *in vitro* was too low to initiate expulsion of the nuclear material. The resiliency of the disc was highlighted in a study in which stiffness of the disc was compared when the disc was intact, after its height had been increased by saline injection, after it had been radially punctured, following removal of NP material and following removal of the CEPs.[14] Surprisingly, there was little difference in stiffness once the disc had adapted to compressive loading. A study by Adams *et al*[15] sought to compare the extent of endplate damage with the variation of compressive stress in the adjacent disc and to observe the response of affected discs to cyclic loading. Motion segments were subjected to a pure compressive force of 300 N for about 15 minutes to eliminate post-mortem superhydration, which resulted in a disc height loss of 0.1 to 0.2 mm. A static compressive load of 2000 N was then applied for 20 minutes to simulate light manual labor. Subsequently, the motion segment was flexed slightly and slowly compressed until damage was identified by a reduction in the gradient of the force-deformation curve. Compressive damage to the disc was induced at a mean force of 7000 N resulting in a permanent compression of about 0.7 mm, cracking of the vertebral endplate, and its supporting trabecular bone and vertical displacement of the NP. Failure due to posterior prolapse was observed in only one of the specimens. Pressure in the NP dropped by 25% and appeared to be directly correlated with vertebral damage. Somewhat surprisingly, subsequent cyclic ramp loading and unloading over 1.5 seconds did not cause the NP to migrate from regions of high stress to low stress which would have equalized the stress distribution. Rather, the stress peaks were accentuated, further reducing nuclear pressure and also significantly reducing the diameter of the hydrostatic NP. This was mainly due to buckling of the inner annular lamellae toward the nucleus and the outer lamellae toward the edge of the vertebral body allowing for migration of the NP because of the additional space provided by the deformation of the damaged endplate. It was suggested that the resulting pressure drop would inhibit synthesis of proteoglycans preventing restoration of the nuclear volume and the increased stress in the AF would inhibit the ability of the cell to repair damage to the collagen matrix. A recent study in which compressive loads were applied to cultured caprine discs showed that high static loads affected cell viability and matrix integrity particularly in the posterior region of the outer annulus suggesting that high compressive static loads increases the vulnerability of IVDs to posterior herniation.[16] Higher frequency sinusoidal loading of ovine motion segments at 5 Hz for tens of thousands of cycles resulted in separation and distortion

TABLE 2. Structural Failures Associated and Their Link to Mechanical Loadings

Loading Type	Possible Resulting Failure
Compression	Annulus tear disc prolapse Endplate damage Disc bulging
Flexion	Disc narrowing
Axial rotation	Annulus tear
Complex loading	Annulus tear Disc prolapse

of the inner- and mid-annular lamellae and diffuse tracking of nucleus material, which occurred in both the posterior and anterior regions.[17,18] Tearing between the inner disc and endplate was also occasionally observed.

Flexion

Although prolonged or repeated anterior flexion may not load spinal tissues to the point of failure, it can greatly increase risk of IVD injury.[17,18] Such loading induces creep in the passive disc tissue, thereby causing alterations in its height and viscoelastic properties and further increasing the laxity of joints and subsequent intervertebral motion. Solomonow *et al*[19] performed cyclical loading of the cat spine by stretching the supraspinal ligament for periods of 50 minutes followed by 10 minutes of rest and observed that the loading produced a reduction of almost 85% in the stabilization reflex of the multifidus muscles which they attributed to desensitization of mechanoreceptors caused by laxity in the viscoelastic disc tissues (narrowing of the disc and development of asymmetrical geometries within its volume). They concluded that occupations which involve repeated flexion of the spine would reduce the stabilization reflex exposing the discs to destabilizing injury. The 10-minute rest period was not enough for recovery from creep, leaving the discs vulnerable to for some time following the cyclic loading. McGill and Brown[20] found that following 20 minutes of deep flexion 30% of the induced creep remained even 50 minutes after resuming normal posture. Similarly, Ekström *et al*[21] found that following 1 hour of 5 Hz compressive vibratory loading of porcine lumbar motion segments, a 1-hour rest period was not sufficient for recovery from creep. Although it is possible to increase muscular tension to compensate for the joint laxity resulting from creep deformation, a study involving human subjects found that complete compensation cannot be achieved.[22]

Axial Rotation

Axial rotation of the spine during vigorous activities may injure the anterior regions of IVDs lying furthest from the center of axial rotation in the posterior annulus. Farfan *et al*[23,24] subjected both motion segments and isolated discs to axial rotation until failure and found that the failure was manifested as separation of the peripheral lamellae of the disc and foraminal occlusion, which correspond to early stages of disc degeneration involving the AF. They hypothesized that repeated torsional loading would lead to radial tears in the annulus, migrating from the NP to the periphery of the disc. However, Adams and Hutton[25] found that most of the resistance to torsion is provided by the compressed facet joint and concluded that torsion alone is less likely to damage IVDs within the physiological range of motion than compression of the disc. In accord with this result, Marshall and McGill[26] found that cyclic axial twisting did not result in damage to the disc, although when preceded or followed by cyclic flexion-extension, axial twisting frequently resulted in radial delamination within the AF.

Complex Loading

Simultaneous application of bending and compressive forces to the spine, as occurs when lifting a heavy object from the floor, can cause spine injury through posterior prolapse of the IVD as demonstrated in the studies by Adams and Hutton[5,7] described above, although a disc is not usually damaged by hyperflexion until the compressive force reaches a critical value. Gradual expulsion of the NP may occur through growth of radial fissures into a posterolateral corner of a disc. Using porcine movement segments, it has also been shown that combining flexion/extension moments with compressive force can produce herniation in the posterior and posterolateral regions of the AF with injury increasing in proportion to the axial compressive force.[27] An alternative paradigm, in which disc herniation was induced in ovine motion segments by increasing the pressure in the NP, found that the incidence of radial annular-endplate tears did not increase when torsion was combined with flexion compared to flexion alone.[28] However, tears did occur at lower NP pressures. The tears on the endplate portion propagated in the direction contralateral to the application of the axial torque affecting only the parallel fibers. Together these results suggest that torsion alone is not responsible for disc injury. However, it makes the disc more vulnerable to injuries normally associated loading during flexion.

CHANGE IN INTERVERTEBRAL DISC CELL HOMEOSTASIS

The IVD has poor vascularization so the primary means by which nutrients and metabolites reach disc cells is diffusion through the CEP and AF. Oxygen levels in the IVD are low since little oxygen is supplied by the vasculature, so cell metabolism is mainly anaerobic.[29,30] This contributes to high concentrations of lactate and low pH conditions. Large amounts of glucose are required for glycolysis-dependent ATP production and IVD cell viability becomes compromised if injury or degeneration interferes with nutrient supply or clearance of metabolites, resulting in glucose insufficiency and lactate accumulation.[31,32] The cellular response to a wide range of mechanical stimuli and modification of the response with aging and degeneration of the IVD are described in a recent review of mechanical transduction and cellular biomechanics.[33] The processes of IVD degeneration and cell death are discussed in another recent review that explores the possible molecular mechanisms that lead to cell death.[34]

Mechanical loading of the IVD alters cell homeostasis through mechanosensitive signaling pathways that regulate the expression of matrix metalloproteinases (MMPs),[35,36] cytokines,[37] and growth factors.[38] Metalloproteinases degrade collagen and proteoglycans in the IVD and are normally strictly regulated such that their catabolic activity is balanced by anabolic activity stimulated by growth factors present in the cells. The response to loading depends critically on the dynamics of the load, including the mode

(compression, bending, shearing, torsion), magnitude, duration, and frequency.[39] Injury which alters the shape (herniation, prolapse) or integrity (tear, rupture) leads to changes in pressure distribution and nutrient diffusion gradients within the IVD resulting in a catabolic shift whereby NP and AF cells synthesize more matrix-degrading enzymes than extracellular matrix components. Cleavage and loss of the proteoglycan aggrecan reduces the water content of the NP, which in turn reduces the ability of the NP to resist compression.[1] When hydrostatic pressure is reduced, IVD cells are subjected to increased shear stress, which stimulates the formation of fibrous tissues in AF cells by upregulating genes involved in synthesis of collagen and production of metalloproteinases,[40] which degrade proteoglycans.[41] Increased shear stress can also increase the production of nitric oxide by chondrocytes, which can reduce the production of proteoglycan and increase apoptosis in the cells within IVD,[42] accelerating IVD degeneration.

Higher levels of proinflammatory and pronociceptive factors have been found in IVDs with signs of degeneration than in healthy IVDs. These factors include the interleukins: IL-1β, IL-6, IL-8, and tumor necrosis factor alpha, nerve growth factor, and brain-derived neurotrophic factor.[43–46] Expression of these factors has also been shown in isolated healthy IVDs subjected to rapid compression injury resulting in endplate fracture.[47] Endplate fracture has been linked to increased catabolic enzyme and proinflammatory gene expression.[48,49] Inflammatory factors released by disc cells can act to increase expression of matrix-degrading catabolic enzymes[35,37] and may also promote the growth of afferent fibers, which are not normally present in healthy IVDs. Ingrowth of nerve fibers into the AF may precipitate low back pain.[50] The molecular mechanisms of nerve fiber ingrowth are discussed in a review on cell signaling pathways related to pain receptors in the degenerated IVD.[51]

A number of studies have analyzed changes in protein synthesis and gene expression in response to mechanical stimuli to the IVD and to isolated NP and AF cells. Fourteen days after injury by compressive loading of human IVDs at 30% per second, glycosaminoglycan levels were reduced in NP cells. AF cells responded to loading by increased release of glycosaminoglycan which was elevated 3 days after loading but returned to control levels with 7 days of loading. Greater MMP and aggrecanase activity was found in injured NP cells after 14 days than control cells indicating greater proteoglycan degradation in injured cells.[40] Shear stress of 1 dyne/cm^2 applied to human AF cells exerted an anabolic effect on collagen I and collagen III genes and catabolic effect of the aggrecan gene. Greater shear stress of 10 dyne/cm^2 also produced an anabolic effect on the collagen I gene but had a catabolic effect on the collagen III and aggrecan genes. Expression of MMP-1 increased significantly following 10 dyne/cm^2 shear stress compared to no shear stress but did not increase following 1 dyne/cm^2.[46] In healthy human NP cells, moderate hydrostatic pressure (0.8–1.7 MPa at a frequency of 0.5 Hz applied for 2 h) increased c-Fos and aggrecan gene expression, but not *MMP-3* gene expression, suggesting a catabolic response. In contrast, application of hydrostatic pressure to AF or degenerate NP cells had no effect on target gene expression.[52] Hydrostatic compression of rabbit NP cells at higher pressure (4 MPa) for 24 hours induced increases in gene expression of inducible nitric oxide synthase and cyclooxygenase-2, indicators of inflammation, and MMP-3, a catabolic enzyme. At the same time, gene expression of tissue inhibitor of MMP-1 (TMP-1) and aggrecan decreased, suggesting that cell homeostasis had shifted to a more catabolic state.[53] The evidence for cytoskeletal remodeling and receptor-mediated signaling as important mechanotransduction events that can regulate downstream effects like gene expression and posttranslational biosynthesis is reviewed in.[33]

CHANGES IN BIOMECHANICAL PROPERTIES

Disc injury and degeneration result in altered biomechanical properties. Thompson *et al*[54] studied the mechanical effects of concentric tears, radial tears, and rim lesions of the AF in ovine lumbar IVDs. The peak resistive moment produced by the disc in extension, lateral bending, and axial rotation was reduced by an anterior rim lesion, impairing the ability of the disc to resist motion. Radial tears contributed to a reduction in the hysteresis of the response to flexion/extension and lateral bending. The resulting reduction in energy dissipation and altered stress profile within the disc could cause overloading of the spinal ligaments, muscles, and zygapophysial joints, thereby impairing their normal function.

Thompson *et al*[55] also examined the correlation between disc tears and mechanical properties of the intervertebral joint and bony part of the vertebral body. A reduced bone elastic modulus was found in specimens with disc tears compared to specimens without tears and the stiffness of the intervertebral joint in response to extension was positively correlated with increasing tear severity. In contrast, torsional stiffness of the joint decreased with increasing severity of rim lesions at L2-L3 and L4-L5 levels of lumbar vertebrae. Rim lesions were also associated with reduced stiffness in flexion and extension which may be linked to a loss of NP pressure.[56] Miyazaki *et al*[57] studied the correlation between the degree of cervical disc degeneration and mobility of the cervical spine from magnetic resonance imagings of patients with symptomatic neck pain. The translational motion initially increased as the degree of degeneration progressed from grade II, representing mild degeneration, to grade III, but subsequently decreased significantly along with angular mobility as degeneration approached more severe levels at grade V. C4-C5 and C5-C6 motion segments were the major contributors to angular mobility of the spine for mildly degenerate discs (grade I and grade II). However, their contribution was significantly diminished for severely degenerate discs (grade V). Fujiwara *et al*[58] found significant disc degeneration-related motion changes for axial rotation, lateral bending, and flexion in human lumbar motion segments, with an increase in segmental motion up to grade IV degeneration

and a subsequent decrease as disc degeneration reached grade V.

CONCLUSION

IVDs experience diverse mechanical stimuli which can result in injury and degeneration. Degeneration-associated alterations of the disc structure modify the biochemistry of disc cells and also the mechanical properties of the IVD. Recent studies have elucidated some of the cellular mechanisms involved in the metabolic responses to mechanical stimuli and their implications for the integrity of the structure of the NP and AF. Remodeling of these structures leads to alterations of their mechanical properties and to their vascularization and innervation. An understanding of the mechanotransduction of signaling pathways in IVDs and the relation between remodeling and mechanical properties may lead to the development of interventions for disc repair and relief of back pain.

Uncited reference

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➢ Key Points

- ❑ Torsion, compression, flexion, and combinations of those loadings can result in a variety of IVD injuries from annular tears to structural failures of the spine.
- ❑ Mechanical loadings of the IVD alter the homeostasis of the cell which in turn accelerates degeneration.
- ❑ Concentric tears, radial tears, and rim lesions of the annulus fibrosis can result in reduced stiffness of the intervertebral joint.

References

1. Adams MA, Roughley PJ. What is intervertebral disc degeneration, and what causes it?. *Spine (Phila Pa 1976)* 2006;31:2151–61.
2. Goel VK, Monroe BT, Gilbertson LG, et al. Interlaminar shear stresses and laminae separation in a disc: finite element analysis of the L3-L4 motion segment subjected to axial compressive loads. *Spine (Phila Pa 1976)* 1995;20:689–98.
3. Osti OL, Vernon-Roberts B, Moore R, Fraser RD. Annular tears and disc degeneration in the lumbar spine. A post-mortem study of 135 discs. *J Bone Joint Surg Br* 1992;74:678–82.
4. Hilton RC, Ball J. Vertebral rim lesions in the dorsolumbar spine. *Ann Rheum Dis* 1984;43:302–7.
5. Adams MA, Hutton WC. Gradual disc prolapse. *Spine (Phila Pa 1976)* 1984;10:524–31.
6. Yu S, Haughton VM, Sether LA, et al. Criteria for classifying normal and degenerated lumbar intervertebral disks. *Radiology* 1989;170:523–6.
7. Adams MA, Hutton WC. Prolapsed intervertebral disc. A hyperflexion injury 1981 Volvo Award in Basic Science. *Spine (Phila Pa 1976)* 1982;7:184–91.
8. Gordon SJ, Yang KH, Mayer PJ, Mace AH Jr, Kish VL, Radin EL. Mechanism of disc rupture: a preliminary report. *Spine (Phila Pa 1976)* 1991;16:450–6.
9. Vernon-Roberts B, Pirie CJ. Healing trabecular microfractures in the bodies of lumbar vertebrae. *Ann Rheum Dis* 1973;32:406–12.
10. Tanaka M, Nakahara S, Inoue H. A pathologic study of discs in the elderly. Separation between the cartilaginous endplate and the vertebral body. *Spine (Phila Pa 1976)* 1992;18:1456–62.
11. Videman T, Battié MC, Gill K, Manninen H, Gibbons LE, Fisher LD. Magnetic resonance imaging findings and their relationships in the thoracic and lumbar spine: insights into the etiopathogenesis of spinal degeneration. *Spine (Phila Pa 1976)* 1995;20:928–35.
12. Pollintine P, Przybyla AS, Dolan P, et al. Neural arch load-bearing in old and degenerated spines. *J Biomech* 2004;37:197–204.
13. Brinkman P. Injury of the annulus fibrosis and disc protrusions. *Spine (Phila Pa 1976)* 1986;11:149–53.
14. Markolf KL, Morris JM. The structural components of the intervertebral disc: a study of their contributions to the ability of the disc to withstand compressive forces. *J Bone Joint Surg Am* 1974;56:675–87.
15. Adams MA, Freeman BJ, Morrison HP, et al. Mechanical initiation of intervertebral disc degeneration. *Spine (Phila Pa 1976)* 2000;25:1625–36.
16. Paul CPL, De Graaf M, Bisschop A, et al. Static axial overloading primes lumbar caprine intervertebral discs for posterior herniation. *PLoS One* 2017;12:e0174278.
17. Wade KR, Schollum ML, Robertson PA, et al. Vibration really does disrupt the disc. A microanatomical investigation. *Spine (Phila Pa 1976)* 2016;41:1185–98.
18. McGill SM. The biomechanics of low back injury: implications on current practice in industry and the clinic. *J Biomech* 1997;30:465–75.
19. Solomonow M, Zhou BH, Baratta RV, Lu Y, Harris M. Biomechanics of increased exposure to lumbar injury caused by cyclic loading: Part 1. Loss of reflexive muscular stabilization. *Spine (Phila Pa 1976)* 1999;24:2426–34.
20. McGill SM, Brown S. Creep response of the lumbar spine to prolonged full flexion. *Clin Biomech* 1992;7:43–6.
21. Ekström L, Kaigle A, Hult E, Holm S, Rostedt M, Hansson T. Intervertebral disc response to cyclic loading—an animal model. *Proc Inst Mech Eng H* 1996;210:249–58.
22. Adams MA, Hutton WC, Stott JRR. The resistance to flexion of the lumbar intervertebral joint. *Spine (Phila Pa 1976)* 1980;5:245–53.
23. Farfan HF. Effects of torsion on the intervertebral joints. *Can J Surg* 1969;12:336–41.
24. Farfan HF, Cossette JW, Robertson GH, Wells RV, Kraus H. The effects of torsion on the lumbar intervertebral joints: the role of torsion in the production of disc degeneration. *J Bone Joint Surg Am* 1970;52:468–97.
25. Adams MA, Hutton WC. The relevance of torsion to the mechanical derangement of the lumbar spine. *Spine (Phila Pa 1976)* 1981;6:241–8.
26. Marshall LW, McGill SM. The role of axial torque in disc herniation. *Clin Biomech* 2010;25:6–9.
27. Callaghan JP, McGill SM. Intervertebral disc herniation: studies on a porcine model exposed to highly repetitive flexion/extension motion with compressive force. *Clin Biomech* 2001;16:28–37.
28. Veres SP, Robertson PA, Broom ND. The influence of torsion on disc herniation when combined with flexion. *Eur Spine J* 2010;19:1468–78.
29. Bartels EM, Fairbank JC, Winlove CP, Urban JP. Oxygen and lactate concentrations measured in vivo in the intervertebral discs of patients with scoliosis and back pain. *Spine (Phila Pa 1976)* 1998;23:1–7.
30. Urban JP, Holm S, Maroudas A, Nachemson A. Nutrition of the inter-vertebral disk. An in vivo study of solute transport. *Clin Orthop Relat Res* 1977;129:101–14.
31. Bibby SR, Jones DA, Ripley RM, et al. Metabolism of the intervertebral disc: effects of low levels of oxygen, glucose, and pH on rates of energy metabolism of bovine nucleus pulposus cells. *Spine (Phila Pa 1976)* 2005;30:487–96.
32. Bibby SR, Urban JP. Effect of nutrient deprivation on the viability of intervertebral disc cells. *Eur Spine J* 2004;13:695–701.

33. Fearing BV, Hernandez PA, Setton LA, Chahine NO. Mechanotransduction and cell biomechanics of the intervertebral disc. *JOR Spine* 2018;1:e1026.
34. Zhang F, Zhao X, Shen H, Zhang C. Molecular mechanisms of cell death in intervertebral disc degeneration. *Int J Mol Med* 2016;37:1439–48.
35. Le Maitre CL, Freemont AJ, Hoyland JA. The role of interleukin-1 in the pathogenesis of human intervertebral disc degeneration. *Arthritis Res Ther* 2005;7:R732–45.
36. Blain E. Mechanical regulation of matrix metalloproteinases. *Front Biosci* 2007;12:507–27.
37. Phillips KL, Chiverton N, Michael AL, et al. The cytokine and chemokine expression profile of nucleus pulposus cells: Implications for degeneration and regeneration of the intervertebral disc. *Arthritis Res Ther* 2013;15:R213.
38. Neidlinger-Wilke C, Galbusera F, Pratsinis H, et al. Mechanical loading of the intervertebral disc: from the macroscopic to the cellular level. *Eur Spine J* 2014;23 (suppl 3):S333–43.
39. Smith RL, Carter DR, Schurman DJ. Pressure and shear differentially alter human articular chondrocyte metabolism: a review. *Clin Orthop Relat Res* 2004;427 (suppl):S89–95.
40. Chou P-H, Wang S-T, Yen M-H, et al. Fluid-induced, shear stress-regulated extracellular matrix and matrix metalloproteinase genes expression on human annulus fibrosus cells. *Stem Cell Res Ther* 2016;7:34.
41. Liu GZ, Ishihara H, Osada R, Kimura T, Tsuji H. Nitric oxide mediates the change of proteoglycan synthesis in the human lumbar intervertebral disc in response to hydrostatic pressure. *Spine (Phila Pa 1976)* 2001;26:134–41.
42. Freemont AJ, Watkins A, Le Maitre C, et al. Nerve growth factor expression and innervation of the painful intervertebral disc. *J Pathol* 2002;197:286–92.
43. Purmessur D, Freemont AJ, Hoyland JA. Expression and regulation of neurotrophins in the nondegenerate and degenerate human intervertebral disc. *Arthritis Res Ther* 2008;10:R99.
44. Gruber HE, Hoelscher GL, Bethea S, Hanley EN Jr. Interleukin 1-beta upregulates brain-derived neurotrophic factor, neurotrophin 3 and neuropilin 2 gene expression and NGF production in annulus cells. *Biotech Histochem* 2012;87:506–11.
45. Krock E, Rosenzweig DH, Chabot-Dore AJ, et al. Painful, degenerating intervertebral discs up-regulate neurite sprouting and CGRP through nociceptive factors. *J Cell Mol Med* 2014;18:1213–25.
46. Alkhatib B, Rosenzweig DH, Krock E, et al. Acute mechanical injury of the human intervertebral disc: link to degeneration and pain. *Eur Cell Mater* 2014;28:98–111.
47. Haschtmann D, Stoyanov JV, Gédet P, Ferguson SJ. Vertebral endplate trauma induces disc cell apoptosis and promotes organ degeneration in vitro. *Eur Spine J* 2008;17:289–99.
48. Wang Y, Videman T, Battie MC. Lumbar vertebral endplate lesions: associations with disc degeneration and back pain history. *Spine (Phila Pa 1976)* 2012;37:1490–6.
49. Fields AJ, Liebenberg EC, Lotz JC. Innervation of pathologies in the lumbar vertebral end plate and intervertebral disc. *Spine J* 2014;14:513–21.
50. Freemont AJ, Peacock TE, Goupille P, Hoyland JA, O'Brien J, Jayson MI. Nerve ingrowth into diseased intervertebral disc in chronic back pain. *Lancet* 1997;350:178–81.
51. Hiyama A, Sakai D, Mochida J. Cell signaling pathways related to pain receptors in the degenerated disk. *Global Spine J* 2013;3:165–74.
52. Le Maitre CL, Frain J, Fotheringham AP, Freemont AJ, Hoyland JA. Human cells derived from degenerate intervertebral discs respond differently to those derived from non-degenerate intervertebral discs following application of dynamic hydrostatic pressure. *Biorheology* 2008;45:563–75.
53. Sowa GA, Coelho JP, Bell KM, et al. Alterations in gene expression in response to compression of nucleus pulposus cells. *Spine J* 2011;11:36–43.
54. Thompson RE, Pearcy MJ, Barker TM. The mechanical effects of intervertebral disc lesions. *Clin Biomech* 2004;19:448–55.
55. Thompson RE, Pearcy MJ, Downing KJ, Manthey BA, Parkinson IH, Fazzalari NL. Disc lesions and the mechanics of the intervertebral joint complex. *Spine (Phila Pa 1976)* 2000;25:3026–35.
56. De Visser H, Rowe C, Pearcy M. A robotic testing facility for the measurement of the mechanics of spinal joints. *Proc Inst Mech Eng H* 2007;221:221–7.
57. Miyazaki M, Hong SW, Yoon SH, et al. Kinematic analysis of the relationship between the grade of disc degeneration and motion unit of the cervical spine. *Spine (Phila Pa 1976)* 2008;33:187–93.
58. Fujiwara A, Lim TH, An HS, et al. The effect of disc degeneration and facet joint osteoarthritis on the segmental flexibility of the lumbar spine. *Spine (Phila Pa 1976)* 2000;25:3036–44.