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Grand Rounds
Pre-Game Warm-Up

James Demetrious, DC, DABCO
Diplomate, American Board of Chiropractic Orthopedists

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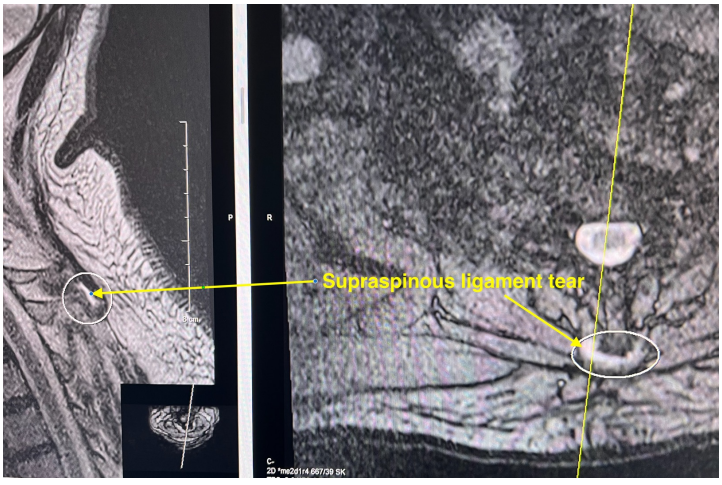
Pre-Game Warm-Ups



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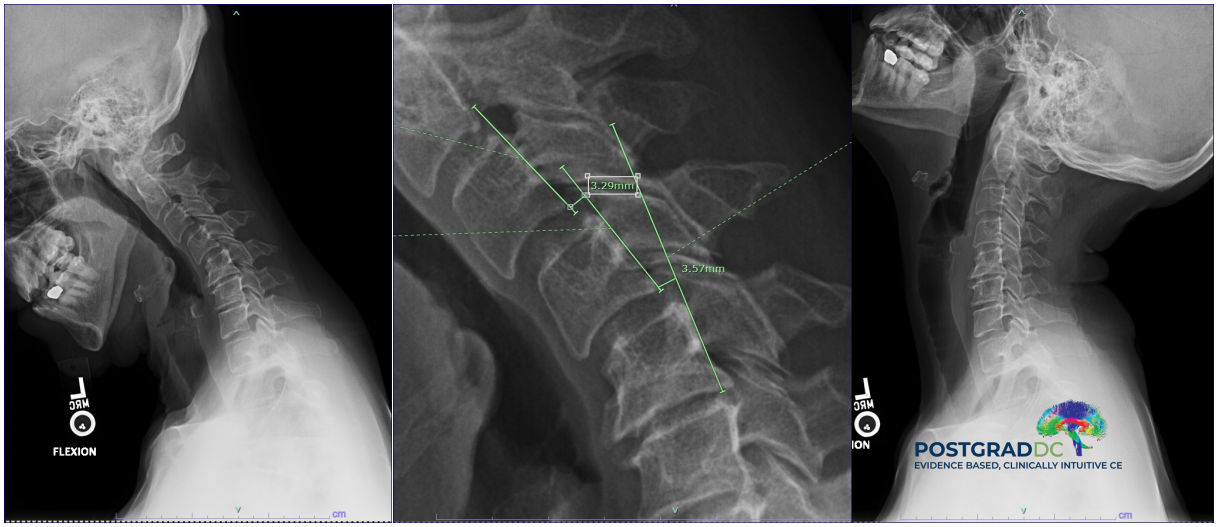
Pre-Game Warm-Ups



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Pre-Game Warm-Ups

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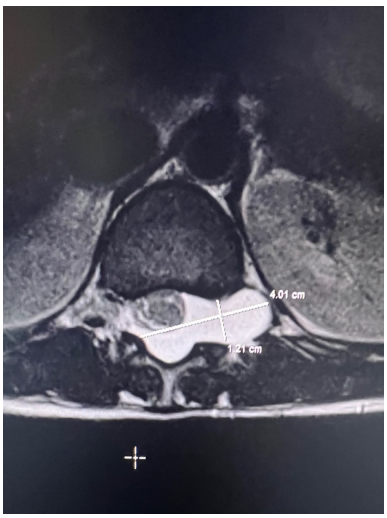
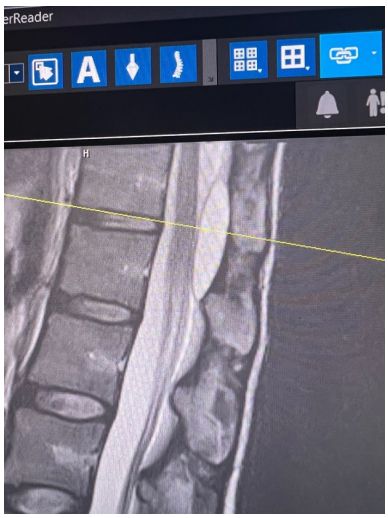
Pre-Game Warm-Ups





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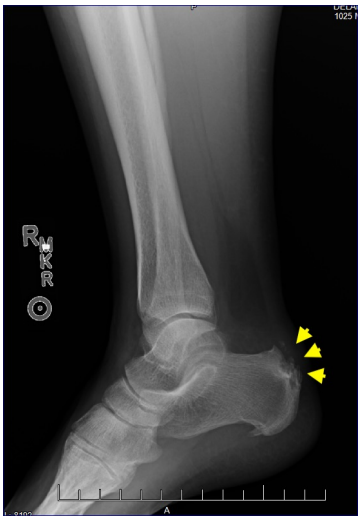
Pre-Game Warm-Ups



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Pre-Game Warm-Ups

Per Bak
Theoretical Physicist
1948-2002

- **Structured Criticality**
  - A property of complex systems in which small events may trigger larger events due to subtle interdependencies between elements.
- **Cascade failure**
  - May occur when one part of the system fails.
  - When this happens, other parts must then compensate for the failed component.

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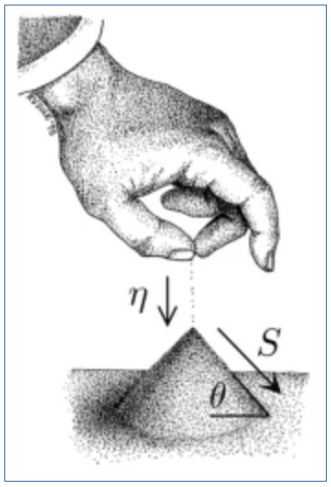
Pre-Game Warm-Ups

Some Thoughts or Thots:

- Some chiropractors favor the term chiropractic subluxation. Some do not.
- In our recent **Clinical Pearl**, Dr. Demetrious offers his thoughts related to structural criticality and cascade failure in biological systems from the work of theoretical physicist Per Bak.
- Through objective and testable biomarkers, perhaps an updated definition could be considered that can coalesce the profession.



8

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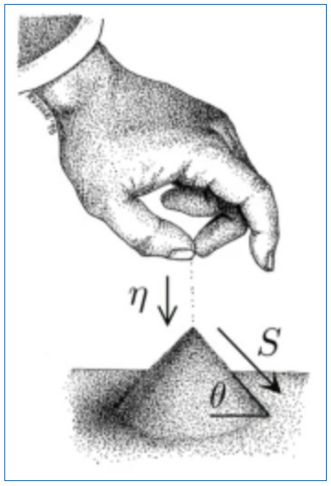
Some Thoughts or Thots:

- One such biomarker could include information gleaned from Harvard studies that assessed pain modulation and the effects of spinal adjustments on the salience system of the brain using fMRI BOLD imaging.
- At **PostGradDC.com**, we seek to advance the chiropractic profession in a manner that is respective to our history, science, philosophy, and art.



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Journal of Integrative Neuroscience

J. Integr. Neurosci. **2024**; 23(5): 98
https://doi.org/10.31083/j.jin2305098

Original Research

The Effects of Chiropractic Spinal Adjustment on EEG in Adults with Alzheimer's and Parkinson's Disease: A Pilot Randomised Cross-over Trial

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Academic Editor: Yoshihiro Noda
Submitted: 11 December 2023 Revised: 7 March 2024 Accepted: 18 March 2024 Published: 11 May 2024

Abstract

Objectives: In this study, we explored the effects of chiropractic spinal adjustments on resting-state electroencephalography (EEG) recordings and early somatosensory evoked potentials (SEPs) in Alzheimer's and Parkinson's disease. **Methods:** In this randomized cross-over study, 14 adults with Alzheimer's disease (average age 67 ± 6 years, 2 females:12 males) and 14 adults with Parkinson's disease (average age 62 ± 11 years, 1 female:13 males) participated. The participants underwent chiropractic spinal adjustments and a control (sham) intervention in a randomized order, with a minimum of one week between each intervention. EEG was recorded before and after each intervention, both during rest and stimulation of the right median nerve. The power-spectra was calculated for resting-state EEG, and the amplitude of the N30 peak was assessed for the SEPs. The source localization was performed on the power-spectra of resting-state EEG and the N30 SEP peak. **Results:** Chiropractic spinal adjustment significantly reduced the N30 peak in individuals with Alzheimer's by 15% ($p = 0.027$). While other outcomes did not reach significance, resting-state EEG showed an increase in absolute power in all frequency bands after chiropractic spinal adjustments in individuals with Alzheimer's and Parkinson's disease. The findings revealed a notable enhancement in connectivity within the Default Mode Network (DMN) at the alpha, beta, and theta frequency bands among individuals undergoing chiropractic adjustments. **Conclusions:** We found that it is feasible to record EEG/SEP in individuals with Alzheimer's and Parkinson's disease. Additionally, a single session of chiropractic spinal adjustment reduced the somatosensory evoked N30 potential and enhancement in connectivity within the DMN at the alpha, beta, and theta frequency bands in individuals with Alzheimer's disease. Future studies may require a larger sample size to estimate the effects of chiropractic spinal adjustment on brain activity. Given the preliminary nature of our findings, caution is warranted when considering the clinical implications. **Clinical Trial Registration:** The study was registered by the Australian New Zealand Clinical Trials Registry (registration number ACTRN12618001217291 and 12618001218280).

Keywords: chiropractic; Parkinson disease; Alzheimer disease; electroencephalography; somatosensory evoked potentials; brain waves; spinal adjustment

1. Introduction

Alzheimer's and Parkinson's disease are the two most prevalent neurodegenerative disorders worldwide [1]. Alzheimer's is characterized as a dementia involving memory loss, confusion, and cognitive impairment [2], while Parkinson's is a movement disorder involving tremors, rigidity, bradykinesia, and postural instability [3]. Although these disorders have distinct features, with Alzheimer's primarily classified as dementia and Parkinson's being a movement disorder, they share several commonalities. Both disorders have a multifactorial etiology, involve an abnormal accumulation and processing of damaged or mutant proteins in the brain, are increasingly prevalent in older age, involve permanent loss of neurons, and may be difficult to treat [1]. In addition, both Alzheimer's and Parkinson's disease involve altered sensorimotor processing in the central nervous system [2,3]. In both Alzheimer's and Parkinson's disease, these alterations may manifest as functional impairments, including

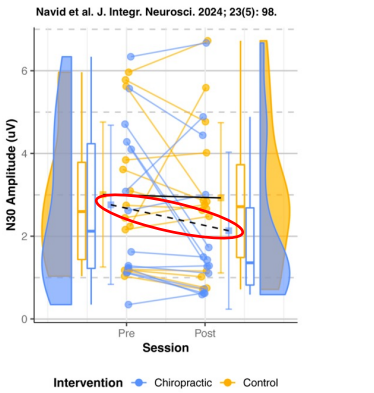

Fig. 6. N30 SEPs amplitude (Alzheimer's Disease). Dots represent the N30 amplitudes from all the analyzed subjects, while the boxplots display the median, 25th, and 75th percentiles. The error bars indicate the mean ± 95% CI. The distribution plots show the density distribution estimated using a Gaussian kernel with a SD of 1.5. The N30 amplitude was similar for the pre-intervention sessions. However, after chiropractic spinal adjustment (represented by the dashed black line), the N30 amplitude significantly decreased, but it remained unchanged after the control intervention (represented by the solid black line). The figure was created using a modified version of the code provided by Allen *et al.* [69]. 95% CI, 95% confidence interval; SD, Standard Deviation.

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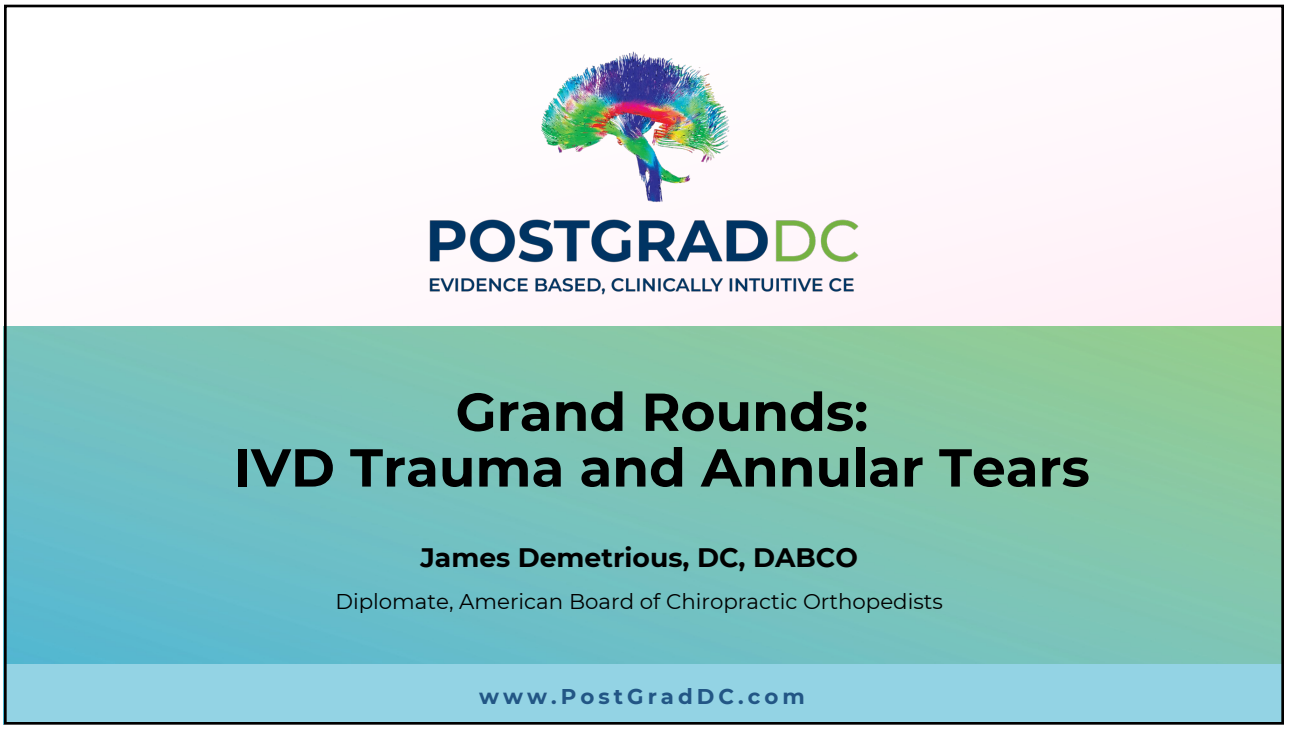
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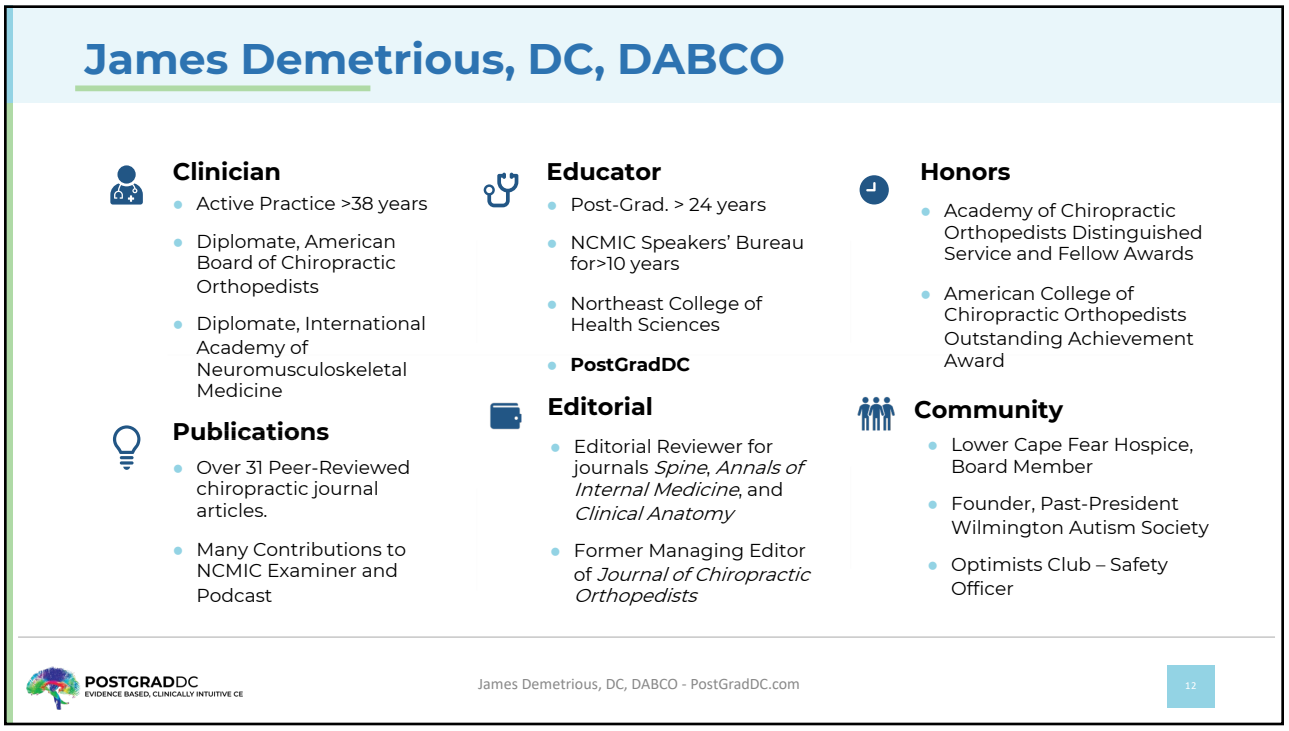
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Diplomate, International Academy of Neuromusculoskeletal Medicine
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Many Contributions to NCMIC Examiner and Podcast
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Founder, Past-President Wilmington Autism Society
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Purpose…

What are identifiable, objective and measurable biomarkers and assessments that may offer insight into the chiropractic subluxation?

- **Modic changes?**
- Peri-articular edema?
- Paraspinal mm. atrophy?
- IVD Desiccation?
- CSF flow?
- HRV?
- fMRI BOLD imaging?
- DTI?
- SPECT?
- Saccades?
- ?

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Syllabus

- The Annular Tear
- Asymptomatic/Symptomatic
- Radicular Affects
- The Role of MRI
- IVD Nutrition and Healing
- IVD Degeneration
- IVD Regeneration?

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IVD Rim Lesion / Annular Tear

Comparative Study > Spine (Phila Pa 1976). 1993 Jul;18(9):1115-22.
doi: 10.1097/00007632-199307000-00001.

Acute injuries to cervical joints. An autopsy study of neck sprain

J R Taylor [1], L T Twomey

Affiliations + expand

PMID: 8362316 DOI: 10.1097/00007632-199307000-00001

Abstract

A comparative study of cervical spines from 16 subjects who died of major trauma and 16 control subjects who died of natural causes, showed clefts in the cartilage plates of the intervertebral discs in 15 of 16 spines from the trauma victims. These were quite distinct from the uncovertebral clefts and central disc fissures that are a normal feature of aging in cervical discs. Posterior disc herniation through a damaged anulus fibrosus and hemarthrosis in facet joints were also observed. No directly comparable lesions were found in the control subjects, but two discs in this group showed "rim lesions," which may be old injuries. Disc lesions are common in injured cervical spines where translation is much greater than in the lumbar spine and these lesions are slow to heal. It is suggested that such injuries could cause the pain experienced by patients with neck sprain.

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Prevalence

Table 2: Age-specific prevalence estimates of degenerative spine imaging findings in asymptomatic patients[a]

Imaging Finding	Age (yr)						
	20	30	40	50	60	70	80
Disk degeneration	37%	52%	68%	80%	88%	93%	96%
Disk signal loss	17%	33%	54%	73%	86%	94%	97%
Disk height loss	24%	34%	45%	56%	67%	76%	84%
Disk bulge	30%	40%	50%	60%	69%	77%	84%
Disk protrusion	29%	31%	33%	36%	38%	40%	43%
Annular fissure	19%	20%	22%	23%	25%	27%	29%
Facet degeneration	4%	9%	18%	32%	50%	69%	83%
Spondylolisthesis	3%	5%	8%	14%	23%	35%	50%

[a] Prevalence rates estimated with a generalized linear mixed-effects model for the age-specific prevalence estimate (binomial outcome) clustering on study and adjusting for the midpoint of each reported age interval of the study.

AJNR Am J Neuroradiol 36:811–16 Apr 2015

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Prevalence

Incidental Findings on Magnetic Resonance Imaging of the Spine in the Asymptomatic Pediatric Population: A Systematic Review

Uma Ramadorai[1] Justin Hire[1] John G. DeVine[2] Erika D. Brodt[3] Joseph R. Dettori[3]

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Address for correspondence John G. DeVine, MD, Department of Orthopaedic Surgery, Georgia Regents University, 1120 15th Street, Augusta, GA 30912, United States (e-mail: JDEVINE@gru.edu).

Evid Based Spine Care J 2014;5:95–100.

Table 2 Summary of MRI findings in asymptomatic pediatric subjects

MRI finding	No. studies	Total events (*n*)	Total subjects (*N*)	Prevalence, % (95% CI)
Disc-related				
Degenerative disc disease[a]	7	109	557	19.6% (16.5%, 23.1%)
Disc herniation/protrusion	4	12	418	2.9% (1.7%, 5.0%)
Disc height/narrowed disc space	2	128	380	33.7% (29.1%, 38.6%)
Endplate changes	2	19	357	5.3% (3.4%, 8.2%)
Bulging disc	1	1	22	4.5% (0.9%, 21.8%)
Nucleus shape	1	176	341	51.6% (46.3%, 56.9%)
Annular tear	1	28	341	8.2% (5.7%, 11.6%)
High intensity zone	1	18	341	5.3% (3.4%, 8.2%)
Nerve root compression	1	31	341	9.1% (6.5%, 12.6%)
Spondylolisthesis/spondylolysis				
Spondylolisthesis	1	8	341	2.3% (1.2%, 4.6%)
Spondylolysis	1	0	22	0% (0%, 13.6%)
Other				
Tumor	1	0	49	0% (0%, 6.1%)
Infection	1	0	49	0% (0%, 6.1%)
Scheuermann-type changes	1	3	39	7.7% (2.7%, 20.3%)
Bone anomalies	1	5	49	10.2% (4.4%, 21.8%)
Transitional vertebra	1	1	39	2.6% (0.5%, 13.2%)

[a] Kjaer et al (2005) reported intermediate/hypointense signal intensity and Tertti et al (1990) reported "abnormal discs"; these findings were determined to be indicative of degenerative disc disease and included in this category.

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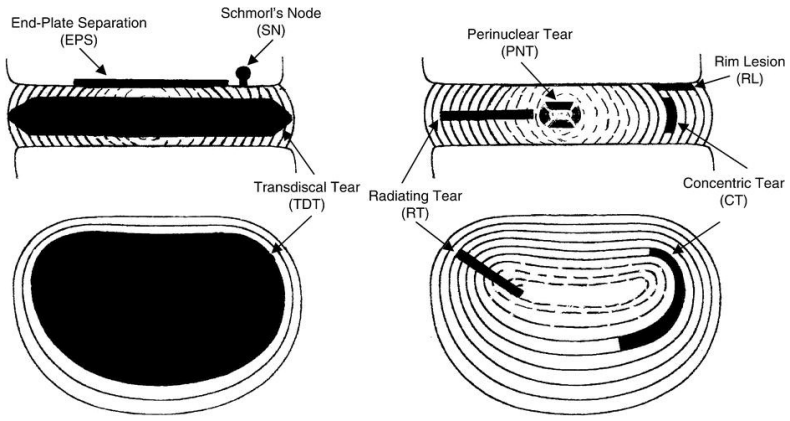
Annular Tears



Perinuclear tears (PNT) and a radiating tear (RT).
Vernon Roberts: Spine, Volume 32(25).December 1, 2007.2797-2804

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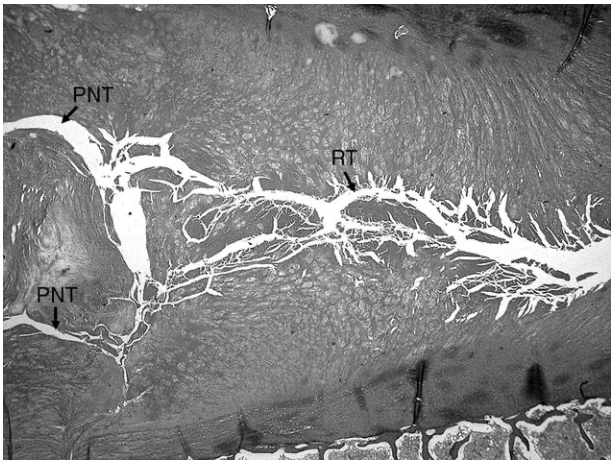
Annular Tears



Vernon Roberts: Spine, Volume 32(25).December 1, 2007.2797-2804

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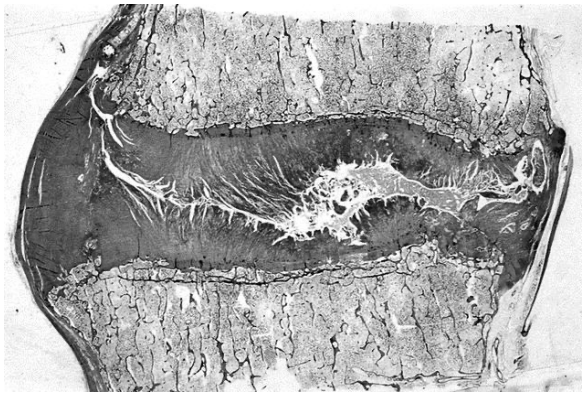
Annular Tears



L4–L5 disc from a 72-year-old man, showing a transdiscal tear with characteristic destructive cavitation of the disc center containing free fragments and the radiating "bottle-brush" pattern of minor clefts.
Vernon Roberts: Spine, Volume 32(25).December 1, 2007.2797-2804

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Annular Tears

> Pain. 2007 Jan;127(1-2):11-6. doi: 10.1016/j.pain.2006.06.034. Epub 2006 Sep 8.

Chemical radiculitis

Baogan Peng [1], Wenwen Wu, Zhenzhou Li, Jidong Guo, Xiaoning Wang

Affiliations + expand

PMID: 16963186 DOI: 10.1016/j.pain.2006.06.034

Abstract

The theory of chemical radiculitis had been put forward about 30 years ago, but as yet it has not been proved by clinical studies. The aim of the current studies was to determine whether the annular tear of a painful disc proved by discography is the cause of radiating leg pain (radiculopathy) in patients with discogenic low back pain. Forty-two patients with discogenic low back pain at single disc level with concomitant radiating leg pain were studied in order to analyse the relationship between site of annular tear and side of radiating leg pain. Electromyogram and motor nerve conduction velocity were monitored to examine nerve root injury. The current studies found that there was a significant positive correlation between the site of annular tear and the side of radiation pain. Abnormalities of electromyogram and reduction of motor nerve conduction velocity were found on the side of radiating leg pain. The studies indicated that leakage of chemical mediators or inflammatory cytokines, which are produced in the painful disc, into epidural space through annular tear could lead to injury to adjacent nerve roots, and it might constitute the primary pathophysiologic mechanism of radiating leg pain in patients with discogenic low back pain but with no disc herniation.

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Annular Tears

International Journal of Molecular Sciences

MDPI

Article

Annulus Fibrosus Injury Induces Acute Neuroinflammation and Chronic Glial Response in Dorsal Root Ganglion and Spinal Cord—An In Vivo Rat Discogenic Pain Model

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† These authors contributed equally to this work.

Abstract: Chronic painful intervertebral disc (IVD) degeneration (i.e., discogenic pain) is a major source of global disability needing improved knowledge on multiple-tissue interactions and how they progress in order improve treatment strategies. This study used an in vivo rat annulus fibrosus (AF) injury-driven discogenic pain model to investigate the acute and chronic changes in IVD degeneration and spinal inflammation, as well as sensitization, inflammation, and remodeling in dorsal root ganglion (DRG) and spinal cord (SC) dorsal horn. AF injury induced moderate IVD degeneration with acute and broad spinal inflammation that progressed to DRG to SC changes within days and weeks, respectively. Specifically, AF injury elevated macrophages in the spine (CD68) and DRGs (Iba1) that peaked at 3 days post-injury, and increased microglia (Iba1) in SC that peaked at 2 weeks post-injury. AF injury also triggered glial responses with elevated GFAP in DRGs and SC at least 8 weeks post-injury. Spinal CD68 and SC neuropeptide Substance P both remained elevated at 8 weeks, suggesting that slow and incomplete IVD healing provides a chronic source of inflammation with continued SC sensitization. We conclude that AF injury-driven IVD degeneration induces acute spinal, DRG, and SC inflammatory crosstalk with sustained glial responses in both DRGs and SC leading to chronic SC sensitization and neural plasticity. The known association of these markers with neuropathic pain suggests that therapeutic strategies for discogenic pain need to target both spinal and nervous systems, with early strategies managing acute inflammatory processes, and late strategies targeting chronic IVD inflammation, SC sensitization, and remodeling.

Keywords: discogenic pain; intervertebral disc degeneration; annulus fibrosus injury; spinal cord; dorsal root ganglion; animal model; macrophage; astrocyte; microglia; satellite glial cell

1. Introduction

Chronic low back pain involves discogenic pain, or back pain with intervertebral disc (IVD) degeneration (IVDD) as the main diagnosis, in about 40% of cases [1–4]. Discogenic pain is a multifactorial and complex condition that is difficult to manage pharmacologically and not well indicated for surgical interventions [5,6]. Structural defects in the annulus fibrosus (AF) and endplate (EP) are specific IVDD phenotypes known to contribute to discogenic pain, and the presence of structural IVD defects and pain distinguishes pathological IVD degeneration from aging [5,6]. AF defects can cause painful processes due to spinal instability (e.g., from nucleus pulposus (NP) depressurization, IVD height loss, or other degenerative changes that cause nerve root compression and irritation) and pro-inflammatory conditions (e.g., from incomplete IVD healing, progressive matrix degradation, neuronal

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Role of MRI for Traumatic Injuries

Kumar and Hayashi *BMC Musculoskeletal Disorders* (2016) 17:310
DOI 10.1186/s12891-016-1169-6

BMC Musculoskeletal Disorders

REVIEW Open Access

Role of magnetic resonance imaging in acute spinal trauma: a pictorial review

Yogesh Kumar[1] and Daichi Hayashi[1,2*]

Abstract

Magnetic resonance imaging (MRI) has been playing an increasingly important role in the spinal trauma patients due to high sensitivity for detection of acute soft tissue and cord injuries. More and more patients are undergoing MRI for spinal trauma in the emergency settings, thus necessitating the interpreting physicians to be familiar with MRI findings in spinal trauma. In this pictorial review, we will first describe the normal anatomy of various ligamentous structures. Indications of MRI in spinal trauma as well as the role of MRI in diagnosing spinal cord and soft tissue injuries will then be discussed. Illustrated cases are mainly of cervical spine trauma, but thoracolumbar spine injuries are also included where appropriate in our review.

Keywords: Spinal trauma, MRI, Spinal cord, Hemorrhage, Ligamentous injury

Indications of spinal MRI

The main indications of MRI in spinal trauma include [2–4]:

1. Radiographic and/or CT scan findings suggestive of ligamentous injury, such as prevertebral hematoma, spondylolisthesis, asymmetric disc space widening, facet joint widening or dislocations, and inter-spinous space widening.
2. To look for epidural hematoma or disc herniation before attempting a closed reduction of cervical facet dislocations.
3. To identify spinal cord abnormalities in patients with impaired neurological status.
4. To exclude clinically suspected ligamentous or occult bony injuries in patients with negative radiographs.
5. To determine the stability of the cervical spine and assess the need for cervical collar in obtunded trauma patients.
6. To differentiate between hemorrhagic and non-hemorrhagic spinal cord injuries for the prognostic significance as the presence of hemorrhage significantly worsens the final clinical outcome.

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Role of MRI for Traumatic Injuries

Table 1 Role of MRI for evaluation of various acute traumatic spinal injuries

Pathologic features	Role of MRI
Ligamentous injury	• Higher sensitivity for detection compared to CT. • Complete tear (seen as discontinuity of ligaments) or partial tear (seen as abnormal signal) can be differentiated. • Helpful in guiding management by differentiating stable from unstable injuries.
Disc damages and herniations	• Detection of abnormal disc signal related to traumatic herniations. • Important to diagnose this before closed reduction as undetected disc herniations can cause worsening cord injury.
Extra medullary hemorrhage	• MRI shows extent of hematoma to help in surgical planning. • Extradural hematoma is commonly encountered and can lead to cord compression.
Vascular injuries	• Enable detection of arterial injuries, which include an intimal flap, pseudoaneurysm, complete occlusion or active extravasation. • Undetected vascular injuries can cause spinal cord infarctions.
Cord injuries	• Detection of hemorrhagic and non-hemorrhagic cord injuries. • This is the single most important role of MRI in spinal trauma evaluation. • Visualized as abnormal cord signal with hemorrhage best seen on gradient recalled echo (GRE) type sequences. • Presence of hemorrhage is the most important poor prognostic factor.
Acute vs old vertebral fracture	• Age-indeterminate fractures identified on radiography and CT can be classified into acute and old fractures based on the presence or absence of bone marrow edema, respectively.
Benign vs malignant fracture	• Differentiation of benign and malignant fractures. • Benign fractures show horizontal band of marrow edema, concave appearance of posterior vertebral margin and lack of soft tissue mass. • Malignant fractures show almost complete involvement of vertebral body, convex posterior margin and associated soft tissue mass.

- According to American College of Radiology (ACR) appropriateness criteria, MRI of spine combined with CT scan is appropriate in the setting of acute spinal trauma if [5]:
  1. National Emergency X-Radiography Utilization Study (NEXUS) or Canadian Cervical-Spine Rule (CCR) criteria are met and there are clinical findings of myelopathy.
  2. NEXUS or CCR criteria are met and there are clinical or imaging findings to suggest ligamentous injury.
  3. NEXUS or CCR criteria indicate imaging and the mechanically unstable spine is anticipated.

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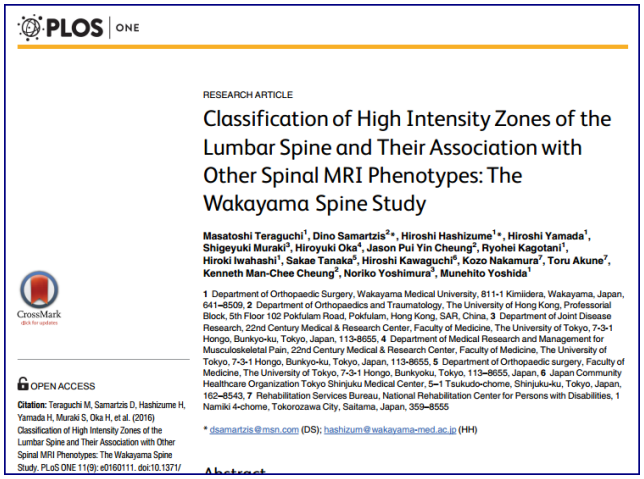
Annular Tears



PLOS ONE

RESEARCH ARTICLE

Classification of High Intensity Zones of the Lumbar Spine and Their Association with Other Spinal MRI Phenotypes: The Wakayama Spine Study

Masatoshi Teraguchi[1], Dino Samartzis[2]*, Hiroshi Hashizume[1]*, Hiroshi Yamada[1], Shigeyuki Muraki[3], Hiroyuki Oka[4], Jason Pui Yin Cheung[2], Ryohei Kagotani[1], Hiroki Iwahashi[1], Sakae Tanaka[5], Hiroshi Kawaguchi[6], Kozo Nakamura[7], Toru Akune[7], Kenneth Man-Chee Cheung[2], Noriko Yoshimura[3], Munehito Yoshida[1]

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Annular Tears

Table 1. Assessment of lumbar High Intensity Zones on MRI.

Variables	Definition
Shape	
Round	Concentric or oval cavity
Fissure	Parallel and transverse layer to the adjacent endplate
Vertical	Vertical layer to the adjacent endplate
Rim	Oblique radiating layer from the adajacent endplate
Enlarged	Greater concentric area than typical round HIZ
Horizontal location within disc	
Posterior	HIZ located in the posterior annulus fibrosus
Anteriror	HIZ located in the anterior annulus fibrosus
Signal type on T1W and T2W HIZ image	
T1W low-intensity type of HIZ	Decreased signal than the bone marrow on T1W sagittal MRI
T1W high-intensity type of HIZ	Increased signal than the bone marrow on T1W sagittal MRI
T1W iso-intensity type of HIZ	Same signal than the bone marrow on T1W sagittal MRI

HIZ: high intensity zones, MRI: magnetic resonance imaging, T1W: T1-weighted, T2W: T2-weighted, MRI: magnetic resonance imaging

doi:10.1371/journal.pone.0160111.t001

PLOS ONE | DOI:10.1371/journal.pone.0160111 September 20, 2016

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Annular Tears

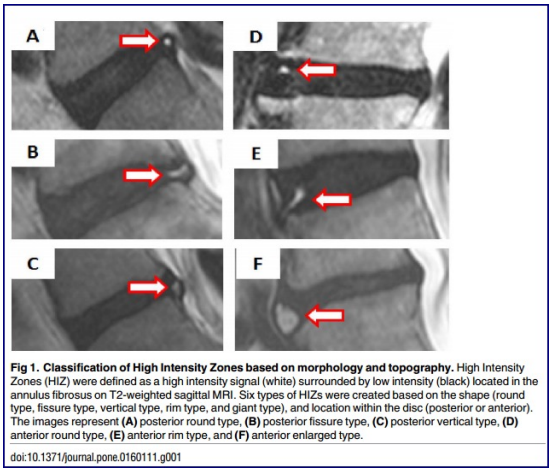

Fig 1. Classification of High Intensity Zones based on morphology and topography. High Intensity Zones (HIZ) were defined as a high intensity signal (white) surrounded by low intensity (black) located in the annulus fibrosus on T2-weighted sagittal MRI. Six types of HIZs were created based on the shape (round type, fissure type, vertical type, rim type, and giant type), and location within the disc (posterior or anterior). The images represent **(A)** posterior round type, **(B)** posterior fissure type, **(C)** posterior vertical type, **(D)** anterior round type, **(E)** anterior rim type, and **(F)** anterior enlarged type.

doi:10.1371/journal.pone.0160111.g001

PLOS ONE | DOI:10.1371/journal.pone.0160111 September 20, 2016

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Annular Tears

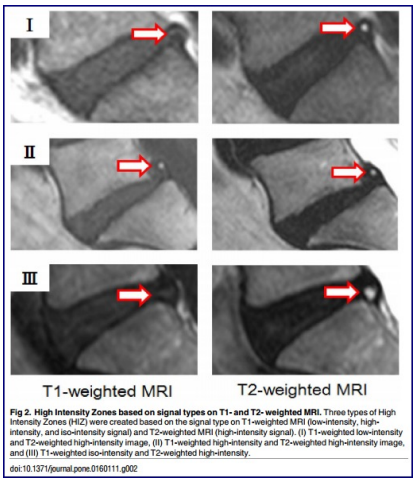

Fig 2. High Intensity Zones based on signal types on T1- and T2- weighted MRI. Three types of High Intensity Zones (HIZ) were created based on the signal type on T1-weighted MRI (low-intensity, high-intensity, and iso-intensity signal) and T2-weighted MRI (high-intensity signal). (I) T1-weighted low-intensity and T2-weighted high-intensity image, (II) T1-weighted high-intensity and T2-weighted high-intensity image, and (III) T1-weighted iso-intensity and T2-weighted high-intensity.

doi:10.1371/journal.pone.0160111.g002

PLOS ONE | DOI:10.1371/journal.pone.0160111 September 20, 2016

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Annular Tears

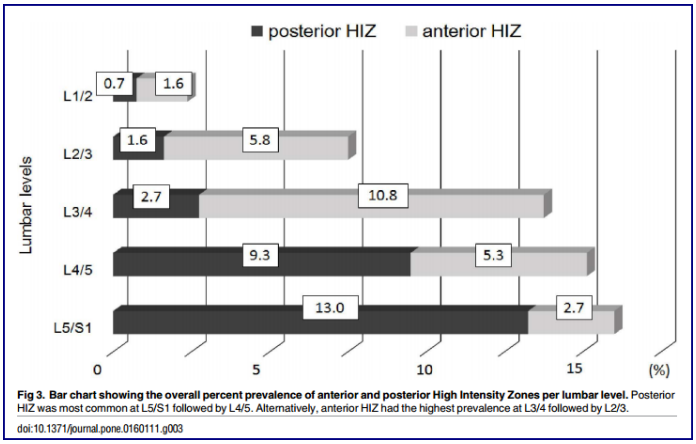

Fig 3. Bar chart showing the overall percent prevalence of anterior and posterior High Intensity Zones per lumbar level. Posterior HIZ was most common at L5/S1 followed by L4/5. Alternatively, anterior HIZ had the highest prevalence at L3/4 followed by L2/3.

doi:10.1371/journal.pone.0160111.g003

PLOS ONE | DOI:10.1371/journal.pone.0160111 September 20, 2016

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Annular Tears

Possible Pathogenesis of Painful Intervertebral Disc Degeneration
Peng, Baogan MD, PhD et al. *Spine*, Volume 31(5), 1 March 2006, pp 560-56

To study the pathogenesis of disc degeneration, meanwhile discriminating between common disc degeneration and painful disc degeneration .

Results. The distinct histologic characteristic of the disc from the patient with discogenic low back pain was the ingrowth of vascularized granulation tissue along torn fissures, extending from the external layer of the anulus fibrosus into the nucleus pulposus.

Conclusions. The findings indicated that degeneration of the painful disc might originate from the injury and subsequent repair of anulus fibrosus. Growth factors, such as bFGF and TGF-[beta]1, macrophages and mast cells might play a key role in the repair of the injured anulus fibrosus and subsequent disc degeneration.

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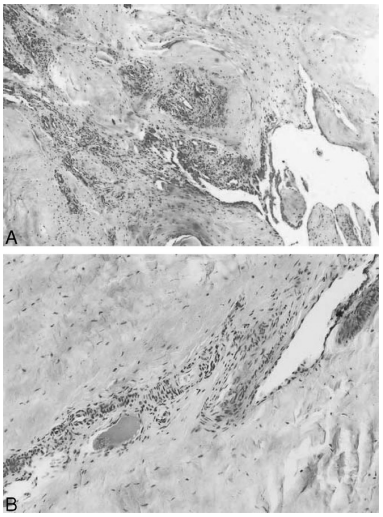
Annular Tears



A, The ingrowth of vascularized granulation tissue into anulus along tear in painful disc.

B, A strip of granulation tissue and surrounding tissue in anulus showing fibrosis in surrounding tissue.

From: Peng: Spine, Volume 31(5).March 1, 2006.560-566

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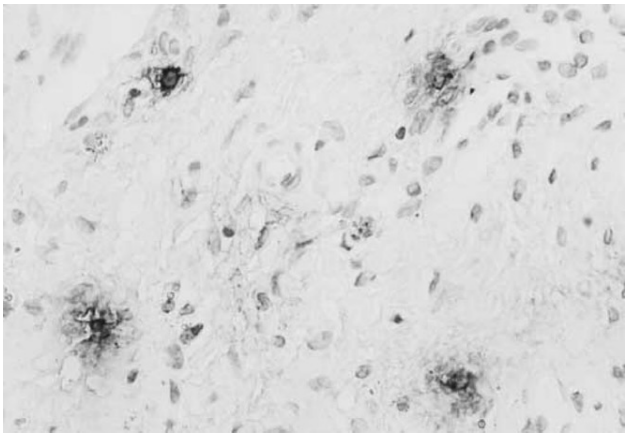
Annular Tears



Mast cells in granulation tissue in painful disc.
From: Peng: Spine, Volume 31(5).March 1, 2006.560-566

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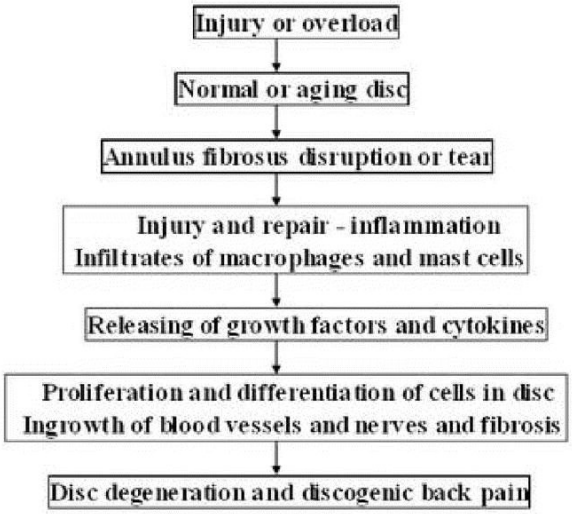
Annular Tears



From: Peng: Spine, Volume 31(5).March 1, 2006.560-566.

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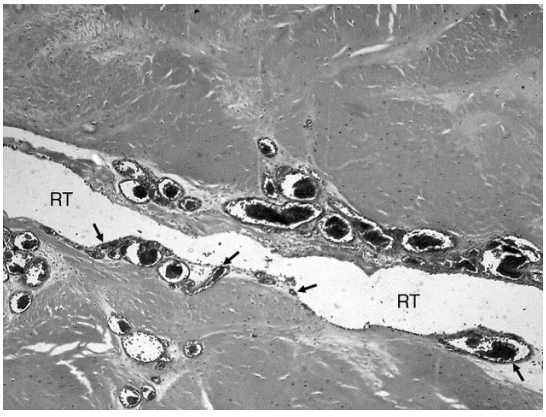
Annular Tears



Neovascularization of a radiating tear (RT) in the L4–L5 disc showing that some vessels attached to the inner surface have walls composed only of a single layer of endothelial cells (arrows).
Vernon Roberts: Spine, Volume 32(25).December 1, 2007.2797-2804

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Annular Tears

Eur Spine J. 2015 Nov;24(11):2496-502. doi: 10.1007/s00586-015-4180-y. Epub 2015 Aug 19.

Relationship between annular tear and presence of Propionibacterium acnes in lumbar intervertebral disc

Zezhu Zhou [1 2], Zhe Chen [1 2], Yuehuan Zheng [3], Peng Cao [4 5], Yu Liang [1 2], Xingkai Zhang [1 2], Wenjian Wu [1 2], Jiaqi Xiao [6], Shijing Qiu [7 8 9]

Affiliations + expand

PMID: 26287263 DOI: 10.1007/s00586-015-4180-y

Abstract

Purpose: Propionibacterium acnes (P. acnes) in the intervertebral disc may result in low back pain. The purpose of this study was to determine how P. acnes accesses the disc.

Methods: Patients with low back pain and/or sciatica were examined using X-ray and MRI before surgery. The intervertebral disc space height was measured on X-ray image. Disc and muscle samples were obtained from 46 patients undergoing discectomy at the lumbar spine. The tear of annulus was inspected before discectomy. In the disc and muscle tissue cultures, 16S rDNA gene specific for P. acnes was examined using PCR.

Results: The discs from 11 (23.9 %) patients were identified as 16S rDNA positive, in which two patients also had 16S rDNA in their muscles. 16S rDNA gene was significantly more likely to appear in the discs with annular tear than those without tear ($P < 0.05$). The disc space height was significantly decreased when the disc contained P. acnes.

Conclusion: P. acnes is significantly more likely to be present in herniated discs with an annular tear than in herniated discs without such a tear. Since in the vast majority of these cases, no P. acnes was found in control muscle samples, a true infection with P. acnes is far more likely than a contamination.

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IVD Nutrition

Nutrition of the Intervertebral Disc.
Spine. 29(23):2700-2709, December 1, 2004.
Urban, Jill P.G. PhD et al.

- Summary of the Background Data. The disc is avascular, and the disc cells depend on diffusion from blood vessels at the disc's margins to supply the nutrients essential for cellular activity and viability and to remove metabolic wastes such as lactic acid. The nutrient supply can fail due to changes in blood supply, sclerosis of the subchondral bone or endplate calcification, all of which can block transport from blood supply to the disc or due to changes in cellular demand.
- Methods. A review of the studies on disc blood supply, solute transport, studies of solute transport in animal and human disc in vitro, and of theoretical modeling studies that have examined factors affecting disc nutrition.
- Results. Small nutrients such as oxygen and glucose are supplied to the disc's cells virtually entirely by diffusion; convective transport, arising from load-induced fluid movement in and out of the disc, has virtually no direct influence on transport of these nutrients.
- Consequently, there are steep concentration gradients of oxygen, glucose, and lactic acid across the disc; oxygen and glucose concentrations are lowest in the center of the nucleus where lactic acid concentrations are greatest. The actual levels of concentration depend on the balance between diffusive transport and cellular demand and can fall to critical levels if the endplate calcifies or nutritional demand increases.
- Conclusions. Loss of nutrient supply can lead to cell death, loss of matrix production, and increase in matrix degradation and hence to disc degeneration.

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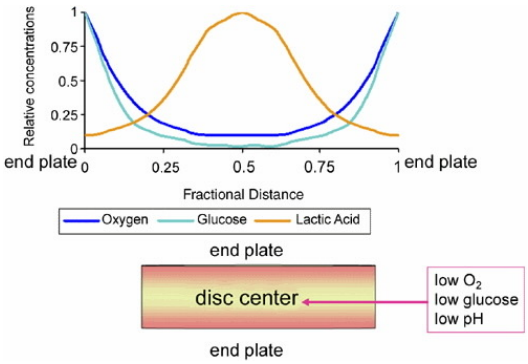
IVD Nutrition

NUTRIENT SUPPLY AND INTERVERTEBRAL DISC METABOLISM
Grunhagen et al. JBJS. Volume 88 Supplement 2, April 2006, p 30–35.



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IVD Nutrition

Spine
SPINE Volume 41, Number 7, pp 568–576

BASIC SCIENCE

Influences of Nutrition Supply and Pathways on the Degenerative Patterns in Human Intervertebral Disc

Qiaoqiao Zhu, BS,* Xin Gao, BS,† Howard B. Levene, MD, PhD,‡ Mark D. Brown, MD, PhD,§ and Weiyong Gu, PhD*·†

"Impairment of different nutrition pathways results in different degenerative patterns."

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IVD Degeneration

INTERNATIONAL JOURNAL of SPINE SURGERY

Pathomechanism and Biomechanics of Degenerative Disc Disease: Features of Healthy and Degenerated Discs

Sertac Kirnaz, Charisse Capadona, Marianne Lintz, Byumsu Kim, Rachel Yerden, Jacob L. Goldberg, Branden Medary, Fabian Sommer, Lynn B. McGrath, JR, Lawrence J. Bonassar and Roger Härtl

Int J Spine Surg 2021, 15 (s1) 10-25
doi: https://doi.org/10.14444/8052
http://ijssurgery.com/content/15/s1/10

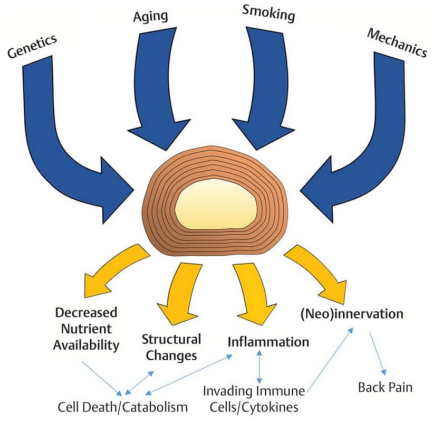

Figure 7. Degenerative disc disease (DDD) in a cascading multifactorial process involving the interaction of risk factors and pathophysiology. Printed with permission from *Biological Approaches to Spinal Disc Repair and Regeneration for Clinicians.*[186]

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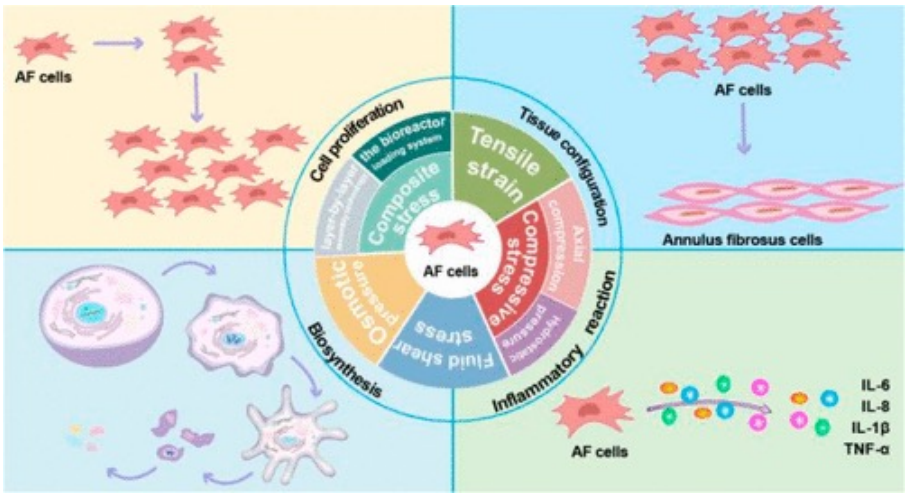
IVD Degeneration



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IVD Degeneration

Effects of controlled dynamic disc distraction on degenerated intervertebral discs: an in vivo study on the rabbit lumbar spine model.
Kroeber et al. *Spine*. 2005 Jan 15;30(2):181-7.

- The current study showed that disc degeneration creates a vicious circle with progressive deterioration in oxygen, nutrient, and waste transport leading to cell death and depletion of the matrix.
- The current results suggest that dynamic mechanical distraction leads to a chronic state of decompression in the anulus, which appears to direct metaplasia of chondrocytes, reduction of the number of cell death, and the concomitant production of fibro-cartilage in the substance of the anulus.
- This results in increase of disc thickness. Early intervention when disc degeneration was initiated seems to be important to maintain disc health or stimulate tissue repair.

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IVD Degeneration

Intradiscal pressure measurements in normal discs, compressed discs and compressed discs treated with axial posterior disc distraction: an experimental study on the rabbit lumbar spine model.
Guehring et al. *Eur Spine J*. 2006 May;15(5):597-604. Epub 2005 Aug 13.

- These data support the hypothesis that temporary external compression leads to moderate disc degeneration as a result of degradation of water-binding disc matrix or affected active pumping mechanisms of nutrients into the disc.
- A stabilization of IVD pressure in discs treated with temporary distraction was observed.

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IVD Degeneration

INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE 37: 1439-1448, 2016

Molecular mechanisms of cell death in intervertebral disc degeneration (Review)

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DOI: 10.3892/ijmm.2016.2573

Abstract. Intervertebral discs (IVDs) are complex structures that consist of three parts, namely, nucleus pulposus, annulus fibrosus and cartilage endplates. With aging, IVDs gradually degenerate as a consequence of many factors, such as microenvironment changes and cell death. Human clinical trial and animal model studies have documented that cell death, particularly apoptosis and autophagy, significantly contribute to IVD degeneration. The mechanisms underlying this phenomenon include the activation of apoptotic pathways and the regulation of autophagy in response to nutrient deprivation and multiple stresses. In this review, we briefly summarize recent progress in understanding the function and regulation of apoptosis and autophagy signaling pathways. In particular, we focus on studies that reveal the functional mechanisms of these pathways in IVD degeneration.

Contents

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Key words: apoptosis, autophagy, nucleus pulposus, annulus fibrosus, cartilage endplate

1. Introduction: Overview of cell death and its intracellular signaling pathways

Cell death is a fundamental biological process that is required for cellular development. On the basis of its morphological features, cell death can be grouped into three main classes, namely, apoptosis, autophagy and necrosis (1). The deregulation of cell death is associated with the etiology, pathogenesis and treatment of many diseases (2-4), particularly degenerative diseases such as cancer, Alzheimer's disease, heart disease and Parkinson's disease (2,5). Over the past few years, increasing evidence has indicated that cell death contributes to degenerative disc disease (6), spinal degenerative disease, and intervertebral disc (IVD) degeneration (7,8). These findings have led to an improved understanding of the etiology of these diseases as well as providing molecular strategies for therapy. Degenerative changes in IVDs due to aging are clinically important as these changes are associated with back pain. Current understanding of the molecular basis of IVD degeneration is principally focused on the regulation of apoptotic and autophagic pathways.

Apoptosis and its signaling pathways. Apoptosis is a process of programmed cell death that eliminates damaged or non-essential cells without causing local inflammation from cell leakage (9). Apoptotic cells exhibit apparent morphological changes, including cell shrinkage and plasma membrane bubbling as well as nuclear condensation and fragmentation (10). Triggering apoptosis requires a group of cysteine proteases known as caspases, which may be activated through intrinsic and extrinsic signaling pathways (11).

The intrinsic pathway, also known as the mitochondrial pathway, is initiated in the mitochondria (11). As shown in Fig. 1, apoptotic signals, such as DNA damage and cytokine deprivation, activate p53, which further initiates the intrinsic pathway by upregulating the p53 upregulated modulator of apoptosis (Puma) and Noxa [also known as phorbol-12-myristate-13-acetate-induced protein 1 (PMAIP1)] (12). These two proteins in turn activate pro-apoptotic proteins, such as Bax and Bak, which eventually results in the efflux of cytochrome c (Cyt.c).Cytochrome c further interacts with the cytosolic protein apoptotic protease activating factor-1 (Apaf-1) to

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IVD Degeneration

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BioMed Research International
Volume 2016, Article ID 1681752, 10 pages
http://dx.doi.org/10.1155/2016/1681752

Research Article

Effect of Static Load on the Nucleus Pulposus of Rabbit Intervertebral Disc Motion Segment in an Organ Culture

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Academic Editor: Panagiotis Korovessis

The development of mechanically active culture systems helps in understanding of the role of mechanical stress in intervertebral disc (IVD) degeneration. Motion segment cultures facilitate the application and control of mechanical loads. The purpose of this study was to establish a culturing method for rabbit IVD motion segments to observe the effect of static load on the whole disc organ. Segments were cultured in custom-made apparatuses under a constant, compressive load (1kg) for 2 weeks. Tissue integrity, matrix synthesis, and matrix gene expression profile were assessed and compared with fresh one. The results showed *ex vivo* culturing of samples gradually destroyed the morphology. Proteoglycan contents and gene expression were decreased and downregulated obviously. However, immunohistochemical staining intensity and collagen type II gene expression were significantly enhanced and upregulated. In contrast, these trends were reversed under constant compression. These results indicated short-term static load stimulated the synthesis of type II collagen; however, constant compression led to progressive degeneration and specifically to proteoglycan. Through this study a loading and organ culturing system for *ex vivo* rabbit IVD motion segments was developed, which can be used to study the effects of mechanical stimulation on the biology of IVDs and the pathomechanics of IVD degeneration.

1. Introduction

Evidence of a link between degenerative intervertebral disc (IVD) and low back pain (LBP) is mounting [1]. Currently, the treatment of diseases related to IVD often involves surgical intervention or long-term rehabilitation therapy. The goals of biological therapy are to prevent or delay IVD degeneration and to alleviate its symptoms by promoting tissue repair. To better prevent and treat LBP a detailed understanding of the mechanisms of IVD degeneration is necessary.

The comprehensive mechanisms and related biological and mechanical pathways of IVD degeneration remain poorly understood [2, 3], even though LBP is a common clinical condition. Biomechanics and IVD degeneration are closely related, and many studies have shown that mechanical loading is one of the major factors leading to IVD [4, 5].

An epidemiological survey has also shown that mechanical loading is a risk factor for LBP [6, 7]. However, weight-bearing mechanical loading is the primary function of IVDs, and it occurs in the natural environment. Mechanical loading also stimulates IVD cells; this stimulation is likely the underlying factor for the maintenance of cartilage cell activity [8, 9]. To better understand the mechanisms of IVD degeneration, an in-depth understanding of its cause and effect relationship with biomechanics is required. Moreover, the establishment of an ideal experimental model might facilitate future related studies.

However, investigating the complex metabolism and signaling cascades that occur in IVDs is difficult using *in vivo* models [10] because of the lack of close control and difficulties with monitoring. In contrast, *ex vivo* culturing systems are more appealing because they allow for better control of

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IVD Degeneration

PLOS ONE

RESEARCH ARTICLE

Constant compression decreases vascular bud and VEGFA expression in a rabbit vertebral endplate ex vivo culture model

Jia-Wen Zhan[1,2], Shang-Quan Wang[1], Min-Shan Feng[2,3], Xu Wei[4], Jie Yu[2], Xun-Lu Yin[2,3], Tao Han[1,2], Li-Guo Zhu[1,2]*

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Abstract

OPEN ACCESS

Citation: Zhan J-W, Wang S-Q, Feng M-S, Wei X, Yu J, Yin X-L, et al. (2020) Constant compression decreases vascular bud and VEGFA expression in a rabbit vertebral endplate ex vivo culture model. PLoS ONE 15(6): e0234747. https://doi.org/10.1371/journal.pone.0234747

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Data Availability Statement: All relevant data are within the paper and its Supporting Information files.

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Summary of background data

The vascular buds in the vertebral endplate (VEP) are the structural foundation of nutrient exchange in the intervertebral disc (IVD). VEGF is closely related to angiogenesis in the endplate and intervertebral disc degeneration (IDD).

Objective

To investigate the effects of static load on vascular buds and VEGF expression in the VEP and to further clarify the relation between IDD and VEGF.

Methods

IVD motion segments were harvested from rabbit lumbar spines and cultured under no-loading conditions (controls) or in custom-made apparatuses under a constant compressive load (0.5 MPa) for up to 14 days. Tissue integrity and the number of vascular buds were determined, and the concentrations and expression of Aggrecan, COL2a1, and VEGFA in the VEPs were assessed after 3, 7, and 14 days of culturing and then compared with those of fresh tissues.

Results

Under the constant compression, the morphological integrity of the VEPs was gradually disrupted, and immunohistochemistry results showed a significant decrease in the levels of Agg and COL2a1. During the static load, the number of vascular buds in the VEPs was gradually reduced from the early stage of culture, and ELISA showed that the constant compressive load caused a significant decrease in the VEGFA and VEGFR2 protein concentrations, which were consistent with the immunohistochemistry results. Western blot and RT-PCR

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IVD Degeneration

Review > Apoptosis. 2013 Jul;18(7):777-85. doi: 10.1007/s10495-013-0839-1.

Cell death in intervertebral disc degeneration

Fan Ding [1], Zeng-wu Shao, Li-ming Xiong

Affiliations + expand

PMID: 23512131 DOI: 10.1007/s10495-013-0839-1

Abstract

Degeneration of intervertebral disc (IVD) is mainly a chronic process of excessive destruction of the extracellular matrix (ECM), and also is thought to be the primary cause of low back pain. Presently, however, the underlying mechanism of IVD degeneration is still not elucidated. Cellular loss from cell death has been believed to contribute to the degradation of ECM and plays an important role in the process of IVD degeneration, but the mechanisms of cell death in degenerated IVD remain unclear. Apoptosis, a very important type of IVD cell death, has been considered to play a crucial role in the process of degeneration. Autophagy, a non-apoptosis death type of programmed cell death, has been considered extensively involved in many pathological and physiological processes, including the degenerative diseases. Thus, the research on cell death in IVD degeneration has become a new focus recently. In this review, by analyzing the available literature pertaining to cell death in IVD and discussing the inducing factors of IVD degeneration, NP cells and ECM in IVD degeneration, apoptotic signal transduction pathways involved in IVD cell death, the relationship of cell death with IVD degeneration and potential therapeutic strategy for IVD degeneration by regulating cell death, we conclude that different stimuli induce cell death in IVD via various signal transduction pathways, and that cell death may play a key role in the degenerative process of IVD. Regulation of cell death could be a potential and attractive therapeutic strategy for IVD degeneration.

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IVD Regeneration

Disc distraction shows evidence of regenerative potential in degenerated intervertebral discs as evaluated by protein expression, magnetic resonance imaging, and messenger ribonucleic acid expression analysis.
Guehring et al. Spine. 2006 Jul 1;31(15):1658-65.

- Distraction results in disc rehydration, stimulated extracellular matrix gene expression, and increased numbers of protein-expressing cells.

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IVD Regeneration

Effects of controlled dynamic disc distraction on degenerated intervertebral discs: an in vivo study on the rabbit lumbar spine model.
Kroeber et al. *Spine*. 2005 Jan 15;30(2):181-7.

- CONCLUSIONS: The results of this study suggest that disc regeneration can be induced by axial dynamic distraction in the rabbit intervertebral disc.
- The decompressed rabbit intervertebral discs showed signs of tissue recovery on a biologic, cellular, and a biomechanical level after 28 days of distraction.

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IVD Regeneration

[Controlled distraction as a therapeutic option in moderate degeneration of the intervertebral disc -- an in vivo study in the rabbit-spine model]
Unglaub et al. *Z Orthop Ihre Grenzgeb*. 2006 Jan-Feb;144(1):68-73.

- The results of this study suggest that disc regeneration can be induced by axial dynamic distraction in the moderately degenerated rabbit intervertebral disc.
- The decompressed rabbit intervertebral discs showed signs of tissue recovery at the cellular and histological levels after temporary disc distraction.

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IVD Regeneration

Review Article | Published: 14 January 2019

IVD progenitor cells: a new horizon for understanding disc homeostasis and repair

Feng-Juan Lyu, Kenneth M. Cheung, Zhaomin Zheng, Hua Wang, Daisuke Sakai & Victor Y. Leung

Nature Reviews Rheumatology **15**, 102–112 (2019) | Cite this article
3027 Accesses | **111** Citations | **16** Altmetric | Metrics

Abstract

Intervertebral disc (IVD) degeneration is associated with low back pain. In IVDs, a high mechanical load, high osmotic pressure and hypoxic conditions create a hostile microenvironment for resident cells. How IVD homeostasis and function are maintained under stress remains to be understood; however, several research groups have reported isolating native endogenous progenitor-like or otherwise proliferative cells from the IVD. The isolation of such cells implies that the IVD might contain a quiescent progenitor-like population that could be activated for IVD repair and regeneration. Increased understanding of endogenous disc progenitor cells will improve our knowledge of IVD homeostasis and, when combined with tissue engineering techniques, might hold promise for future therapeutic applications. In this Review, the characteristics of progenitor cells in different IVD compartments are discussed, as well as the potency of different cell populations within the IVD. The stem cell characteristics of these cells are also compared with those of mesenchymal stromal cells. On the basis of existing evidence, whether and how IVD degeneration and the hostile microenvironment might affect endogenous progenitor cell function are considered, and ways to channel the potential of these cells for IVD repair are suggested.

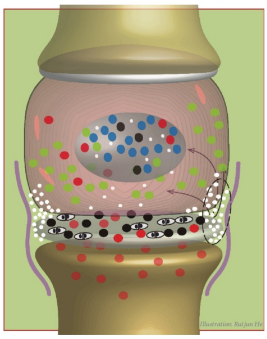

FIGURE 1: Schematic overview of the location of different kinds of IVDSCs. The stem cells located in IVD and the adjacent vertebras are indicated with dots. Elliptical broken line indicates the area of stem cell niche. The arrows indicate the possible migration pathways of SCNSCs. BMSC: bone marrow-derived stem cells; SCNSC: stem cell niche-derived stem cells; CESC: cartilage end plate-derived stem cells; NPSC: nucleus pulposus-derived stem cells; AFSC: annulus fibrosus-derived stem cells; CEPC: cartilage end plate cells. AFC: annulus fibrosus cells.

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IVD Regeneration

Review > ACS Biomater Sci Eng. 2024 Jan 8;10(1):219-233.
doi: 10.1021/acsbiomaterials.3c01091. Epub 2023 Dec 27.

Mechanical Factors Regulate Annulus Fibrosus (AF) Injury Repair and Remodeling: A Review

Zihan Wang [1], Xin Chen [1], Nan Chen [1], Hongjie Yan [1], Ke Wu [1], Jitao Li [2], Qingyuan Ru [1], Rongrong Deng [1], Xin Liu [1], Ran Kang [1 3]

Affiliations + expand
PMID: 38149967 DOI: 10.1021/acsbiomaterials.3c01091

Abstract

Low back pain is a common chronic disease that can severely affect the patient's work and daily life. The breakdown of spinal mechanical homeostasis caused by intervertebral disc (IVD) degeneration is a leading cause of low back pain. Annulus fibrosus (AF), as the outer layer structure of the IVD, is often the first affected part. AF injury caused by consistent stress overload will further accelerate IVD degeneration. Therefore, regulating AF injury repair and remodeling should be the primary goal of the IVD repair strategy. Mechanical stimulation has been shown to promote AF regeneration and repair, but most studies only focus on the effect of single stress on AF, and lack realistic models and methods that can mimic the actual mechanical environment of AF. In this article, we review the effects of different types of stress stimulation on AF injury repair and remodeling, suggest possible beneficial load combinations, and explore the underlying molecular mechanisms. It will provide the theoretical basis for designing better tissue engineering therapy using mechanical factors to regulate AF injury repair and remodeling in the future.

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IVD Regeneration

> Spine (Phila Pa 1976). 2021 Apr 1;46(7):421-432. doi: 10.1097/BRS.0000000000003816.

Effects of Axial Compression and Distraction on Vascular Bud and VEGFA Expression in the Vertebral Endplate of an Ex Vivo Rabbit Spinal Motion Segment Culture Model

Jia-Wen Zhan [1], Shang-Quan Wang, Min-Shan Feng, Jing-Hua Gao, Xu Wei, Jie Yu, Xun-Lu Yin, He Yin, Kai Sun, Ming Chen, Rui Xie, Ping Zhang, Li-Guo Zhu

Affiliations + expand
PMID: 33186278 DOI: 10.1097/BRS.0000000000003816

Abstract

Study design: An ex vivo study of the rabbit's vertebral endplate.

Objective: The aim of this study was to assess the effect of axial compression and distraction on vascular buds and vascular endothelial growth factor (VEGFA) expression of the vertebral endplate (VEP).

Summary of background data: The abnormal load can lead to intervertebral disc degeneration (IDD), whereas axial distraction can delay this process. The effects of different mechanical loads on the intervertebral disc (IVD) have been hypothesized to be related to changes in the vascular buds of the VEP; moreover, the process that might involve the vascular endothelial growth factor (VEGF) within the VEP.

Methods: Rabbit spinal segments (n = 40) were harvested and randomly classified into four groups: Control group, no stress was applied; Group A, a constant compressive load applied; Group B, compression load removed for a fixed time daily on a continuous basis, and substituted with a distraction load for 30 minutes; and Group C, compression removed for 30 minutes for a fixed period daily on a continuous basis. Tissue specimens were collected before the culture (day 0) and on day 14 post-culture of each group for analysis of IVDs' morphology, and protein and mRNA expression of Aggrecan, COL2al, VEGFA, and vascular endothelial growth factor receptor 2 of the VEPs.

Results: Application of axial distraction and dynamic load compression significantly delayed time- and constant compression-mediated VEP changes and IDD. Moreover, the degree of degeneration was associated with loss of vascular buds, as well as the downregulation of VEGFA and its receptor.

Conclusion: The regulation of vascular buds and VEGF expression in the VEP represents one of the mechanisms of axial distraction and dynamic loading.Level of Evidence: N/A.

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Questions?

- Thoughts about annular tears?
- Pain generators/complicators?
- Chiropractic means to benefit annular tears?
- Indications/contraindications of chiropractic techniques?
- Experience with regenerative medicine?
- Thoughts?

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Thank you!

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Upcoming Grand Rounds Schedule

The First Tuesday of the Month at 8PM EST

Upcoming Rounds

- **Septmber 3, 2024 – IVD Protrusions and Extrusions**
- **Additional live qualifying CAD classes will be available at the end of the year.**

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