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Lumbar Discogenic Pain: State-of-the-Art Review

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Abstract

Objective. To test the null hypotheses that: lumbar intervertebral discs cannot be a source of pain; discs are not a source of pain; painful lumbar discs cannot be diagnosed; and there is no pathology that causes discogenic pain.

Methods. Philosophical essay and discourse with reference to the literature.

Results. Anatomic and physiologic evidence denies the proposition that disc cannot be a source of pain. In patients with back pain, discs can be source of pain. No studies have refuted the ability of disc stimulation to diagnose discogenic pain. Studies warn only that disc stimulation may have a false-positive rate of 10% or less. Internal disc disruption is the leading cause of discogenic pain. Discogenic pain correlates with altered morphology on computerized tomography scan, with changes on magnetic resonance imaging, and with internal biophysical features of the disc. The morphological and biophysical features of discogenic pain have been produced in biomechanics studies and in laboratory animals.

Conclusions. All of the null hypotheses that have been raised against the concept of discogenic pain and its diagnosis have each been refuted by one or more studies. Although studies have raised concerns, none has sustained any null hypothesis. Discogenic pain can occur and can be diagnosed if strict operational criteria are used to reduce the likelihood of false-positive results.

Key Words. Back Pain; Intervertebral Disc; Discography; Diagnosis

Introduction

The causes of low back pain are not obvious. Fractures, tumors, and infections are rare causes, but for most cases, there is no evident disease that causes back pain; there is no readily detected injury that does so. Back pain begs an explanation.

When an established explanation is lacking, philosophers and scientists are entitled to raise conjectures. They can postulate what the cause may be. At one extreme, they might postulate that back pain is entirely psychosocial: that there is nothing wrong with the lumbar spine, and that the complaint of pain is a psychological disturbance. At the other extreme, they might postulate that back pain is a nociceptive phenomenon, with the source of pain lying among the constituent structures of the lumbar spine.

One such postulate is that the pain could stem from an intervertebral disc. As a conjecture, this is a perfectly valid suggestion. The discs are components of the lumbar spine, and if they were to hurt, it seems reasonable that the patient would complain of back pain. For ease of reference, that pain can be called discogenic pain.

Simply raising a conjecture, however, does not make it true. Nor does proselytizing—saying it over and over again—make it true. In fact, there is no way of proving any conjecture to be true, in an absolute sense. The scientific method relies not on proving a conjecture but on repeatedly attempting to refute it [1]. Credence in the conjecture grows if arguments against it are consistently refuted, and if experiments undertaken to test the conjecture consistently fail to refute it. Under those conditions, the conjecture is promoted to being acceptably true, for the time being, until evidence eventually refutes it.

The concept of discogenic pain implies various subordinate conjectures. Stated simply these are:

- Discs can hurt.
- Discs do hurt.
- Discs are affected by pathology that can make them hurt.

Satisfying these requirements would alone vindicate the concept; but in a clinical context, two additional responsibilities—rather than criteria—arise:

- Painful discs can be diagnosed, and
- doing so is clinically useful.

If cast in a converse, refutable sense, these criteria and responsibilities define criteria and experiments that can be applied to test the concept:

- Discs cannot hurt.
- Discs do not hurt.
- There is no pathology that causes pain.
- Discogenic pain cannot be diagnosed, and
- doing so is not clinically useful.

Refuting these opposing conjectures serves to raise the credibility of the concept.

At one time or another, during the history of spine science, each of these negative conjectures has been raised to discredit the concept of discogenic pain. Upon close analysis, it transpires that the experiments conducted, and the evidence collected, have failed to refute the concept.

Discs Cannot Hurt

The concept of discogenic pain was first proposed by the pioneers of lumbar discography, in the 1940s [2–4]. They observed that, during discography, patients often reported reproduction of their back pain. Indeed, authorities of the time, as eminent as Inman and Saunders, proposed that the lumbar discs could be a source of back pain [5].

However, the concept did not gain traction because it was commonly held, at the time, that the lumbar intervertebral discs lacked a nerve supply and, therefore, could not possibly be a source of pain. Indeed, this view was maintained as late as 1979 and 1980 [6,7] and was the pivotal argument against discogenic pain for some 30 years.

This argument was overturned by the demonstration in 1980 and 1981 that the lumbar discs did have a nerve supply [8–10]. Moreover, searches of the literature [10–12] revealed that evidence for this innervation had been available since 1959 [13], 1947 [14], and 1940 [15], but had either been ignored or suppressed, in order to refute the concept of discogenic pain.

The demonstration of a nerve supply showed that the lumbar discs were endowed with the necessary anatomical apparatus for them to be painful. This refuted the opposition that disc cannot hurt because they lack a nerve supply. When challenged on this issue at a seminar at the Royal Adelaide Hospital in 1990, Dr. Charles Aprill encapsulated the argument with a succinct reply that is worthy of contemplation and record: “If God didn’t mean for the discs to hurt, why did he give them a nerve supply?”.

Discs Do Not Hurt

Showing that discs had a nerve supply does not constitute evidence that these nerves are physiologically active, or that they transmit nociception. That requires physiological studies in subjects who can report if they feel pain or not.

The earliest studies in this regard were conducted in the 1940s, when investigators pressed the back of lumbar discs, using a blunt probe, in patients undergoing spine surgery under local anesthesia [16,17]. Probing the disc reproduced back pain. Injecting discs with hypertonic saline also reproduces back pain [18]. Similar observations were repeated in 1991, in a study in which structures in addition to the discs, such as the back muscles, zygapophysial joints, and ligaments were pressed with probes or squeezed with forceps. That study found that of all structures in the lumbar spine, the discs were the most potent source of experimentally evoked back pain.

A potential criticism of these studies is that they were conducted in patients with back pain who might not be reliable witnesses. Essentially, the accusation is that, in patients with back pain, probing any structure might evoke pain. To some extent, this accusation is dispelled by the observation that discs are more often painful, and more painful, than other structures when stimulated experimentally [19]. Nonetheless, it would be more convincing if discs were painful in subjects who did not have back pain.

Analogous studies have not been conducted in normal volunteers. Ethical constraints prevent volunteers from undergoing open surgery to gain access to their discs for experimental purposes. Nor is it anatomically possible to probe the back of discs with needles, for the dural sac and its contents obstruct access. However, normal volunteers have undergone discography. In these subjects, it has been shown that discs can be made to hurt, if stimulated strongly enough [20,21]. In this regard, discography is a less potent physical stimulus than probing the posterior surfaces of discs, because the inner anulus of an intact disc buffers the nerve endings in the outer third of the anulus from diffuse pressure exerted internally in the nucleus pulposus. In contrast, a fine probe on the external anulus has virtually immediate access to nociceptive nerve endings in the outer third.

Collectively, this evidence refutes the opposition that discs do not hurt. Clearly, they can be painful, when sufficiently stimulated mechanically.

Not Diagnosable

Whereas it might be accepted that discs are endowed with the apparatus by which to hurt and can be made to

hurt experimentally, a crucial question for clinical practice is whether or not painful discs in patients can be detected. This requires a diagnostic test that is valid.

In this regard, discogenic pain is not amenable to conventional means of assessing diagnostic tests. For many tests, it is possible to correlate the results of the test with the results of a physical reference standard, such as a biopsy, a post-mortem result, or an observation at surgery. Such correlations can be pursued for conditions such as infections, tumors, and diseases of the blood, because a physical reference standard is available. In contrast, pain is a physiological symptom; it cannot be photographed, radiographed, or biopsied. There is no physical reference standard for discogenic pain. However, this does not preclude the diagnosis of discogenic pain. Nor does it preclude the validation of tests for discogenic pain. The requirement is only that a process other than the conventional one be used.

In conventional circumstances, an experiment would be conducted so as to yield data that complete a contingency table, as depicted in Table 1. Cases in cell "a" represent true-positive responses, and cases in cell "d" are true-negative cases. Cases in cell "c" are false-negative cases, and cases in cell "b" are false-positive cases. The sensitivity of the test would be a/(a + c), and its specificity would be d/(b + d). The false-positive rate would be b/(b + d). These calculations require a reference standard that is dependably positive and negative.

When a reference standard is lacking, such a table cannot be completed. However, a partial reference standard might be available that allows part of the table to be estimated. For example, although there might not be a reference standard for positive presence of the index condition, there might nevertheless be a reference standard that dependably excludes the condition. Correlation of the diagnostic test against that standard would allow the completion of at least the second column of the table (Table 2). The resulting data do not constitute an accurate measure of the specificity of the test and its false-positive rate because, by definition, the data will not have been drawn from a sample of subjects that might have had the condition that the test is designed to detect. The data will, therefore, be heavily biased toward the negative. However, and nevertheless, the data can provide an estimate of the false-positive rate, which can be called the imputed false-positive rate. If the value of "b" is large, the validity of the test is rendered suspect because the false-positive rate is likely to be large; but if "b" is small, or tolerably so, the validity of the test has withstood challenge. This is the strategy that has been followed to test the validity of a diagnostic test for lumbar discogenic pain. The reference standard is that discs in asymptomatic patients should not be painful.

Table 1 The design of a contingency table by which to assess the validity of a diagnostic test

	Reference Standard	
Diagnostic Test	Positive	Negative
Positive	a	b
Negative	c	d

Table 2 The design of a contingency table by which to test the validity of a diagnostic test when only a reference standard for true-negative responses is available

	Reference Standard
Diagnostic Test	Negative
Positive	b
Negative	d

A large value of "b" implies a possibly large false-positive rate of the test.

The concept of discogenic pain translates into the proposition that, in a particular patient, their pain stems from a particular disc (or discs). For a diagnostic test of this proposition to be valid, the test must be able to distinguish between symptomatic and asymptomatic discs, and the test must not be positive for reasons other than that the index disc is the source of pain.

The pioneers of lumbar discography observed that their patients' back pain was reproduced when contrast medium was injected into certain discs [2–4], and others also noted this phenomenon [22–26]. This observation inspired disc stimulation as the basis of a diagnostic test for discogenic pain.

Any stimulation test, however, inherits certain liabilities. For a stimulation test to be valid:

- It should not be positive in normal volunteers, or
- at least it should not be positive below a particular threshold of stimulation; and
- it should not be positive for reasons other than the target structure is symptomatic, such as hyperalgesia.

If these criteria are not satisfied, the validity of the test lapses. Since the adoption of stimulation as a diagnostic test for discogenic pain, several studies have investigated if it does fail these criteria.

Normal Volunteers

The first approach was to determine if disc stimulation was positive in normal volunteers, who had no back pain. The earliest study was published only in the form of an abstract, but provided encouraging results. Massie and Stevens [27] reported the responses to discography of 52

normal subjects and 570 patients. They found that morphologically abnormal discs occurred in asymptomatic subjects but far more commonly in patients. In patients, although more than one disc might appear abnormal morphologically, usually only one was found to be symptomatic on provocation discography. However, in asymptomatic subjects, abnormal discs were rarely painful on provocation discography.

A later study, conducted on volunteer prisoners, claimed that disc stimulation was often painful [28]. However, this study was subsequently discredited on technical and psychosocial grounds [29].

The first fully reported, rigorous study assessed the responses to disc stimulation of 10 normal volunteers [30]. It found that no subject satisfied the criteria for a positive response, and the authors concluded that disc stimulation was not confounded by false-positive responses.

Later, this study was criticized on the grounds that its sample was demographically not representative of patients in whom disc stimulation is typically undertaken. A replication study was undertaken in a more representative sample. That study transparently provided comprehensive data [20]. Analysis of those data yields conclusions that differ from those tendered by the authors.

The authors did not study normal volunteers. They used a surrogate group of 10 patients who had undergone cervical surgery, were free of pain, and who had not had back pain. Some critics might complain that such subjects are not representative of totally asymptomatic, normal volunteers; or that patients with cervical disc disease might have cryptic lumbar disc disease. However, given the difficulties inherent in recruiting volunteers for invasive studies, more gracious readers might accept this surrogate group as tolerable, under the circumstances.

In addition, the authors performed provocation discography on two other groups of subjects. There were 10 subjects who had undergone surgery for chronic neck pain, and whose neck pain persisted; but they did not have back pain. There were six patients with somatization disorder; but although discography was initiated in these six patients, it was not completed in two.

The authors rated as positive any patient or subject who reported severe pain after stimulation of any disc at any pressure (Table 3). Under those conditions, they found a low imputed false-positive rate among asymptomatic volunteers, but alarmingly high rates among the other subjects (Table 4).

Ostensibly, these data seem to suggest that disc stimulation is confounded by false-positive responses, but this conclusion is subject to the criteria used by the authors for a positive response, namely: severe pain from any disc at any pressure of stimulation. These criteria do not reflect the operational criteria for disc stimulation for they do not correct for threshold of stimulation.

Table 3 An abridged version of the data of Carragee et al. [20] showing the pressures of injection and pain scores of patients in three, clinically different group after disc stimulation

	L2-3		L3-4		L4-5		L5-S1	
Group	psi	VAS	psi	VAS	psi	VAS	psi	VAS
Neck surgery, no back pain								
1			100	0	100	0	**25**	**9**
2			100	0	80	0	40	0
3			80	4	50	0	20	4
4			100	0	80	2	100	0
5			100	0	30	0	10	2
6			100	0	80	0	100	0
7			100	0	50	2	100	0
8			100	0	100	0	100	1
9			100	0	100	0	100	0
10			100	0	80	0	30	0
Neck surgery, chronic pain								
11	100	0	100	0	100	4		
12	100	0	80	0	100	2		
13			80	4	**12**	**9**	**50**	**6**
14			100	0	**20**	**6**	40	0
15			100	1	80	0	80	0
16			30	4	100	0	40	2
17			100	0	100	0	100	2
18			**80**	**10**	**50**	**10**	**20**	**8**
19			100	0	20	0	100	0
20			100	0	80	0	**50**	**8**
Somatization								
21			**25**	**6**	100	0	30	0
22			25	1	12	0	**12**	**10**
23			100	0	80	4	20	0
24			100	0	**20**	**8**	**100**	**6**
25			100	0	**50**	**5**		
26			**50**	**5**				

In order to enable comparison with other data, the pain scores have been converted from a 0–5 scale, used in the original study, to a 0–10 visual analog score. The responses rated as positive are shown in bold.
VAS = visual analog score for pain.

Any normal structure that is innervated is potentially painful if stimulated sufficiently strongly. However, there may be a threshold below which normal structures are not painful. In the context of disc stimulation, this has been determined.

A study was performed in currently asymptomatic volunteers who, variously, had no past history of back pain or a history of only occasional back pain [21]. Their discs were stimulated by injection of contrast medium. Injection was continued, and pressure of injection was increased either

Table 4 The imputed false-positive rate of disc stimulation in three categories of subjects, whose original data are shown in Table 3

Category of Subject	Imputed False-Positive Rate	95% Confidence Intervals
Asymptomatic	1/10 = 10%	0–29%
Chronic pain	4/10 = 40%	10–70%
Somatization	3/4 = 75%	33–100%

until the subject reported pain, or until the pressure of injection reached 100 psi. Reported was the cumulative probability that a normal subject would report pain of a particular intensity at a particular pressure of injection (Table 5).

In detail, these data show that a compound sliding scale could be used to define a normal threshold. Physicians could accept a pressure of 30, 40, or 70 psi as a threshold, provided that patients did not report pain that was more severe than 2, 5, or 6. However, for immediate purposes, the data show that no normal volunteers experienced pain of any intensity at pressures of stimulation up to and including 20 psi. Thus, 20 psi defines an absolute threshold at which normal discs should not be painful.

If this manometric criterion is applied to the data of Table 3, reductions occur in the number of discs and number of patients with positive responses (Table 6). Among asymptomatic subjects, false-positive responses disappear. In patients with chronic pain, the prevalence of positive responses reduces to 3/10; and in patients with somatization, the prevalence reduces to 2/6 (Table 7).

The threshold of 20 psi is not without a correlate in symptomatic patients. Two studies have graphed the distribution of pressures at which patients with back pain report pain during disc stimulation [31,32].

In the first study [31], three subgroups of responses could be discerned upon visual inspection of the data: a low-pressure group, a mid-pressure group, and a high-pressure group (Figure 1). The low-pressure responses implied distinctly symptomatic discs, because of their sensitivity to stimulation; the high-pressure responses implied normal discs that responded only because high pressures were applied; and the mid-pressure responses were indeterminate, in that they might or might have been symptomatic. Conspicuously, however, the overlap between the low-pressure and mid-pressure responses occurred at 25 psi; and there were no mid-pressure responses below

Table 5 The responses to disc stimulation of subjects with no history of back pain (No) and subjects with a history of occasional back pain only (Occ), according to the pressure of stimulation and the intensity of pain evoked

			Pain Score (0–10)						
			0	1	2	3	4	5	6
Pressure of injection (psi)	100	Occ	0.30	0.40	0.25	0.25	0.25	0.10	0.00
		No	0.17	0.48	0.30	0.22	0.09	0.04	0.04
	90	Occ	0.35	0.40	0.25	0.25	0.25	0.10	0.00
		No	0.22	0.43	0.30	0.22	0.09	0.04	0.04
	80	Occ	0.55	0.30	0.25	0.25	0.25	0.10	0.00
		No	0.22	0.43	0.30	0.22	0.09	0.04	0.04
	70	Occ	0.55	0.30	0.25	0.25	0.25	0.10	**0.00**
		No	0.52	0.30	0.17	0.14	0.04	0.00	**0.00**
	60	Occ	0.65	0.30	0.25	0.25	0.25	0.10	**0.00**
		No	0.65	0.30	0.17	0.12	0.04	0.00	**0.00**
	50	Occ	0.75	0.20	0.15	0.15	0.15	0.06	**0.00**
		No	0.83	0.17	0.09	0.06	0.04	0.00	**0.00**
	40	Occ	0.80	0.15	0.10	0.10	0.10	**0.00**	**0.00**
		No	0.96	0.04	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
	30	Occ	0.95	0.05	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
		No	1.00	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
	20	Occ	1.00	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
		No	1.00	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**

The tabulated figures are the cumulative frequency of responses, which reflect the chances of pain of a particular intensity occurring at a particular pressure of injection. The line indicates the boundary below which normal volunteers do not experience pain. From Derby et al. [21].

Table 6 The data of Table 3 showing the discs and subjects with a positive response to disc stimulation after adjusting the threshold of stimulation to 20 psi

	L2-3		L3-4		L4-5		L5-S1	
Group	psi	VAS	Psi	VAS	psi	VAS	psi	VAS
Neck surgery, no back pain								
1			(20	0)	(20	0)	(20	0)
2			(20	0)	(20	0)	(20	0)
3			(20	0)	(20	0)	(20	0)
4			(20	0)	(20	0)	(20	0)
5			(20	0)	(20	0)	(20	0)
6			(20	0)	(20	0)	(20	0)
7			(20	0)	(20	0)	(20	0)
8			(20	0)	(20	0)	(20	0)
9			(20	0)	(20	0)	(20	0)
10			(20	0)	(20	0)	(20	0)
Neck surgery, chronic pain								
11	(20	0)	(20	0)	(20	0)		
12	(20	0)	(20	0)	(20	0)		
13			(20	0)	**12**	**9**	(20	0)
14			(20	0)	**20**	**6**	(20	0)
15			(20	0)	(20	0)	(20	0)
16			(20	0)	(20	0)	(20	0)
17			(20	0)	(20	0)	(20	0)
18			(20	0)	(20	0)	**20**	**8**
19			(20	0)	(20	0)	(20	0)
20			(20	0)	(20	0)	(20	0)
Somatization								
21			(20	0)	(20	0)	(20	0)
22			(20	0)	12	0	**12**	**10**
23			(20	0)	(20	0)	(20	0)
24			(20	0)	**20**	**8**	**100**	**6**
25			100	0	(20	0)		
26			(20	0)				

Responses in which pain occurred at higher pressures are assumed to have had no pain at 20 psi. The responses rated as positive are shown in bold.
VAS = visual analog score for pain.

20 psi. Given the normative data of Table 5, the low-pressure discs clearly qualify as abnormal, because they were painful at pressures at which normal volunteers do not perceive pain. Mid-pressure responses may or may not be abnormal. For those cases, the sliding scale of composite thresholds of Table 5 applies. Discs would be abnormal if the pain evoked exceeded the boundary for pain scores depicted in Table 5, but pressures of stimulation did not exceed the boundary for pressure.

In the second study [32], the distributions of responses in symptomatic patients were subjected to rigorous mathematical analysis, and two distinct subgroups were identified (Figure 2). As in the previous study [31], responses at low pressures of stimulation suggest highly sensitive symptomatic discs. This group had a mean pressure of 10 psi and overlapped with the second group at around 20 psi. According to these data, adopting a threshold of 20 psi captures most of the patients with highly sensitive discs, and only the low end of the indeterminate group of middle- and high-pressure responses. At pressures greater than 10 psi, discs would be classed as symptomatic only if the pain evoked was of an intensity greater than the corresponding threshold of pain for that pressure, as depicted in Table 5.

It is conspicuous in Tables 5 and 7 that the imputed false-positive rates have large 95% confidence intervals. The confidence intervals for patients with somatization, in particular, are so wide as to be almost meaningless. This arises because the sample sizes (10 and 6) are so small. This means that the data cannot be definitive; they are at best only sentinel.

A systematic review, however, overcame this problem [33]. It collected all data from all studies on disc stimulation and subjected them to meta-analysis. Doing so increased the sample size and increased the confidence in the resulting estimate. It found that the imputed false-positive rate of disc stimulation did not exceed 10% and was possibly as low as 6%. This rate compares more than favorably with the false-positive rates of accepted tests in medical practice. More particularly, although the false-positive rate of disc stimulation is nonzero, it is too low to invalidate disc stimulation as a diagnostic test.

Hyperalgesia

Hyperalgesia describes a state in which a patient or subject reports pain, or pain of greater intensity than expected, for reasons other than a noxious lesion in the structure stimulated. Hyperalgesia allows a structure to appear to be painful upon stimulation and appear to be the source of the patient's accustomed pain, when it is not the actual source of pain. It appears to be painful only because other mechanisms are operating. Those mechanisms may be central or segmental.

The model of central hyperalgesia supposes that, for psychological reasons or because the patient has pain in remote regions elsewhere, noxious stimulation of normal

Table 7 The imputed false-positive rate of disc stimulation in three categories of subjects, whose data are shown in Table 6

Category of Subject	Imputed False-Positive Rate	95% Confidence Intervals
Asymptomatic	0/10 = 0%	0–28%
Chronic pain	3/10 = 30%	2–58%
Somatization	2/6 = 33%	0–60%

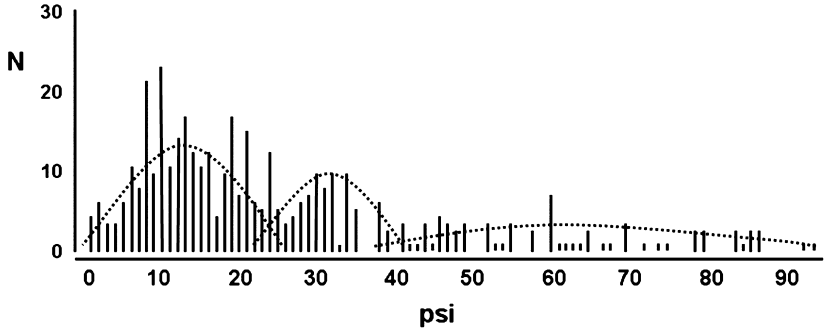

Figure 1 The distribution of pressures at which symptomatic patients reported reproduction of their pain upon disc stimulation. The distribution implies three overlapping subgroups. Based on O'Neill et al. [31].

structures will make them appear more painful than normal. In the case of disc stimulation, central hyperalgesia risks making the disc appear to be the source of the patient's pain, but the response is false-positive because the disc is actually not abnormal and painful. There are no tests to determine if a patient has central hyperalgesia, but there are means by which to reduce false-positive responses ostensibly due to possible central hyperalgesia.

In philosophical terms, the model of central hyperalgesia can be cast as a competing hypothesis. The model predicts that anything that is stimulated will appear painful. In particular, it predicts that in a patient with central hyperalgesia, i.e., generalized sensitivity to pain, any and all discs will be painful to stimulation. This prediction can be tested. The test requires stimulation of adjacent discs. If all discs that are tested appear painful, the response is consistent with the predictions of the competing model. However, if only one disc (or perhaps two discs) is painful but others are not, the competing model is refuted. The presence of asymptomatic discs refutes the proposition that the patient has generalized hyperalgesia and, therefore, refutes the accusation that the response to disc stimulation is false.

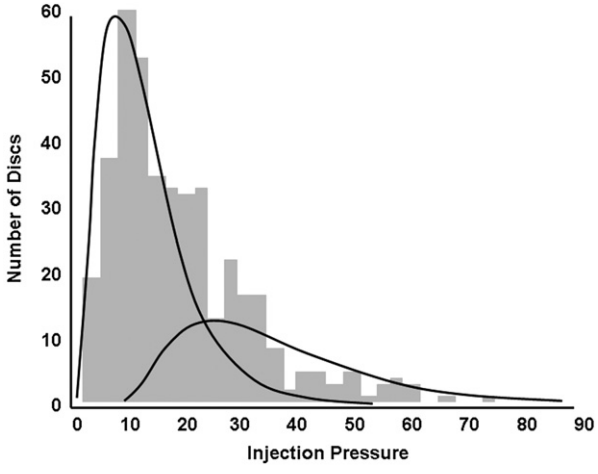

Figure 2 The distribution of pressures at which symptomatic patients reported reproduction of their pain upon disc stimulation. The histograms depict the raw data. The curves identify two overlapping subgroups. Based on O'Neill and Kurgansky [32].

For this reason, an operational requirement of disc stimulation is that anatomical controls be used. The patient must be able to distinguish a painful disc from adjacent discs that are not painful. If one disc is painful but two others are not, the response cannot be false because of central hyperalgesia. If three discs are tested and all three are painful, the physician cannot be certain that the response is not false. If two discs are painful but one is not, the interpretation of the response is potentially vexatious. On balance, the response is unlikely to be false, because the model of central hyperalgesia predicts that all discs should be painful. However, physicians need to be cautious in interpreting such responses lest the responses of the patient are only random.

A study of a large number of patients showed that their responses to disc stimulation are not complicated by central hyperalgesia [34]. Patients are able to discriminate between symptomatic and asymptomatic discs. Discs classified as positive are painful at significantly lower pressures of stimulation than discs classified as negative and discs in normal volunteers; and they are significantly more painful across a range of pressures (Figure 3). Meanwhile, negative discs are indistinguishable from discs in normal volunteers, with respect to the threshold pressure at which they become painful, and the intensity of pain evoked (Figure 3). This shows that, whereas patients may have one or more discs that are distinctly symptomatic, they also have discs that respond like normal, asymptomatic discs. This is incompatible with these patients having central hyperalgesia that renders any and all discs painful. Therefore, their positive responses cannot be dismissed as being false-positive because of central hyperalgesia.

Psychometrics

Several studies have applied psychometric tests on theory that psychological distress might cause central hyperalgesia, or that patients with psychological distress are likely to have exaggerated responses to disc stimulation that

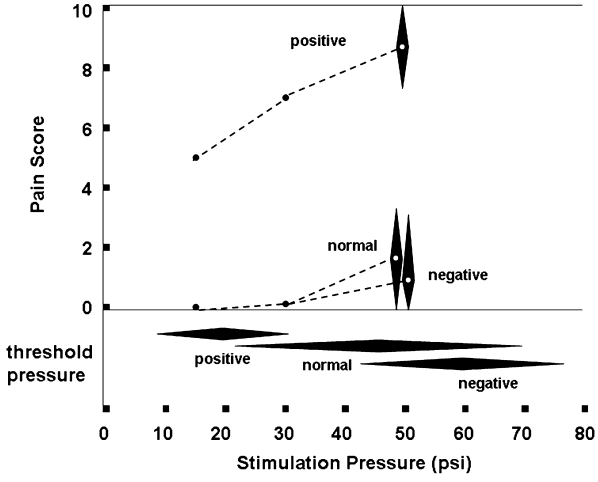

Figure 3 The data from a study of normal volunteers and patients with discs that were positive or negative to disc stimulation 35 showing the threshold pressures at which discs became painful in each of the three groups and their pain scores at 15, 30, and 50 psi.

render disc stimulation invalid. The results of these studies have varied.

Two studies measured the frequency of false-positive responses that were defined as pain evoked by stimulation of a disc that was not internally disrupted. Such responses are not necessarily false-positive for it has not been shown that internal disruption is necessary for a disc to be painful, and that there are no conditions other than internal disc disruption that render a disc painful. Nevertheless, the definition used serves reasonably for the sentinel purposes for which the studies were conducted.

One of the studies [35] found that scores greater than 70 on the scales for hysteria, hypochondriasis, or depression on the Minnesota Multiphasic Personality Inventory (MMPI) were associated with a greater prevalence of false-positive responses. However, although statistically and clinically significant, the association was not absolute. Some 60% of patients with elevated scores were likely to report false-positive response, compared with 30–40% of unaffected patients. This does not render disc stimulation prohibited in patients with elevated scores, because about 40% of affected patients do not report aberrant responses; and the MMPI does not predict individually which patients will and which patients won't have aberrant responses to disc stimulation. These results simply warn physicians that patients with scores above 70 might have exaggerated pain responses.

The second study [36] found that patients with abnormal pain drawings were prone to false-positive responses. However, only 50% of such patients had exaggerated responses to disc stimulation; the other 50% did not. So, an abnormal pain drawing does not disqualify a patient from investigation; it simply warns physicians to expect aberrant responses.

Neither of these studies threatens the validity of disc stimulation as a diagnostic test. They warn only of the possibility of exaggerated responses to disc stimulation in certain types of patients. Whereas such responses complicate disc stimulation, they do not invalidate it. If patients have exaggerated responses, they will not have painless control levels. In the absence of painless controls, positive responses cannot be held to be true-positive, and the results of the test become indeterminate. Thus, the studies warn physicians that, in patients' elevated scores on the MMPI, or with abnormal pain drawings, indeterminate results are likely; but not all such patients will necessarily have indeterminate results.

Two studies, based on small samples (6 and 20), warned that the false-positive rate of disc stimulation could be high in patients with somatization disorders [37]. This was not borne out in a subsequent, larger study (of 50 patients and 50 controls) that found no difference in the frequency of positive responses in patients with and without somatization disorder [38].

A study using the Distress and Risk Assessment Method found no correlation between psychometric variables and the positive rate of disc stimulation [39]. Nor was there any difference in the intensity of pain evoked, at either 15 psi or 50 psi stimulation.

Thus, although concerns and conjectures have been raised about the influence of psychometric features on the response to disc stimulation, none has been fully substantiated. Distress does not influence responses, and the influence of somatization has been denied. Elevated scores on the MMPI, or abnormal pain drawings, do not invalidate disc stimulation; they no more than render responses more difficult to interpret.

Segmental Hyperalgesia

Segmental hyperalgesia is a different phenomenon. It means that a normal structure may appear painful, when stimulated, if there is an actual source of pain among the other structures innervated by the same spinal cord segments as the structure stimulated. A study warned of this phenomenon in the context of disc stimulation. It showed that discs could appear to be painful upon stimulation in subjects who had no back pain but who had painful iliac crest donor sites [40].

This observation does not invalidate disc stimulation as a diagnostic test, but it warns physicians to be careful about competing sources of pain when performing disc stimulation. Possible sources such as iliac crest donor sites would be obvious, but others are more cryptic.

One study explored the possibility that patients with discogenic pain might also have another source of pain. In that study, 86 patients underwent disc stimulation and controlled, diagnostic blocks of their zygapophysial joints [41]. The majority of patients had positive responses to either disc stimulation or zygapophysial joint blocks, but not to both. Only three patients had positive responses to both. Their responses were compatible either with the disc and zygapophysial joints both being sources of pain, or with the disc stimulation being false-positive because of segmental hyperalgesia caused by zygapophysial joint pain. Irrespective of the explanation, the rarity of combined positive responses indicates that the false-positive rate of disc stimulation attributable to segmental hyperalgesia from the zygapophysial joints must be less than 5%.

Some physicians might care to tolerate such low probabilities of other structures being cryptic sources of pain and segmental hyperalgesia. However, in the interests of optimizing the validity of disc stimulation, it would seem pertinent and wise to clear patients of zygapophysial joint pain and possibly also sacroiliac joint pain before undertaking disc stimulation.

There Is No Pathology

Discitis is mercifully a rare condition but one that is patently painful, and severely so. This condition alone refutes in its broadest terms the opposition that there is no pathology that renders lumbar discs painful. However, the opposition could be cast more specifically as there is no common condition that renders discs painful. Yet there is evidence to the contrary.

Internal disc disruption is a condition characterized by degradation of the nuclear matrix and the development of fissures inside the disc, which are initially radial in disposition but which can extend circumferentially between the lamellae of the outer anulus. For descriptive purposes, these fissures can be graded according to the extent to which they penetrate the anulus (Figure 4). Grade I, II, and III fissures reach the inner, middle, and outer third of the anulus, respectively, and become grade IV when they spread circumferentially. Critically, this condition is restricted to the internal structure of the disc; the outer anulus may bulge over a fissure, but the outer anulus remains essentially intact, i.e., there is no penetrating defect through the entire anulus.

Because the anulus is externally intact, this condition cannot be detected by conventional computerized tomography (CT), but it can be seen if contrast medium is injected into the nucleus pulposus and viewed under CT. The contrast medium fills the fissure and depicts its extent (Figure 5).

There is an imperfect but nevertheless strong correlation between a disc having a grade III (or IV) fissure and being painful upon disc stimulation. An early study showed that some 70% of discs with a grade III fissure are painful, and some 70% of painful discs have a grade III fissure [42]. A subsequent, large study showed that radial fissures are independent of age changes and degenerative changes in the affected segment, but are strongly associated with the disc being painful [43] (Table 8). Other studies have repeatedly underscored this association (Table 9). Not all grade III or IV fissures are painful, but having a grade III or IV fissure seems to be a requisite for the disc to be painful. It is uncommon for discs to be painful when affected by no fissures or only grade I or II fissures (Table 9).

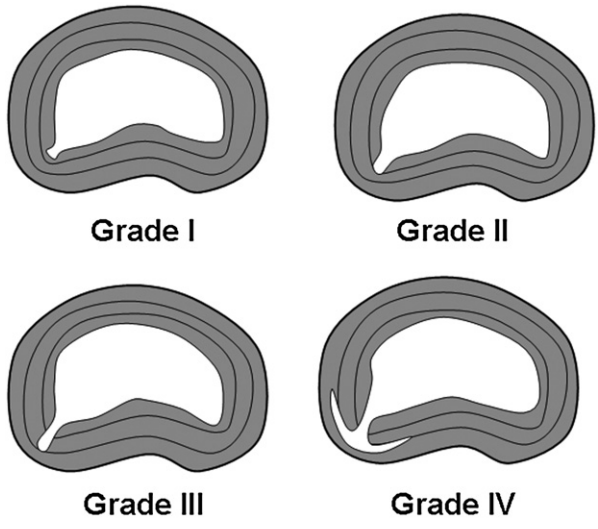

Figure 4 Sketches of the appearance of various grades of radial fissures in lumbar intervertebral discs.

Internally disrupted discs exhibit striking biophysical properties. Stress profilometry is a procedure in which a probe is used to measure the stresses across a diameter of the disc [48,49]. In a normal disc, the stresses are uniform from the inner, anterior anulus, across the nucleus, to the posterior anulus, with a small peak in the posterior anulus [50] (Figure 6). In a disc with internal disruption, nuclear stresses are reduced, irregular, and may be zero in places, while the posterior anulus exhibits increased stresses [50] (Figure 6).

These physiologic (biomechanical) features are objective, and cannot be invented or feigned by patients. They indicate that the nuclear matrix must have changed, for it is no longer functioning properly. The nucleus is no longer bearing compression load properly, if at all. Meanwhile, normal compression loads are offset onto the posterior anulus and accentuated.

These physical properties independently correlate with pain. Reduced nuclear stress and increased stress in the anulus each correlate strongly with reproduction of pain when the disc is stimulated [51] (Table 10).

The mechanisms by which discs are rendered painful by internal disruption have not been established directly. The

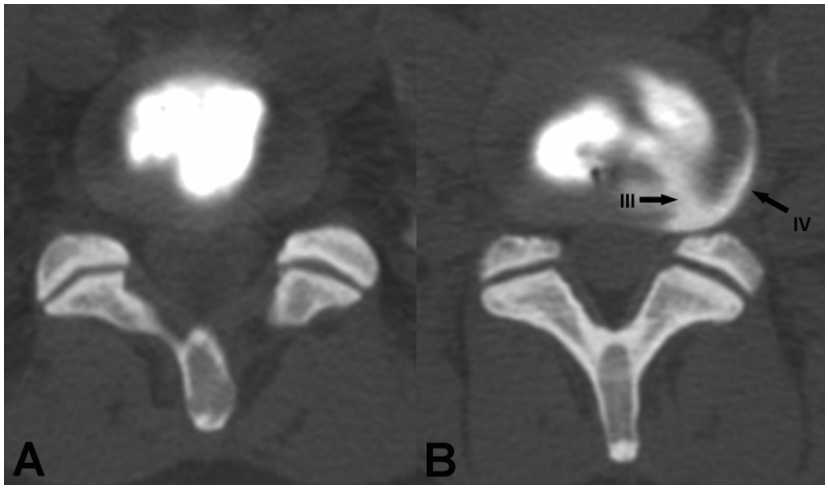

Figure 5 Computerized tomography scans of discs into whose nucleus contrast medium has been injected. A: normal disc. B: a disc with a grade III radial fissure that spreads circumferential to become a grade IV fissure. Images kindly provided by Dr. Milton Landers, Wichita, Kansas.

Table 8 The correlation between the grade of annular disruption and reproduction of pain by disc stimulation

Pain Reproduction	Annular Disruption			
	Grade III	Grade II	Grade I	Grade 0
Exact	43	29	6	4
Similar	32	36	21	8
Dissimilar	9	11	6	2
None	16	24	67	86

The numbers refer to the number of patients exhibiting the features tabulated. Based on Moneta et al. [43]. $\chi^2 = 148$; $P < 0.001$.

determination of these mechanisms would require intricate experiments involving the insertion of microelectrodes and micropipettes into painful disc and onto the nerves that subtend them. However, possible mechanisms can be reasonably postulated.

The increased stresses seen in the posterior anulus on stress profilometry suggest that the posterior anulus could be a source of mechanical pain. In particular, the anulus around the apex of radial fissures would be especially vulnerable. In that sector of the anulus, fewer lamellae of the anulus remain intact, but they are still subject to normal compression loads and to radial tension. Therefore, the stress per lamella must be greater in these surviving lamellae. For mechanical nociception to occur, all that is required is for this relative

Table 9 The association between grades of anulus disruption and reproduction of pain upon disc stimulation, as found in four studies. A: Aprill and Bogduk [44]. B: Smith et al. [45]. C. Lim et al. [46]. D: Kokkonen et al. [47]

	Anulus Disruption			Anulus Disruption	
A	Grade III, IV	Grade 0-II	B	Grade III, IV	Grade 0-II
Pain	38	0	Pain	39	5
Not pain	37	31	Not pain	67	51
$P = 0.000$			$P = 0.000$		
	Anulus Disruption			Anulus Disruption	
C	Grade III, IV	Grade 0-II	D	Grade III, IV	Grade 0-II
Pain	33	27	Pain	16	31
Not pain	1	36	Not pain	11	54
$P = 0.000$			$P = 0.003$		

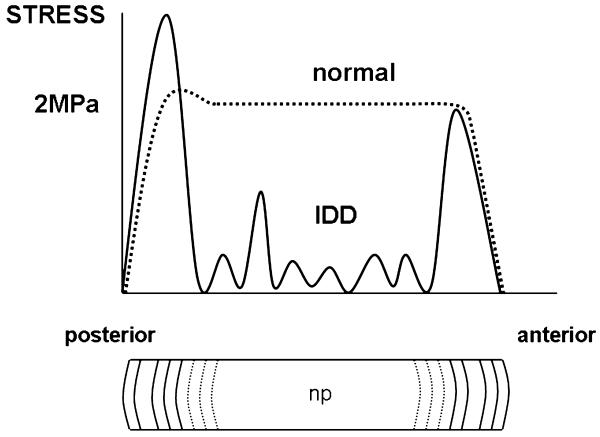

Figure 6 A sketch of the features of a normal disc and on affected by internal disc disruption (IDD) under stress profilometry. The graph shows the magnitude of the stress within the disc across a diameter that pass from the anterior anulus to the posterior anulus. In a normal disc, the stresses are uniform. In a disc with IDD, the stresses in the nucleus pulposus (np) are irregular, decreased, and may be zero, but the stress in the posterior anulus is increased substantially above normal.

stress to exceed the threshold for mechanical transduction of nociception.

Another potential mechanism of pain is chemical nociception. Degraded matrix materials contain inflammatory chemicals, cytokines, and noxious agents such as nitric oxide [52], which are capable of stimulating or facilitating nociceptors. These agents could elicit chemical nociception alone, or they could sensitize the ambient nociceptors to mechanical stimulation.

Table 10 The correlation between abnormal stress profiles and pain upon stimulation of a lumbar intervertebral disc

	Disc	
Biophysical Properties	Painful	Not Painful
Nuclear stress		
Depressurized	11	0
Normal	7	13
	Fisher's exact test; $P = 0.017$	
Annular stress		
Stressed	17	2
Normal	1	11
	Fisher's exact test; $P = 0.001$	

Based on McNally et al. [51].

Circumstantial evidence supports such postulates. In addition to their normal innervation, injured lumbar discs can acquire a neoinnervation [53–58]. New nerves are particularly found along radial fissures [57,58] and extend into the deeper anulus, and even into the nucleus [53,54,56]. Although the majority of these nerves are sympathetic efferents, a substantial proportion carry the markers of nociceptive afferents [56]. The presence of such nerves around radial fissures is consonant with the affected sector of the anulus being a source of pain. Neoinnervation is significantly greater in discs that are painful upon disc stimulation than asymptomatic discs [54].

Etiology

Biomechanics studies have shown that vertebral endplates are subject to fatigue failure under compression [48]. Failure, in the form of small fractures, can occur when loads as small as 50% of the ultimate compression strength of the endplate are applied, after as few as 1,000 or even 100 repetitions [50,59]. Such loads and repetitions are encountered during normal, moderate to heavy work activities. Therefore, endplate fractures do not need major trauma to be the precipitating event.

It has also been shown that immediately upon incurring an endplate fracture, the affected disc exhibits features of the abnormal stress profile of internal disruption. Nuclear stress is lowered, and stress in the posterior anulus rises [48]. The magnitudes of changes seen acutely in biomechanics experiments are not as large as those seen in discs with established internal disruption, but in quality and direction, they are the same.

Animal studies have now shown that the features of internal disc disruption can be induced experimentally by fracturing a vertebral endplate. Doing so causes changes in the nature and content of proteoglycans, reduction in water content, reduction in nuclear pressure, and delamination of the inner anulus [60,61]. Endplate trauma also induces increased activity of lactate dehydrogenase and matrix metalloproteinases; and induces cell death through the expression of genes for cell-death receptors, such as Fas and tumor necrosis factor α [62].

These animal studies show that the nuclear matrix is degraded by endplate trauma [60–62]. Degradation of the matrix implies impaired function, and that is what stress profilometry reveals [48,51].

Magnetic Resonance Imaging (MRI)

Two features evident on MRI correlate strongly with the affected disc being painful upon disc stimulation: high-intensity zone (HIZ) lesions and Modic lesions. The former affect the anulus fibrosus, the latter affect the vertebral endplate.

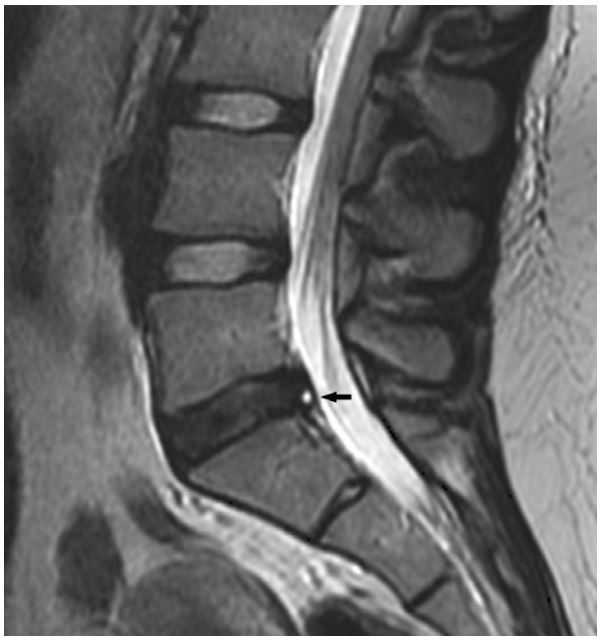

Figure 7 A sagittal magnetic resonance scan of a lumbar spine showing a high-intensity zone (arrow) in the posterior anulus of the L5 disc. Image kindly provided by Dr. Milton Landers, Wichita, Kansas.

HIZs

HIZs are defined as spots of intensely high signal within the posterior anulus of a disc viewed in heavily T2-weighted MR images [44] (Figure 7). They represent the appearance, in sagittal images, of large radial or circumferential fissures [44]. They are not simply fissures or gray spots within the anulus. Their intensity must rival that of the cerebrospinal fluid [44]. Failure to heed this criterion can result in asymptomatic fissures being misrepresented as HIZs.

Only one study has estimated the prevalence of HIZs in patients. It found that 28% (±4%) of 500 consecutive patients exhibited the feature [44]. Other studies have reported only prevalence among discs on which disc stimulation was performed. HIZs are not a sign of back pain, for they can occur in asymptomatic individuals [63,64]; but when evident in a patient with back pain, they strongly implicate the affected disc as the source of pain.

Several studies have investigated the correlation between the presence of HIZs and the reproduction of back pain upon disc to stimulation (Table 11). All studies agree on the high specificity of the sign. That means that it is unlikely to be false-positive, when present. Where studies have differed is in the sensitivity of the HIZ (Table 11). Lower sensitivity correlates with lower prevalence, as does higher specificity. This suggests that differences between studies are due to differences in the samples studied, differences in the acquisition sequences used to detect the sign, or to differences in propensity of observer to underread the sign. Nevertheless, there is good consistency between studies with respect to the positive likelihood ratio of the HIZ (Table 11). Only two studies had likelihood ratios whose 95% confidence intervals did not overlap with those of the other 10 studies, and only one study had confidence intervals that did not match those of the pooled data.

The indicative likelihood ratio of an HIZ is 3.8, with 95% confidence intervals of 3.1 to 4.5. If the prevalence of internal disc disruption is 46% (see later), a likelihood ratio

Table 11 The sensitivity, specificity, and likelihood ratio of the high-intensity zone as a predictor of the affected disc being painful, as reported by 12 studies

Sample Size	Sensitivity	Specificity	Likelihood Ratio	95% CI	Source
142	0.37	1.00	∞		[64]
120	0.82	0.89	7.5	4.0–14.1	[44]
256	0.45	0.94	7.5	3.7–15.1	[65]
152	0.27	0.95	5.4	1.7–17.1	[66]
101	0.52	0.90	5.2	2.4–11.2	[67]
155	0.81	0.79	3.9	2.5–6.0	[68]
178	0.57	0.84	3.6	2.2–5.7	[69]
109	0.45	0.84	2.8	1.4–5.5	[70]
152	0.26	0.90	2.6	1.2–5.8	[47]
97	0.56	0.70	1.9	1.2–3.0	[46]
116	0.27	0.85	1.8	0.9–3.8	[71]
80	0.09	0.93	1.3	0.3–5.4	[72]
1,658	0.45	0.88	3.8	3.1–4.5	ALL

The prevalence represents the number of discs studied that showed the sign.
95% CI = 95% confidence interval.

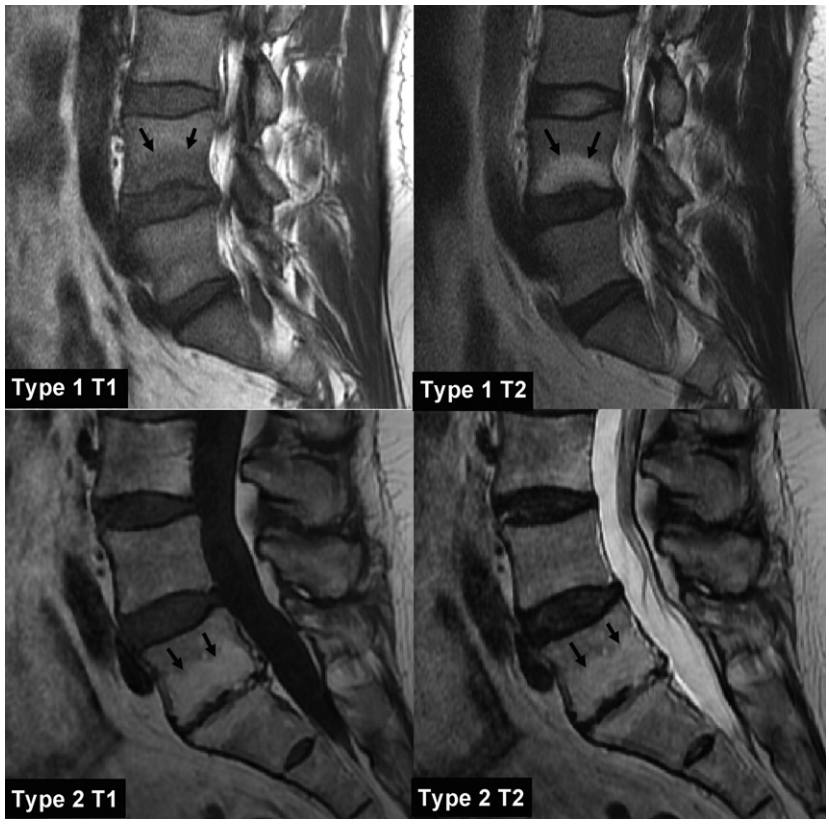

Figure 8 Type 1 and Type 2 Modic changes in T1- and T2-weighted sagittal magnetic resonance imaging scans. Images kindly provided by Dr. Tim Maus, Rochester, Minnesota.

of 4 means that an investigator can be 73% confident that the affected disc will be painful on disc stimulation. This figure indicates that an HIZ is not absolutely diagnostic of a painful disc, but its presence substantially increases the chances that the affected disc will be the source of pain.

Modic Changes

Modic changes are patches of abnormal signal in the vertebral bodies adjacent to a disc [73]. They occur as three types [74]. Type 1 changes appear hypo-intense of T1-weighted MR images and hyper-intense on T2-weighted images (Figure 8). Type 2 changes appear hyper-intense on both T1-weighted and T2-weighted images (Figure 7). Type 3 changes appear hypo-intense on both T1-weighted and T2-weighted images.

Type 1 changes represent inflammatory edema surrounding the disc. They are associated with disruption and fissuring of the endplate, and the presence of interleukin 6, interleukin 8, and prostaglandin E2 [74]. They can resolve, or evolve into Type 2 changes [74]. Type 2 changes represent fatty infiltration, ostensibly after the acute inflammation represented by Type 1 changes. They tend to persist and not change in appearance [74]. Type 3 changes probably represent sclerosis of the vertebral body [74]. Type 3 changes are not related to pain, but Types 1 and 2 are.

Modic changes are reasonably common. They occur in between 19% and 59% of patients with chronic low back pain [74]. Across all studies that have measured the prevalence, the median figure is 36% [75].

In population studies, Type 1 and Type 2 changes occur significantly more often in patients with back pain than in asymptomatic individuals [74,75], with odds ratios ranging between 2.0 and 19.9 [75]. They are clearly a marker of back pain and imply that the affected disc is the source of pain.

Type 1 and Type 2 changes correlate with the affected disc being painful on disc stimulation. The pooled data suggest a likelihood ratio of 3.4 with 95% confidence limits of 2.8 and 4.1 (Table 12). Two of six studies have been dissonant with this estimate [46,69], but the other four are fully concordant with it, including the largest study, of 2,457 patients [76]. The latter study also showed that the association with discogenic pain was stronger with Type 1 changes.

Across all studies, Modic changes have a high specificity, which means that they are unlikely to be false-positive. Studies have differed only over the sensitivity of the sign, i.e., its ability to detect all discs that are painful. A likelihood ratio of 3.4 means that investigators can be 69% confident that the affected disc will be the source of pain.

Table 12 The sensitivity, specificity, and likelihood ratio of Modic changes as predictors of the affected disc being painful, as reported by 12 studies

Sample	Sensitivity	Specificity	Likelihood Ratio	95% CI	Source
2,457	0.25	0.94	4.2	3.3–5.2	[76]
152	0.23	0.97	7.7	1.9–31.6	[77]
101	0.22	0.95	4.4	1.3–15.0	[67]
255	0.18	0.90	1.8	0.9–3.5	[78]
178	0.14	0.87	1.1	0.5–2.6	[69]
97	0.09	0.83	0.52	0.2–1.8	[46]
3,240	0.24	0.83	3.4	2.8–4.1	ALL

The prevalence represents the number of discs studied that showed the sign.
95% CI = 95% confidence interval of likelihood ratio.

Prevalence

Several studies have measured the prevalence of internal disc disruption in patients with chronic back pain who undergo invasive investigations. Adjusting for sample sizes, the results have been consistent.

The first study found a prevalence of 39% (29–49%) in 92 consecutive patients [79]. This constituted a worst-case estimate because the study used strict diagnostic criteria and measured the prevalence only of single-level disease; it did not count internal disc disruption at two or more levels. In a second study, the prevalence was lower (26%) but with confidence intervals (18–34%), consistent with the first study [80]. A third study found a prevalence of 42%, with confidence intervals of 34–49% [81].

A fourth study [82] encountered positive responses to disc stimulation in 3 of 13 patients with mild back pain. That study portrayed this figure as representing the false-positive rate of disc stimulation, but that conclusion is based on the self-serving assumption that patients with mild back pain cannot have discogenic pain. There is no objective basis for that assumption. A competing interpretation, which is more plausible biologically, is that discogenic pain can occur in patients with mild back pain. Whereupon, the study in question actually provides an estimate of the prevalence of discogenic pain among patients with mild back pain (23%; 0–46%), and this estimate is consonant with the prevalence in patients with chronic severe pain.

Synthesis

Internal disc disruption is the most extensively studied cause of low back pain. Clinical studies, biomechanics studies, imaging studies, and animal studies paint a common picture (Figure 9). The condition is defined by degradation of the nuclear matrix and the development of radial fissures. These changes are detectable on CT-discography, and they correlate strongly with the disc being painful. Internally disrupted discs exhibit characteristic, abnormal physical properties; the nucleus is depressurized, and stresses in the posterior anulus are increased. Each of these features correlates with the disc being painful. Fatigue failure of the vertebral endplate is implicated as the precipitating cause. Endplate fracture initiates the biophysical changes of internal disc disruption. Endplate fracture initiates the degradation of the nuclear matrix. Endplate fractures are reflected by Modic

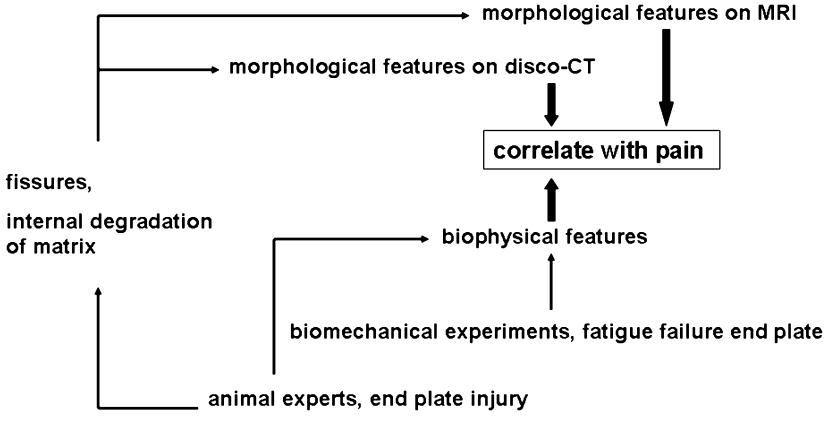

Figure 9 The correlations between animal experiments, biomechanics studies, and imaging studies, and the morphological and biophysical features of internal disc disruption, and their relationship to pain. CT = computerized tomography; MRI = magnetic resonance imaging.

changes on MRI, and radial fissures by HIZs. The condition is not uncommon and accounts for some 40% of patients with chronic low back pain.

Clinical Utility

Clinical utility can be cast or measured in various ways. One domain, often invoked for assessing the utility of disc stimulation, is therapeutic utility. It asks if making the diagnosis of discogenic pain leads to improved outcome after treatment; but this is only one domain of clinical utility; and it can be cast as positive therapeutic utility. A converse domain is negative therapeutic utility, which asks if making the diagnosis prevents misadventure through inappropriate treatment. An additional domain is diagnostic utility, which asks if making the diagnosis serves a useful purpose even if treatment is not available.

Positive Therapeutic Utility

The experiment to prove positive therapeutic utility for disc stimulation is demanding and has not been conducted. It would require patients to undergo disc stimulation, but the results would be masked, yet the patients would then nevertheless proceed to treatment. Thereafter, their response to treatment would be correlated with their response to disc stimulation (Table 13). Positive therapeutic utility would arise if it emerged that success rates of treatment were significantly higher in those patients in whom the correct disc, according to disc stimulation, had been treated.

Several difficulties apply to such a study. It would require patients to agree to undergo disc stimulation. Those who treat the patients must be prepared and able to do so without the results of the diagnostic test. The treatment must be target specific, i.e., designed to treat selectively only a painful disc; treatments that do not target specific discs do not require a specific, segmental diagnosis. The treatment must have a reasonable chance of success, in order to generate the required numbers in the first column of the contingency table (Table 13); its success rate would have to be substantially greater than that of a placebo. Large numbers of patients would be required in order to overcome the potential influence of chance. Given that most symptomatic discs occur at L4-5 and L5-S1, there is a 0.50 probability that treatment could be directed at the correct disc by chance alone.

Table 13 The format of a contingency table by which to assess the positive therapeutic utility of disc stimulation

According to Results of Disc Stimulation		Response to Treatment: Success	Response to Treatment: Failure
Segment treated	Correct	a	b
	Incorrect	c	d

Table 14 The results of the study of Colhoun et al. [85] for the predictive validity of discography with response to posterior or anterior lumbar fusion as the criterion standard

	Response to Treatment	
Discography	Success	Failure
Positive	121	16
Negative	16	15

Of the treatments currently available for discogenic pain, the most widely practiced is surgery, in the form of arthrodesis. Other inventions, such as disc arthroplasty and various intradiscal therapies are purportedly specific for symptomatic discs, but their success rates are either low or have not been established.

One study purported to show that disc stimulation did not influence surgical outcome [83], but it was not an appropriate test of disc stimulation. It compared the outcomes from arthrodesis in earlier patients in whom disc stimulation had not been undertaken and later patients who had undergone disc stimulation. Notwithstanding the limitations of using historical controls, this study did not comply with contemporary standards of disc stimulation. Pain scores were not recorded and manometric controls were not applied. Indeed, the report states that all discs were subjected to high-pressure injections. Consequently, the validity of the response to disc stimulation comes into question.

One study did not provide usable data [84] because it did not compare the outcomes of patients whose discography was positive or negative. Rather, it compared the outcomes of two different types of surgical treatment. It reported that patients with positive discography at low pressures of injection more often had better outcomes when treated with interbody fusion than when treated with intertransverse fusion. Although this study hints that discography is a useful test, the study is more a test of two types of treatment than a test of the predictive validity of discography.

Only one study has provided usable data [85]. It compared the success rates of arthrodesis in patients with positive responses or negative responses to disc stimulation. Success was defined as complete or significant improvement in symptoms, resumption of work or normal duties, and no requirement for analgesics. For predicting this success, disc stimulation had a sensitivity of 0.88, a specificity of 0.48, and a positive likelihood ratio of 1.7 (95% confidence intervals: 1.2–2.4) (Table 14).

This study provides prima facie evidence that discography is predictive of a successful response to surgical treatment; but a positive likelihood ratio of 1.7 indicates only a

low strength of prediction. This low value arises because most of the patients were positive to discography and most had a successful outcome; too few patients who were negative to discography underwent treatment, probably because the surgeons were reluctant to operate on such patients. The validity of discography would have been stronger had more patients negative to discography been treated and if more of them failed treatment. As the data stand, they indicate that patients with negative discography have essentially a 50% chance of successful outcome, whereas those with positive discography have an 88% chance.

Another study, published only in abstract form [86], compared the outcomes of surgery in patients whose responses strictly satisfied, or not, the criteria for a positive response to disc stimulation, as prescribed by the International Spine Intervention Society [87], i.e., exact reproduction of pain, upon stimulating a disc at a pressure of less than 15 psi, provided that adjacent discs are not painful. Patients were three times more likely to have a favorable outcome from surgery if their responses strictly satisfied the criteria.

Negative Therapeutic Utility

In principle, disc stimulation has potentially great, negative therapeutic utility. If disc stimulation is negative, or if it is indeterminate because too many levels are positive, surgery would not be indicated. Identifying such responses should prevent gratuitous surgery and, thereby, protect patients from failed surgery.

The negative therapeutic utility of disc stimulation has not been quantified. Either patients with negative responses do not participate further in studies or they undergo surgery, despite negative responses, but their outcomes are not reported.

Disc stimulation has been deprecated on the grounds that it only leads to more surgery. This may be an impression held by some critics, but it has not been validated. It may be that some surgeons are intent on operating, regardless of the results of disc stimulation, and undertake the test only as a routine ritual. In that event, disc stimulation is not at fault, for the decision to operate has already been taken. In contrast, however, disc stimulation serves to inform surgeons and is more often likely to be negative than positive. A negative outcome, if reported and heeded, should lead to less surgery being undertaken.

Diagnostic Utility

It is distressing for patients, with any disease, not to know why they are suffering. In such cases, making a diagnosis provides an explanation. Doing serves to allay distress over not knowing, and serves to terminate the continued pursuit of a diagnosis, which is likely to be futile. In the case of back pain, patients face an additional risk. In the absence of a diagnosis, they risk being accused of malingering or having psychogenic pain (or some euphemism thereof). Establishing a diagnosis protects them from such false accusations. In these respects, diagnostic utility arises even if there is no treatment available for the condition.

There are many conditions known to medicine, and many more in the past, for which there has been no proven or successful treatment. Examples include motor neuron disease and multiple sclerosis. For such conditions, the absence of a treatment has not, and does not, preclude pursuing and determining the diagnosis. Establishing the correct diagnosis protects patients from undergoing treatments that are not appropriate for the condition diagnosed; it also opens up future possibilities.

As research continues, new treatments for particular conditions arise. Patients with the condition become eligible to participate in trials of the new treatment, or eligible to have the treatment if and once it is proven. In the case of lumbar discogenic pain, various therapies, involving devices or injections, are under development. None is suitable for indiscriminate application to all discs, symptomatic and normal; each is designed to target symptomatic discs. Under these circumstances, establishing a diagnosis of discogenic pain serves two purposes on behalf of patients. They might avail themselves of trials of these new interventions, or they can be informed that research is being undertaken to look for a treatment for the particular condition that they have.

Pivotal to all of these merits of diagnostic utility is the balance between necessity and the stress of undergoing disc stimulation. The procedure is not pleasant and should not be undertaken presumptuously or gratuitously. The treating physician and the patient should discuss and determine if they need to know if the patient has discogenic pain when the options for treatment may be limited or only speculative.

When the certainty of diagnosis is not crucial, disc stimulation may not be warranted. In such cases, MRI can provide a diagnostic confidence of 70% if Modic changes or HIZs are evident. Whereupon, MRI constitutes a suitable substitute or surrogate to disc stimulation.

Synopsis

Disc stimulation is often accused of having not clinical utility because it does not influence management. This accusation is false because it is based on a limited interpretation of clinical utility. Disc stimulation provides information and virtually by definition that information influences management. That information may not lead to a cure for the patient but influence management it does.

Disc stimulation has intrinsic diagnostic utility. It establishes that the patient has a genuine, detectable reason for their pain. This allays the distress of not knowing and protects patients from false accusations and from the continued pursuit of a diagnosis. It brings about closure. Thereafter, having a diagnosis protects patients from the futile pursuit

of inappropriate treatment that has no chance of relieving discogenic pain; or it may open up the possibility of appropriate treatment. That treatment may be of a conventional nature, such as arthrodesis, or it may be a recent innovation. None of these benefits arise if the patient has not been tested and the diagnosis remains unknown.

Complications

Discitis

Concerns about discitis, as a complication of discography, were raised in 1987. Fraser et al. [88] referred to rates of 0.1% reported in the literature. They reported their own experience of six cases of discitis in 222 patients in whom discography had been performed, between 1978 and 1980, using 18-gauge needles without a stylette; and four cases in 210 patients when styletted 18-gauge and 22-gauge needles were used between 1983 and 1984. Subsequently, they advocated using prophylactic, intradiscal injection of antibiotic medications during discography [89]. After adopting this measure, they encountered no cases of discitis in 127 patients.

Prompted by these concerns, other physicians adopted prophylactic antibiotic medications as the standard of care during disc stimulation. Subsequent data suggest that this may have been on overreaction.

A review of the published articles that provided data on the prevalence of discitis found no statistically significant difference between the rates encountered in studies using antibiotic medications and those that did not use antibiotic medications [90]. The pooled data indicate that the indicative prevalence of discitis when antibiotic medications are not used is 0.24%, with confidence intervals of 0.11–0.37% (Table 15). Although the prevalence of discitis when prophylactic antibiotic medications are used is nominally zero, the confidence interval of this estimate is 0–2.9%, which overlaps the competing estimate. It would take a sample of 3,489 patients with zero cases of discitis to prove empirically that prophylactic antibiotic medications are effective. Studies totaling this sample size and showing a 0% prevalence of discitis have not been published.

Thus, although discitis is potentially a complication of disc stimulation, the prevalence is low, and a prophylactic effect of intradiscal antibiotic medications has not been established. Careful attention to preparation of the skin, and strict aseptic handling of the needles, may be all that is required to minimize the risk of discitis. In the absence of empirical evidence to the contrary, it becomes a matter of personal choice if physicians wish to use prophylactic antibiotic medications during disc stimulation.

Morbidity

A study has warned that discography is associated with accelerated degenerative changes and an increased incidence of subsequent disc herniation, 10 years after discography [98]. Analysis of the data presented, however, indicates that whereas the results might be regarded as sentinel, they are not all conclusive.

Table 15 The number of cases of discitis reported in various studies of discography and disc stimulation that did and did not use prophylactic antibiotic medications

	Patients	Discitis	Source
No antibiotic medications	1,014	1	[91]
	123	0	[92]
	716	1	[93]
	500	3	[94]
	210	4	[88]
	2,014	2	[95]
	124	0	[96]
	164	1	[97]
	26	0	[20]
	200	0	[90]
	5,091	12	Total
Prevalence (%)		0.24	
95% CI		0.11–0.37	
Antibiotic medications	127	0	[90]
Prevalence (%)		0	
95% CI		0–2.9	

95% CI = 95% confidence interval.

On the question of degenerative disc disease, the study reported a statistically significant association between higher grades of degeneration and having undergone discography (Table 16). However, chi-squared analysis is rather generous as a statistical test and can show statistical significance when only a small trend is present. Deeper analysis reveals that, for the sample sizes acquired, the confidence intervals of the prevalence of higher grades of degeneration overlap and so, are not significantly different (Table 16). Thus, although the data show a trend toward higher grades of degeneration, they lack sufficient power to show so conclusively. This trend would need to be confirmed by another, better powered study.

Similarly, although Modic changes arose more frequently among patients who had undergone discography, the confidence intervals of the prevalence in each group overlapped and so, were not significantly different (Table 17). Curiously, the prevalence of Modic changes in the control group (11%) was substantially less than the median prevalence of these changes in population studies (36%) [99], which calls into question if the control group was correctly representative of patients with low back pain.

On the question of disc herniation, the study provided data that are outrightly significant statistically (Table 18). Disc herniations were encountered more than twice as often in patients who had undergone discography. Many

Table 16 The prevalence of degenerative changes in control subjects and in patients 10 years after undergoing discography

	Numbers		Proportions	
	Discography	Control	Discography	Control
Degeneration				
Grade I–II	50	67	0.32	0.45
95% CI			0.25–0.39	0.37–0.53
Grade III–IV	76	66	0.49	0.44
95% CI			0.41–0.57	0.32–0.52
Grade V	29	17	0.19	0.11
95% CI			0.13–0.25	0.06–0.16
	$P = 0.03$ (chi-squared test)			

Based on the data of Carragee et al. [98].
95% CI = 95% confidence interval.

of these were only broad-based bulges, which might be dismissed as clinically insignificant, but foraminal herniations and extrusions were 2–5 times more common (Table 18). It is notable, however, that whereas the prevalence of disc herniations in the discography group is essentially equal to that in the general population, the prevalence in the control group is substantially less [99,100], which calls into question how representative the control group is. For some reason, the control group is less affected than the general population.

Table 17 The prevalence of Modic changes in control subjects and in patients 10 years after undergoing discography

	Discography	Control
Sample size	155	150
Modic changes		
Number	29	16
Proportion	0.19	0.11
95% CI	0.13–0.25	0.06–0.16

Based on the data of Carragee et al. [98].
95% CI = 95% confidence interval.

Notwithstanding these arguments of statistics, the potential risk of increased degenerative changes may be dismissed as clinically insignificant, for there is only a weak association between degenerative changes and back pain [101]. Of greater concern clinically is the potential risk of disc herniation. This one study raises the spectre of increased risk, but alone this study does not prove it. If discography does induce disc herniation in the long term, there should be a veritable epidemic of disc herniations among patients who have had prior discography. Long-term reviews of large samples of such patients would readily reveal if they have an inordinate prevalence of disc herniation. Such studies have yet to be reported.

Table 18 The prevalence of disc herniations in control subjects and in patients 10 years after undergoing discography

	Numbers		Proportions	
Feature	Discography	Control	Discography	Control
Sample size	155	150		
Disc herniation	55	22	0.35	0.15
			0.27–0.43	0.09–0.21
Broad-based	13	4	0.08	0.03
			0.04–0.12	0.00–0.06
Paracentral	9	5		
Foraminal	13	6	0.21	0.08
Extrusion	10	2	0.15–0.27	0.03–0.15

Based on the data of Carragee et al. [98].

Frontiers

Contemporary research has focused on developing an analgesic test for lumbar discogenic pain. The attraction of an analgesic test is that it would circumvent all the liabilities of provocation tests. The local anesthetic either relieves the pain or it does not. There is no requirement for manometric or other controls that complicate disc stimulation. A successful analgesic test would serve to corroborate the results of disc stimulation or, perhaps, replace disc stimulation in the future.

Nerve Blocks

The anatomy of the lumbar discs is not conducive to using nerve blocks to anesthetize a disc. The disc is innervated from multiple sources across multiple aspects of the disc. However, the posterior anulus has been implicated as the likely source of pain, and the posterior anulus is innervated by the sinuvertebral nerves which are potentially accessible in the intervertebral foramen.

One study explored this possibility and found that sustained relief of pain could be achieved in some 70% of patients with discs found painful on disc stimulation, but the specificity of the blocks performed could not be assured [102]. Technical problems involved with securing target-specific blocks of the sinuvertebral nerves have still to be overcome.

Intradiscal Blocks

An alternative form of block is to inject local anesthetic into the nucleus of the disc. The objective is to relieve pain by anesthetizing the nerve endings within the painful disc.

One study [103] found that simply injecting local anesthetic at the time of disc stimulation is not effective. Doing so does not relieve pain any more often, or to any significantly greater degree, than injecting contrast medium alone. Indeed, only 2 of 30 patients reported greater than 50% reduction of their pain, and none reported complete relief.

Different outcomes have been reported by investigators who introduced a catheter into the painful disc or discs at the time of disc stimulation, but waited until the completion of disc stimulation and post-discography CT scanning before injecting local anesthetic [104]. They found that approximately 40% of 28 subjects reported 50% relief of pain, 28% reported 75% relief, and 11% reported complete relief. The authors concluded that these outcomes corroborated the responses to disc stimulation in 80% of their patients, but several limitations apply.

Control blocks were not used. Therefore, it is not evident that the extent to which the positive responses to local anesthetic were confounded by false-positive responses. Furthermore, vexatious is the meaning of 50% relief of pain. The basis of incomplete relief could be psychosocial or physiological, but without controls no one can tell.

Intradiscal anesthesia is subject to various vicissitudes. In different patients, the actual source of pain may differ. For example, it is evident that HIZs, which represent lesions in the anulus, correlate with pain, but independently of the correlation with Modic changes, which represent lesions in the endplate. This suggests that some patients may have pain from the anulus whereas others have pain from the endplate, yet both have discogenic pain. Local anesthetic injected into the nucleus may fail to anesthetize one but not the other source; or it may fail to anesthetize either.

The current convention is to inject local anesthetic into the nucleus and trust that it reaches the outer anulus around radial fissures; but material within the fissure may prevent local anesthetic reaching the fundus of the fissure in adequate concentrations to fully anesthetize the nociceptors contained thereabouts. One way to deal with this limitation could be to abandon injection into the nucleus and, instead, place injections directly into the fundus of the fissure, in order to maximize the concentration of local anesthetic at the presumed site of pain. With clever technique, this is technically possible, but has not yet been explored.

Currently, analgesic tests for discogenic pain are still in evolution. For a test to be convincing, it will need to reliably produce complete relief of pain that is validated under controlled conditions.

Prognostic Blocks

Intradiscal blocks have been assessed as a prognostic test for surgery. One study [105] showed that patients whose pain was relieved by intradiscal local anesthetic had better outcomes, on the average, after arthrodesis, than patients who pain was not relieved. However, only group data were reported. They showed that mean scores for pain and disability were better in those patients whose pain was relieved by disc blocks, but both groups of patients nevertheless responded to treatment, on average. The lack of categorical data prevents a comparison of the success rates for surgery and, therefore, prevents an estimation of the predictive value of a positive response to blocks. Furthermore, the fact that patients responded to surgery despite not being relieved by blocks augers that response to disc blocks will not be a clinically significant criterion for avoiding surgery.

Discussion

Discogenic pain and discography are different entities. One is a concept; the other is a diagnostic test. The criteria for validating (or refuting) each are different.

Over the 70 years or so since it was first advanced, the concept of discogenic pain has met with resistance. Intriguingly, that resistance and attempts to refute the concept were all ex cathedra pronouncements, not based on experimental evidence. Serially, those pronouncements were refuted by empirical data. It was said that discs could not hurt because they lacked a nerve supply; but then a

nerve supply was demonstrated. It was said that discs could not hurt and, therefore, did not hurt; until studies showed them to be the most sensitive of all structures in the lumbar spine to noxious stimulation. In essence, basic science and clinical research refuted the rhetoric that was used to deny discogenic pain. Thereby and therefore, the concept survives.

More complex has been the defense of provocation discography as a diagnostic test for discogenic pain. Provocation discography cannot be tested in the conventional manner by comparing it with a material criterion standard. The only available means to impugn provocation discography is to find a high, imputed false-positive rate. Attempts to do so have failed. At worst, the false-positive rate is 10%, which is quite acceptable for clinical practice. If strict operational criteria are applied, embracing pressure of injection and intensity of the pain evoked, the false-positive rate reduces to zero. False-positive rates might be greater in patients with psychological issues, but only marginally. Psychological distress warns physicians to be careful when interpreting the test, but psychological distress is not a contraindication for the test.

Internal disc disruption is a pathologic condition that can cause discogenic pain and to whose diagnosis provocation discography contributes. It is the most extensively studied and best understood cause of chronic low back pain. It has characteristic morphological and biophysical features, each of which correlates with the affected disc being painful. The condition has an etiology. It has been produced experimentally in laboratory studies and in experimental animals. The condition can express itself on MRI and accounts for some 40% of chronic low back pain.

Numerically, discogenic pain, provocation discography, and internal disc disruption are compromised by partial figures. The correlation between discogenic pain and grade III fissures in the anulus is 70%, but not 100%. The correlation between provocation discography and Modic lesions or HIZs is 70%, but not 100%. The MR features occur in 30% of patients, but not in all patients. Internal disc disruption accounts for 40% of patients, but not all patients with chronic low back pain.

Critics use these partial figures as an excuse to disparage the concepts and procedures, seemingly on the basis that correlations and prevalence rates are not worthy unless they are perfect or provide a singular explanation for back pain. This is an unrealistic expectation. Although partial, the correlations are nevertheless statistically significant, and the prevalence rates are substantial. Discogenic pain, provocation discography, and internal disc disruption are modest but legitimate contributions to the understanding of low back pain. They provide one answer but not the only answer to the question of back pain.

Lumbar discs can be injured and suffer internal disc disruption. Internal disc disruption can become painful. Its features can sometimes be found on MRI. The condition can be diagnosed with reasonable certainty by provocation discography. Not all patients with chronic low back pain have this condition, but 40% do.

What is curious is why discogenic pain and provocation discography have met with such sustained, and at times vehement, opposition since their inception. Whenever it has appeared, the slightest negative evidence has been embraced to condemn the concept of the procedure. However, as shown in this review, all attempts to refute the concept of discogenic pain or to discredit provocation discography have consistently failed. Conjecture and refutation are the hallmarks of scientific inquiry [1]. Notwithstanding emotional or political prejudices, when a conjecture survives refutation, it is allowed to stand. Such is the current status of discogenic pain and provocation discography.

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