Narrative Review

A regional interdependence model of musculoskeletal dysfunction: research, mechanisms, and clinical implications

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The term 'regional interdependence' or RI has recently been introduced into the vernacular of physical therapy and rehabilitation literature as a clinical model of musculoskeletal assessment and intervention. The underlying premise of this model is that seemingly unrelated impairments in remote anatomical regions of the body may contribute to and be associated with a patient's primary report of symptoms. The clinical implication of this premise is that interventions directed at one region of the body will often have effects at remote and seeming unrelated areas. The formalized concept of RI is relatively new and was originally derived in an inductive manner from a variety of earlier publications and clinical observations. However, recent literature has provided additional support to the concept. The primary purpose of this article will be to further refine the operational definition for the concept of RI, examine supporting literature, discuss possible clinically relevant mechanisms, and conclude with a discussion of the implications of these findings on clinical practice and research.

Keywords: Physical therapy, Regional interdependence, Rehabilitation

Introduction

'Regional interdependence' or 'RI' is the term that has been utilized to describe the clinical observations related to the relationship purported to exist between regions of the body, specifically with respect to the management of musculoskeletal disorders.[1] There is a growing body of literature demonstrating that interventions applied to one anatomical region can influence the outcome and function of other regions of the body that may be seemingly unrelated.[2–7] Despite the growing interest, controversy exists regarding the relevance of the RI model in physical therapy research and practice.[8] Therefore, RI warrants further examination and scientific scrutiny.

RI was initially defined and proposed as a part of a basic manipulation skills educational CD-ROM developed by Wainner *et al.* in 2001.[9] The concept of RI stemmed from the review of literature during which they observed that regions of the body appeared to be musculoskeletally linked.[10–12] Erhard and Bowling alluded to this concept in 1977 when they stated: 'Dysfunction in any unit of the system will cause delivery of abnormal stresses to other segments of the system with the development of a subsequent dysfunction here as well'.[13] Although Erhard's observation preceded Wainner's, RI was not proposed as a formal concept and did not gain wider recognition as a model of assessment and treatment in the peer-reviewed literature until Wainner *et al.* described it in an editorial in 2007.[1] At that time, it was proposed primarily as a clinical model to be considered and incorporated in the context of a 'test-treat-retest' approach[14] to treating patients with musculoskeletal disorders. Commentary in response to the original RI editorial countered the suggestion that RI was the result of musculoskeletal factors and suggested that RI may also involve a neurophysiological response.[8] The points made by Bialosky *et al.* in the response brought to light the fact that while the primary interest of RI has been physical manifestations (typically pain and range-of-motion) involving the musculoskeletal system, the mechanisms underlying these primary manifestations can be much more complex involving other physiological systems.[15] Any condition or disorder initiates a series of responses that involves multiple systems of the body. Not only musculoskeletal but also neurophysiological, somatovisceral, and biopsychosocial responses occur when a disorder or condition

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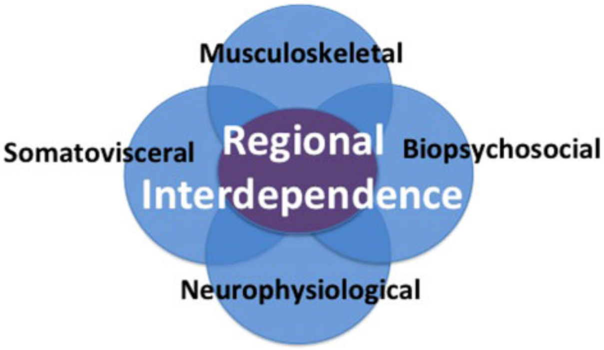

Figure 1 Regional interdependence involves the coordinated and integrated action of multiple systems including musculoskeletal, biopsychosocial, neurophysiological, and somatovisceral.

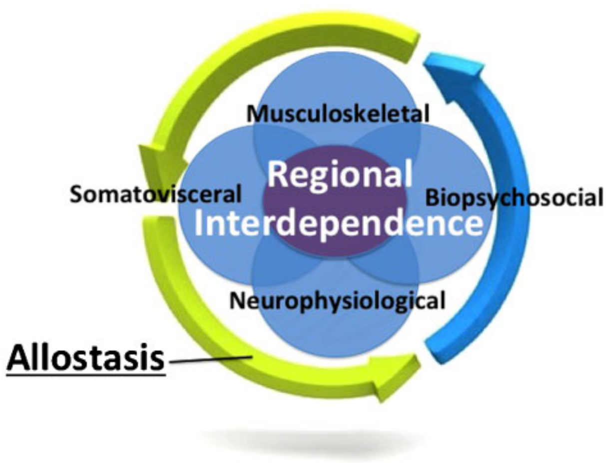

Figure 2 The allostatic process is responsible for the regulation and integration of biopsychosocial, neurophysiological, somatovisceral, and musculoskeletal responses.

disrupts homeostasis[16,17] (Fig. 1). These allostatic responses are all pieces of an integrated physiological process that functions to restore equilibrium and promote recovery[18,19] (Fig. 2). The RI model as defined represents the musculoskeletal manifestation of a larger interdependent process by which other systems may be involved in eliciting these musculoskeletal changes.

The biomedical model of disease has served as the foundation for assessment and treatment in the clinical management of patients and it is taught in first-professional physical therapists programs as a primary model for managing patients with musculoskeletal disorders. In this model, clinical management decisions are predicated on the identification of a pathoanatomical source tissue. However, interventions and treatment plans focused upon a single pathological structure can often result in poor outcomes, in particular with spinal disorders for which a pathoanatomic source tissue cannot be identified in the majority of cases.[20,21] In addition, clinical decision making based on a single pathological finding has been credited as contributing to these poor results.[22] Therefore, in orthopedic clinical settings, the biomedical model should be expanded to include identification of other factors or regions that may contribute to the patient's complaints. The RI model of assessment and treatment provides a framework to incorporate this expanded focus.

The purpose of this article is to propose a revised operational definition for the concept of Regional Interdependence based on current best evidence and supporting literature. In addition, this article will explore the literature underlying the concept of RI, as well as the implications of the RI model for clinical practice and research.

RI Defined and Redefined

RI was originally defined as a concept that seemingly unrelated impairments in remote anatomical regions could contribute to and be associated with a patient's primary complaint.[1] The definition was limited in that it considered the musculoskeletal system as the primary source as well as manifestation of impairments and did not consider other systems as sources or factors that could contribute to the impairments. Therefore, the current definition may be incomplete or misleading and requires further refinement. A more comprehensive definition of RI would be 'the concept that a patient's primary musculoskeletal symptom(s) may be directly or indirectly related or influenced by impairments from *various body regions and systems* regardless of proximity to the primary symptom(s)'. In this definition, impairments are not limited to the musculoskeletal system and include those that may originate from other systems, which may contribute to or influence the patient's primary musculoskeletal complaint(s). Validating this definition, therefore, requires researchers to demonstrate that impairments in one region of the body or one system of the body can have a direct or indirect influence upon the musculoskeletal symptoms and function of another region of the body.[7,8,23–29]

Origins of RI

RI is a musculoskeletal model born out of earlier clinical reports and clinical observation. In other words, clinicians treating one region of the body, such as the hip, noticed that signs and symptoms in areas remote to the area of treatment, such as the knee, were altered. From this insight followed the observation that impairments located in one region of the body could also be affected or were associated with the musculoskeletal function and symptoms of a completely separate region.

The concept that the function and health of one region of the body could potentially affect the function of another region is not novel. In 1944, Inman and Saunders[30] stated that both clinical and experimental evidence indicated that pain could be experienced over a considerable distance from the site of the local lesion and in 1959, Slocum[31] stated that it was not uncommon for a baseball pitcher with an injured toe or foot to lose the effectiveness of the shoulder joint.

From these published beginnings, backed by clinical observation and established clinical practice patterns, additional works under experimental conditions began to appear that supported the clinical interdependent relationship between regions of the body. Cleland *et al.*,[3] Fernandez-de-las-Penas *et al.*,[32] and Gonzalez-Iglesias *et al.*[33] have all demonstrated that interventions focused on the thoracic spine could affect impairments in the cervical region. Similarly, Currier *et al.*[4] and Souza and Powers[6] have both provided evidence that treatment of the hip could alleviate impairments located at the knee. Since it was editorialized in 2007, multiple studies have been published that directly reference the concept of RI (Table 1).

Evidence for RI

An electronic search was conducted using PubMed, Medline, Google Scholar, and the Cochrane Library. The pool of articles was initially screened for studies that included the words 'regional interdependence' and were also relevant to musculoskeletal and orthopedic physical therapy. Because the term 'regional interdependence' is relatively new, the literature with direct reference to its usage is somewhat limited. Using the described search method, 16 articles were found that specifically utilize or describe the term 'regional interdependence' and are listed in Table 1. An even larger number of studies exist in the literature that supports the concept of RI but do not directly reference the model (Table 2). A similar search method was utilized to identify these articles. Keywords utilized for the search consisted of the regions of interest (i.e. lumbar spine and knee). The results were then screened for articles relevant to the topic. The reference list of the relevant articles was then examined to determine whether additional articles existed that were not identified in the previous search. The most relevant publications from the search will be described in the following sections.

Clinical Studies

Lower quarter

The majority of lower extremity literature supporting the concept and model of RI is related to the lumbopelvic region (Tables 1 and 2). Low back pain has been positively associated with hip osteoarthritis, fractures, and following total hip replacement surgery.[34–36] Stupar *et al.* has also demonstrated a positive relationship between low back pain and the presence of knee osteoarthritis.[34] Additionally, decreased strength, neuromuscular control, range of motion, and mobility of the lower quarter have all demonstrated a positive association with the presence of low back pain and impairments.[37–40] A relationship between the foot and ankle and the lumbosacral region has been proposed in publications by Cibulka[11] and Rothbart and Estabrook.[41] Kosashvili *et al.*[42] demonstrated that a positive correlation exists between a pes planus position in the foot and low back pain. Similarly, Brantingham *et al.*[43] established a potential positive relationship between ankle impairment and lumbar pain.

While the preponderance of literature has focused on the lumbopelvic region, there have also been a recent number of publications related to the knee. Powers[44] has suggested that proximal factors such as hip impairment may play a contributory role in knee injuries. Bogla *et al.*,[45] Finnoff *et al.*,[46] Souza *et al.*,[6] and Rowe *et al.*[47] have all demonstrated that deficits in hip strength and abnormal hip mechanics are positively correlated with knee pain (Table 2). Although it is common clinical practice to assess and treat the foot and ankle in patients with other lower quarter impairments, very few studies aside from those mentioned previously have looked specifically at the influence that the ankle or foot can have on outcomes related to the hip, pelvis, or lumbar spine. Molgaard *et al.*[48] studied high school students with patellofemoral pain (PFPS) found greater navicular drop, navicular drift, and dorsiflexion in the subjects with PFPS compared with healthy students (Table 2).

Upper quarter

Like the lower quarter, there is also evidence of RI relationships in the upper quarter. (Table 2). Studies by Cleland *et al.*[3] and Gonzales-Iglesias *et al.*[33] linking cervical pain to thoracic interventions have been mentioned previously. Additionally, Strunce *et al.*,[7] Boyles *et al.*,[2] and Mintken[5] have demonstrated that interventions focused on the thoracic spine have the potential to alter shoulder symptoms. Yoo *et al.*[49] demonstrated that sympathetic blocks at the thoracic spine could improve upper extremity neuropathic pain and Berglund *et al.*[50] showed that pain and dysfunction of the thoracic spine is positively correlated with the presence of lateral elbow pain. For a more in depth discussion, the reader is directed to a systematic review by Walser *et al.*[51] that discusses the effect of thoracic manipulation on various musculoskeletal conditions.

While not as prevalent, numerous studies have also linked impairments in the cervical spine and upper quarter. Berglund *et al.*[50] surveyed subjects with lateral elbow pain and found 70% of subjects also reported pain in the cervical and thoracic regions compared to 16% in the asymptomatic control group.

Table 1 Studies with direct mention of regional interdependence

Authors	Title and journal	Regions	Design	Number of subjects	Level of evidence*
Systematic reviews and meta analyses					
Walser RF, Meserve BB, Boucher TR[51]	The effectiveness of thoracic spine manipulation for the management of musculoskeletal conditions: a systematic review and meta-analysis of randomized clinical trials. *J Man Manip Ther* 2009	Thoracic spine and various musculoskeletal conditions	Systematic review of cohort RCTs	N/A	Level 2a
Randomized control trials and experimental studies					
Bunn EA, Grindstaff TL, Hart JM, Hertel J, Ingersoll CD[103]	Effects of paraspinal fatigue on lower extremity motoneuron excitability in individuals with a history of low back pain. *J Electrophysiol Kinesiol* 2011	Lumbar spine and lower extremity	Cohort	20	Level 2b
de Oliveira Grassi D, Zanelli de Souza M, Belissa Ferrareto S, Imaculada de Lima Montebelo M, Caldeira de Oliveira Guirro E[104]	Immediate and lasting improvements in weight distribution seen in baropodometry following a high-velocity, low-amplitude thrust manipulation of the sacroiliac joint. *Man Ther* 2011	Sacroiliac joint and lower extremity	Prospective cohort	20	Level 2b
Iverson CA, Sutlive TG, Crowell MS, Morrell RL, Perkins MW, Garber MB, Moore JH, Wainner RS[105]	Lumbopelvic manipulation for the treatment of patients with patellofemoral pain syndrome: development of a clinical prediction rule. *J Orthop Sports Phys Ther* 2008	Lumbar spine and knee	Cohort CPR	50	Level 2b
Mintken PE, Cleland JA, Carpenter KJ, Bieniek ML, Keirns M, Whitman JM[5]	Some factors predict successful short-term outcomes in individuals with shoulder pain receiving cervicothoracic manipulation: a single-arm trial. *Phys Ther* 2010	Cervicothoracic spine and shoulder	Cohort CPR	80	Level 2b
Strunce JB, Walker MJ, Boyles RE, Young BA[7]	The immediate effects of thoracic spine and rib manipulation on subjects with primary complaints of shoulder pain. *J Man Manip Ther* 2009	Thoracic spine and shoulder	Cohort	21	Level 2b
Case studies					
Burns SA, Mintken PE, Austin GP[106]	Clinical decision making in a patient with secondary hip-spine syndrome. *Physiother Theory Pract* 2011	Hip and lumbar spine	Case study	1	Level 4
Lowry CD, Cleland JA, Dyke K[107]	Management of patients with patellofemoral pain syndrome using a multimodal approach: A case series. *J Orthop Sports Phys Ther* 2008	Knee and multiple regions	Case series	5	Level 4
Vaughn DW[108]	Isolated knee pain: a case report highlighting regional interdependence. *J Orthop Sports Phys Ther* 2008	Knee and pelvis	Case study	1	Level 4
Welsh C, Hanney WJ, Podschun L, Kolber MJ[109]	Rehabilitation of a female dancer with patellofemoral pain syndrome: applying concepts of regional interdependence in practice. *N Am J Sports Phys Ther* 2010	Knee and multiple regions	Case study	1	Level 4

Table 1 Continued

Authors	Title and journal	Regions	Design	Number of subjects	Level of evidence*
Clinical commentaries					
Lucado A, Kolber M, Echternach J, Cheng MS[53]	Subacromial impingement syndrome and lateral epicondylalgia in tennis players. *Phys Ther Rev* 2010	Shoulder and elbow			
Isabel de-la-Llave-Rincon, A., Puentedura EJ., Fernandez-de-las-Penas C[110]	Clinical presentation and manual therapy for upper quadrant musculoskeletal conditions. *J Man Manip Ther* 2011	Upper quadrant			
Reiman MP, Weisbach PC, Glynn PE[111]	The hips influence on low back pain: a distal link to a proximal problem. *J Sport Rehabil* 2009	Hip and lumbar spine			
Sueki DG, Chaconas EJ[26]	The effects of thoracic manipulation of shoulder function: a regional interdependence model. *Phys Ther Rev* 2011	Thoracic spine and shoulder			
Editorials					
Wainner RS, Whitman JM, Cleland JA, Flynn TW[1]	Regional interdependence: a musculoskeletal examination model whose time has come. *J Orthop Sports Phys Ther* 2007	Not applicable			
Bialosky JE, Bishop MD, George SZ[8]	Regional interdependence: a musculoskeletal examination model whose time has come. *J Orthop Sports Phys Ther* 2008	Not applicable			

Note: RCT: randomized control trial; CPR: clinical prediction rule.
*Oxford Centre for Evidence-Based Medicine Levels of Evidence Criteria: 2a, systematic review of cohort studies; 2b, individual cohort study; 3a, systematic review of case control studies; 3b, individual case control study; 4, case series.

Table 2 Evidence of regional interdependence

Quarter	Regions	Study	Type of study	Number of subjects	Level of evidence*
Lower quarter	Hip and lumbar	Arab AM, Nourbakhsh MR (2010)[37]	Cross-sectional cohort	300	Level 2b
		Arab AM, Nourbakhsh MR (2010);[37] Arab *et al.* (2011)[40]	Cohort	20	Level 2b
		Ben-Galim P *et al.* (2007)[35]	Prospective cohort	25	Level 2b
		Di Lorenzo L *et al.* (2007)[36]	Prospective cohort	37	Level 2b
		Ellison JB *et al.* (1990)[112]	Case–control	150	Level 3b
		Kendall KD *et al.* (2010)[113]	Quasi-experiment cohort	20	Level 2b
		Mellin G (1988)[39]	Case–control	476	Level 3b
		Nadler SF *et al.* (2000)[114]	Cohort	210	Level 2b
		Nelson-Wong *et al.* (2009)[115]	Prospective cohort	43	Level 2b
		Paquet N *et al.* (1994)[116]	Case–control	20	Level 3b
		Stupar M *et al.* (2010)[34]	Population-based cohort	983	Level 2b
		van Dillen LR *et al.* (2008)[117]	Case–control	48	Level 3b
		Yoshimoto H *et al.* (2005)[118]	Retrospective case–control	150	Level 3b
		Deyle GD *et al.* (2005)[119]	Prospecitve cohort	134	Level 2b
	Knee and lumbar	Deyle GD *et al.* (2000)[120]	RCT of cohort	83	Level 2b
		Stupar M *et al.* (2010)[34]	Population-based cohort	983	Level 2b
		Suri P *et al.* (2010)[121]	Case–ontrol	1389	Level 3b
	Foot/ankle and lumbar	Bjonness T (1975)[122]	Case–control	93	Level 3b
		Brantingham JW *et al.* (2006)[43]	Case–control	100	Level 3b
		Kosashvili Y *et al.* (2008)[42]	Retrospective case–control	97 279	Level 3b
	Hip and knee	Astephen JL *et al.* (2008)[90]	Cross-sectional case–control	181	Level 3b
		Bennell KL *et al.* (2007)[123]	RCT of cohort	88	Level 2b
		Bolgla LA *et al.* (2011);[45] Bolgla LA *et al.* (2008)[124]	Cross-sectional case–control	18	Level 3b
		Currier LL *et al.* (2007)[4]	Cohort CPR	60	Level 2b
		Finnoff JY *et al.* (2011)[46]	Prospective cohort	98	Level 2b
		Rowe J *et al.* (2007)[47]	Case–control	19	Level 3b
		Souza RB *et al.* (2009)[6]	Cross-sectional case–control	41	Level 3b
	Ankle and knee	Astephen JL *et al.* (2008)[90]	Cross-sectional case–control	181	Level 3b
		Molgaard C *et al.* (2011)[48]	Case–control	299	Level 3b
Upper quarter	Thoracic and cervical spine	Cleland JA *et al.* (2005)[3]	Cohort RCT	36	Level 2b
		Cleland JA *et al.* (2010)[102]	Cohort CPR	140	
		Fernandez-de-las-Penas C *et al.* (2009)[32]	Cohort	45	Level 2b
		Gonzalez-Iglesias J *et al.* (2009)[33]	Cohort RCT	45	Level 2b
	Thoracic spine and shoulder	Boyles RE *et al.* (2010)[2]	Cohort	56	Level 2b
		Mintkin PE *et al.* (2010)[5]	Cohort CPR	80	Level 2b
	Thoracic spine and upper extremity	Strunce JB *et al.* (2009)[7]	Cohort	21	Level 2b
		Berglund *et al.* (2008)[50]	Cohort	62	Level 2b
	Cervical spine and upper extremity	Berglund *et al.* (2008)[50]	Cohort	62	Level 2b
		Suter E *et al.* (2002)[52]	Cohort	16	Level 2b
		Vicenzino B *et al.* (1996)[125]	Cohort RCT	15	Level 2b
	Shoulder and elbow	No known experimental studies			
	Elbow and hand	No known experimental studies			
Upper and lower quarter	Lower extremity and shoulder	Klein MG *et al.* (2000)[55]	Cohort	194	Level 2b

Note: RCT: randomized control trial; CPR: clinical prediction rule.
*Oxford Centre for Evidence-Based Medicine Levels of Evidence Criteria: 2a, systematic review of cohort studies; 2b, individual cohort study; 3a, systematic review of case control studies; 3b, individual case control study; 4, case series.

Vicenzino *et al.*[25] has linked cervical manipulation with decreases in pressure pain threshold and increases in grip strength in subjects with lateral elbow pain. Suter *et al.*[52] demonstrated an increase in bicep muscle strength and a decrease in muscle inhibition following cervical manipulation. Clinically, and in published reviews,[53,54] it has been hypothesized that the function of the shoulder can directly influence impairments at the elbow and hand, but to date, no studies have validated this hypothesis. Like the lower quarter studies, much of the research was not designed specifically to study the RI model, yet the results of the studies suggest that RI may be a viable concept and model.

Upper and lower quarter

While the vast majority of available research has focused on establishing a relationship between adjacent regions of the upper or lower quarter, the RI model suggests that a patient's primary musculoskeletal symptoms may be influenced by impairments regardless of proximity to the patient's primary symptoms. There is a small amount of evidence that is beginning to suggest that these relationships extend beyond adjacent regions of the body to more remote sites (Table 2). As mentioned previously, Kosashvili *et al.*[42] and Brantingham *et al.*[43] both established a potential positive relationship between ankle and foot impairment and lumbar pain. In the upper quarter, Berglund *et al.*[50] established a potential relationship between the thoracic spine and elbow impairments.

These studies emphasize relationships between upper or lower quarter regions. However, theoretically impairments in the the lower quarter could influence the function of the upper quarter and similarly, dysfunction in the upper quarter could have an impact upon the function of the lower quarter. Klein *et al.*[55] screened polio survivors and the results of the study suggest that lower extremity weakness may predisposed subjects to shoulder overuse symptoms and has the potential to negatively influence the function of the shoulder. While it is only one study in a specific sample pool and does not establish a direct linkage between the upper and lower quarter, the results do seem to support the concept that regions of the body are interrelated and may influence symptoms irrespective of their proximity. Considerably, more research is needed in order to determine if clinically meaningful relationships exist beyond adjacent regions and extend to the upper and lower quarters.

Proposed Mechanisms

The RI model has its roots in clinical practice and has been utilized primarily to support clinical decision-making. Even before recent clinical research appearing to support the model, clinicians and researchers have speculated about physiological and biomechanical mechanisms underlying these long-standing clinical observations. In 1955, Steindler[56] proposed a model based on a kinetic mechanical engineering model. He termed this relationship the 'Kinetic Chain' and in his model, he described the body as a series of interconnected joints where the movement of one joint directly effects the movement of other joints above and below. His model is based primarily upon the biomechanical relationship between regions of the body. For example, decreased dorsiflexion in the talocrural joint can produce biomechanical compensatory changes in knee, hip, and lumbar spine. The recent literature demonstrating interdependent relationships between the thoracic spine/cervical spine and the hip/knee are examples of this potential biomechanical link or kinetic chain.[3,4,44]

Bialosky *et al.* have suggested that RI may be the result of neurophysiological mechanisms or the combined interaction between biomechanical and neurophysiological mechanisms.[15] This observation has its basis in recent work related to temporal summation and pain perception related to manual therapy interventions.[24,57,58] The result of this work combined with prior research has led to the suggestion that neurophysiological mechanisms play a major role in the physiological effects experienced by patients.[58] Like the biomechanical proposition mentioned previously, more research is needed before any definitive conclusions or statements can be made.

While the mechanisms previously discussed provide feasible explanations for the RI model, neither have been definitively established or well investigated. It is unlikely that a single mechanism or body system explanation is sufficient, thus a more comprehensive model is needed. The revised definition of RI acknowledges that biomechanical and neurophysiological factors may account for musculoskeletal responses seen in conjunction with treating impairments, but it expands upon the previous definition and includes the provision that *various body regions and systems* may contribute to these observed musculoskeletal responses and their associated clinical outcomes and likely also include other factors (Fig. 1). From a clinical management perspective, the redefined RI model is more comprehensive then the original definition and allows for the consideration and subsequent management of numerous factors including other body regions and systems that may be contributing to a patient's musculoskeletal symptoms.

The redefined concept of RI proposes that:

- Response(s) to a disorder or condition and the associated clinical outcome(s) are not limited to local and adjacent regions of the body but can involve a neuromusculoskeletal response that may be more widespread.

- Multiple systems respond to impairment and may influence the function of the neuromusculoskeletal system and associated symptoms.

Response to any disorder or condition is not limited to local and adjacent regions of the body but can involve a neuromusculoskeletal response that may be more widespread

The musculoskeletal interdependence between regions of the body does not exist in isolation. Changes in the musculoskeletal system must also be accompanied by changes in neurophysiology because these and other systems work in concert to perform tasks. Interventional-based studies have demonstrated that treatments targeting one area of the body can affect neuromuscular performance in remote regions of the body. It has been demonstrated that manual therapy and spinal manipulation can alter local and distal motoneuron excitability. Of particular interest to the RI model are the effects of spinal manipulation on distal neuromuscular function. Suter *et al.*[59,60] has demonstrated that thrust manipulation of the sacroiliac joint decreased motor inhibition of the knee extensor muscles, while Dishman *et al.*[61] showed that lumbar spinal manipulation increased electromyographic (EMG) activity remotely in the gastrocnemius muscle. Additionally, Murphy *et al.*[62] and Dishman *et al.*[61,63] showed that manipulation of the lumbosacral region has the potential to produce a decrease in distal neuromuscular function as measure by the magnitude of the tibial nerve H-reflex. These studies may be reflective of an interventional effect on nerve and muscular function beyond the immediate and adjacent regions of the body. While the evidence supporting a neurophysiological relationship between lumbosacral manipulation and remote lower extremity neurophysiological responses exists, a recent follow-up study by Suter *et al.*[59] has suggested that manipulation may not have a significant effect on distal motoneuron excitability (H-reflex testing). It is unclear whether these studies refute the previous studies, are indicative of the variability normally seen when utilizing H-reflex as an outcome measure, or whether magnitude and direction of response are preferentially influenced. In either case, a potential relationship exists between interventions targeting one region of the body and the neuromuscular performance in regions remote to the area of intervention that warrants further exploration.

Multiple systems respond to impairment and may influence the function of the musculoskeletal system

A previously noted, the body appears to utilize physiological mechanisms in an integrated fashion in order to adapt or reduce the loads or stress placed upon involved structures. There is an interdependence that exists between regions of the body, as well as, other systems. In the initial model of RI, it was inferred that the adapting structures were musculoskeletal in nature. In the revised model of RI, it is proposed that not only neurophysiological[8] and musculoskeletal[1] structures but biopsychosocial[64] and somatovisceral[65] systems can all potentially affect the function of the musculoskeletal system (Fig. 3).

Biopsychosocial Considerations

The biopsychosocial model proposes that the experience of pain and resultant responses stem from the interaction of biological, psychological, and social factors.[66,67] The recognition of an association between physiology and psychology is not new and dates as far back as 350 BC. Both Aristotle[19] and Abu Zayd Al-Balkhi[68] suggested that health was tied to the interweaving of the psyche and its biological manifestations and a large body of current literature supports such a relationship.[27,67,69–73]

Bialosky *et al.*,[74] George *et al.*,[27,75] and Fritz *et al.*[76] have all demonstrated that factors such as fear avoidance, pain catastrophizing, and anticipation can impact musculoskeletal function and pain. Moseley[77,78] and Butler and Page[79] have demonstrated that altering a patient's perception of pain allows for improved neuromuscular function. Similarly, Moseley[28] and van Oosterwijck *et al.*[80] have demonstrated that educating patients about pain mechanisms may subsequently alter neuromuscular function and pain. Bialosky *et al.*[57] has demonstrated that a subject's expectations can affect the pain perceptions following an intervention. In addition, a clinician's attitude towards a patient's treatment and recovery has the potential to impact the prognosis of a patient both negatively and positively.[74,81]

Depression,[82] post-traumatic stress,[83,84] fear avoidance,[75,76,85] anxiety,[86] pain catastrophizing,[87] and negative emotions[88] have all been demonstrated to exert influence upon musculoskeletal pain. An in-depth discussion regarding specific psychological impairments observed in patients with musculoskeletal disorders and their underlying physiological mechanisms are beyond the scope of this paper. However, given the strong influence of biopsychosocial factors and potential to be positively influenced, it is important for clinicians to understand and consider the interdependent relationship between biopsychosocial, neurophysiological, and musculoskeletal factors when assessing and treating patients.

Referred, Somatovisceral, and Radicular Pain: Special Considerations

Referred and radicular pain and their relationship with RI have some unique considerations. By definition, referred pain is pain that is perceived in a location other than the actual site of painful

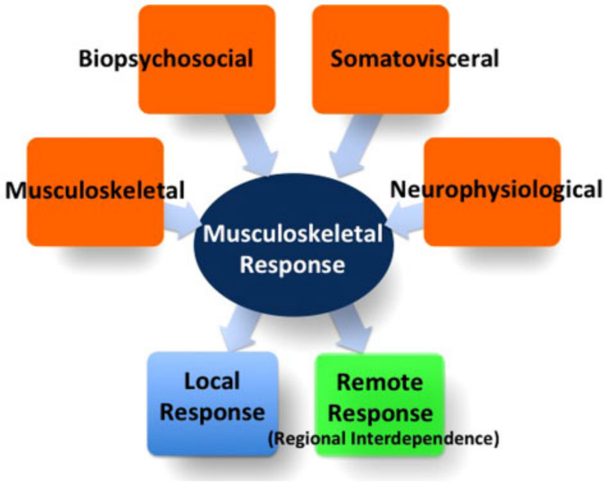

Figure 3 Multiple systems can contribute to a musculoskeletal response by the body. Both local and remote responses occur, but the Regional Interdependence Model represents remote responses by the body.

stimulus or source of symptoms (tissue symptom generator).[89] For example, primary hip disorders can refer pain into the lower extremity,[4,44] but it can also exhibit impairments that affect symptoms and musculoskeletal responses without the referral of pain, as in the case with patients with knee osteoarthritis.[90] Both of these examples would fall within the definition of RI. In this instance, referred pain is a special case with the hip disorder being the source of symptoms. However, hip impairments may not necessarily refer pain, but may be associated and influence remote symptoms in other regions of the body.

It is well supported in literature that somatovisceral tissue can be a source of referred pain as well as mimic musculoskeletal pain.[65,91] For example, left shoulder pain can be due to heart disorders, right shoulder pain can be the result of liver disorders, and low back pain can be the product of urogenital disorders.[92] It is not known whether somatovisceral structures may be a source of disability and limitations in musculoskeletal function, but literature suggests that such a relationship may exist.[93] In a longitudinal study of women's health, Smith *et al.*[29,94] found that in women, menstrual cramping, incontinence, gastrointestinal symptoms, and respiratory problems were all associated with the development of low back pain. This is not to suggest a causal relationship, but simply that somatovisceral structures have the potential to contribute to musculoskeletal symptoms and should be screened as potential contributors to these symptoms. Clinically, the consideration of somatovisceral structures as a source of symptoms, in particular with regard to Red Flag findings, is a routine and recommended component of a physical therapist's practice[95] and if suspected, referral to appropriate health care practitioner is warranted.

Acute radicular pain can be defined as pain that originates from the spinal nerve roots and is experienced remotely from the site of the nerve root lesion.[96] As was the case with referred pain, radicular pain also represents a special case of RI (musculoskeletal symptoms experienced remotely to the affected region), which is a modification of the original description by Wainner *et al.*[1] With radicular pain, the nerve root is the source of symptoms, but it may also result in other local and remote impairments that contribute to the source of symptoms. These related impairments may contribute to that patient's source of symptoms within the RI model, but would be distinct from true acute nerve root pain. Examples of such impairments would be abnormal motor responses[97] and limited nerve root mobility.[97,98]

Clinical Implications

The RI model does not suggest that the biomedical model should be abandoned, but instead modified to include additional considerations and concepts. Assessment and management strategies should seek to identify pathoanatomical tissues that may be the source of the patient's symptoms. Unfortunately, a single underlying pathoanatomical cause that is responsible for a patient's primary and secondary complaints often cannot be identified in patients with musculoskeletal disorders, particularly those with spine problems.[99] Therefore, while clinicians should initially seek to identify a specific pathoanatomic source of the patient's symptoms, in particular red-flag conditions, they should also consider impairments of other systems or regions that may be directly or indirectly associated with the patient's complaints. There is some research to suggest that such an expanded approach can produce positive results. Trials utilizing a multi-modal treatment approach supported by RI concepts have demonstrated efficacy.[3,100–102] The RI model should be viewed as an integrative model that eliminates the dichotomy of having to choose between a biomedical, neurophysiological, or biopsychosocial model. It uses pathoanatomy as a starting point and expands the search to look for the other factors that may contribute to the patient's symptoms.

Future Research

The concept of RI is still preliminary and speculative. Therefore, basic science as well as clinical research is required to more fully develop the model described in this paper. Specifically, evidence derived from prospective studies with the specific purpose of testing hypotheses related to RI concepts is required to establish a viable theory and validate a working model of RI.

The majority of supporting evidence that does exist has been taken from various musculoskeletal-related studies with other purposes and used inductively to construct the concept of RI. The revised RI model proposes that impairments in one region of the body can influence the musculoskeletal and neuromuscular function and symptoms in other remote regions of the body. Researchers should continue to focus on exploratory studies to establish potential new relationships, but should also focus on validating the studies that already exist with specific RI hypotheses in mind. Researchers have begun to validate the relationship between the thoracic spine and cervical impairments and also the hip and knee, but further validation is required. In addition, the revised RI model states that the interdependence between regions of the body may involve the musculoskeletal system, but that neurophysiological, biopsychosocial, and somatovisceral systems can also influence musculoskeletal function both locally and at remote sites. Research is needed to further establish whether and how such relationships exist and how they may influence clinical practice.

Conclusions

The revised definition of RI refers to the concept and clinical model that a patient's primary musculoskeletal symptom(s) may be directly or indirectly related to or influenced by impairments from various body systems regardless of proximity to the primary symptom(s). Although initial local treatment of a patient's primary complaint is typically a first step in clinical management, RI is a model that may be helpful in identifying treatment strategies for recalcitrant and persistent symptoms that may be due to associated functional limitations and impairments in more distant body regions as well as other body systems. The model of RI is in its infancy and will no doubt change and evolve as our understanding is informed from the results of future, formal investigations. The model presented in this paper is meant to serve as a framework for clinicians and researchers alike as they seek to identify the factors that may contribute to a patient's impairments as well as for stimulating future research.

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