Central Sensitization in Chronic Non-specific Low Back Pain

The possibility of the presence of central sensitization (CS) among chronic non-specific low back pain (CNSLBP) patients to predict treatment response by related outcome measures has not been adequately explored. The purpose of this study was to determine the effects of 'McKenzie exercise program' (MEP) and 'Conventional physiotherapy program' (CPP) on various outcomes for subjects having CNSLBP with or without CS, investigate whether any difference in outcome was related to CS, pain, pressure pain threshold, disability, fear-avoidance beliefs, trunk flexors & extensors muscles endurance, and Global rating of change scores for overall improvements. The present study tests whether MEP reduces CS better in CNSLBP patients having CS compared to CPP. McKenzie exercises are effective in reducing central sensitization, pain, disability, and fear-avoidance beliefs but they do not improve trunk flexors and extensors endurance in CNSLBP patients with central sensitization.

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Scholars' Press

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PREFACE

The possibility of the presence of central sensitization (CS) among chronic non-specific low back pain (CNSLBP) patients to predict treatment response by related outcome measures has not been adequately explored. The book aims to determine and discuss the effects of 'McKenzie exercise program' (MEP) and 'Conventional physiotherapy program' (CPP) on various outcomes for subjects having CNSLBP with or without CS, investigate whether any difference in outcome was related to CS, pain, pressure pain threshold, disability, fear-avoidance beliefs, trunk flexors & extensors muscles endurance, and Global rating of change scores for overall improvements.

McKenzie exercises are effective in reducing central sensitization, pain, disability and fear avoidance beliefs but it does not improve trunk flexors and extensors endurance in CNSLBP patients with central sensitization.

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LIST OFABBREVIATIONS

CNSLBP– Chronic Non-specific Low Back Pain

LBP -Low Back Pain

CLBP – Chronic Low Back Pain

CSI-G - Central Sensitization Inventory- Gujarati

FABs - Fear Avoidance Beliefs

NPRS - Numerical Pain Rating Scale

PPT –Pressure Pain Threshold

CNS – Central Nervous System

RMDQ-G- Roland Morris Disability Questionnaire-Gujarati version

FABQ-G - Fear Avoidance Beliefs Questionnaire-Gujarati version

GROC – Global Rate of Change Scale

ICC– Intra-class Correlation Coefficient

RCT - Randomized Control Trial

SD – Standard Deviation

BMI – Body Mass Index

ANOVA – Analysis of Variance

ITT – Intention to Treat Analysis

MDC – Minimum Detectable Change

1

INTRODUCTION

"Research is creating new knowledge" -Neil Armstrong

This chapter of the book is intended to gather information regarding the background, prevalence, classification, etiopathology and treatment guidelines of chronic non-specific low back pain (CNSLBP). As the study intends to check the efficacy of McKenzie exercise program in contrast to conventional physiotherapy program, a detailed information gathering is necessary. Moreover, the presence of central sensitization in LBP patients and how the above intervention strategies influence the same would require a detailed and thorough knowledge of the central sensitization pathology. Hence, this chapter will form on above details and describe the same.

Low back pain is a common disorder and nearly everyone is affected by it at some time or other in their life. For most of the people affected by low back pain, have substantial pain and/or disability which is short lived and they usually return to their normal activities regardless of any treatment they received. But a small proportion of patients, however, develop chronic pain and disability.

Chronic non-specific low back pain (CNSLBP) is a major health related issue, whose prevention and treatment are highly varied. The primary focus of this book is to contribute to the understanding of central sensitization issue governing various outcome measures in response to McKenzie exercise program in day-to-day clinical practice. The investigations were carried out on three themes (a) Cross-cultural translation and adaptation of Central sensitization inventory into Gujarati version; (b) Cross-cultural translation and adaptation of Fear-avoidance beliefs questionnaire into Gujarati version; and (c) comparing the effectiveness of McKenzie exercise program and Conventional physiotherapy program for reducing central sensitization among CNSLBP patients.

Three studies were conducted to answer questions relating to each of these topics. The book work presented here has resulted in several research papers

from the School of Physiotherapy, RK University, Rajkot, and The Sarvajanik College of Physiotherapy, Rampura, Surat, India. These research papers address the issues of cross-cultural adaptation of central sensitization inventory and fear-avoidance beliefs questionnaire into Gujarati language and explore the effectiveness of McKenzie exercise program for reducing central sensitization among CNSLBP patients. The list of publications is provided after the References in this book.

1.1 Background of the Study

Low back pain (LBP) is the commonest condition which is defined as pain and discomfort in the lumbosacral region, between the space of twelfth rib and the gluteal crease. The recommended 'diagnostic triage' defined three types of back pain: 1) non-specific low back pain; 2) back pain with nerve root symptoms; and 3) back pain resulting from serious pathology (e.g. malignancy, fracture, ankylosing spondylitis, infection). Among them, the Non-specific LBP, in which there is no known pathoanatomic basis, is usually a benign condition but without suitable management will turn into chronic low back pain (CLBP)'. Moreover, the traditional classification system, classifies LBP according to its duration from the onset, as acute (<6 weeks), sub-acute (6 weeks - 12 weeks), and chronic (≥12 weeks)' [1, 2].

1.1.1 Definitions of LBP

Non-specific LBP was defined as *"not attributed to identifiable known specific pathology (e.g. infection, inflammatory process, tumor, osteoporosis, fracture or radicular syndrome)"* [3]. Chronic non-specific low back pain (CNSLBP), is considered to be a complex multidimensional bio-psycho-social pain disorder, where precise etiology remains undefined [4-6].

1.1.2 Definitions of Pain

The International Association for the Study of Pain (IASP) define pain as *"an unpleasant sensory and affective experience associated with actual or potential tissue damage or described in terms of such damage"* [7]. According to the definition, pain is a complex and subjective experience comprising different dimensions of pain independent of the identification of tissue

damage. Three main dimensions are proposed: the sensory-discriminative, affective-motivational and cognitive-evaluative[8]. Pain intensity (how much it hurts), pain quality (the physical sensations), and pain localization are aspects of the sensory-discriminative dimension[9]. The affective dimension is often described in terms of anxiety, depression, frustration, anger, and disgust, and the cognitive dimension is evaluated by thoughts and beliefs about pain [10, 11]. Pain is influenced by a variety of psychological variables, previous experiences, is related to personal meanings, and influenced by cultural learning[12, 13]. Pain is a dynamic process demanding attention and a powerful motivational drive to avoid or handle threats [14-16].

1.1.3 Types of Pain

According to the duration of the symptoms, there are two main types of pain, acute and chronic. The acute pain is temporarily related to theinjury that resolves along the appropriate healing time, normally responds to analgesic drugs and to the treatment of the main cause of injury. Moreover, this type of pain does not last more than three months, the intensity of the pain is higher at the beginning and gradually decrease as healing take place, the central nervous system is rarely affected, and normally it disappears when the tissue has healed [17]. The second type of pain is known as chronic pain. It is defined as any pain that lasts more than 3 months, may arise from an initial injury, such as rotator cuff tear, or there may be an ongoing cause, for instance, a disease. However, there is not always a clear cause behind it. Chronic pain is linked very often with sleeplessness, tiredness, and lack of motivation. As a consequence of the pain the movements of the affected person become limited, and flexibility and strength are lost. All these changes may lead to disability and despair. Some studies have suggested some of the causes of chronic pain and have investigated the several alterations that are widely spread across the nervous system contributing to the complicated pain phenotypes. Moreover, they have explored how the age, gender, stress, and fears can influence the risk of developing persistent pain [18]. From the viewpoint of the pathophysiologic mechanisms behind the pain, we can differentiate three types: nociceptive, neuropathic and the one caused by central sensitization pain. Nociceptive pain is described as pain that arises

from a present or threatened damage, activating the nociceptors and not affecting the neural tissue, is classified regarding the noxious stimulus where arise from: thermal (heat and cold), mechanical (tearing) and chemical (iodine in a wound).

The second type is the neuropathic pain, is caused by a damage or disease that affects the somatosensory nervous system, and it has an effect on peripheral or on central nervous system. This pain does not occur in all patients and the mechanisms which cause neuropathic pain are unclear. The nerve fibers may be damaged, injured or not functioning well. In fact, the injuries affect the function of the nerve at the site of injury and around it. Consequently, incorrect signals are sent to the brain. The brain interprets that these signals are coming from the pain receptors in the skin or organs where in fact it is not. Some features of this pain are allodynia, hyperalgesia, and hyperpathia. The last one is central sensitization, nociceptive neurons in the CNS (central nervous system) increases their sensitivity to their normal or sub-threshold afferent input [19]. The latest findings of brain neuroimaging have shown that there is not only one center of pain, but many. These brain parts, that work as a pain center are called ignition nodes and include clusters of nodes used for sensation, movement, emotions, and memory, in chronic pain the pain experience involve them. Motor cortex, cingulate cortex, prefrontal cortex, amygdala, sensory cortex, hypothalamus, cerebellum, hippocampus and spinal cord are the brain parts that usually are active during the pain experience, in addition, within them, there are electrical and chemical links, this system made up by cortical mechanisms are known as a pain neuromatrix, and the activation of this system will create the pain perception, that is called **pain neurotag**. However the brain imaging techniques have demonstrated that some cortical areas are involved more frequently than others: frontal cortex, premotor cortex, thalamus and anterior cingulate cortex, insular and sensorimotor cortex. Recently, some studies have shown through magnetic spectroscopy data that there are important neurochemical changes in the anterior cingulate cortex, thalamus, and prefrontal cortex subjects with chronic low back pain in comparison to healthy controls[20-22].

1.1.4 Central Sensitization

Central sensitization (CS) is a condition of the nervous system that is related to the development and maintenance of chronic pain. When CS happens, the nervous system goes through a process called “wind-up” and gets regulated in a continuous state of high reactivity. This continuous, or regulated, the state of reactivity, later on, maintains pain even after the initial injury might have healed.

The CS has got two main properties named as ‘allodynia’ and ‘hyperalgesia’. Both involve an enhanced sensitivity to pain and the sensation of touch. Allodynia occurs when a person feels pain with things that are normally not painful. For example, chronic pain patients often feel pain even with things as simple as a touch. In these cases, the sensation of touch passes through the nervous system. As the nervous system is in a constant state of increased reactivity, the sensation is registered in the brain as painful or disturbing even when it really shouldn’t, given that the sensation itself was that of a simple touch. ‘Hyperalgesia occurs when an actual painful stimulus is perceived more excessively painful than it should’. For example, a simple knock, which ordinarily should be mildly painful, sends the chronic pain patient into severe pain. Here again, the sensation of pain passes through the nervous system, which is in a heightened state of high reactivity, and the pain is noted in the brain as a highly increased level of pain’.

Beside CS there is Peripheral sensitization (PS), which is an increased sensitivity to an afferent nerve stimulus. This happens after there has been an injury or cell damage to the body area, and produces a flare response due to nociceptors producing plenty of neuropeptides. This results in an increased sensitivity to touch and heat stimuli that are referred to as primary allodynia or primary hyperalgesia if the stimulus was not a painful one prior to the injury. For example a gentle touch to the skin which before the injury is not painful but after is perceived as pain[23].

1.1.5 Central Sensitization and CLBP

Few studies reported the presence of central sensitization as hyperalgesia to pressure to sites unrelated to the lumbopelvic region in patients with CLBP,

indicating generalized or widespread hyperalgesia at least in sub-group of patients with CLBP [24-27]. Flor*et al* first demonstrated cortical hyperactivity and reorganization in patients with CLBP [28]. Two studies evaluating brain morphology reported 'a loss of grey matter volume in patients with CLBP compared with healthy controls' [29, 30]. The role of various psychological factors in the maintenance and development of chronic symptoms has frequently been reported in the literature. Catastrophizing [31], depressive feelings[32], and fear avoidance [33-35] have been described to occur in patients with CLBP.

1.2 Prevalence

LBP is well recognized to be an enormously common health problem that most people experience at some point in their life [36-39]. LBP is the most important cause of activity limitation and absence from work all over the world[40], and it causes a huge economic burden on persons, families, communities, industry, and administrations [41-43]. Until 20 years ago, it was mainly considered as a problem limited to Western countries[44]; however, since that time an ever-increasing amount of research has established that low back pain is also a very important problem in low- and middle-income countries[45-48].

1.2.1 Prevalence in India

In India, LBP prevalence has been found to range from 6.2% to 92% with an increasein prevalence with age and female preponderance [49]. AhdhiG S et al [50] reported that the prevalence of LBP for Indian population was found to be 42% and the majority of women (60.9%) with LBP experienced moderate disability. Hameed P S reported that 51% of information technology employees are having LBP in India [51].

1.2.2 Prevalence in Western Countries

Meucci RD, Fassa AG, and Faria NMX[52]in a systematic review estimated the worldwide prevalence of chronic low back pain according to age and sex. They found that CLBP prevalence was 4.2% in individuals aged between 24 and 39 years old and 19.6% in those aged between 20 and 59. Of nine

studies with individuals aged 18 and above, six reported CLBP between 3.9% and 10.2% and three, prevalence between 13.1% and 20.3%. In the Brazilian older population, CLBP prevalence was 25.4%. Freburger JK et al [53]stated that the prevalence of CLBP rose significantly over the 14-year interval, from 3.9% (95% CI:3.4–4.4) in 1992 to 10.2% (95% CI:9.3–11.0) in 2006 in a representative sample of North Carolina households. Hoy D[54] in their systematic review calculated the global prevalence of LBP and stated that the mean±SEM point prevalence was figured out to be 11.9±2.0%, and the 1-month prevalence was figured out to be 23.2±2.9%.

1.3 Aetiology

LBP is initiated by a physical problem which is normally mechanical in nature i.e. symptoms are exacerbated by movement. This is true for the non-specific or benign LBP where a specific cause (e.g. a prolapsed intervertebral disc or a spinal tumor) has been ruled out through diagnostic triage. Pain can arise from any innervated (receives a nerve supply) structure these include vertebrae, intervertebral discs, dura and nerve root sleeves, facet joint capsules, ligament and fascia, and muscle.

Waddell[5] states that: *For more than 100 years, orthodox medicine, orthopedics, and biomechanics have searched for a structural cause for back pain.* Nachemson, Waddell, and Norlund [55] suggested that it is very difficult to identify a single cause for back pain and in about85% of people with back pain, no clear pathology can be established. This lack of a clear pathology and subsequent diagnosis has led to varying negative classifications (malingering etc) where it is thought that symptoms are fabricated or exaggerated for secondary gain[5, 56]. This type of 'labeling' has the potential to be extremely destructive to the self and identity of those so categorized.

1.4 Relevant Clinical Anatomy

1.4.1 Anatomy of Lumbar Spine

The anatomy of the lumbar spine is complex with bony elements consisting of the vertebrae, the intervertebral discs between the vertebral bodies, the ligaments reinforcing and passively supporting the vertebrae as well as the

musculature actively supporting and providing movement, and finally, the spinal cord and nerves innervating the local musculature [57]. From an evolutionary comparative anatomy perspective, the present lumbar morphology of *Homo sapiens* represents a gross structure encompassing a wide and short pelvis, long flexible lumbar column and both comparatively large hip extensors (gluteal and hamstring musculature) and small lumbar extensors (erector spinae and multifidus)[58].

1.4.2 Lumbar Vertebrae

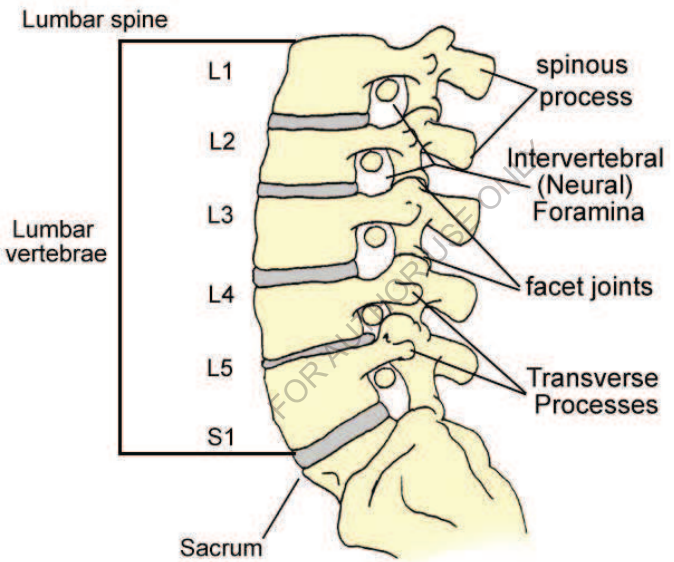


Figure-1.1: Lateral view of the human lumbar spine[59]

The lumbar spine consists of the 5 vertebrae from L1 to L5 and encompassing the L5-S1lumbopelvic junction, though, in a small number of modern humans (~3-5%) the presence of 6th lumbar vertebra has been noted[58]. The vertebrae consist of the vertebral body, which is the major load bearing component, and the vertebral arch consisting of the pedicle, transverse process, lamina, spinous process and superior and inferior articular processes. The pedicles and lamina form the lateral pillar and roof of the spinal canal protecting the

spinal cord and proximal spinal nerves, and the combined elements of the vertebral arch serve as attachments for muscles and ligaments, levers for muscular contraction to act against, and articulations with adjacent vertebrae [57].

1.4.3 Articulations of Lumbar Vertebrae

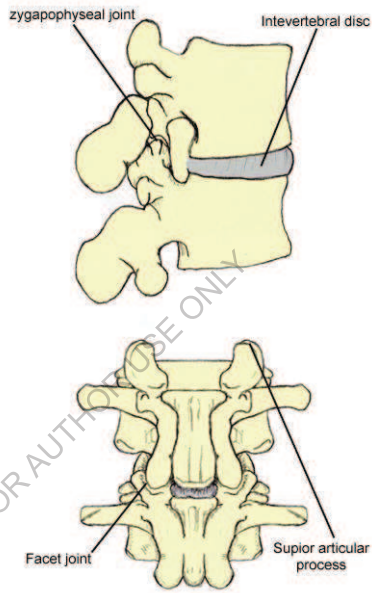


Figure-1.2:The three-joint complex is formed between two lumbar vertebrae[59]

The vertebrae articulate with one another through two joint types; the symphyses between the vertebral bodies (intervertebral discs), and the synovial joints between the articular processes (zygapophyseal or facet joints). The intervertebral discs join adjacent vertebrae by means of a thin layer of hyaline cartilage (known as the endplate) and are composed of the nucleus pulposus (the gelatinous centre providing hydrostatic properties to changes in pressure) and the annulus fibrosus (composed of the outer fibers of the lamellae which are differentially oriented in adjacent lamellae)[60]. The

facet joints are where the two articular processes meet and are enclosed by a thin articular capsule.

1.4.4 The Ligaments of Lumbar Vertebrae

A number of ligaments also provide passive stability to the vertebraeincluding the anterior and posterior longitudinal ligaments surrounding the vertebral body, and the interspinous ligaments including the ligament flava and spinous ligaments[57].

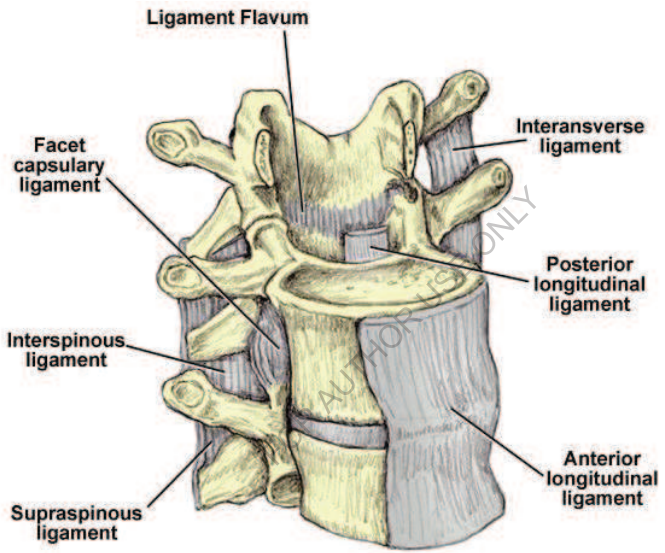


Figure-1.3: Antero-lateral view of the lumbar spine showing the multiple ligaments of the lumbar vertebrae [59]

1.4.5 The Lumbar Musculature

The lumbar musculature, include the superficial Erector Spinae (ES; i.e. iliocostalis lumborum and longissimus thoracis) and both deep and superficial Lumbar Multifidus (MF), both of which provide stability to the lumbar spine[61-63]. These muscles originate at the sacrum, spinous processes, and iliac crest and are covered by the thoracolumbar fascia[57] which has recently been highlighted to also provide a contributory role in spinal stability, static posture,

and movement [64]. The muscles receive innervations from the posterior rami of the lumbar spinal nerves[57].

The complexity of the structures within the lumbar spine presents a number of potential mechanisms for pain originating from the area. Indeed many of the structures noted have been evidenced to be implicated in LBP.

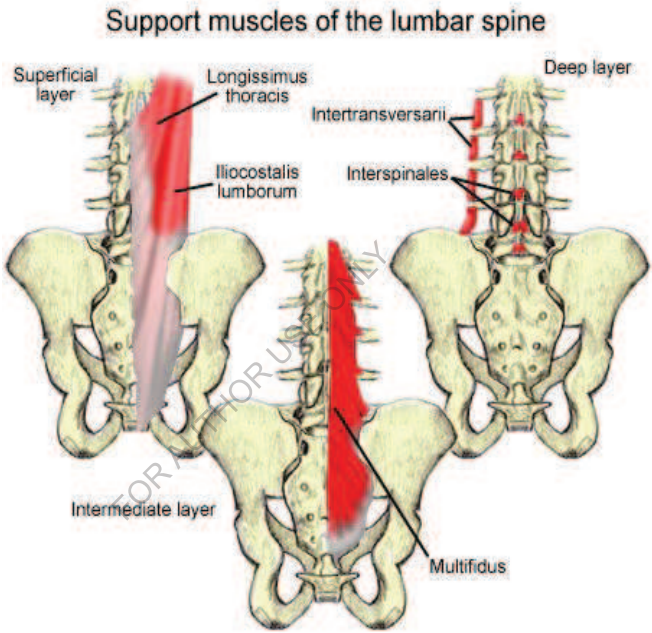


Figure-1.4: Lumbar spinal muscles [59]

1.5 Pathophysiology of Chronic Non-Specific Low Back Pain

1.5.1 Non-Specific Low Back Pain

In the majority of cases (85%) pain is not attributable to specific pathology or nerveroot compression [65] and is defined as non-specific. In some cases, patients with non-specific pain may have radiological signs of spondylolysis and spondylolisthesis (forward slipping of the lumbar vertebrae) but a considerable proportion of diagnosed patients are asymptomatic and

therefore the radiological signs cannot always be directly related to the pathology [66].Patients with non-specific low back pain may also present with referred pain (pain that radiates into the hips and legs) in addition to back pain. Referred pain can originate from a number of different tissues in the back including muscles, fascia, periosteum, ligaments, facet joints, intervertebral disc or epidural structures. It can be hard to localize the exact source of referred pain affecting the hip, groin, and thighs. This type of pain does not generally radiate further than the knee [5].

1.5.2 Classification of Non-Specific Low Back Pain

The link between symptoms and pathology in non-specific low back pain is not clear cut and a number of different approaches to classification have been proposed (e.g. fissures in the intervertebral disc, facet joint degeneration) [67, 68]. While there is no agreement regarding the signs and symptoms that characterize non-specific low back pain, [69] the most widely acknowledged criteria by health professionals are *Acute (<6 weeks duration; Subacute (6 weeks to 3 months); Chronic (>3months)* [70]. The six-week cut off period for acute low back pain is based on epidemiological data that suggests that 90% of patients with an acute attack is fully improved within six weeks [5].

This very simple method of categorization takes no account of severity, the dynamic and random nature of back pain or psychological and social factors [71]. Croft et al stress the limitations of this classification system and propose that the mostimportant concept is the pattern of back pain over long periods of the individual's life [72]. Croft et al found that 90% of patients stopped consulting and returned to work after 6 weeks but 60% or more still had symptoms a year later[72]. Back pain often manifests as a chronic problem with a jumbled pattern of irritable symptoms and periods of relative freedom from pain and disability interspersed with acute episodes, exacerbations, and recurrences that can be very hard to manage [72]. The term “CNSLBP” is often used when sub-classifying LBP patients [5, 73].

1.5.3 Heterogeneous Group of LBP Patients

The term was initially derived from a diagnostic triage, where patients were sub-classified based on pathoanatomical/radiological symptoms into (1) nerve root problem, (2) serious spinal pathology and (3) CNSLBP with no radiological evidence of either of the former pathologies[74]. A specific diagnosis can be established in less than 20%-25% of these cases[75], with the remaining 75% of cases, where there was a lack of radiological evidence of pathology causing pain, being classified as having CNSLBP[5, 73]. It has been claimed that CNSLBP is one of the most challenging and unrewarding pain syndromes to manage in clinical medicine as no clear diagnostic approach or management strategy has been shown to be of clear benefit [76, 77]. A number of different types of interventions have been evaluated with little success in finding the most optimal treatment that consistently improves clinical outcomes [78-81]. The lack of success has been attributed to the fact that most RCTs investigate the efficacy of specific treatments on broadly defined heterogeneous groups of CNSLBP patients, where specific treatment may be effective in one subgroup, detrimental in other subgroup and entirely ineffective in another subgroup of patients [82, 83]. Thiseffect was described by Rose as a "wash-out effect" where the results in one sub-group are being counteracted by the opposite results from patients in another sub-group[84].

It is argued that this CNSLBP population contains a large heterogeneous group of patients for whom the clinical presentation, prognosis and subsequently the best type of intervention varies considerably [85-87]. It has been proposed that application of interventions that are matched to a specific homogeneous subgroup of CNSLBP would be more likely to result in successful outcomes [88, 89]and indeed, studies investigating interventions in specific syndromes or categories of patients appear to have good outcomes [90-95]. The use of a classification-based approach has also been shown superior to therapy based on clinical practice guidelines in improving disability and faster return to work status in patients with work-related LBP [96]. Nevertheless, studies applying specific interventions matched to a specific subgroup of patients with CNSLBP are far outnumbered by studies that explore specific treatments in a broad heterogeneous group of LBP.

1.6 Conventional Physiotherapy For Non-Specific Low Back Pain

The main types of therapeutic exercise relevant to chronic low back pain (CLBP) include: (1) general physical activity (e.g., advice to remain active), (2) aerobic (e.g., brisk walking, cycling), (3) aquatic (e.g., swimming, exercise classes in a pool), (4) directional preference (e.g., McKenzie), (5) flexibility (e.g., stretching, yoga, Pilates), (6) proprioceptive/coordination (e.g., wobble board, stability ball), (7) stabilization (e.g., targeting abdominal and trunk muscles), and (8) strengthening (e.g., lifting weights) [97].

The European guidelines for the management of chronic nonspecific low back pain have recommended conservative treatments such as cognitive behavioral therapy, a supervised exercise program, educational interventions, Back schools (for short-term improvement), manipulations and multidisciplinary (bio-psycho-social) treatment can be considered. The use of physical therapy modalities including TENS not recommended. The short-term use of NSAIDs and weak opioids noradrenergic - serotoninergic antidepressants, muscle relaxants, and capsicum plasters can be recommended for pain relief except the use of Gabapentin as pharmacological treatments. Moreover, the guidelines do not recommend any invasive treatments including Acupuncture, trigger point injections, intradiscal injections and prolotherapy are not recommended. Percutaneous electrical nerve stimulation (PENS) and neuro-reflexotherapy can be considered. Surgery for CNSLBP cannot be recommended unless 2 years of all other recommended conservative treatments – including multidisciplinary approaches with combined programs of cognitive intervention and exercises have failed [1].

1.7 McKenzie Concept

The McKenzie method is a comprehensive approach to spinal pain, including CLBP, which includes both an assessment and an intervention consisting primarily of directional preference exercises. The goal of the McKenzie assessment is to classify patients with CLBP according to the type of therapy to which they are most likely to respond. Because it combines assessment

and intervention, the McKenzie method is commonly referred to as *mechanical diagnosis and therapy* (MDT)[98, 99]. One of the principal tenets of MDT is centralization, which refers to the sequential and lasting abolition of distal referred symptoms, as well as subsequent abolition of any remaining spinal pain in response to a single direction of repeated movements or sustained postures. According to MDT, patients may be classified into one of three mechanical syndromes: derangement, dysfunction, or postural [100, 101].Derangement syndrome is the most common and indicates that centralization can be achieved with directional preference movements. Dysfunction syndrome is found only in patients with chronic symptoms and is characterized by intermittent pain produced only at end-range in a single direction of restricted movement. The adherent nerve root is a particular type of dysfunction that typically follows an episode of radicular pain after which pain can be elicited when the nerve root and its adhering scar tissue are stretched. The postural syndrome is likewise intermittent, but the pain is typically midline or symmetrical, produced only by sustained slouched sitting, and subsequently abolished by posture correction (restoring the lumbar lordosis); it is typically not seen in CLBP. The minority of patients who cannot be classified into one of these three syndromes would be termed *other*.

1.7.1 Theory behind McKenzie Method

In general, exercises are used to strengthen muscles, increase soft tissue stability, restore range of movement, improve cardiovascular conditioning, increase proprioception, and reduce the fear of movement. Most McKenzie method exercises are intended to directly and promptly diminish and eliminate patients' symptoms by providing beneficial and corrective mechanical directional end-range loads to the underlying pain generator [102].The anatomic means by which these rapid pain changes occur is addressed in an article by Wetzel and Donelson [103]. Treatment with the McKenzie method may also provide psychological mechanism–related benefits.

1.7.2 Psychological Mechanisms

In some patients with particularly severe or prolonged CLBP or psychological co-morbidities such as anxiety or depression, maladaptive illness behavior

may become established. This type of behavior may manifest itself as fear of engaging in any activity or movement that has previously been associated with symptoms of CLBP. As time passes, virtually all activities gain this association, leading to a generalized fear of movement in an attempt to minimize exacerbations. Engaging in any form of supervised exercise therapy under the guidance of an experienced clinician able to gradually increase the type, dose, frequency, or intensity of movements can help break this cycle and demonstrate that not all movements or activities need be painful.

1.7.3 Indication

This intervention is generally indicated for patients with nonspecific mechanical CLBP, recurrent LBP, and those classified as centralizers following MDT. Mechanical LBP patients who may respond to the McKenzie method are those whose symptoms are affected by changes in postures and activities (e.g., the pain made worse by sitting and bending, but better with walking or moving). Such a history is often indicative of a directional preference for an extension, which can be confirmed during the repeated end-range testing of the physical examination. Such mechanical responsiveness to changes in posture and activity has been commonly reported [104-107].Recurrent LBP patients who report recurring LBP are routinely found to have a directional preference, are centralizers and are therefore ideal treatment candidates. Still, even if a patient has responded to some other form of treatment for past LBP but is irritated with recurrences and in need of further treatment, they are often pleased with the ability to self-manage their pain with this intervention.

1.7.4 Centralizers

At least six studies have reported on the favorable prognosis for patients who were categorized as centralizers if treatment is directed by the patients' directional preference [108-113]. A systematic review (SR) similarly concluded that centralization, when elicited, predicts a high probability of a good treatment outcome, again as long as treatment is guided by the assessment findings [114].These patients might be considered ideal patients to experience an excellent treatment response with this approach. Initial clues for potentially

responsive patients emerge during the history taking and then are confirmed with the repeated end-range movement portion of the physical testing.

1.7.5 The Evidence for the efficacy of McKenzie Method

The Cochrane Collaboration conducted a Systematic review (SR) in 2004 on all forms of exercise therapy for acute, subacute, and chronic LBP [79].A total of 61 RCTs were identified, including 43 RCTs related to CLBP. Although results were generally favorable, this review combined all forms of exercise therapy, including stabilization, strengthening, stretching, directional preference, aerobic, and others. As such, these conclusions are not specific to the McKenzie method and pertain only to isolated components (i.e., directional preference exercise). This review identified few RCTs related to the McKenzie method for acute, subacute, and chronic LBP [104, 115-117].

The American Pain Society and American College of Physicians CPG committee conducted an SR in 2007 on non-pharmacologic therapies for acute and chronic LBP [118]. That review identified two SRs related to McKenzie exercise, and both were considered of higher quality [119, 120]. One found no clear difference between the McKenzie method and other types of exercise [120]. The other SR found that the McKenzie method was more effective than other interventions on short-term pain and disability, but no difference in effectiveness was observed for intermediate-term disability [119]. These SRs included eight additional RCTs related to the McKenzie method [121-124]. This SR did not make any conclusions specific to exercises used in the McKenzie method.

Two SRs related to the McKenzie method have thus far been conducted [119, 120].Their conclusions were similar and indicated there was limited evidence with respect to CLBP. Another SR examined the evidence regarding the effectiveness of physical therapy–directed exercise interventions after patients had been classified using symptom response methods [125].This included mixed duration LBP (some chronic, but mostly subacute). Four of five of the included studies were related to the McKenzie method. All articles scored sixor more by physiotherapy evidence database (PEDro) rating (suggesting high methodological quality), and four of five found that a directed exercise

program implemented according to patient response was significantly better than control or comparison groups. The authors noted a positive trend, but few studies have investigated this phenomenon. One unique RCT was identified in this study that was not included in the aforementioned reviews [102].A recent SR on unloaded movement facilitation exercise in CLBP identified another unique RCT related to the McKenzie method [126, 127].

An RCT conducted by Petersen *et al* [115]included patients with LBP with or without leg pain who had symptoms lasting longer than 8 weeks. Participants were randomized to either the McKenzie method or strengthening exercises for 8 months in an outpatient clinic and 2 months at home. At the 8-month follow-up, there was a decrease in pain scores (Manniche) in the McKenzie group, but only a small decrease in the training group (*P* values not reported). The difference in pain between the two groups was not statistically significant. There was also a decrease in disability scores (Manniche) in both groups (*P* values not reported). The difference in disability between the two groups was not statistically significant. This study was considered of lower quality.

An RCT conducted by Long *et al*[102] included patients with LBP with or without neurologic involvement (duration of symptoms not reported). Participants were assigned 6 sessions over 2 weeks of (1) McKenzie method, (2) opposite directional preference exercises, or (3) active nonspecific exercises. After the treatment period, there was a significant reduction in pain scores (visual analog score, 0-10) in all three groups. The difference in pain between groups was statistically significant, with the largest improvement in the McKenzie group. There was also a significant reduction in disability scores (Roland Morris Disability Questionnaire) in all three groups. The difference in disability between groups was borderline non-significant, with the largest improvement in the McKenzie group.

An RCT by Miller *et al*[127] included patients with CLBP and symptoms lasting longer than 7 weeks. Participants were randomized to either the McKenzie method or stabilization exercises for 6 weeks. After the treatment period, there was a statistically significant reduction in pain scores (Short-form McGill Pain

Questionnaire) in the McKenzie group but not in the stabilization group. The difference in pain between groups was not statistically significant. There was no significant change in disability (Functional Status Questionnaire) in either group, and there were no significant differences between groups.

1.8 Clinical Diagnosis of Central Sensitization

Recently, a clinical method was developed for the differential diagnosis between common nociceptive pain and CS in CLBP using an algorithm based on three diagnostic criteria: (a) The disparity between the experience of pain and the extent of damage or disease; (b) A distribution of pain anatomically unreasonable (i.e. bilateral pain/mirror, pain varying in anatomical location, large pain areas with a non-segmental distribution, widespread pain, and/or allodynia / hyperalgesia outside the segmental area of supposed primary nociception), and (c) Hypersensitivity of the senses not associated to the musculoskeletal system [128].

CS is typically described as disproportionate and diffuse pain distribution, implying that the severity of pain and related reported or perceived disability are inconsistent with the nature and extent of injury or pathology [128, 129].

1.9 Significance of The Study

Hoy D et al [130] stated that LBP causes more global disability than any other condition and also described in results of their study that out of all 291 conditions studied in the Global Burden of Disease 2010 Study, LBP ranked highest in terms of years lived with disability (YLDs), and sixth in terms of overall disability-adjusted life years (DALYs). Ekman M, Johnell O, and Lidgren L [131] estimated that the total cost of LBP was 1860 million EUR in Sweden in 2001 and the indirect costs were due to lost productivity accounted for 84% of the total cost. The prognosis for CNSLBP is generally poor and associated disability seems to be more persistent. The present study has the potential to improve our understanding of CNSLBP, as the methodology allows for the simultaneous assessment of pain, central sensitization, and disability, and fear-avoidance beliefs. The unique information provided about CNSLBP disability could assist in the development of effective treatments for CNSLBP by identifying specific target groups for these treatments. Ultimately,

this could serve to improve patient outcomes and reduce health care costs. Gujarati version of CSI will be useful in detecting CS in Gujarati speaking patient population. Similarly, Gujarati version of FABQ will be very useful. This study may contribute to develop awareness among physiotherapists about the presence of CS in CNSLBP population and would help them to detect Central Sensitization and decide appropriate intervention for this entity. There is very less literature available regarding the occurrence of CS in CNSLBP patients. Hence this study is adding new information to the existing body of knowledge.

1.10 Statement of the Problem

It is known that there are various interventions verified as treatment strategies in CNSLBP considering that CNSLBP consists of homogeneous subgroups. However, it is argued that based on various factors such as clinical presentation and prognosis there could be heterogeneous subgroups. Especially in patients with central sensitization, it may be difficult to find the best treatment intervention. Therefore this present study aimed to check and verify the efficacy of McKenzie exercises program in contrast with conventional physiotherapy program in a subgroup of CNSLBP patients with CS and without CS.

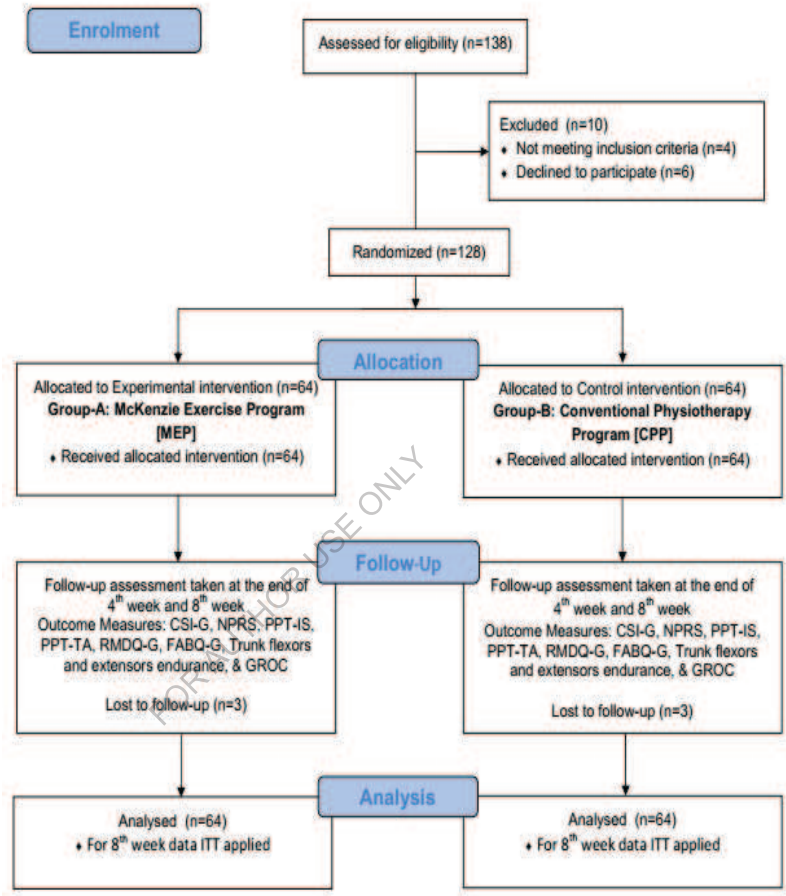
1.11 Review of Literature

1.11.1 Introduction

This literature review provides the background and justification for the research undertaken. In this chapter, an attempt has been made to give an overview of various aspects and issues of this study through the review of existing literature. It has helped to identify the contradictions, gaps, inconsistencies or discrepancies in the previous studies on the subject.

1.11.2 Low Back Pain

Low back pain (LBP) is a significant clinical, social, and financial problem frequently observed with prevalence ranging from 8% to 56% in the USA and it is estimated that 28% people experience disabling LBP sometime during their lives, 14% experience episodes lasting at least two weeks, 8% of the entire working population will be disabled in any given year[132]. Volinn E [44] highlighted the fact that the 22 high-income countries, on which the research



**ITT - Intention To Treat Analysis*

Figure-1.5: CONSORT 2010 Flow Diagram of Main Study

attention has largely been centered, represent less than 15% of the world's population. However, more recent reports from Tibet[133], Turkey[134, 135], and China[136]suggest that prevalence rates in non-European countries are not

that dissimilar from Western countries with one-year prevalence in adults in these research studies is between 36% and 64%.

Chronic low back pain (CLBP) is sometimes defined as back pain that lasts for more than 7–12 weeks and many others classify frequently repeated back pain as chronic pain since it intermittently affects an individual over a long period [137]. Very little is known about the precise causes despite the high prevalence and high incidence of LBP [138].Degenerative changes were seen in imaging studies in the structures of the lumbar vertebral column and as well in musculoskeletal structures do not explain the symptoms of LBP; as they are also seen in normal healthy subjects[139, 140] and consistently there is a weak association between symptoms of LBP and imaging results[66].In approximately 85% of the patients with LBP a precise pathoanatomic diagnosis cannot be given, hence these patients are considered having nonspecific LBP [138].It is observed that only 25% of the variance of back pain intensity can be explained by the combined contribution of pathology and psychosocial factors [141], hence it is imperative that further exploration of contributing factors and underlying mechanisms should be done.

1.11.3 Central Sensitization

Abnormal pain processing in the central nervous system (CNS) rather than from actual damage and/or injury to anatomic structures of body may lead to increased neuronal response and central sensitization (CS) [142-144] and this may be responsible for mechanical hyperalgesia, allodynia, and/or referred pain which is frequently seen in chronic pain syndromes [144-148].CS is described by the International Association for the Study of Pain(IASP) as: *"Increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input"[149].*CS is also defined as "an augmentation of responsiveness of central neurons to input from unimodal and polymodal receptors"[150]. The outcome of the processes involved in CS is an increased responsiveness to a variety of peripheral stimuli including mechanical pressure, chemical substances, light, sound, heat, cold, and electrical stimuli. The increased sensitivity to various stimuli results in a largely decreased load tolerance of the neuromusculoskeletal

system. Although the precise mechanism of CS is not fully understood; several contributing mechanisms have been put forward: It may be an altered sensory processing in the brain [151], malfunctioning of descending anti-nociceptive mechanisms [152], increased activity of pain facilitatory pathways, temporal summation of second pain or windup[151, 153], and long-term potentiation of neuronal synapses in the anterior cingulate cortex[154]. Besides the above top-down mechanisms included in the pathophysiology of CS, it is important to understand that there are bottom-up mechanisms as well. For example, peripheral injury and other forms of stressors trigger the release of pro-inflammatory cytokines, with the consequent activation of spinal cord glia with cyclo-oxygenase-2 and prostaglandin E2 expression in the CNS[155-158].

"Wind up" denotes to a central spinal mechanism in which repetitive noxious stimulation results in a slow temporal summation that is experienced in humans as increased pain [159]. It leads to facilitation of ascending pain mechanisms and the literature also describes that there are alterations in the descending inhibitory pathways those arising from the periaqueductal gray matter and the rostral ventral medulla in the brainstem [160].The work of these descending inhibitory pathways is to "focus" the excitation of the dorsal horn neurons, to generate an urgent, localized, and rapid nociceptive signal to biologically relevant stimuli, thereby suppressing surrounding extraneous neuronal activity[161, 162], and breakdown of one or more components of these inhibitory systems can result in CS[162].It is recognized that there are facilitatory pathways originating from the brainstem; besides descending inhibitory pathways. Centers in the forebrain are capable of wielding powerful influences on various nuclei of the brainstem[163], including the nuclei recognized as the origin of the descending facilitatory pathway[162].

The activity in descending pathways can be modulated, as it is not constant; for example by the level of alertness, attention, anticipation, and stress[164].It has been identified that forebrain functions such as cognitions, attention, emotions, motivation, and/or stress as personal factors may regulate the actual pain experience[162].To name this facilitatory influence, the 'cognitive-emotional sensitization' term has been coined[165].Functional imaging studies

have shown in healthy subjects that pain catastrophizing and anticipations were related to the neural processing of nociceptive stimuli; which are psychosocial and cognitive factors [166, 167]. During the last few decades, great efforts have been made to untangle how the brain processes pain and to decode involved neuronal mechanisms using functional imaging studies [168].

1.11.4 Central Sensitization in CLBP Patients

The intent of this narrative review is to search and analyze the available literature regarding CS and altered central pain processing in CLBP patients. It was done by a comprehensive computerized search on Science Direct, National Library of Medicine (Pubmed), Biomed Central, Google Scholar, CINAHL, Pubmed Central and Oxford Press. The key words "chronic low back pain" was used in combination with following terminologies: central sensitization, hyperalgesia, temporal summation, central pain processing, cortical reorganization, pain inhibition, pain facilitation, diffuse noxious inhibitory controls (DNICs) and widespread pain. Additionally, reference lists of most pertinent articles were searched to increase the search accuracy, as much as possible. We have included all the available studies which are evaluating the concept of central sensitization (CS) in conservatively treated CLBP patients.

1.11.4.1 Does Segmental and Extrasegmental Sensitization exist in CLBP patients?

Hyperalgesia is showed by "a lowered pain threshold because of sensitization of nociceptive afferents or an increasing pain intensity as a function of graded nociceptive stimulation" in many chronic unexplained disorders, such as Fibromyalgia, Chronic regional pain syndrome (CRPS), Whiplash Associated Disorders (WADs) to detect CS [169]. In patients with LBP, lower thresholds may be found in areas innervated by spinal segments neighboring to the spinal segments of the primary source of pain perception. These findings are termed as segmental CS[170]. If pain referral and many areas of hyperalgesia are found away from the site of the symptomatic area of back pain then this is termed as widespread or extra-segmental CS [170]. Sixteen studies are found

that deals with a sensitivity of various types of stimuli in CLBP patients. Details of the study are shown in the Table-1.1.

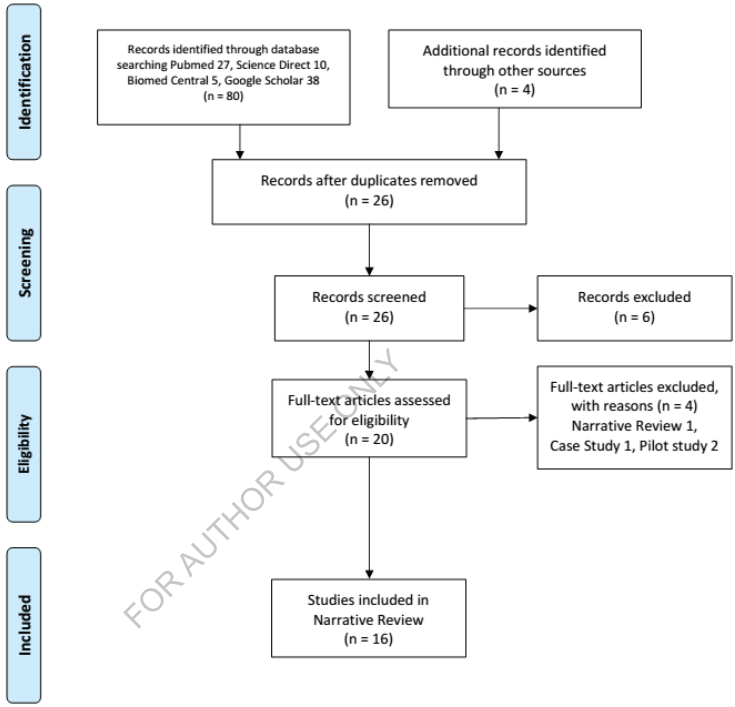


Figure 1.6: Flow Diagram of Literature Search

This Table-1.1 describes the results of these studies in relation to the presence or absence of the central sensitization (CS+ or CS-) in CLBP patients.

Table 2.1: Summary of the included Studies in Review of Literature

Author/ Publication Year	Design	Population studied	Stimulus used	Outcome measures[including Assessment of CS]	Central sensitization YesCS+/ No CS-	Results of the study	Level of evidence/Limitations of study
Hyperalgesia (mechanical &/or electrical stimuli)							
Peters and Schmidt[171](1992)	Case control study	20 CLBP 20 HCs	Electrical pain stimulus, Mechanical pressure	Algometry- Pain perception threshold, & Maximum pain tolerance	No	Higher PPT & MPT in CLBP group. Supports adaptation theory/DNIC	Level IV(172)
Clauw et al [25] (1999)	Cross-sectional pilot study	45 CLBP patients	Mechanical pressure	Algometry, MRI, SF-36, Psychosocial variables	Yes	CLBP patients had more tender points (5.2±5.4) in comparison with 1 to 3.5 in general population.	Level IV
Giesecke et al[24] (2004)	Case-control study	11 CLBP 16 Fibro-myalgia 11 HCs	Mechanical Pressure	Pressure pain threshold, fMRI	Yes	Low PPT found in CLBP patients	Level IV Small sample size
Giesbrecht and Battie[26] (2005)	Case-control study	30 CLBP females 30 HCs female	Mechanical Pressure	Pressure pain threshold (Electronic Algometry)	Yes	Significantly lower PPT in CLBP patients in comparison with HC	Level IV Only females
Laursen et al [27] (2005)	Case-control study	40 female patients - 10FM/whiplash, 10 endometriosis, 10 LBP, 10 Rheumatoid	Mechanical Pressure	Pressure pain threshold (Electronic Algometry), SF-36	Yes	lower values of PPT in CLBP patients in comparison with HC	Level IV Small sample of CLBP patients;

		arthritis Compared with 41 female HCs.					Only female patients.
O'Neill et al [173] (2007)	Case-control study	12 CLBP 12 HC	Mechanical pressure, Hypertonic saline injection	Pressure pain threshold Supra-threshold stimulation Experimentally induced muscle pain	Yes	Significant difference between LBP and HC in pain threshold or pain tolerance.	Level IV Small sample size. Selection bias
Meeus et al[174] (2010)	Experimental case-control study	26 Chronic Fatigue Syndrome 21 CLBP 31 HC	Mechanical pressure, Aerobic exercises	Pressure pain threshold Venous blood sampling (Nitric Oxide level)	No	No difference between LBP and HC in pain threshold	Level IV Selection bias. Individual difference. Duration of exercise
Hyperalgesia (thermal stimuli)							
Lautenbacher et al [175](1990)	Cross-sectional study	19 CLBP 19 HC	Thermal stimuli, cold	VAS, Tonic &phasic threshold, Somatosensory perception	No	No difference in threshold between CLBP andHCs but SSP is decreased	Level IV Small sample size
Derbyshire et al[176]2002	Cross-	16 CLBP	Thermal stimuli	Thermal pain	Yes	Patients experienced higher	Level IV

	sectional Case control study	16 HC		perception Regional cerebral blood flow (rCBF) VAS rating		VAS score at higher temperature compared with HCs; Small difference between LBP and HCs in rCBF for thermal stimuli	Small sample size
Wind up							
Arntz et al [177] (1991)	Pre-post repeated measure design	22 CLBP 21 HC	Electrical pain stimulus	VAS	No	Both the groups showed habituation	Level IV Methodological Flaw
Kleinbohl et al [178](1999)	Case-control study	15 CLBP 15 headache patients 23 HCs	Tonic & Phasic heat stimuli	Pain threshold Index of Sensitization	Yes	LBP patients showed stronger & early sensitization	Level IV Selection bias
Flor et al [179] (2002)	Case-control study	30 CLBP 30 HCs	Electrical pain stimuli Repeated stimulation at different intensities	Pain threshold Pain tolerance threshold Somatosensory perception	Yes	Elevated pain threshold in CLBP group, Decrease in pain threshold in HCSupportsCS+	Level IV
Diers et al [180] (2007)	Cross-sectional Case control study	14 CLBP 11 HCs	Electrical intracutaneous& intramuscular stimulus	Pain threshold Pain tolerance	Yes	Sensitization occurs in all CLBP patients but not in HCs	Level IV Small sample size

DNIC							
Julien et al[181] (2005)	Cross-over trial	30 Fibromyalgia30 CLBP 30 HCs	Immersion in noxious cold water at 12ºC	VAS rating during ascending or descending sessions (spatial summation)	No	The deficit of endogenous pain inhibitory systems found in fibromyalgia but not in chronic low back pain.	Level IV Methodological Flaw
Endogenous inhibition during exercise							
Hoffman et al [182](2005)	Repeated measure design/clinical trial	8 CLBP 10 HCs	Mechanical pressure	PPT	No	Pressure pain perception can be reduced after aerobic exercise in LBP patients and HCs	Level IV Small sample size
Flexion reflex							
Peters et al [183] (1992)	Mixed between-within group design	12 CLBP 12 oral surgery 12 HCs	Electrical pain stimulation	Nociceptive flexion reflex threshold	No	No significant difference between CLBP and HCs; No role of DNIC/supports adaptation theory	Level IV Small sample size

1.11.4.2 Presence of Hyperalgesia in CLBP Patients

There are four studies, which reported hyperalgesia to pressure to sites unrelated to the lumbopelvic area in CLBP patients, indicating generalized or widespread hyperalgesia at least in a subgroup of CLBP patients[24-27]. It was observed that there is a decreased pressure pain threshold (PPT) in a population of CLBP patients with and without radiation distal to the knee, both at sites related to lumbar area (paraspinal lumbar muscles) and unrelated to the lumbar area (extensor muscle of the wrist, finger, etc)[26]. Also, contradictory results were reported in the literature suggesting that CLBP patients do not experience sensitization[174].In a study conducted by O'Neill et al, pressure pain thresholds (PPTs) in tibialis anterior muscle were found significantly lower in CLBP patients, whereas PPTs of infraspinatus muscle were not different from healthy controls, suggesting segmental sensitization[173]. Lautenbacher et al [175] found no differences in pain threshold between patients with CLBP and HC when contact heat was used on the right hand using a Peltier-thermode, but in another study by Derbyshire et al [176] reported that the patients experienced significantly higher pain ratings on Visual Analog Scale (VAS) compared with healthy subjects, suggesting widespread hyperalgesia, but no allodynia (as there were no differences in VAS between patients and control group for the non-painful stimulation).After administering the hypertonic saline injection, patients with herniated disk confirmed by MRI exhibited considerably higher pain intensity, duration, and larger areas of pain referral in both infraspinatus and tibialis anterior muscles in comparison with healthy controls, indicating widespread sensitization in these patients with CLBP[173].

In studies, where repeated pain stimulation is applied or continuous stimulation is applied; demonstrates the phenomena of enhanced temporal summation (wind-up)[177-180].In various studies, to induce temporal summation mechanical, electrical or thermal stimulation have been used (See Table-1.1Wind-up).

The endogenous pain control system whose deficiency is supposed to contribute to chronic musculoskeletal pain is represented by DNIC-like mechanisms [184, 185].The DNIC-like mechanisms originate from the serotonergic dorsoreticular subnucleus in the caudal medulla, is activated by nociceptive afferents and in turn modulates the impending noxious input by the inhibition of wide dynamic range neurons in the

dorsal horn[186].It can be facilitated by serotonergic and opioidergic-agents and inhibited by opioid antagonists and serotoninantagonists, respectively[187-189].

The initiation of endogenous pain inhibitory systems by the spatial summation test was assessed[181] using immersion of different surfaces of the arm in circulating noxious cold (12ºC) water. Both patients with CLBP and healthy controls perceived their pain in a different manner during the ascending and descending sessions. The descending session resulted in smaller pain intensity and unpleasantness, which the authors ascribed to a full recruitment of inhibitory systems at the beginning of the descending session in contrast to agradual recruitment during the ascending session. During the ascending session, pain perception remained static, regardless the stimulated area, whereas a correlation was observed between pain and stimulated area during the descending session. Hence the observations from this study do not support a deficit of this endogenous pain inhibitory system in CLBP.

In normal conditions, pain thresholds increase during physical activity because of the release of endogenous opioids, growth factors[190], and other strong inhibitory mechanisms (descending inhibition) engineered by the CNS[191].However, in patients with CLBP, pain ratings from an experimentally induced pressure pain stimulus increased in response to submaximal aerobic exercise[182], as they are in healthy controls [192], indicating normal pain processing in response to exercise. Meeus M et al studied pain response in relation to exercise in patients with chronic fatigue syndrome and chronic widespread pain, in patients with CLBP, and in pain-free sedentary controls. The absence of endogenous inhibition during exercise was only seen in patients with chronic fatigue and chronic widespread pain, but not in the group of CLBP patients [174].

Most of the above-mentioned studies are based on the patients' pain assessment, which is an actually subjective measurement. Measuring the minimal intensity of transcutaneous electrical stimulation essential to elicit a spinal reflex may provide a better objective measurement of spinal hyperexcitability and CS [193]. The minimal intensity of the stimulus that is sufficient to evoke a reflex at a well-defined latency, known as the reflex threshold, usually represents the minimal stimulus intensity required to elicit a perception of pain [194]. Peters ML et al elicited a nociceptive

flexion reflex after noxious stimulation in CLBP patients [183]. There was no differences observed in nociceptive flexion reflex (RIII) threshold between CLBP patients and healthy controls after noxious electrical stimulation of the ankle [183]. Hence, there is no evidence to suggest that spinal reflexes are varied in CLBP patients.

1.11.4.3 Altered Brain Function in CLBP

Flor*et al* first showed that cortical hyperactivity and reorganization in CLBP patients[28].Diers *et al*[180] used EEG to evaluate brain responses in relation to pain in patients with CLBP. No significant differences were observed in pain threshold, but patients exhibited extra-segmental sensitization when repeated stimulation was applied to evoke temporal summation, but no significant sensitization was seen among healthy controls [180]. Evidence for augmented central pain processing has been found in studies using fMRI[24]. In a positron emission tomography study [176]conducted on CLBP patients and HCs with thermal pain stimulation; the regional cerebral blood flow correlated partially well with subjective pain experience in many brain areas, such as the cerebellum, thalamus, midbrain, etc. in both the groups. Hence these data provide some initial evidence for altered central pain processing in CLBP patients [176].

1.11.4.4 Cognitive-Emotional Sensitization

Following characteristics namely, Catastrophizing[31], depressive feelings[32], and fear avoidance[33-35] have been reported to occur in CLBP patients. Inappropriate beliefs have been linked with the development of overstated pain perception [195, 196] or other negative effects. All these psychological factors are cited as yellow flags as they are associated with a poor prognosis, may heighten facilitatory pathways in the CNS, leads to sensitization of dorsal horn spinal cord neurons. Initial research findings suggest that cognitive and emotional factors can contribute and/or may sustain the mechanisms of CS in CLBP patients.

1.11.5 Research Gap

The purpose of this review of the literature was to review and evaluate the existing scientific literature regarding the role of CS in CLBP of different aetiologies. Different assessment methodologies were utilized for evaluating the phenomenon of CS,

intending to understand the different changes in pain sensitivity observed in this population. Nine out of the 16 articles that were considered in this narrative review seems to support an emerging key role for CS in CLBP. This was confirmed through by means of different parameters like pain perception threshold, pain tolerance, pain ratings etc. All these findings are considered clinical manifestations of CS [197]. Furthermore, similar findings have been previously seen in some other chronic pain conditions such as whiplash injury [198]or fibromyalgia [24], suggesting these conditions are caused by the same altered central pain processing mechanism. CS demonstrates itself at different degrees over a continuum from no CS at all to severe CS. Although prevalent in chronic pain, generalized central hypersensitivity is not present in every patient [199]. For instance, in some populations (e.g., fibromyalgia), CS may be the characteristic feature of the disorder. In others, such as in CLBP, not all patients have CS, but only a subgroup of them has it. There are many studies which suggest that chronic pain should be seen from a "Central" viewpoint. Changes in ascending and descending central modulatory mechanisms for the perception of pain, which is termed as "neuronal plasticity" [161] may be responsible for CS. CS may involve both functional changes and structural changes in the CNS [200, 201].

Though there were many studies that indicate the presence of altered central pain mechanisms in CLBP patients resultsare ambiguous. Some studies observed reduced pain thresholds suggestive of extra-segmental hyperalgesia [24-27], some other studies only observed a segmental hyperalgesia [173], and while some authors did not find hyperalgesia at all [171, 180, 202]. Same results were found when temporal summation was experimentally induced in CLBP patients [180, 202]. Now it is understood that functional organization of the adult brain is not fixed, but plastic changes of the primary cortical areas may happen as a result of injury, stimulation, and training[203]. Continued painful stimulation may result in cortical changes [28, 204].There is growing evidence that changes in the brain structure, brain function, and brain chemistry may happen in CLBP patients [24, 28, 29, 205]. Functional brain-imaging techniques are especially useful to visualize the brain structures engaged in pain processing during evoked pain and to understand the mysteries of brain circuitry.

In a narrative review by Sanzarello, I et al[206] stated that CNSLBP is the most frequent musculoskeletal disorder across the world for which there is evidence that can be clinically identified as a cluster of signs and symptoms which

indicatepresence of CS pain. At present clinicians and patients, both are not satisfied with the label of 'medically unexplained symptoms'. This line of approach gives a comprehensible diagnosis for the presence of CS in a subgroup of CNSLBP patients, and this can direct the clinicians for certain specific pharmacological and non-pharmacological treatment for CS. In future, physiotherapists can explore the non-pharmacological or exercise-based treatments for CS in CNSLBP in their clinical trials.

So far there is no gold standard available for diagnosis of CS [144]. Different clinical and laboratory methods are used for detecting potential involvement of CS in musculoskeletal pain conditions (i.e., QST and brain imaging techniques), without having any comparatively superior or reliable method. All of them evaluated the same basic concept of CS but in its different expressions related to the different aspects of sensitization [207]. For example, widespread hyperalgesia, which is an expression of CS, can be evaluated quantitatively in a standardized way by using pressure algometry. Most studies of this review assessed the presence of CS in laboratory conditions and used costly and complex equipment; which is not available for most of the clinicians. Further investigation regarding the assessment of CS in CLBP is required in order to provide new assessment methodologies for CS, which is simple and less costly for the clinicians. With this viewpoint, the recently proposed 'Central Sensitization Inventory' should be investigated in CLBP patients [208].

There is no study available in the literature, which directly deals with the presence of CS in CNSLBP patients and its treatment by McKenzie exercise program and Conventional physiotherapy program. This study will be very useful in adding new information to the existing knowledge base in terms of detecting CS and treating by physiotherapeutic means.

1.11.6 Conclusion

Most of the literature reviewed here suggests that the CNS becomes centrally sensitized in a subgroup of patients with CLBP. However, the significance of this involvement is just starting to become clearer. This could be an active topic of future research. More studies are necessary for providing definite evidence for the clinical importance of CS.

2

OBJECTIVES OF THE STUDY

"Science is simply common sense at its best, that is, rigidly accurate in observation, and merciless to fallacy in logic."

— **Thomas Henry Huxley**

This thesis has three studies; which includes two studies pertaining to translation and validation of 'Central sensitization inventory' and 'Fear-avoidance beliefs questionnaire' into Gujarati language. The third study is the main study which deals with central sensitization issue in chronic non-specific low back pain. The translated and validated version of CSI-G and FABQ-G was used in the main study as outcome measures.

2.1 Objectives of the Study

The main objective of the book was to investigate whether McKenzie exercise program is more beneficial in centrally sensitized CNSLBP patients in terms of various outcome measures such as pain, central sensitization, pressure pain threshold, disabilities, fear avoidance beliefs, trunk flexors, trunk extensors endurance, and patient satisfaction.

2.1.1 Priori Objectives

(a) To translate and culturally adapt Central Sensitization Inventory (CSI) into Gujarati language and check test-retest reliability and content validity of Gujarati version of CSI.

(b) To translate and culturally adapt Fear Avoidance Belief Questionnaire (FABQ) into Gujarati language and check test-retest reliability and content validity of Gujarati version of FABQ.

2.1.2 Primary Objectives

(a) To review the literature for patients with chronic non-specific low back pain to examine to what extent subgrouping and targeted treatment have been used previously, and furthermore examine if the use of classification systems [CS+ & CS-] influenced the outcome.

(b) To identify the proportion of patients with CNSLBP experiencing central sensitization in terms of severity classification by using CSI-G.

(c) To find the presence of CS in CNSLBP patients in terms of, those who display lower pressure pain thresholds (PPT) by pressure algometry.

(d) To establish a scientific evidence to use McKenzie exercise program for benefits of patients having CS in CNSLBP patients.

(e) To establish a scientific base for future research for CS in CNSLBP patients.

2.1.3 Secondary Objectives

(a) To find the presence of fear-avoidance beliefs in CNSLBP patients in terms of, those who display higher score on FABQ-G and does it correlates with presence of CS in terms of CSI-G scores among CNSLBP patients?

(b) To find presence of disabilities in CNSLBP patients in terms of, those who display higher score on RMDQ-G and does it correlates with presence of CS in terms of CSI-G scores among CNSLBP patients?

2.1.4 Hypothesis

Comparisons are made between following two groups, based on these eightoutcome measurements at the end of 4th week and 8th week after implementation of the respective intervention: 1) Numerical pain rating scale, 2) Pressure pain threshold, 3) CSI-G scores, 4) Roland Morris Disability Questionnaire-G, 5) Fear-avoidance Beliefs Questionnaire-G, 6) Trunk flexor endurance, 7) Trunk extensor endurance scores, and 8) GROC scores.

Group A: - McKenzie Exercise Program [MEP]

Group B: - Conventional Physiotherapy Program [CPP]

1) Numerical Pain Rating Scale:

- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on NPRS scores in reducing pain in patients with CNSLBP having the presence of CS.
- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on NPRS scores in reducing pain in patients with CNSLBP not having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on NPRS scores in reducing pain in patients with CNSLBP having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on NPRS scores in reducing pain in patients with CNSLBP not having the presence of CS.

2) Pressure pain threshold:

- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on PPT scores in improving the perception of mechanical pressure pain in patients with CNSLBP having the presence of CS.
- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on PPT scores in improving the perception of mechanical pressure pain in patients with CNSLBP not having the presence of CS.
- **Alternative Hypothesis (H_1):**There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on PPT scores in improving the perception of mechanical pressure pain in patients with CNSLBP having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on PPT scores in improving the perception of mechanical pressure pain in patients with CNSLBP not having the presence of CS.

3) Central Sensitization Inventory-Gujarati

- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on CSI-G scores in reducing pain sensitization in patients with CNSLBP having the presence of CS.
- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on CSI-G scores in reducing pain sensitization in patients with CNSLBP not having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on CSI-G scores in reducing pain sensitization in patients with CNSLBP having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on CSI-G scores in reducing pain sensitization in patients with CNSLBP not having the presence of CS.

4) Fear-Avoidance Beliefs Questionnaire-Gujarati

- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on FABQ-G and its subscales FABQ-W-G & FABQ-PA-G scores in reducing FABs in patients with CNSLBP having the presence of CS.
- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on FABQ-G and its subscales FABQ-W-G & FABQ-PA-G scores in reducing FABs in patients with CNSLBP not having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on FABQ-G and its subscales FABQ-W-G & FABQ-PA-G scores in reducing FABs in patients with CNSLBP having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on FABQ-G and its subscales FABQ-W-G & FABQ-PA-G scores in reducing FABs in patients with CNSLBP not having the presence of CS.

5) Roland Morris Disability Questionnaire-Gujarati

- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on RMDQ-G scores in reducing disability in patients with CNSLBP having the presence of CS.
- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on RMDQ-G scores in reducing disability in patients with CNSLBP not having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on RMDQ-G scores in reducing disability in patients with CNSLBP having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on RMDQ-G scores in reducing disability in patients with CNSLBP not having the presence of CS.

6) Trunk Flexor Endurance

- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on trunk flexors endurance scores in patients with CNSLBP having the presence of CS.
- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on trunk flexors endurance scores in patients with CNSLBP not having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on trunk flexors endurance scores in patients with CNSLBP having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on trunk flexors endurance scores in patients with CNSLBP not having the presence of CS.

7) Trunk Extensor Endurance

- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on trunk extensors endurance scores in patients with CNSLBP having the presence of CS.
- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on trunk extensors endurance scores in patients with CNSLBP not having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on trunk extensors endurance scores in patients with CNSLBP having the presence of CS.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on trunk extensors endurance scores in patients with CNSLBP not having the presence of CS.

8) Global Rate of Change Scale

- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on GROC scores in demonstrating an overall improvement in patients with CNSLBP having the presence of CS at the end of 8^{th} week.
- **Null Hypothesis (H_0):** There is no difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on GROC scores in demonstrating an overall improvement in patients with CNSLBP not having the presence of CS at the end of 8^{th} week.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on GROC scores in demonstrating an overall improvement in patients with CNSLBP having the presence of CS at the end of 8^{th} week.
- **Alternative Hypothesis (H_1):** There is a difference in the effectiveness of 'McKenzie program' and 'Conventional physiotherapy program' on GROC scores in demonstrating an overall improvement in patients with CNSLBP not having the presence of CS at the end of 8^{th} week.

3

MATERIALS AND METHODS

"We must revisit the idea that science is a methodology and not ontology."

- Deepak Chopra

3.1 Introduction

This chapter includes a detailed description of the research methodology, participants selected to participate in the study and the outcomes used in the study. The measurements obtained and the statistical procedures used in the analysis of the data were also discussed. Participants were also recruited by sending circulars to the various local hospitals and clinics in Surat. The purpose of this chapter is to describe the research, the subject recruitment process and the treatment protocol followed as well as the assessments and the type of measurements recorded.

3.2 Study Design

Research design plays a very significant role in making any research successful and reliable as it decides the fate of proposal and its outcome. The design of the study depends upon the purpose of the research, the findings of the data collection and the other needs of the research. The present study is a single-blind, randomized, controlled clinical trial with two different treatments. It is a multivariate repeated measure ANOVA design; where the subject was assessed on three occasions i.e. at the baseline before treatment, at the end of 4^{th} week and at the end of 8^{th} week.

Translation, cross-cultural adaptation, and psychometric testing design were adopted for CSI and FABQ questionnaires.

3.3 Study Population

The patients of Surat, those coming to Orthopaedic Physiotherapy department with a clinical diagnosis of Chronic Non-specific Low Back Pain, during the period of January 2015 to May 2017 were considered as the study population.

3.4 Study Setting

Orthopedic Physiotherapy Outpatient Department, Hajee A.M. Lockhat & Dr. A.M. Moolla Sarvajanik Hospital, Rampura, Surat

3.5 Study Duration

The duration of January 2014 to June 2017 includes from the inception of study to final preparation of the thesis.

3.6 Approvals and Registrations

The Institutional Ethical Committee of Nirmal Hospital Pvt. Ltd. had approved the research protocol. Subsequently, the protocol was registered retrospectively in Clinical Trial Registry of India bearing registration number CTRI/2017/007683. The Doctoral Research Committee of School of Physiotherapy, RK University periodically monitored the progress of research with a mandate to submit a report every six months to the RK University.

3.7 Sample Size and Sample Selection

The power of a statistical test is the probability that a test will reject the null hypothesis when the null hypothesis is false. That is, power reflects the probability of not committing a type II error. The two major factors affecting the power of a study are the sample size and the effect size.

The sample size was calculated from G-power-3.1.7 software [209] by using following entries in the software interface: Level of significance (α) is kept 0.05; power (1-β) = 0.8. It shows a total sample size required is 128 i.e. 64 for each group. [Two independent groups: Means: Difference between two independent means (two groups)]

The sample size was again calculated from G-power-3.1.7 software by using: Level of significance (α) is kept 0.05; power (1-β) = 0.8; effect size 0.28; the number of treatment groups were 2 and number of times measurement taken were 3. It shows a total sample size required is 126 i.e. each group gets 63 subjects. [Repeated measure: Within-between interactions, MANOVA approach] In this study, a total sample size of 128(64 for each group) was taken.

3.8 Sampling Technique

Sampling is concerned with choosing a subset of individuals from a statistical population to estimate characteristics of a whole population. In the present research, a Prospective Random Sampling was used to select and allocate CNSLBP patients to experimental and control groups.

3.9 Selection Criteria

Inclusion criteria and exclusion criteria are set of predefined characteristics used to identify subjects as the target population for a research study. Inclusion criteria should respond to the scientific objectives of the study and proper selection may optimize the validity of the study, and improve its feasibility; specifically, good selection criteria will ensure the homogeneity of the sample population and reduce confounding bias in the study.

3.9.1 Inclusion Criteria

(a) CNSLBP for three months or longer;
(b) Age between 18 and 50 years;
(c) No radiation of low back pain;
(d) Normal neurological findings of lumbosacral nerve, including deep tendon reflexes, plantar response, and voluntary muscle action, straight leg raising, and sensory function.

3.9.2 Exclusion Criteria

(a) Having systemic disease and specific conditions such as neoplasm, fractures, spondylolisthesis, spondylolysis, spinal stenosis, ankylosing spondylitis, previous low back surgery;
(b) Taking medication for specific psychological problems;
(c) Being pregnant;
(d) Receiving conflicting or ongoing co-interventions;
(e) Having nerve root related symptoms.

3.10 Tools and Materials

Model- ALGO-AN-01, Capacity 20 Kg, Units- Kg & N, Load Division value 200gm, Accuracy- ±0.5%. Orchid Scientifics, Nashik.

Figure-3.1: Pressure Algometer

3.11 Procedure of the Study

The purpose of this study was explained and a written informed consent was obtained from all the subjects. Subjects were preliminary screened based on the inclusion and exclusion criteria. Subjects were allocated into two groups, group A and group B using lottery method. As the patient turned up after fulfilling the inclusion criteria, they were given the sealed envelope containing their allotment and as per the pre-decided allotment, they went to either experimental or control group.

Descriptions of groups were as follows:

Group-A (Experimental Group): Subjects were given **McKenzie Exercise Program.**

Group-B (Control Group): Subjects were administered **Conventional Physiotherapy Program**.

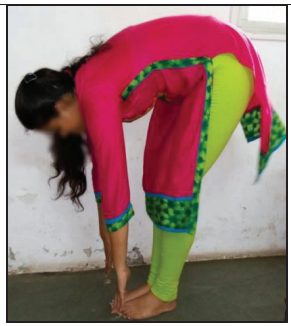
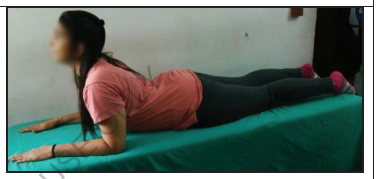
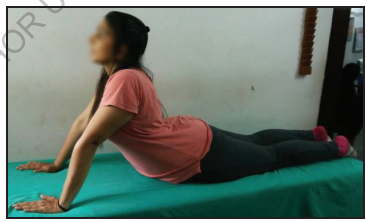
All the subjects completed demographic details and physical examination performed by the researcher. On the first day of the study, all subjects underwent a baseline assessment prior to any intervention using CSI-G, NPRS, PPT, RMDQ-G, FABQ-G, and Trunk flexors & extensors endurance. All the measurements were taken by the researcher of the study.

3.11.1 Sequence of exercises for Experimental Group (McKenzie Exercise Program)

This exercise program is illustrated here in Table-3.1.

Table-3.1: McKenzie Exercise Program

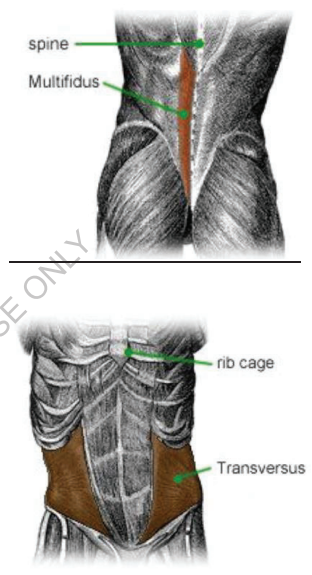
Week	*McKenzie Exercise Program* [210]	*Figure-3.2: Pictures of McKenzie Exercises* *(As and where Applicable)*
0-2 weeks	Presentation of the method, including history and general information about the McKenzie method Completion of the exercises after initial evaluation and indication of movement direction preference: flexion, extension, or lateral shift of the spine Education component: basic information about low back pain and spinal anatomy; mechanical pain; how and why to do exercises; and types of responses that can occur in response to the exercise program Guidance on completing the exercises at home	
3-4 weeks	Progression of the exercises defined after first session and progression in line with the responses of each patient Educational component: basic information about the most likely causes of low back pain, emphasizing posture when seated for a prolonged time; practice on finding the correct seated position and maintenance of lumbar lordosis while seated Guidance on continuing the exercises at home	

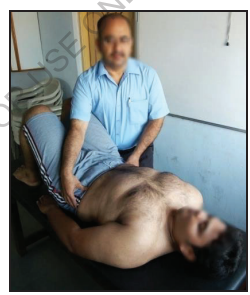
5-6 weeks	Progression of the exercises defined after second session and progression toward other position in line with the responses of the patient Educational component: basic information about the most likely causes of low back pain, emphasizing work on bending positions; standing up; relaxing after vigorous activity; remaining in standing position for prolonged periods; lying down; and resting, coughing, and sneezing Guidance on continuing the exercises at home	
7-8 weeks	Progression of the exercises defined after third session and progression toward other positions in line with the responses of the patient Educational component, review of the most important points since the first week	  

3.11.2 Sequence of exercises for Control Group (Conventional Physiotherapy Program)

This exercise program is illustrated here in Table-3.2.

Table-3.2: Conventional Physiotherapy Program

Week	*Conventional Physiotherapy Program* [211]	*Figure-3.3: Pictures of Conventional Physiotherapy Program*
0-2 weeks	**"Contracting core muscles"** The first two week's treatment is focused on educating the patient regarding the deepcore muscles which are often under-used in patients with lower back pain. Before moreactive exercises can beperformed thepatient first must have control andconfidence in activating these important core muscles. There are two main deep (core) stabilising muscles that support the lower back: the Multifidus muscle and the Transversus abdominis muscle. **Stage 1: Education** The patient is educated regarding the above coremuscles in terms of their importance for the prevention of lower back pain. **Stage 2 – Contractions** The patient lies supine with a neutral spine position and flexed knees. Physiotherapist explains how tocontract core muscles with bio-feedback (palpation). It is important that the	**"Contracting core muscles"** 

	patientunderstands that he/she should contract the coremuscles without affecting his/her breathing. The external muscles (rectus abdominus/obliques should remain relaxed). **Patient contact** : 1 hour **Home exercises** Contractions – Patient lies supine and practices contractions while using self-palpation. **Dosage** 3 x 10 contractions 2 x per day 5 days per week	
3-4 weeks	**"Endurance contractions"** The third&fourth week of treatment focuses on longerand more controlled contractions of the core muscles. The patient also graduates to contracting his/her core muscles in different positions. **Stage 1 – Education** The physiotherapist explains the importance of core muscles in regards to posture and endurance. **Stage 2 – Endurance contractions** Starting in asupine position the patient practicesholding the contractions for 10 seconds, then 20 seconds, then 30 seconds until a contraction of up to 5 minutes is possible. **Stage 3 – Endurance**	**"Endurance contractions"**  

	contractions in postures and movements Once the patient has mastered the contractions over a long time period he/she can practice holding them in postures such as sitting, kneeling, on hands and knees and standing. Further to this the patient cantry to hold the contractions throughout ADL movements such as sitting at a computer or getting out of a car. **Patient contact** : 1 hour **Home exercises** Endurance contractions – supine, sitting, kneeling, standing and then in ADL movements. **Dosage** 3 x 10 x 1 minute contractions in each position and ADL movement. 1 x per day for 5 days.	
5-6 weeks	**"Stability contractions"** The essence of all core muscle training is to increase both endurance and stability in the trunk and spine in order to provide a more stable base for arm and leg movements. Therefore week 5& 6 is to introduce active movements of the arms and legs whilst holding the core in a contracted state. All exercises should be completed in a slow, controlled manner with little movement of the pelvic girdle.	**"Stability contractions"**   **Bridging**

Below is a toolkit of exercises to be used by the physiotherapist.

Stage 1 – Education

The physiotherapist explains the importance of core muscles in regards to trunk/spine stability and arm/leg movements.

Stage 2 – Stability contractions

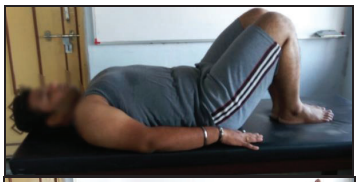
Exercise 1 – Bridging

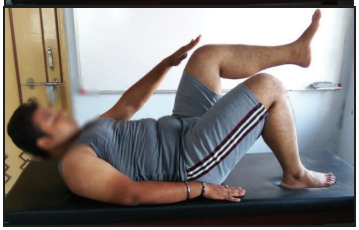
Patient lies supine with knees flexed and arms by his/her side. Core muscles are contracted simultaneously with gluteal muscles and the patient lifts trunk upwards until spine is in neutral position. The position is held for 3 deep breaths or 10 seconds.

Exercise 2 - Leg slides

Patientlies supine with knees flexed and arms by his/her side. Core muscles are contracted and the patient slowly slides one leg along the floor (extension) until the back of the knee is 5cm from the floor before returning the leg to the previous position. This is repeated using the other leg.

Exercise 3 – Single leg & arm raises





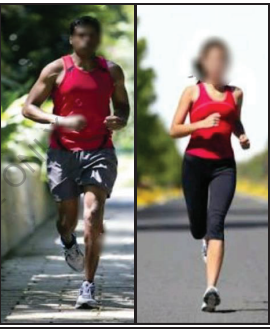
Single leg and arm raise

Quadruped

Segmental Rotation

	Patient lies supine with a neutral spine and, after contracting the core muscles, raises one leg so that the knee joint is at 90 degrees. He/she then raises the arm on the same side to touch the knee. Both limbs are then slowly returned to their starting position. This is repeated with the other leg and arm and then, as a next step, opposing leg and arm raises can be tried. Patient is on hands and knees with a neutral spine position. Core muscles are contracted and patient raises right arm to be parallel with the floor. The patient then stretches the arm away from him/her and holds it there for 3 deep breaths. This is repeated for all 4 limbs. The next level is to rise opposite limbs (e.g. right leg and left arm). Patient lies supine with a neutral spine and legs flexed. Core muscles are contracted and the patient slowly rotates his/her legs to the left (A) until a slight stretch is felt. The position is held for 3 deep breaths and then the knees are returned to the starting position. The exercise is then repeated to the right side (B).	

	Patient contact : 1 hour **Home exercises** The exercises prescribed along with the dosage will depend on the patient's individual capacity to complete the exercises during the one hour contact with the physiotherapist. A dosage example is given below upon which each physiotherapist may base their treatment. **Dosage** Exercise 1 – Bridging: 3 x 10 second holds 3 x per day x 5 days Exercise 2 – Leg Slide: 1 set of 10 slides per leg 3 x per day 5 days per week Exercise 3 - Single Leg & Arm Raises: 1 set 10 raises each side (+ opposite limbs); 3 x per day 5 days per week Exercise 4 - "Quadriped": 1 set 10 raises each side (+ opposite limbs); 3 x per day 5 days per week Exercise 5 – Segmental Rotation: 1 set 10 rotations to each side 3 x per day	
7-8 weeks	**"Stability contractions & ADL training"** The final week of treatment will involve continued use of the toolkit of exercises described in Week 5&6 as well as specific functional training on those ADL movements which have	

	previously given the patient the most problems. For example, if the patient has trouble lifting from floor level, the physiotherapist will educate and assist the patient in breaking down the movement to see how it can be improved or adjusted in order to avoid pain.	 

All the 128 subjects received McKenzie exercise program or conventional physiotherapy for 45-60 minutes with 2-minute rest between two different exercises. The researcher had practiced enough before doing it on the subjects. All exercises were done 5 days a week for 8 weeks under supervision of a physiotherapist. The exercises were progressed as per given protocol as above.

Subjects of both the groups were instructed to discontinue if they had any form of discomfort during the procedure but none of them reported any adverse reactions. All the subjects were advised not to participate in any other physical program during the study, to remain as active as possible and to avoid aggravating activities such as sustained positions for longer than 15 minutes. Reassessments for both groups were taken post-treatment at the end of 4^{th} week and 8^{th}week. All procedures were conducted in accordance with the Declaration of Helsinki.

3.12 Outcome Tools

- Central Sensitization Inventory – Gujarati (CSI-G)
- Numeric pain rating scale (NPRS) form
- Pain Pressure Threshold (PPT)
- Roland-Morris Disability Questionnaire - Gujarati version (RMDQ-G)
- Fear Avoidance Beliefs Questionnaire - Gujarati version (FABQ-G)
- Trunk Flexors and Extensors Endurance
- Global Rate of Change Scale (GROC)

(a) Central Sensitization Inventory-Gujarati (CSI-G):

Tom G. Mayer et al [212]developed the Central Sensitization Inventory (CSI), which identifies key symptoms associated with Central Sensitivity Syndromes, and quantifies the degree of these symptoms. The utility of the CSI, to differentiate among different types of chronic pain patients that presumably have different levels of CS impairment, was then evaluated. Their studies demonstrated the psychometric strength, clinical utility, and the initial construct validity of the CSI in evaluating CS-related clinical symptoms in chronic pain populations. Neblett Randy et al [213]in their study found that CSI have high reliability and validity (test-retest reliability = 0.82; Cronbach's alpha = 0.88). Neblett Randy et al [129]in analyses of their study revealed that the patients with FM reported the highest CSI scores and the normative population the lowest ($P < 0.05$). Analyses also demonstrated that the prevalence of previously diagnosed CSSs and related disorders was highest in the FM group and lowest in the normative group ($P < 0.001$). Taken together, these 2 studies demonstrate the psychometric strength, clinical utility, and the initial construct validity of the CSI in evaluating CS-related clinical symptoms in chronic pain populations.

The clinical goal of this CSI is to help better assess symptoms thought to be associated with CS in order to aid clinicians in syndrome categorization, sensitivity, severity identification, and treatment planning, to help minimize, or possibly avoid unnecessary diagnostics and treatment procedures. Neblett R *et al* determined that a CSI score of 40 out of 100 best distinguished between the CSS patient group and a non-patient comparison sample (N=129) [213].

(b) Numeric pain rating scale (NPRS):

The intensity of back pain was assessed with NPRS. Using an 11–point scale, ranging from 0 (no pain) to 10 (worst pain imaginable), subjects were asked to answer the following question: on a scale 0 to 10, where 0 corresponds to no pain and 10 to the worst imaginable pain, select the single number that best represents your pain intensity. The scale has been shown to have adequate reliability, validity, and responsiveness in patients with CLBP [214].

(c) Pain Pressure Threshold (PPT):

Objective measures of sensory changes through quantitative sensory testing (i.e. pressure algometry) may help identify central sensitization of nociceptive pathways in CLBP population [215-218]. Pressure stimuli were measured using a handheld digital algometer (Orchid Scientifics, Nashik). A pain detection threshold was measured on the Infraspinatus muscle and Tibialis anterior muscle. The pressure was increased at a rate of approximately 1 Kg/s. Subjects had to report when the feeling of pressure alone changed into a feeling of pressure and pain (Pain Detection Threshold). The mean of two measurements, taken 30seconds apart from each other, was used.

(d) Roland-Morris disability questionnaire - Gujarati version (RMDQ-G):

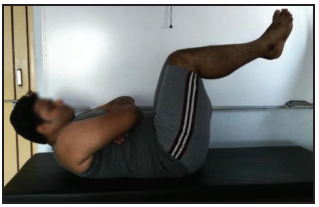
The RMDQ is a disability measure in which greater levels of disability are reflected by higher numbers on a 24-point YES/NO scale[219]. Patients were asked to place a check mark beside a statement if it applies to them. Disability score for each patient was determined as the total of items checked. The degree of disability is scaled with RMDQ score as 0-8 for minimal disability, 9-16 for moderate disability and 17-24 for significant disability. The RMDQ-G has shown to have good internal and external validity, as well as adequate internal consistency [219, 220].

(e) Fear-Avoidance Beliefs Questionnaire – Gujarati version (FABQ-G):

FABQ was developed by Waddell *et al*[221] to measure fear-avoidance beliefs in LBP patients. It is a 16-item, self-reporting questionnaire, in which each item is graded on a 7-point Likert scale strongly disagree to strongly agree. The FABQ score is calculated by adding up individual item scores. A higher total score indicates a higher level of fear avoidance beliefs. The FABQ has demonstrated high levels of

internal consistency (Cronbach's alpha= 0.88) and test-retest reliability (r= 0.95) [221]. For ease the use, the original FABQ is translated and validated by the researcher for Gujarati speaking subjects with CLBP[222].

(f) Trunk Flexors and Extensors Endurance:



(A)

(B)

Figure-3.4: (A) Trunk Flexors Endurance Test (B) Trunk Extensors Endurance Test

Flexor Endurance test: For evaluating flexor endurance, subjects were asked to lie in a supine position and to raise the lower extremities with 90° flexion of the hip and knee joint. The subject is asked to maintain maximal flexion of the cervical spine, pelvic stability being maintained through gluteal muscle contraction. The subject is asked to maintain this position for as long as possible, to a maximum of 300 seconds (Figure-3.4 (A)). Endurance time (in seconds) is recorded by an examiner [223].

Extensor Endurance test: The subject is placed prone with the legs extended while holding the sternum off the floor. A small pillow is placed under the lower abdomen to decrease the lumbar lordosis. The subject is asked to maintain maximal flexion of the cervical spine, pelvic stability being maintained through gluteal muscle contraction. The subject is asked to maintain this position for as long as possible, to a maximum of 300 seconds (Figure-3.4 (B)). Endurance time (in seconds) is recorded by an examiner (extensor endurance test) [223].

(g) Global Rate of Change Scale:

The 11-point GROC has been shown to be responsive with an MCID of 2 points [224]. This outcome is used as post-test only.

3.13Cross-Cultural Adaptation of Gujarati Version of CSI

3.13.1 The CSI-G Questionnaire

The CSI-G contains a Part-A of 25 statements related to current health symptoms. Each of these items is measured on a 5-point temporal Likert scale, with the following numeric rating scale: never (0), rarely (1), sometimes (2), often (3), and always (4). A cumulative score ranges from 0 to 100. Additionally, information is collected in Part-B on previously diagnosed CS and related conditions.

3.13.2 Translation of CSI

A written letter of permission for cross-cultural adaptation of CSI-G and to assess reliability and validity of its Gujarati version was obtained from the original author and was sanctioned by the study guide. Guidelines proposed by Beaton and Guillemin were followed [225].

Stage 1: Forward translation (English to Gujarati) Two bilingual translators whose mother tongue was Gujarati, one of medical background and was aware of the concepts and other was unaware of the translation objectives with no medical background and this was useful in eliciting unexpected meanings from the original tool, translated CSI from English to Gujarati. This stage evolved two forward translations T1 and T2.

Stage 2: Working from the original questionnaire as well as the first translator's (T1) and the second translator's (T2) versions, **Synthesis** of T1 and T2 were done by resolving discrepancies after a reconciliation meeting between two translators leading to common translation - T-12.

Stage 3: Back translation (Gujarati to English) of the version T-12 was done by two English speaking professional back translators (BT 1 and BT 2) blinded to the original version, to identify inconsistencies in the words and concepts of the synthesized version. The back-translated and the Gujarati versions were revised by translators and investigators accordingly until consensus was reached.

Stage 4: Expert committee review consisted of all the translators, language professional and researchers, who after resolving all sorts of incongruities or

obscurities established a pre-final version (Gujarati) after consensus were reached.

Stage 5: 20 Gujarati speaking CLBP patients, were asked about their understanding of each questionnaire item and give feedback. All of the findings were re-evaluated by the expert committee, but none of the items were modified because of difficulties in comprehension.

The translation procedures were based on previously published guidelines [225, 226]. Figure-3.5 shows the steps in the process of translation. The committee's considerations were around four areas: semantic equivalence (the meaning of words), idiomatic equivalence (equivalent expression for idioms and colloquialisms), experiential equivalence (the target cultural context), and conceptual equivalence (the validity of the concept).

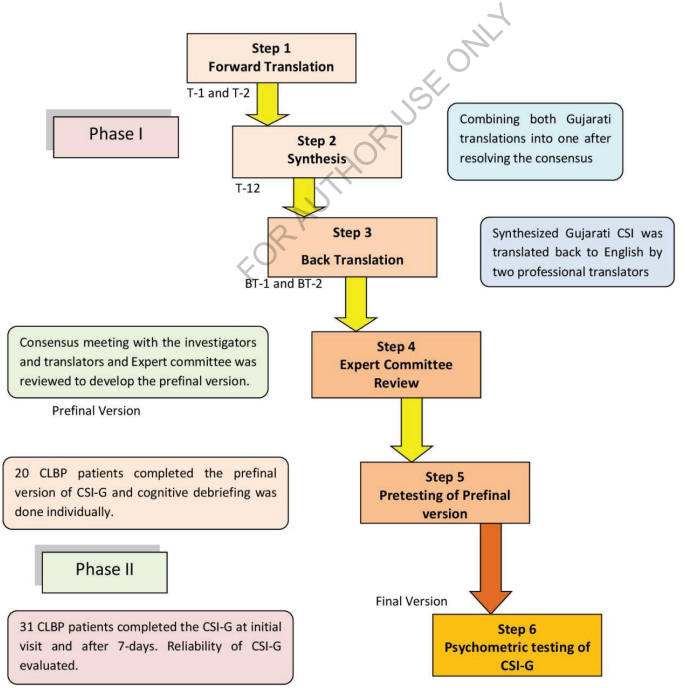


Figure-3.5: Flowchart of the study design of CSI-G

3.13.3 Content Validity of CSI-G

Content validity was evaluated through review criteria given by McKenzie *et al*[227]. Twenty-three health care professionals were approached consisting of experienced Spine Surgeons, Orthopaedic Surgeons, Neurologists, Psychiatrists, Physicians and Physiotherapy Lecturers with mean experience of 15±8.56 years in the field of Low back pain. Nature and purpose of the study were explained to the professionals and informed written consent was obtained from all professionals along with self-filled professional information. Each professional was contacted personally for their expert opinion and was asked to complete an evaluation form to rate the content equivalence, relevance and representativeness of each item in the Gujarati version of CSI on a 7-point Likert scale from strongly disagree to strongly agree.

3.13.4 Test-Retest Reliability of CSI-G

Thirty-one patients[228] aged 30 to 65 years of both genders and who were diagnosed of CNSLBP by an orthopaedic surgeon and were able to read and write Gujarati were included in the study as they turned up to the various physiotherapy departments of Surat city and after being thoroughly informed about the procedure were recruited taking their written consent. Exclusion criteria were infections, low back surgery, malignancy, cardiovascular or respiratory problem, pregnancy, and menstruation during testing days, the presence of any systemic disease, communication problems, and cognitive impairment. CSI-G was collected for each patient 2 two times with an intermediate interval of 7-days to allow wash out the memory of response given[221].No significant physiotherapy treatment was given during this time interval.

3.13.5 Construct Validity of CSI-G

Construct validity is frequently measured as convergent and divergent validity and factor analysis. In this study, convergent validity was evaluated by parallel questionnaires FABQ-G, RMDQ-G. Besides this pain pressure threshold and NPRS also support the concept of the convergent validity in this study. Divergent validity was tested by Pearson correlation coefficients by showing that the CSI-G measurement concept is different from the measurement concept of trunk flexors

endurance and trunk extensor endurance. In addition, factor analysis was done for construct validity.

Construct validity was assessed by calculating Pearson's correlation coefficients (r)[229] comparing the extent to which expected relationships between the various constructswere fulfilled using the CSI-G. Expected relationships were based on the literature. The **r values** yield the degree of correlation between two measures where 0= no correlation between two scores and 1 or –1 = the absolute correlation between two scores.

Pearson's correlation coefficients are interpreted as follows: 0.00 to 0.19 = very weak correlation;0.20 to 0.39 = weak correlation; 0.40 to 0.69 = moderate correlation; 0.70 to 0.89 = strong correlation; and 0.90 to 1 =very strong correlation [230, 231].

Based on previous studies with similar objectives and our clinical experience we hypothesized the following relationships between the various constructs a priori:

1. CSI-G and FABQ-G would have a high correlation.
2. CSI-G and PPT-IS & PPT-TA would have a high correlation.
3. NPRS would have moderate to high correlations with CSI-G.
4. CSI-G and RMDQ-G would have moderate to high correlations.
5. CSI-G and trunk flexors & extensors endurance would have low to a negative correlation.

3.13.6 Factor Analysis of CSI-G

A principal component analysis[232, 233] was run to establish construct validity of the items in the scale. The acceptable level of communalities and factor loadings for items would be 0.5 and Eigenvalue more than one would be considered for component factors. An item analysis was done to check the reliability of the scale components and its Cronbach's alpha. For the data reduction the following norms were considered: Principal component analysis, Varimax rotation, Communalities >0.5, Factor loading >0.5 (as the study sample size is more than120), Sample size 128, KMO/MSA >0.45, Anti-image correlation matrix >0.45, Correlation matrix >30% and Eigenvalue>1.

3.14 Cross-Cultural Adaptation of Gujarati Version of FABQ

3.14.1 FABQ-G Questionnaire

The FABQ-G with two subscales Fear Avoidance Belief Questionnaire-Work (FABQ-G-W) and Fear Avoidance Belief Questionnaire-Physical activity (FABQ-G-PA) was used for data collection.

3.14.2 Translation of FABQ

A written letter of permission for cross-cultural adaptation of FABQ and to assess reliability and validity of its Gujarati version was obtained from the original author, Gordon Waddell Orthopaedic Department, Scotland (UK) and was sanctioned by the study guide. Guidelines proposed by Beaton and Guillemin were followed [225]. These steps were carried out by a person who was not the part of the study.

Stage 1: Forward translation (English to Gujarati) Two bilingual translators whose mother tongue was Gujarati, one of medical background and was aware of the concepts and other was unaware of the translation objectives with no medical background and this was useful in eliciting unexpected meanings from the original tool, translated FABQ from English to Gujarati. This stage evolved two forward translations T1 and T2.

Stage 2: Working from the original questionnaire as well as the first translator's (T1) and the second translator's (T2) versions, **Synthesis** of T1 and T2 were done by resolving discrepancies after a reconciliation meeting between two translators leading to common translation - T-12.

Stage 3: Back translation (Gujarati to English) of the version T-12 was done by two English speaking professional back translators (BT 1 and BT 2) blinded to the original version, to identify inconsistencies in the words and concepts of the synthesized version. The back-translated and the Gujarati versions were revised by translators and investigators accordingly until consensus was reached.

Stage 4: Expert committee review consisted of all the translators, language professional and researchers, who after resolving all sorts of incongruities or obscurities established a pre-final version (Gujarati) after consensus were reached.

Stage 5: 20 Gujarati speaking CLBP patients, were asked about their understanding of each questionnaire item and give feedback. All of the findings were re-evaluated by the expert committee, but none of the items were modified because of difficulties in comprehension.

The translation procedures were based on previously published guidelines [225, 226]. Figure-3.6 shows the steps in the process of translation. The committee's considerations were around four areas: semantic equivalence (the meaning of words), idiomatic equivalence (equivalent expression for idioms and colloquialisms), experiential equivalence (the target cultural context), and conceptual equivalence (the validity of the concept). In FABQ-G item number-8 (I have a claim for compensation for my pain) is omitted because in India no such compensation exists. Hence FABQ-G is having 15 items as against 16 items in original English version. Penultimate version of the FABQ-G questionnaire was applied on 20 patients with CLBP to determine whether all questions were clear and comprehensible. No modification to the questionnaire was required at this phase and the final FABQ-G was then developed and subjected to further psychometric testing.

3.14.3 Content Validity of FABQ-G

Content validity was evaluated through review criteria given by McKenzie *et al*[227]. Twenty professionals were approached consisting of experienced Spine surgeons, Orthopaedics, Neurologists, Psychiatrists, Physicians and Physiotherapy Lecturers with mean experience of 11±7.56 years in the field of Low back pain. Nature and purpose of the study were explained to the professionals and informed written consent was obtained from all professionals along with self- filled professional information. Each professional was contacted personally for their expert opinion and was asked to complete an evaluation form to rate the content equivalence, relevance and representativeness of each item in the Gujarati version of FABQ on a 7-point Likert scale from 'strongly disagree' to 'strongly agree'.

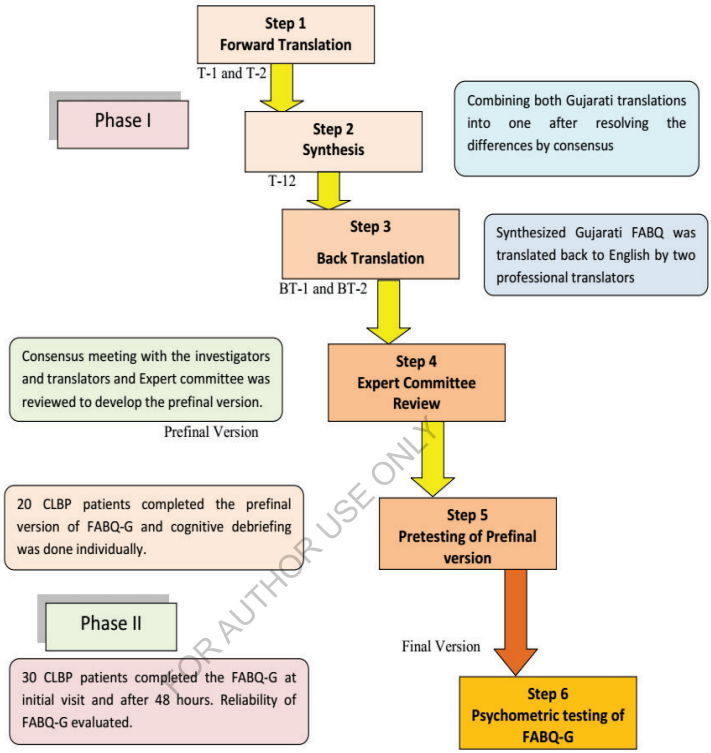


Figure-3.6: Flowchart of the Study Design of FABQ-G

3.14.4 Test-Retest Reliability of FABQ-G

Thirty patients [228] aged 20 to 60 of both genders and who were diagnosed of CLBP with or without radiation symptoms by an orthopaedic and were able to read and write Gujarati were included in the study as they turned up to the various physiotherapy departments of Surat city and after being thoroughly informed about the procedure were recruited taking their written consent. Exclusion criteria were infections, low back surgery, malignancy, cardiovascular or respiratory problem, pregnancy, and menstruation during testing days, the presence of any systemic

disease, communication problems, and cognitive impairment. FABQ-G was collected for each patient two times with an intermediate interval of 48 hours [221].No active or significant physiotherapy treatment was given during this time interval.

3.14.5 Construct Validity of FABQ-G

Construct validity is frequently measured as convergent and divergent validity and factor analysis. In this study, convergent validity was evaluated by a parallel questionnaire CSI-G and RMDQ-G. Besides these, PPT and NPRS measurement also support convergent validity of FABQ-G. Divergent validity was tested by Pearson correlation coefficients by showing that the FABQ-G measurement concept is different from the measurement concept of trunk flexors and extensors endurance. In addition, factor analysis was done for construct validity.

Construct validity was assessed by calculating Pearson's correlation coefficients (r)[229] comparing the extent to which expected relationships between the various constructs were fulfilled using the FABQ-G. All the expected relationships were based on the literature. The **r values** yield the degree of correlation between two measures where 0= no correlation between two scores and 1 or –1 = the absolute correlation between two scores.

Pearson's correlation coefficients are interpreted as follows: 0.00 to 0.19 = very weak correlation;0.20 to 0.39 = weak correlation; 0.40 to 0.69 = moderate correlation; 0.70 to 0.89 = strong correlation; and 0.90 to 1 =very strong correlation [230, 231].

Based on previous studies with similar objectives and our clinical experience we hypothesized the following relationships between the various constructs a priori:

1. FABQ-G and CSI-G would have a high correlation.
2. FABQ-G and PPT-IS & PPT-TA would have moderate to high correlation.
3. NPRS would have moderate to high correlations with FABQ-G.
4. FABQ-G and RMDQ-G would have moderate to high correlations.
5. FABQ-G and trunk flexors & extensors endurance would have low to a negative correlation.

3.14.6 Factor Analysis of FABQ-G

A principal component analysis [232, 233] was run to establish construct validity of the items in the scale. The acceptable level of communalities and factor loadings for items would be 0.5 and Eigenvalue more than one would be considered for component factors. An item analysis was done to check the reliability of the scale components and its Cronbach's alpha. For the data reduction the following norms were considered: Principal component analysis, Varimax rotation, Communalities >0.5, Factor loading >0.5 (as the study sample size is more than 120), Sample size 128, KMO/MSA >0.45, Anti-image correlation matrix >0.45, Correlation matrix >30% and Eigenvalue>1.

4

RESULTS

"If I could, I would always work in silence and obscurity,

and let my efforts be known by their results."

-Emile Bronte

Statistical analysis is a component of research which involves collecting and scrutinizing every data sample. A sample, in statistics, is a representative selection drawn from a total population. Statistical analysis can describe the nature of the data and explore how the data relates to the underlying population. This may create a valid model to predict scenarios that will help guide future actions. This chapter includes a detailed description of the participants selected to participate in the study and the outcomes used in the study. The measurements obtained and the statistical procedures used in the analysis of the data were also discussed. Participants were also recruited by sending circulars to the various local hospitals and clinics in Surat. This chapter presents the outcome of the analysis of the data. The results appearing as non-significant have been presented in the text only, and no tables and graphs are given for such results. It is a single-blind, randomized, controlled clinical trial with two different treatments. The analyses follow the design of the study as described in chapter 1, i.e. a multivariate repeated measure ANOVA design.

4.1 Statistical Analysis and Results for Cross-cultural Adaptation of CSI-G Study

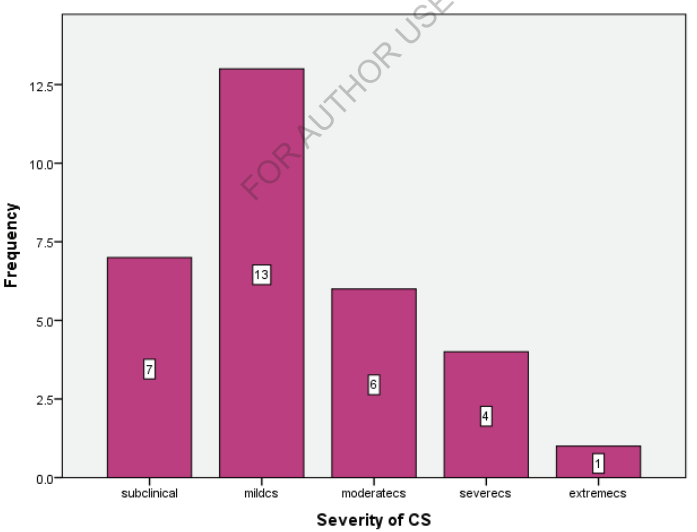
4.1.1 Statistical Analyses of CSI-G Questionnaire Study

Internal consistency of the CSI-G was examined with Cronbach's α coefficient. Cronbach's α values range from 0 to 1, where values above 0.7 indicate adequate internal consistency for a scale [234]. Intra-class correlation coefficients (ICC, model two-way random, type absolute agreement) were calculated for examining the test-retest reliability. The ICC values ranges from 0 to 1; 1= perfect reliability, 0.90 to 0.99 = very high correlation; 0.70 to 0.89 = high correlation; 0.50 to 0.69 = moderate correlation; 0.26 to 0.49 = low correlation and 0.00 to 0.25 =little, if any, reliability [235]. The agreement was determined by the Bland-Altman method in which the individual differences were plotted against the individual mean scores. The

significance level was set at 5%[236]. The standard error of measurement (SEM=Average SD x √1-ICC) was used to determine the measurement error. The SEM was then converted into the Minimal Detectable Change (MDC), which expresses the minimal magnitude of change that likely reflects true change rather than measurement error. The $MDC_{95\%}$ was estimated from the SEM and calculated as 1.96 √2 × SEM[237].

4.1.2 Results of CSI-G Questionnaire Study

The present study used 31 CLBP patients. From this sample, 23 subjects were females (74.2%) and 8 subjects were males (25.8%). The mean age was 52.77(±13.20) years. The severity level of CS in those patients as described by Neblett Randy et al [238] is shown in this bar graph (Graph-4.1) which describes five categories of CSI severity ranging from Subclinical (0-29), Mild (30-39), Moderate (40-49), Severe (50-59) and Extreme (60-100) and the CSI-G item wise score distribution for all the 25 items with range, SD and mean is shown in Graph-4.1.



Graph-4.1: Distribution of CSI-G scores in the sample depicting severity of CS

4.1.2.1 Internal Consistency

Internal consistent is an assessment of how reliable test items that are designed to measure the same construct actually do so. A construct is an underlying theme, characteristic, or skill. A high degree of internal consistency indicates that items meant to assess the same construct yield similar scores. There are a variety of internal consistency measures. Usually, they involve determining how highly these items are correlated and how well they predict each other. Cronbach's alpha is one commonly used measure. To use internal consistency measures, items usually should be in a single measurement instrument and administered to a group of people on one occasion in order to avoid confounding variables. Internal consistency is usually measured with Cronbach's alpha, a statistic calculated from the pairwise correlations between items. Internal consistency ranges between negative infinity and one. A commonly accepted rule of thumb for describing internal consistency is as follows [239]:

Table-4.1: Interpretation of Cronbach's Alpha

Cronbach's Alpha	Internal Consistency
α ≥ 0.9	Excellent
0.9 > α ≥ 0.8	Good
0.8 > α ≥ 0.7	Acceptable
0.7 > α ≥ 0.6	Questionable
0.6 > α ≥ 0.5	Poor
0.5 > α	Unacceptable

CSI-G exhibited excellent internal consistency shown by a Cronbach's α value of 0.914.

4.1.2.2 Test-Retest Reliability of CSI-G

The CSI-G was filled out twice by 31 CLBP patients. The CSI-G mean total scores of the first and second assessment were, respectively, 44.16(± 13.8) and 43.96 (± 13.2).

The ICC in the CLBP patients, based on the total scores of the first and second assessment, was 0.971 (ICC 2,1; 95% CI = 0.941–0.986; p<0.001).An analysis of

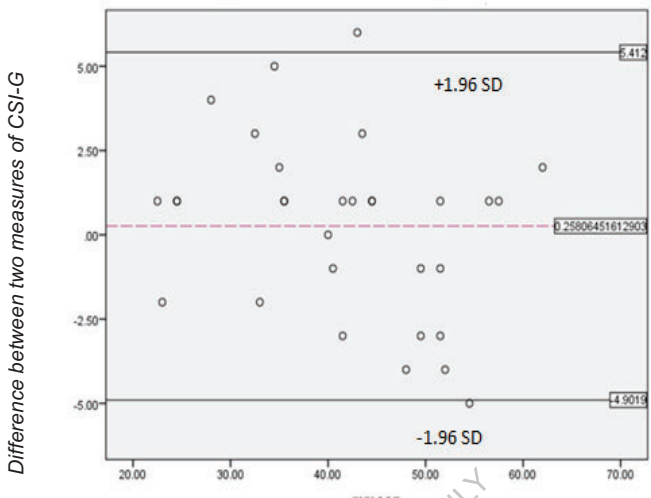
individual item scores revealed that 24 out of 25 items showed an ICC >0.85 (range 0.852–0.993) except item number 10 (ICC 2,1; 0.662; p<0.001).

Table-4.2: Test-Retest Item-wise Correlation 'r' Of CSI-G

Item No.	'r'- value	Item No.	'r'- value
1	0.991	14	0.962
2	0.985	15	0.915
3	0.981	16	0.986
4	0.981	17	0.962
5	0.992	18	0.960
6	0.947	19	0.696
7	0.988	20	0.852
8	0.993	21	0.982
9	0.871	22	0.983
10	0.662	23	0.986
11	0.988	24	0.965
12	0.985	25	0.926
13	0.868	------	------

4.1.2.3 Limits of Agreement of CSI-G Scores

The Bland-Altman Plot (Graph-4.2) shows the difference in total scores against the mean total scores for both the CLBP patients. The mean difference approached zero, indicating that no bias had occurred. In CLBP patients, one outlier was seen outside the 95% CI band. The Bland-Altman analysis showed that the mean difference was 0.258±2.632 for the CSI-G.



Graph-4.2: Bland-Altman Plot for measuring with-in subject variation and the limits of agreement of CSI-G scores

4.1.2.4 SEM and MDC Calculation for CSI-G

The SEM is a measure of precision and a reliability measure that assesses response stability as a standard error in a set of repeated scores. The MDC, a statistical estimate is the minimum amount of change in a patient's score which isn't due to the result of measurement error. The SEM for the CSI-G was 1.837.Calculations revealed an MDC of 5.092 points for CSI-G (scale range = 0–100).

4.1.2.5 Construct Validity of CSI-G

Construct validity is considered an overarching term to assess the measurement procedure used to measure a given construct because it incorporates a number of other forms of validity (i.e., content validity, convergent and divergent validity, and criterion validity) that help in the assessment of such construct validity.

The CSI-G total score was significantly positively correlated with FABQ-G, PPT-IS, PPT-TA, and RMDQ-G, but there were negative correlations obtained for trunk flexors and extensors endurance with CSI-G (Table-4.3).

Table-4.3: Correlation between various constructs (N=128) with CSI-G

	NPRS Base-line	PPT-IS Base-line	PPT-TA Base-line	CSI Base-line Total	RMDQ Base-line Total	FABQ Total Base-line	Trunk Extensors Endurance Baseline	Trunk Flexors Endurance Baseline
NPRS	1	0.014	-0.020	0.081	0.441**	0.172	-0.031	-0.029
Baseline		0.879	0.819	0.362	0.000	0.053	0.727	0.746
PPT-IS		1	0.497**	-0.107	-0.065	-0.125	0.374**	0.338**
Baseline			0.000	0.229	0.469	0.158	0.000	0.000
PPT-TA			1	0.172*	0.291**	0.123	0.325**	0.099
Baseline				0.045	0.001	0.168	0.000	0.265
CSI				1	0.527**	0.455**	-0.171*	-0.273**
Baseline Total					0.000	0.000	0.045	0.002
RMDQ					1	0.514**	-0.073	-0.229**
Baseline Total						0.000	0.410	0.009
FABQ Total						1	-0.137	-0.266**
Baseline							0.124	0.002
Trunk							1	0.851**
Extensors								0.000
Endurance								
Baseline								
Trunk Flexors								1
Endurance								
Baseline								

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

4.1.2.6 Factorial Validity of CSI-G

The results of factor analyses (N=128) of the 25 items of the CSI-G are presented in Table-4.4. The initial analysis considering factors more than one Eigenvalue produced a six-factor solution with 69.65% total variance in the principal component analysis with varimax rotation.

Table-4.4: Varimax Rotated Factor Loading Matrix of the CSI-G

Items	Factor-1	Factor-2	Factor-3	Factor-4	Factor-5	Factor-6
CSI-G_Q1			0.573			
CSI-G _Q2	0.721					
CSI-G _Q3	0.539					
CSI-G _Q4	0.455					
CSI-G _Q5				0.840		
CSI-G _Q6	0.702					
CSI-G _Q7		0.808				
CSI-G _Q8	0.592					
CSI-G _Q9	0.548					
CSI-G _Q10				0.619		
CSI-G _Q11		0.620				
CSI-G _Q12			0.698			
CSI-G _Q13			0.848			
CSI-G _Q14						0.567
CSI-G _Q15				0.529		
CSI-G _Q16	0.653					
CSI-G _Q17	0.772					
CSI-G_Q18	0.804					
CSI-G_Q19						0.804
CSI-G_Q20		0.768				
CSI-G_Q21		0.580				
CSI-G_Q22		0.670				
CSI-G_Q23			0.476			
CSI-G_Q24					0.833	
CSI-G_Q25	0.441					
% of total variance explained	19.25%	13.56%	12.80%	11.55%	6.72%	9.96%

Factor loading of 0.4 or more was displayed here.

Table-4.5 shows the results of item analysis for the sixfactors derived with their respective items of the CSI-G questionnaire and its internal consistency (Cronbach's Alpha).

Table-4.5: Internal consistency of CSI-G Factors with items

Factors	Items Included	Cronbach's Alpha
Factor-1	2, 3, 4, 6, 8, 9, 16, 17 & 18	0.912
Factor-2	7, 11, 20, 21, 22, & 25	0.773
Factor-3	1, 12, 13, & 23	0.782
Factor-4	5, 10, & 15	0.728
Factor-5	24	NA
Factor-6	14, & 19	0.348

4.2 Statistical Analyses and Results for Cross-cultural Adaptation of FABQ-G Study

4.2.1 Statistical Analyses of FABQ-G Questionnaire Study

Descriptive statistics (percentages, means, and standard deviations) were used to describe demographic characteristics within the study. All analyses of reliability and validity described in the research methods were conducted using SPSS statistical package (version 20.0) with 95% confidence interval (CI) limits. As proposed by Waddell et al [221] the score of each FABQ-G subscale was analyzed independently. Seven of the 11 items (item: 6, 7, 9–12, and 15) in the FABQ-G-W subscale and 4 of the 5 items (item: 2–5) in the FABQ-G-PA subscale were summed up to reach total scores (42 and 24, respectively). The five remaining questions were used as delusive items [221].

The translation procedures were based on previously published guidelines [225, 226]. Figure-3.6 shows the steps in the process of translation. The committee's considerations were around four areas: semantic equivalence (the meaning of words), idiomatic equivalence (equivalent expression for idioms and colloquialisms), experiential equivalence (the target cultural context), and conceptual equivalence (the validity of the concept). In FABQ-G item number-8 (I have a claim for compensation for my pain) is omitted because in India no such compensation exists. Hence FABQ-G is having 15 items as against 16 items in original English version. Penultimate version of the FABQ-G questionnaire was applied on 20 patients with CLBP to determine whether all questions were clear and comprehensible. No modification to the questionnaire was required at this phase and the final FABQ-G was then developed and subjected to further psychometric testing.

ICCs were calculated for examining the test-retest reliability. A Bland-Altman plot was constructed in which the *individual* differences were plotted against the individual mean scores. Significance level was set at 5%. The ICC values ranges from 0 to 1; 1 = perfect reliability, 0.90 to 0.99 = very high correlation; 0.70 to 0.89 = high correlation; 0.50 to 0.69 = moderate correlation; 0.26 to 0.49 = low correlation and 0.00 to 0.25 =little, if any, reliability [235].

4.2.2 Results of FABQ-G Questionnaire Study

The FABQ-G was filled out twice by 30 CLBP patients. From this sample, 19 subjects were females (63.3%) and 11 subjects were males (36.7%). The mean age was 41.8 (± 11.36) years (range 21-59 years).

4.2.2.1 Internal Consistency of FABQ-G

FABQ-G exhibited excellent internal consistency shown by a Cronbach's α value of 0.843 with scale mean 66.66±5.60 (Table-4.6).

Table-4.6: FABQ-G scores at baseline and after 48 hours (n=30)

Score	FABQ-G at Baseline			FABQ-G at Retest		
	Mean (SD)	Range	Cronbach's α (CI)	Mean (SD)	Range	Cronbach's α (CI)
FABQ-G (Total)	66.66 (5.60)	57-77	0.843 (0.747-0.914)	67.00 (5.9)	55-78	0.846 (0.752-0.916)
FABQ-G-W	32.20 (2.68)	27-37	0.652 (0.422-0.813)	32.00 (2.71)	26-36	0.583 (0.306-0.776)
FABQ-G-PA	20.63 (1.88)	17-23	0.654 (0.355-0.819)	21.10 (1.66)	17-24	0.594 (0.290-0.788)

4.2.2.2 Test-Retest Reliability of FABQ-G

The FABQ-G mean total scores of the first and second assessment were 66.66(±5.6) and 67.00 (±5.9). The ICC in the CLBP patients, based on the total scores of the first and second assessment, was 0.915 (ICC (2,1); 95% CI = 0.823–0.960; p<0.001). The test-retest reliability of the questionnaire was also high with an ICC (2,1) of 0.864 for the FABQ-G-W and of 0.818 for the FABQ-G-PA (Table-4.7).

Table-4.7: Reliability data for FABQ-G

Testing Measure	ICC	95%CI	SEM	MDC
FABQ-G (Total)	0.915	0.823-0.960	1.676	4.645
FABQ-G-W	0.864	0.715-0.935	0.993	2.753
FABQ-G-PA	0.818	0.617-0.913	0.755	2.092

An analysis of individual item scores revealed that item numbers 1, 2, 3, 5, 6, 7, 9, 10, 11, 13 and 14 showed an ICC >0.70 indicating high to very high correlation. Item numbers 4, 15 and 16 showed an ICC = 0.5 to 0.69 indicating moderate correlation; and only item 12 showed an ICC of 0.26 to 0.49 indicating low correlation (Table-4.8).

4.2.2.3 Limits of Agreement of FABQ-G Scores

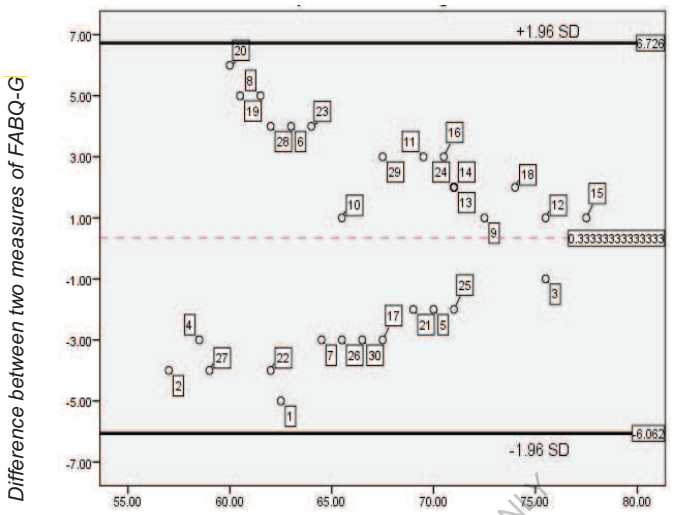
The Bland-Altman Plot (Graph-4.3) shows the difference in total scores against the mean total scores for the CLBP patients. The mean difference approached zero, indicating that no bias had occurred. In CLBP patients, no outlier was seen outside the 95% CI band. The Bland-Altman analysis showed that the mean difference was 0.333±3.262 for the FABQ-G and the limits of agreement were -6.062 to 6.726.

4.2.2.4 SEM and MDC Calculation for FABQ-G

The SEM for the FABQ-G was 1.676 and calculations revealed an MDC of 4.645 points. The SEM for the FABQ-G-W was 0.993 and calculations revealed an MDC of 2.753 points. The SEM for the FABQ-G-PA was 0.755 and calculations revealed an MDC of 2.092 points (Table-4.7).

Table-4.8: Item-wise Reliability of FABQ-G

Items	ICC	95% CI
Item 1	0.965	0.925-0.984
Item 2	0.829	0.641-0.918
Item 3	0.893	0.777-0.949
Item 4	0.564	0.085-0.793
Item 5	0.749	0.468-0.881
Item 6	0.740	0.458-0.876
Item 7	0.869	0.724-0.938
Item 8	Omitted Item *	---------
Item 9	0.866	0.718-0.936
Item 10	0.758	0.498-0.884
Item 11	0.858	0.700-0.933
Item 12	0.453	0.246-0.739
Item 13	0.808	0.595-0.909
Item 14	0.751	0.485-0.881
Item 15	0.630	0.213-0.825
Item 16	0.644	0.244-0.831
FABQ-G-W	0.864	0.715-0.935
FABQ-G-PA	0.818	0.617-0.913
FABQ-G(Full Scale)	0.915	0.823-0.960
* Not applicable in India		



Graph-4.3:Bland-Altman Plot showing the limits of agreement of FABQ-G scores

4.2.2.5 Construct Validity for FABQ-G

The pain intensity score had a high correlation with FABQ-W (r=0.819; p<0.01), and with the FABQ-PA (r=0.852; p<0.01) for subjects with CLBP showing good convergent validity with FABQ-G.

The FABQ-G total score was significantly positively correlated with CSI-G, PPT-IS, PPT-TA, and RMDQ-G, but there were no correlations obtained for trunk flexors &extensors endurance with FABQ-G (Table-4.9).

Table-4.9: Correlation between various constructs (N=128) with FABQ-G

	NPRS Base-line	PPT-IS Base-line	PPT-TA Base-line	CSI Base-line Total	RMDQ Base-line Total	FABQ Total Base-line	Trunk Extensors Endurance Baseline	Trunk Flexors Endurance Baseline
NPRS Baseline	1	0.014	-0.020	0.081	0.441**	0.172	-0.031	-0.029
		0.879	0.819	0.362	0.000	0.053	0.727	0.746
PPT-IS Baseline		1	0.497**	-0.107	-0.065	-0.125	0.374**	0.338**
			0.000	0.229	0.469	0.158	0.000	0.000
PPT-TA Baseline			1	0.172*	0.291**	0.123	0.325**	0.099
				0.045	0.001	0.168	0.000	0.265
CSI Baseline Total				1	0.527**	0.455**	-0.171*	-0.273**
					0.000	0.000	0.045	0.002
RMDQ Baseline Total					1	0.514**	-0.073	-0.229**
						0.000	0.410	0.009
FABQ Total Baseline						1	-0.137	-0.266**
							0.124	0.002
Trunk Extensors Endurance Baseline							1	0.851**
								0.000
Trunk Flexors Endurance Baseline								1

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

4.2.2.6 Factorial Validity of FABQ-G

The results of factor analyses of the 15 items of the FABQ-G are presented in Table-4.10. Item Q-8 of the original questionnaire was omitted as it is not applicable in our country. Three factors were extracted for the FABQ-G, which accounted for 74.56% of the total variance in the principal component analysis with varimax rotation.

Table-4.10: Varimax Rotated Factor Loading Matrix of the FABQ-G

Item	Factor-1	Factor-2	Factor-3
Q-1		0.736	
Q-2		0.840	
Q-3		0.873	
Q-4		0.793	
Q-5		0.779	
Q-6			0.661
Q-7		0.775	
Q-8	Omitted item*		
Q-9			0.657
Q-10	0.580		
Q-11	0.779		
Q-12	0.787		
Q-13	0.811		
Q-14	0.879		
Q-15	0.860		
Q-16	0.755		
% of total variance explained	32.452%	32.43%	9.668%

Factor loading of 0.4 or more was displayed here.

** Not applicable in India*

4.3 Statistical Analysis of Main Study

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS™) version 20 for Windows. Prior to final analysis, data were screened for transcription errors, bivariate correlation, normality assumptions, homogeneity of variance, as prerequisites for parametric calculations of the analysis of difference and analysis of related measures. Alpha level was set at 0.05 to control for type I error and confidence interval was set at 95% for all statistical analysis.

Content validity was estimated using means and test-retest reliability estimated by intraclass correlation coefficient (ICC). Descriptive statistics including mean, standard deviation and percentage were analyzed. Independent t-test was used for baseline comparisons. Repeated measures Multivariate ANOVA was used for Within-group and between-group comparisons at each follow-up period.

To control for the effect of dropouts in the follow-up studies, intention-to-treat analyses were calculated [240]. All important statistical tests were repeated by one or, if possible, 2 commonly feasible methods of intention-to-treat analysis using the last observed response ("carry forward"), respectively assuming that all missing responses were constant ("constant value") (i.e., all of the dropout subjects showed no difference between the groups).

Six subjects (3 from the treatment group and 3 from the control group) failed to return for the end of 8th-week re-evaluation. All 6 subjects improved and did not seek further care for their low back pain, citing busy schedules as the reason for not returning to complete the study. It was decided to account for the missing data from at the end of the 8th week by performing an intention-to-treat analysis utilizing the ***last observation carried forward*** (LOCF) model [241, 242]. This technique involves using the last recorded value for each outcome measure and applying it to the remaining missing value(s).

To find out and quantify the outcome of treatments, the number needed to treat (NNT) and efficacy were calculated. Pearson's correlation coefficient statistics was done to find the relationship between central sensitization and fear avoidance beliefs & disability.

4.3.1 Normality of Data

Normality of data was found for most of the variables except few for the main study data but repeated measure ANOVA was used for the main study based on following explanations described for correcting for violations of the assumptions of sphericity. It is the condition where the variances of the differences between all combinations of related groups and levels are not equal which is linked to the homogeneity assumption violation and causing the test to become too liberal & increase in the

Type I error rate. So as to produce a more valid critical *F*-value & reduce the increase in Type I error rate corrections have been developed by a statistic called epsilon (ε). An epsilon (ε) of 1 indicates that the condition of sphericity is exactly met [243]. If epsilon decreases below 1 (i.e., ε < 1), indicates a greater violation of sphericity. Both the Greenhouse-Geisser and the Huynd-Feldt procedures attempt to estimate epsilon (ε). By estimating epsilon (ε), all these procedures then use their sphericity estimate (ε) to correct the degrees of freedom for the *F*-distribution [243].

4.4 Results for Main Study

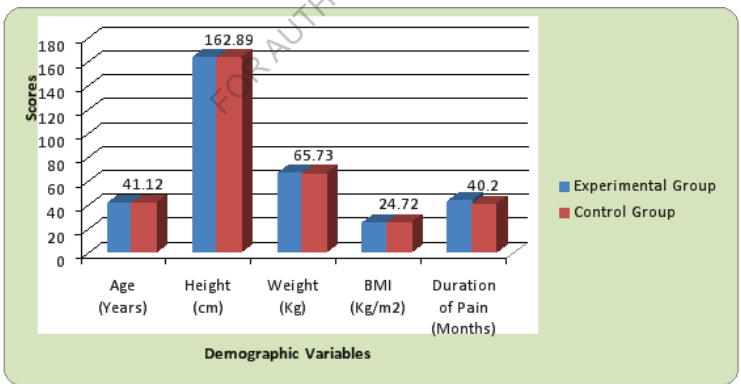
The main aims of the book were to investigate whether McKenzie exercise program is more beneficial in centrally sensitized CNSLBP patients in terms of various outcome measures. So comparisons are made between following two groups, based on these eight outcome measurements at the end of 4th week and 8th week after implementation of the respective intervention: 1) Numerical pain rating scale, 2) Pressure pain threshold, 3) CSI-G scores, 4) Roland Morris Disability Questionnaire-G, 5) Fear-avoidance Beliefs Questionnaire-G, 6) Trunk flexor endurance, 7) Trunk extensor endurance scores, and 8) GROC scores. The present study is a single-blind, randomized, controlled clinical trial with two different treatment groups (MEP & CPP). It is a multivariate repeated measure ANOVA design; where the subject was assessed on three occasions i.e. at the baseline before treatment, at the end of 4th week and at the end of 8th week.

4.4.1 Descriptive Statistics of the Main Study

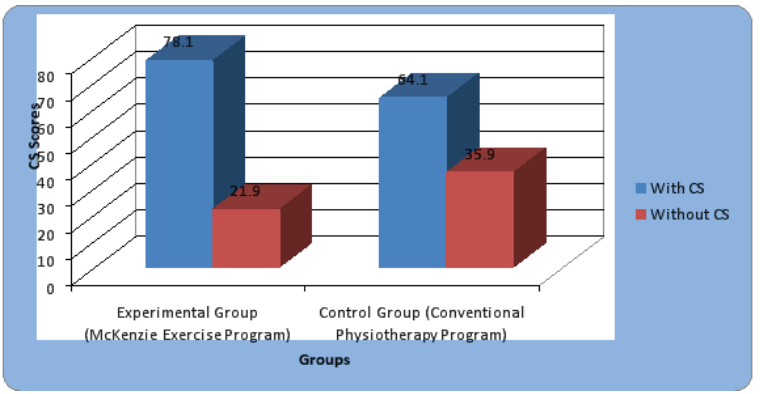
Table-4.11 represents descriptive statistics of age, weight, height, Body Mass Index (BMI), duration of pain symptoms and presence of CS among 64 subjects per group for 128 subjects in both the groups.

Table-4.11: Demographic characteristics of subjects in both groups

Characteristics	Experimental Group [n=64] Mean ± SD	Control Group [n=64] Mean ±SD	P-value
Age (years)	41.33±7.27	41.12±7.76	0.879
Height (cm)	163.14±5.43	162.89±5.25	0.792
Weight (kg)	66.15±7.89	65.73±8.93	0.778
BMI (kg/m^2)	24.88±2.97	24.72±2.76	0.762
Duration of Pain (months)	42.96±29.33	40.20±30.6	0.599
With CS (>40 CSI score)	50 (78.1%)	41 (64.1%)	0.000
Without CS (<40 CSI score)	14 (21.9%)	23 (35.9%)	0.017
Male Female	28(56%) 36(46.2%)	22(44%) 42(53.8%)	0.396 0.497



Graph-4.4: Graphical Presentation of demographic data of CNSLBP patients



Graph-4.5: Graphical Presentation of Presence of CS in Experimental and Control Group

4.4.2 Severity Levels of CS in the Main Study

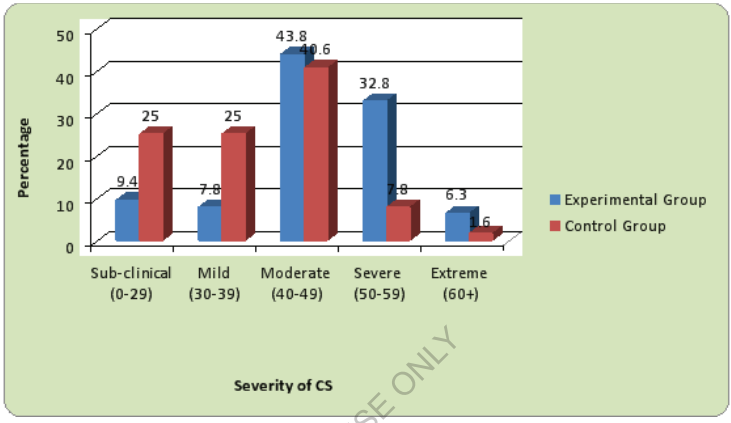
The CSI severity levels were determined by Neblett Randy et al [244] which states that compared to a single cut-off score, categorical rating scales offer better clinical utility inassessing a patient's symptom presentation, making initial treatment decisions, and identifying meaningful clinical changes in response to treatment. Though, it is established that a cut-off score above 40 in CSI indicates the presence of CS.

Table-4.12: Severity levels of CS present in the study sample (N=128)

Groups	Subclinical 0-29	Mild 30-39	Moderate 40-49	Severe 50-59	Extreme 60+
Experimental Group	6 (9.4%)	5 (7.8%)	28 (43.8%)	21 (32.8%)	4 (6.3%)
Control Group	16 (25%)	16 (25%)	26 (40.6%)	5 (7.8%)	1 (1.6%)

There are many instruments like Beck Depression Inventory (BDI), Pain Disability Questionnaire (PDQ), Oswestry Disability Inventory (ODI), and the Insomnia Severity Index (ISI) etc which measures a specific clinically relevant symptom dimension, and score levels suggest a degree of severity, such as mild, moderate, and severe. On

the similar logic, CSI categories based on severity levels were developed by Neblett Randy et al [244]. The Table-15 and Graph-4.6show the distribution of severity levels among CNSLBP patients in this study sample.



Graph-4.6: Graphical Presentation of Severity Levels of CS among CNSLBP patients

4.4.3 Baseline Comparisons of Experimental and Control Group

Table-4.13 shows the baseline comparison of all the outcome measures between the groups. The p-value observed for each measure is more than 0.05except for CSI-G, PPT-TA, and RMDQ-G.

Table-4.13: Baseline Comparisons of Subjects in Both Groups

Outcome measures	Experimental Group [n=64] Mean ± SD	Control Group [n=64] Mean ± SD	t – value	P – value
CSI-G	45.68±11.00	42.34±11.04	1.912	0.054
NPRS	7.60±0.63	7.39±0.65	1.918	0.057
PPT-IS	5.39±1.35	5.62±1.22	-0.977	0.330
PPT-TA	5.03±1.13	5.47±0.88	-2.448	0.016
RMDQ-G	12.81±3.54	11.62±3.21	1.987	0.049
FABQ-G	54.51±9.31	52.46±8.72	1.283	0.202
FABQ-G-W	25.5±4.70	24.35±4.38	1.419	0.158
FABW-G-PA	16.07±2.86	15.78±2.37	0.639	0.524
Trunk Flexor Endurance	43.25±6.87	44.00±8.88	0.534	0.594
Trunk Extensor Endurance	48.78±9.64	48.48±12.38	-0.151	0.880

4.4.4 Mean and SD of Dependent Variables at the end of 4th Week and 8th Week

Table-4.14 shows the mean and SD of all outcome measures for each follow-up period in both the groups.

Table-4.14: Means and SD of Variables at each follow-up period

Follow Up At	Outcome Measure	Experimental Group [n=64] Mean ± SD	Control Group [n=64] Mean ± SD
Week 4	CSI-G	23.42±9.41	28.21±9.32
	NPRS	3.70±0.75	5.14±1.05
	PPT-IS	6.57±1.32	5.78±1.30
	PPT-TA	6.66±0.88	5.71±0.95
	RMDQ-G	6.28±2.77	8.42±2.48
	FABQ-G	33.96±9.59	41.59±7.69
	FABQ-G-W	15.89±4.40	19.64±3.75
	FABW-G-PA	11.03±3.53	13.29±2.06
	Trunk Flexor Endurance	54.89±7.82	69.70±12.23
	Trunk Extensor Endurance	60.70±9.99	75.00±13.03
Week 8	CSI-G	11.17±7.97	21.17±8.83
	NPRS	0.562±0.87	3.06±1.42
	PPT-IS	7.60±1.34	6.04±1.32
	PPT-TA	8.20±1.34	6.10±1.12
	RMDQ-G	1.75±2.05	5.79±2.88
	FABQ-G	21.68±9.65	34.41±6.45
	FABQ-G-W	10.09±4.35	15.74±3.54
	FABQ-G-PA	6.68±4.03	11.46±1.94
	Trunk Flexor Endurance	64.78±9.66	95.39±20.97
	Trunk Extensor Endurance	70.96±13.30	101.93±19.34
	GROC	6.63±0.58	4.55±1.21

4.4.5 The Between Group Comparison of Result of Experimental and Control Group

Table-4.13 & Table-4.14 represents mean comparisons of outcome measures between the control group and experimental group. Table-4.15 represents Multivariate ANOVA result of between-group (experimental &control) analysis, Table-4.16 represents Multivariate ANOVA result of between-group (No CS & CS), Table-4.17 represents Multivariate ANOVA result of Within-group (experimental & control) analysis and it is observed that the P-value of all the measures was found to be less than 0.05 indicating a significant difference between the groups. The effect sizes of the differences between the groups are mentioned in terms of Partial Eta squared.

Table-4.15: Between-group comparison of various outcomes measures for experimental and control group

Outcome Measure	F	P-value	Effect Size (Partial Eta Squared)
CSI-G	24.980	0.000	0.167
NPRS	87.820	0.000	0.413
PPT-IS	10.82	0.001	0.080
PPT-TA	24.00	0.000	0.161
RMDQ-G	22.569	0.000	0.153
FABQ-G	31.06	0.000	0.199
FABQ-G-W	2.218	0.139	0.018
FABW-G-PA	52.010	0.000	0.299
Trunk Flexor Endurance	85.10	0.000	0.405
Trunk Extensor Endurance	58.17	0.000	0.318

4.4.6 Between Group Comparison Results for CS and No CS Group

Table-16 shows the between group comparison of CSI-G, NPRS, PPT-IS, PPT-TA, RMDQ-G and FABQ-G, FABQ-G-W, FABQ-G-PA for patients who are having the presence of CS and those who are not having it irrespective of treatment group they belong to.

Table-4.16: Between-group comparison of various outcomes measures for CS and No CS group

Outcome Measure	F	P-value	Effect Size (Partial Eta squared)
CSI-G	103.214	0.000	0.452
NPRS	4.940	0.028	0.038
PPT-IS	1.244	0.267	0.010
PPT-TA	2.200	0.140	0.017
RMDQ-G	14.263	.000	0.102
FABQ-G	21.11	0.000	0.145
FABQ-G-W	8.930	0.003	0.086
FABW-G-PA	20.00	0.000	0.141
Trunk Flexor Endurance	8.53	0.004	0.064
Trunk Extensor Endurance	8.58	0.001	0.068

4.4.7 Within-Group Comparison Results with Interaction

This Table-4.17 shows the within-group comparison and time interaction for all the outcome measures.

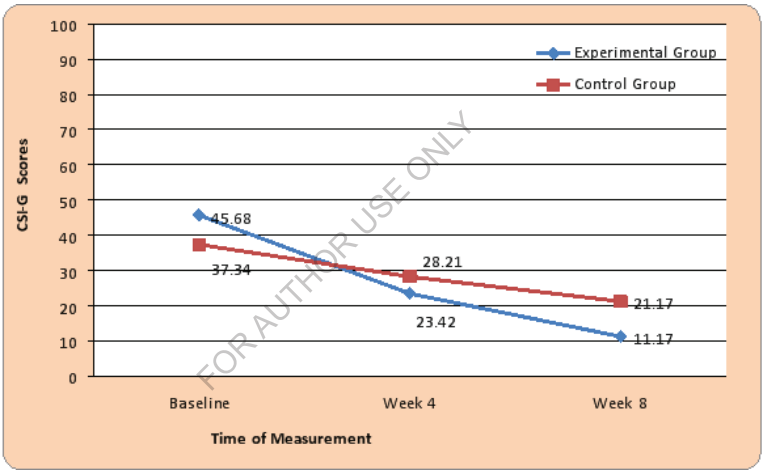
Table-4.17: Repeated measure multivariate ANOVA for within-group comparison

Outcome Measure	F	P-value	Effect Size (Partial Eta Squared)
CSI-G	487.410	0.000	0.796
CSI-G*GroupExp/Control	24.980	0.000	0.167
CSI-G*Group CS/No CS	103.214	0.000	0.452
NPRS	1552.83	0.000	0.925
NPRS*GroupExp/Control	87.820	0.000	0.413
NPRS*Group CS/No CS	4.940	0.028	0.038
PPT-IS	304.476	0.000	0.709
PPT-IS*GroupExp/Control	10.82	0.001	0.080
PPT-IS*Group CS/No CS	1.244	0.267	0.010
PPT-TA	292.75	0.000	0.701
PPT-TA*GroupExp/Control	24.00	0.000	0.161
PPT-TA*Group CS/No CS	2.200	0.140	0.017
RMDQ-G	448.28	0.000	0.782
RMDQ-G*GroupExp/Control	52.130	0.000	0.102
RMDQ-G*GroupCS/NoCS	16.530	0.000	0.153
FABQ-G	604.40	0.000	0.829
FABQ-G*GroupExp/Control	31.06	0.000	0.199
FABQ-G*Group CS/NoCS	21.11	0.000	0.145
FABQ-G-W	563.28	0.000	0.822
FABQ-G-W*GroupExp/Control	2.218	0.139	0.018
FABQ-G-W*Group CS/NoCS	8.930	0.003	0.086
FABQ-G-PA	492.33	0.000	0.801
FABQ-G-PA*GroupExp/Control	52.010	0.000	0.299
FABQ-G-PA*Group CS/NoCS	20.00	0.000	0.141
Trunk Flexor Endurance	562.36	0.000	0.818
Trunk Flexor Endurance*GroupExp/Control	85.10	0.000	0.405
Trunk Flexor Endurance*GroupCS/NoCS	8.53	0.004	0.064
Trunk Extensor Endurance	574.06	0.001	0.821
Trunk Extensor	58.17	0.001	0.318
Trunk Extensor	8.58	0.001	0.068

(a) CSI-G

A repeated measure multivariate ANOVA with Greenhouse-Geisser correction between-group analysis showed that the experimental and control groups were

different statistically with F = 24.980, p<0.000 and also showed that a between-group analysis of CS and No CS groups were different statistically with F = 103.214, p<0.000(Table-4.15& Table-4.16).The within-group repeated measure multivariate ANOVA with Greenhouse-Geisser correction showed the significant statistical difference with F= 487.410, p<0.000 (Table-4.17).Experimental/Control Group*time of measurement interaction analysis showed that the groups were different statistically with F = 24.98, p<0.000 (Graph-4.7). The CS/No CS Group*time of measurement interaction analysis showed that the groups were different statistically with F= 103.214, p<0.000 (Table-4.17).

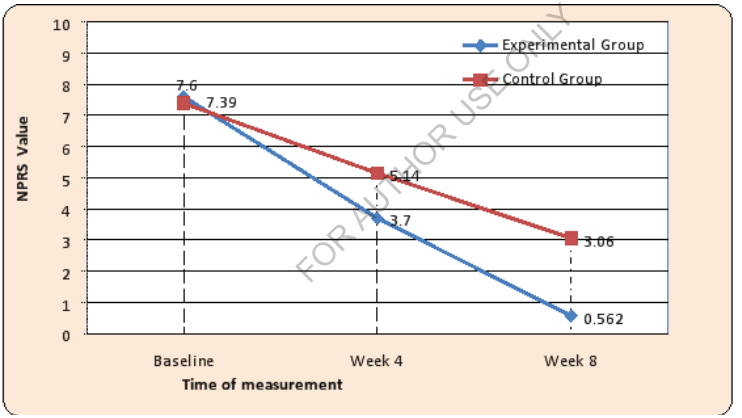


Graph-4.7: Mean Values of CSI-G measurements

Multivariate test results showed that the comparison of CS subjects in both Experimental and control group for the time measurements were different statistically at 4th week with F=4.943,p<0.033 & 8th week with F=1.821, p<0.186.The comparison of No CS subjects in both Experimental and control group for the time measurements were different statistically at 4thweek with F=22.738, p<0.000 &8thweek with F=103.500, p<0.000.

(b) NPRS

A repeated measure multivariate ANOVA with Greenhouse-Geisser correction between-group analysis showed that the experimental and control groups were different statistically with F = 87.820, p<0.000 and also showed that a between-group analysis of CS and No CS groups were different statistically with F = 4.940, p<0.028 (Table-4.15& Table-4.16).The within-group repeated measure multivariate ANOVA with Greenhouse-Geisser correction showed the significant statistical difference with F=1552.83, p<0.000 (Table-4.17). Experimental/Control Group* time of measurement interaction analysis showed that the groups were different statistically with F=87.82, p<0.000 (Graph-4.8). The CS/No CS Group*time of measurement interaction analysis showed that the groups were different statistically with F= 4.94, p<0.028(Table-4.17).

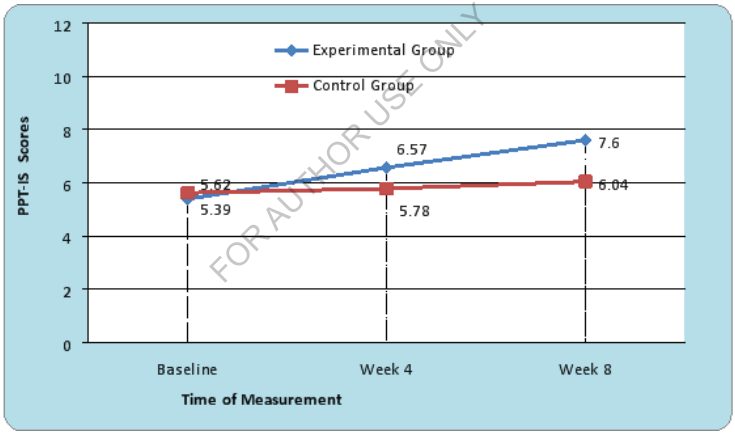


Graph-4.8: Mean Values of NPRS measurements

Multivariate test results showed that the comparison of CS subjects in both Experimental and control group for the time measurements were different statistically at 4th week with F=0.314,p<0.579 & 8th week with F=3.049, p<0.090.The comparison of No CS subjects in both Experimental and control group for the time measurements were different statistically at 4th week with F=209.857, p<0.000 & 8thweek with F=411.377, p<0.000.

(c) PPT-IS

A repeated measure multivariate ANOVA with Greenhouse-Geisser correction between-group analysis showed that the experimental and control groups were different statistically with F=10.82, p<0.000 and also showed that a between-group analysis of CS and NO CS groups were different statistically with F=1.244, p<0.267 (Table-4.15& Table-4.16). The within-group repeated measure multivariate ANOVA with Greenhouse-Geisser correction showed the significant statistical difference with F=304.476, p<0.000 (Table-4.17). Experimental/Control Group* time of measurement interaction analysis showed that the groups were different statistically with F =10.82, p<0.001 (Graph-4.9). The CS/No CS Group*time of measurement interaction analysis showed that the groups were different statistically with F= 1.244, p<0.0267(Table-4.17).

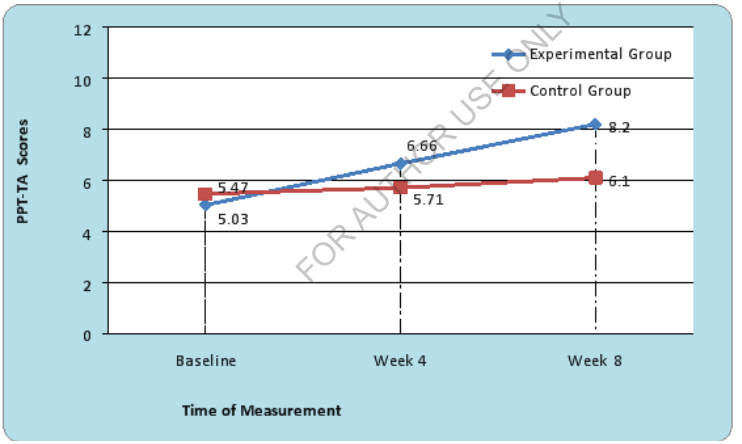


Graph-4.9: Mean Values of PPT-IS measurements

Multivariate test results showed that the comparison of CS subjects in both Experimental and control group for the time measurements were different statistically at 4th week with F=0.399,p<0.532 & 8th week with F=1.918, p<0.175.The comparison of No CS subjects in both Experimental and control group for the time measurements were different statistically at 4thweek with F=36.674, p<0.000 &8thweek with F=128.406, p<.000.

(d) PPT-TA

A repeated measure multivariate ANOVA with Greenhouse-Geisser correction between-group analysis showed that the experimental and control groups were different statistically with F=24.00, p<0.000 and also showed that a between-group analysis of CS and NoCS groups were different statistically with F=2.200, p<0.140 (Table-4.15& Table-4.16). The within-group repeated measure multivariate ANOVA with Greenhouse-Geisser correction showed the significant statistical difference with F=292.75, p<0.000 (Table-4.17).Experimental/Control Group* time of measurement interaction analysis showed that the groups were different statistically with F =24.00, p<0.000 (Graph-4.10). The CS/No CS Group*time of measurement interaction analysis showed that the groups were different statistically with F=2.200, p<0.140(Table-4.17).

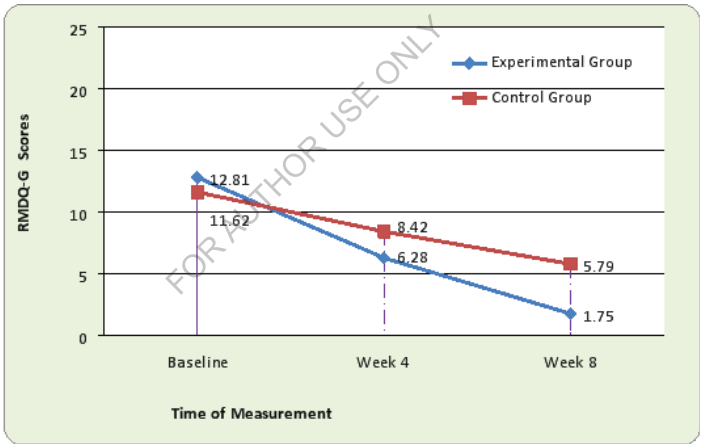


Graph-4.10: Mean Values of PPT-TA measurements

Multivariate test results showed that the comparison of CS subjects in both Experimental and control group for the time measurements were different statistically at 4th week with F=3.471,p<0.071 & 8th week with F=6.649, p<0.014.The comparison of No CS subjects in both Experimental and control group for the time measurements were different statistically at 4thweek with F=6.649, p<0.014 &8thweek with F=92.920, p<0.000.

(e) RMDQ-G

A repeated measure multivariate ANOVA with Greenhouse-Geisser correction between-group analysis showed that the experimental and control groups were different statistically with F = 22.569, p<0.001 and also showed that a between-group analysis of CS and NoCS groups were different statistically with F = 14.263, p<0.001 (Table-4.15& Table-4.16). The within-group repeated measure multivariate ANOVA with Greenhouse-Geisser correction showed the significant statistical difference with F=448.28, p<0.001 (Table-4.17). Experimental/Control Group*time of measurement interaction analysis showed that the groups were different statistically with F = 52.13, p<0.001 (Graph-4.11). The CS/NoCS Group*time of measurement interaction analysis showed that the groups were different statistically with F= 16.53, p<0.001(Table-4.17).

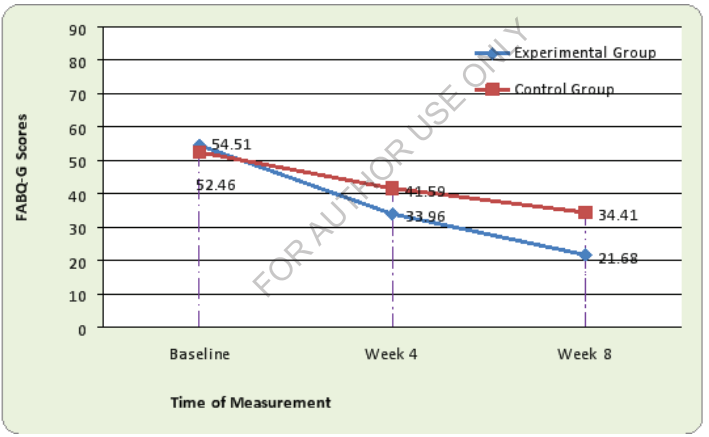


Graph-4.11: Mean Values of RMDQ-G measurements

Multivariate test results showed that the comparison of CS subjects in both Experimental and control group for the time measurements were different statistically at 4th week with F=1.369, p<0.250 & 8th week with F=0.030, p<0.864.The comparison of No CS subjects in both Experimental and control group for the time measurements were different statistically at 4thweek with F=71.703, p<0.001&8th week with F=300.476, p<0.001.

(f) FABQ-G

A repeated measure multivariate ANOVA with Greenhouse-Geisser correction between-group analysis showed that the experimental and control groups were different statistically with F =31.06, p<0.001 and also showed that a between-group analysis of CS and NoCS groups were different statistically with F =21.11, p<0.001 (Table-4.15& Table-4.16). The within-group repeated measure multivariate ANOVA with Greenhouse-Geisser correction showed the significant statistical difference with F=604.40, p<0.001 (Table-4.17). Experimental/Control Group* time of measurement interaction analysis showed that the groups were different statistically with F =31.06, p<0.001 (Graph-4.12). The CS/NoCS Group*time of measurement interaction analysis showed that the groups were different statistically with F=21.11, p<0.001(Table-4.17).

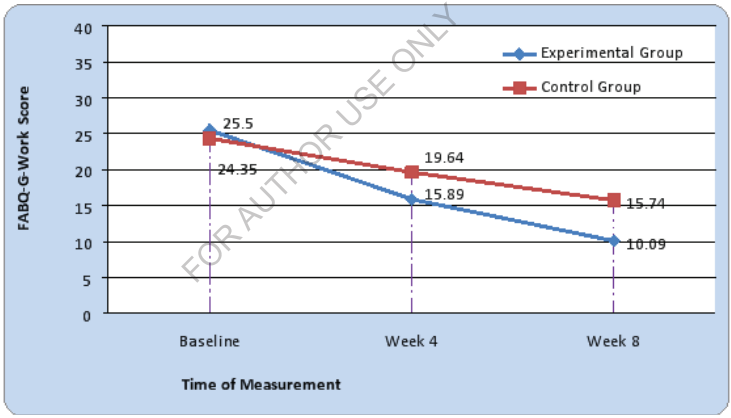


Graph-4.12: Mean Values of FABQ-G measurements

Multivariate test results showed that the comparison of CS subjects in both Experimental and control group for the time measurements were different statistically at 4th week with F=5.703,p<0.023,& 8th week with F=0.330, p<0.569.The comparison of NoCS subjects in both Experimental and control group for the time measurements were different statistically at 4thweek with F=64.832, p<0.001&8th week with F=185.991, p<0.001.

(g) FABQ-G-W

A repeated measure multivariate ANOVA with Greenhouse-Geisser correction between-group analysis showed that the experimental and control groups were different statistically with F =2.218, p<0.139 and also showed that a between-group analysis of CS and NoCS groups were different statistically with F =8.930, p<0.003 (Table-4.15& Table-4.16). The within-group repeated measure multivariate ANOVA with Greenhouse-Geisser correction showed the significant statistical difference with F=563.28, p<0.001 (Table-4.17).Experimental/Control Group* time of measurement interaction analysis showed that the groups were different statistically with F =2.218, p<0.139 (Graph-4.13). The CS/NoCS Group*time of measurement interaction analysis showed that the groups were different statistically with F= 8.930, p<0.003(Table-4.17).

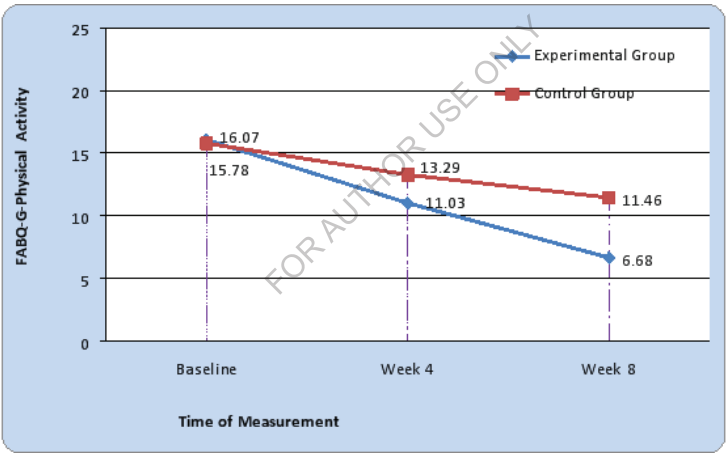


Graph-4.13: Mean Values of FABQ-G-W measurements

Multivariate test results showed that the comparison of CS subjects in both Experimental and control group for the time measurements were different statistically at 4th week with F=5.376, p<0.027 & 8th week with F=0.914, p<0.346.The comparison of No CS subjects in both Experimental and control group for the time measurements were different statistically at 4th week with F=67.318, p<0.001& 8th week with F=166.179, p<0.001.

(h) FABQ-G-PA

A repeated measure multivariate ANOVA with Greenhouse-Geisser correction between-group analysis showed that the experimental and control groups were different statistically with F=52.010, p<0.001 and also showed that a between-group analysis of CS and NoCS groups were different statistically with F=20.00, p<0.001 (Table-4.15& Table-4.16).The within-group repeated measure multivariate ANOVA with Greenhouse-Geisser correction showed the significant statistical difference with F=492.33, p<0.001 (Table-4.17). Experimental/Control Group* time of measurement interaction analysis showed that the groups were different statistically with F =52.010, p<0.001 (Graph-4.14). The CS/NoCS Group*time of measurement interaction analysis showed that the groups were different statistically with F= 20.00, p<0.001(Table-4.17).

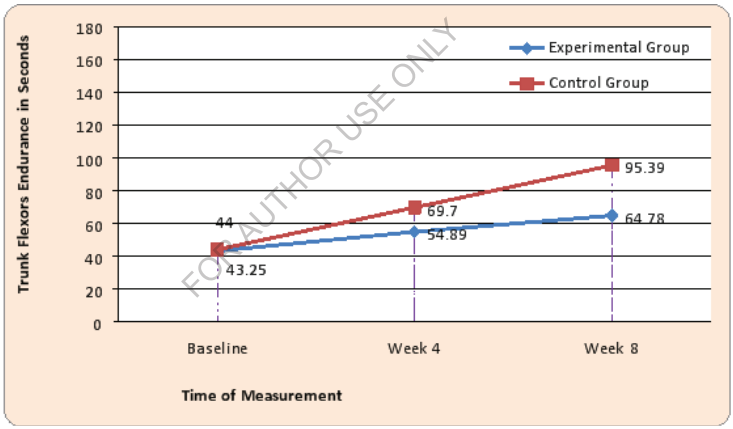


Graph-4.14: Mean Values of FABQ-G-PA measurements

Multivariate test results showed that the comparison of CS subjects in both Experimental and control group for the time measurements were different statistically at 4thweek with F=2.357,p<0.134 & 8th week with F=0.245, p<0.627.The comparison of NoCS subjects in both Experimental and control group for the time measurements were different statistically at 4thweek with F=32.328, p<0.001&8th week with F=98.869, p<0.001.

(i) Trunk Flexors Endurance

A repeated measure multivariate ANOVA with Greenhouse-Geisser correction between-group analysis showed that the experimental and control groups were different statistically with F =85.10, p<0.001 and also showed that a between-group analysis of CS and NoCS groups were different statistically with F=8.53, p<0.004 (Table-4.15& Table-4.16). The within-group repeated measure multivariate ANOVA with Greenhouse-Geisser correction showed the significant statistical difference with F=562.36, p<0.001 (Table-4.17). Experimental/Control Group* time of measurement interaction analysis showed that the groups were different statistically with F =85.10, p<0.001 (Graph-4.15). The CS/NoCS Group*time of measurement interaction analysis showed that the groups were different statistically with F= 8.53, p<0.004 (Table-4.17).

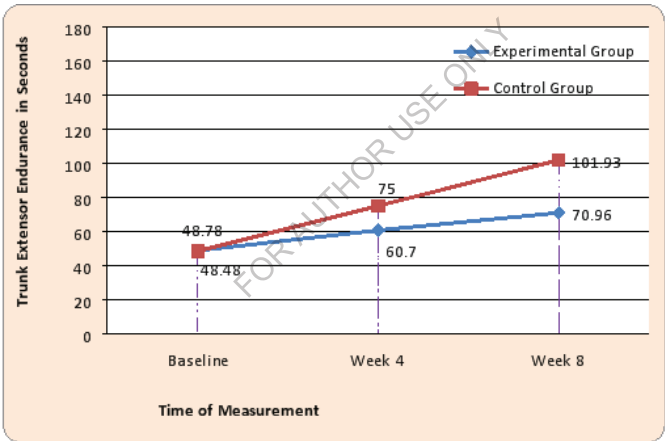


Graph-4.15: Mean Values of Trunk Flexors Endurance measurements

Multivariate test results showed that the comparison of CS subjects in both Experimental and control group for the time measurements were different statistically at 4th week with F=4.047,p<0.052& 8th week with F=5.818, p<0.021.The comparison of NoCS subjects in both Experimental and control group for the time measurements were different statistically at 4thweek with F=71.357, p<0.001&8th week with F=137.034, p<0.001.

(j) Trunk Extensors Endurance

A repeated measure multivariate ANOVA with Greenhouse-Geisser correction between-group analysis showed that the experimental and control groups were different statistically with F=58.17, p<0.001 and also showed that a between-group analysis of CS and NoCS groups were different statistically with F=8.58, p<0.001 (Table-4.15& Table-4.16). The within-group repeated measure multivariate ANOVA with Greenhouse-Geisser correction showed the significant statistical difference with F=574.06, p<0.001 (Table-4.17). Experimental/ControlGroup* time of measurement interaction analysis showed that the groups were different statistically with F =58.17, p<0.001 (Graph-4.16).The CS/NoCS Group*time of measurement interaction analysis showed that the groups were different statistically with F=8.58, p<0.001 (Table-4.17).



Graph-4.16: Mean Values of Trunk Extensors Endurance measurements

Multivariate test results showed that the comparison of CS subjects in both Experimental and control group for the time measurements were different statistically at 4th week with F=2.034,p<0.163 & 8th week with F=5.257, p<0.028.The comparison of NoCS subjects in both Experimental and control group for the time measurements were different statistically at 4thweek with F=64.483, p<0.001&8th week with F=138.287, p<0.001.

4.4.8 Comparison of Global Rate of Change Scores between Experimental and Control Group

Table-4.18 shows the patient satisfaction feedback Comparison between Experimental and Control Group after the interventions at 8th week. The experimental group showed significant difference with p-value<0.001.

Table-4.18: Global rate of change (GROC) scores at 8th week

	Experimental Group	Control Group	t-value	p-value
GROC (8th Week)	6.63±0.58	4.5±1.21	12.05	0.001

4.4.9 Risk of Benefit, Numbers Needed To Treat, and Efficacy of Treatment

Table-4.19: Showing Risk of Benefit, NNT, and Efficacy of Treatment

MDC of CSI-G	No. of patients Improved/not improved [Experi-mental Group n=61]	No. of patients Improved/not improved [Control Group n=61]	Experi-mental Group [Risk of Benefit]	Control Group [Risk of Benefit]	ARR/RD [Risk of Benefit]	NNT [for Risk of Benefit]	Efficacy of McKenzie Treatment [1-RR]
5	61/0	59/2	100%	96.72%	3.28%	30	100%
10	61/0	43/17	100%	70.49%	29.51%	3	100%
15	57/4	25/35	93.44%	40.98%	52.46%	2	88.75%
20	53/8	14/46	86.88%	22.95%	63.94%	2	82.85%

ARR (for Benefit) = Absolute Risk Reduction; RD (for Benefit) = Risk Difference;Efficacy of Treatment = 1 - Risk Ratio (RR = Risk in experimental group/Risk in Control Group); MDC= Minimum Detectable Change

The minimum detectable change[235] for CSI-G was 5.09. Considering this, a calculation of the percentage of patients benefitted for 5, 10, 15 and 20 points as the difference on a scale of a total of 100 points for CSI-G (Table-4.20). From the above risk difference for the benefit was calculated. Then the risk difference was converted

to number needed to treat (NNT- for benefit). The efficacy of McKenzie program was also more than 82% for any of the difference.

4.4.10 Correlation between CSI-G and FABQ-G & RMDQ-G

Table-4.20: Showing correlation of CSI-G with FABQ-G and its subscales, and RMDQ-G

	FABQ-G	FABQ-G-Work	FABQ-G-Physical Activity	RMDQ-G
CSI-G	0.568**	0.525**	0.449**	0.642**
** Correlation is significant at the 0.001 level.				

Pearson's correlation coefficient revealed that CSI-G had a positive correlation with FABQ-G scores and RMDQ-G scores. It showed that the correlation between CSI-G and FABQ-G score was 0.568, $p<0.001$; and FABQ-G-W score was 0.525, $p<0.001$; FABQ-G-PA score was 0.449, $p<0.001$; and with the RMDQ-G score it was 0.642, $p<0.001$.

5

DISCUSSION

"Having excluded the impossible, whatever remains and unlikely it may be, that must be the truth.

- Arthur Conan Doyle

5.1 Introduction

This chapter discusses the only most important findings of this study. It provides a detailed discussion on the reliability and validity of Gujarati version of Central Sensitization Inventory and Fear-Avoidance Beliefs Questionnaire. It also discusses the combined and individual effects of McKenzie Exercise Program and Conventional Physiotherapy Program on CNLBP with CS or without CS. In this chapter, an endeavor has been made to discuss the results obtained from the data analyses which are given in Chapter-4. The results have been discussed in the light of hypotheses formulated for the study, theoretical models available on the subject, and the studies already conducted in this regard.

5.2 Cross-Cultural Adaptation Of CSI-G Questionnaire Study

The aim of cross-cultural adaptation of a questionnaire is to achieve equivalence between the original and adapted questionnaire in another language. It is a process of preparing a questionnaire for use in another setting [225].

5.2.1 Discussion of CSI-G Questionnaire Study

The aim of this study was to translate and cross-culturally adapt the CSI into Gujarati and to check content validity, face validity, internal consistency, test-retest reliability, agreement and minimum detectable change (MDC) of CSI-G in CLBP patients. As a first step in analyzing the psychometric validation of the CSI-G, the questionnaire was translated from English into Gujarati and finalized in a consensus meeting including Gujarati-speaking researchers from Surat. In our opinion, the translation into Gujarati was appropriate, since the data collection did not reveal any confusion or problems mentioned by the participants.

The test-retest reliability showed excellent Cronbach's α value (0.914) and ICC value (ICC = 0.971) for CLBP patients, which confirms that the CSI-G is a psychometrically

robust questionnaire. This study indicates that the CSI-G is a reliable and usable instrument in Gujarati culture. This is in accordance with coefficients described earlier in other studies [238, 245, 246]. This is also in conformity with the findings of Mayer et al [247], in which Pearson's correlation (r =0.82) was used. Pearson's correlation is a commonly used measure in test-retest reliability assessment, however, it is correct to use the ICC due to its sensitivity to any bias between or among measurement times[248].

Mayer et al [247] used only healthy controls and 5-days of the time interval for test-retest analyses in their study, so it is possible that the consistency of filling out the CSI twice was more compared to CLBP patients. In the present study, a 7-days interval was chosen, thereby reducing the likelihood of remembering the responses given during the first assessment considering the high number of the items and also answers from the first assessment were held back.

The SEM and MDC provide researchers and clinicians with some direction for true changes in the measurement, which is not due to random measurement error. The result showed an MDC of 5.092 points for CSI-G (Scale range 0-100). Scores at or above this MDC value are likely to be due to patient improvement instead of measurement error. Estimated minimal meaningful changes should be greater than the MDC value.

No relevant information could be made out of Part-B of CSI-G as most of the patients found it difficult to understand the labels of diagnosed diseases mentioned in this section. Whoever scored high on Part-A of CSI-G were able to say "yes" to one or more diagnoses of Part-B suggesting this could be an extra sign of CS.
The convergent validity of the CSI-G was supported by the pattern of correlations with the RMDQ-G ($r=0.527^{**}$, $p<0.000$), FABQ-G ($r=0.455^{**}$, $p<0.000$) and PPT-TA ($r=0.172^{*}$, $p<0.045$) in our study. The divergent validity is seen by negative correlation with trunk extensors endurance ($r=-0.171^{*}$, $p<0.045$) and trunk flexors endurance ($r=-0.273^{**}$, $p<0.002$).

In our study, we found a 6-factor solution from factor analysis of CSI-G. The internal consistency of factors 1, 2, 3 and 4 was good, with Cronbach's alphas of respectively

0.912, 0.773, 0.782, and 0.728. The Cronbach's alpha for factor 5 could not be calculated as it has loaded only one item (Item-24) and factor 6 was considered poor with a value of 0.348.

Mayer T G et al [247] found a 4-factors solution for the factor analysis of their original English version of CSI that accounted for 53.4% of the variance in the dataset. The factors were labelled for meaningfulness, and the variance is provided here: (a) Factor 1 – Physical Symptoms (30.9%), (b) Factor 2 – Emotional Distress (7.2%), (c) Factor 3 – Headache/Jaw Symptoms (10.1%), and (d) Factor 4 – Urological Symptoms (5.2%).

Kregel J et al [246] also found a 4-factor solution in their study of Dutch translation of CSI where factor 1 consists of items 2, 6, 8, 9, 17, and 25, and is named "General disability and physical symptoms"; items 4, 7, 10, 13, 18, 19, and 20 load on factor 2 which was named "Higher central sensitivity"; factor 3 consists of items 11, 14, and 21, and is named "Urological and dermatological symptoms"; and Factor 4 consists of items 3, 12, 13, 15, 16, and 17, which is named "Emotional distress". Items 1, 5, 22, 23, and 24 did not load on any of the factors (i.e. factor loading <0.40) and were dropped from the subsequent confirmatory factor analyses. PitanceL et al [245] found a 5-factor solution for the factor analysis of French translation of CSI. Cuesta-VargasA let al[249] found a one-factor solution to be the best fit for the Spanish version of the CSI.

5.2.2 Conclusion of CSI-G Questionnaire Study

Our results suggest that the CSI-G has been successfully translated and cross-culturally adapted from English to Gujarati. The preliminary evidence generated by the psychometric testing showed that the CSI-G demonstrates psychometric properties similar to the English version. This study provides us with the evidence that the CSI-G is a reliable and valid measure to assess CS in Gujarati-speaking CLBP patients. The CSI-G total scores were significantly positively correlated with FABQ-G, PPT-IS, PPT-TA, and RMDQ-G, but were negatively correlated with trunk flexors and extensors endurance scores. The results of factor analyses of 25 items of CSI-G produced a six-factor solution, which accounted for 69.85% of the total

variance in the principal component analysis with varimax rotation. Responsiveness of the CSI-G should be evaluated in further studies.

5.3 Cross-Cultural Adaptation of FABQ-G Questionnaire Study

The aim of cross-cultural adaptation of a questionnaire is to achieve equivalence between the original and adapted questionnaire in another language. It is a process of preparing a questionnaire for use in another setting [225, 226].

5.3.1 Discussion of FABQ-G Questionnaire Study

This study describes for the first time the psychometric properties of a cross-cultural translation of the FABQ into Gujarati. In general, all the patients clearly understood the translated version. As a first step in analyzing the psychometric validation of the FABQ-G, the questionnaire was translated from English into Gujarati and finalized in a consensus meeting including Gujarati-speaking researchers from Surat. In our opinion, the translation into Gujarati was appropriate, since the data collection did not reveal any confusion or problems mentioned by the participants. Test-retest reliability was excellent when the FABQ-G was administered twice with a gap of 48-hours in a CLBP sample. The test-retest reliability showed excellent ICC value for CLBP patients (FABQ-G =0.915; FABQ-G-W 0.864 and FABQ-G-PA 0.818), which confirms that the FABQ-G is a psychometrically robust questionnaire. The pain intensity score had a high correlation with FABQ-W ($r=0.819$; $p<0.01$), and with the FABQ-PA ($r=0.852$; $p<0.01$) for subjects with CLBP showing good convergent validity with FABQ-G. Item-8 of FABQ was omitted in Gujarati translation as compensation claims for CLBP is not applicable in India.

The close correlations among the items showed that the FABQ-G-W and FABQ-G-PA subscales were internally consistent and similar to the original. Our findings are similar with the Swiss-German (FABQ-W:0.89 & FABQ-PA:0.82)[250], German (FABQ-Work1:0.89; FABQ-Work2:0.94; & FABQ-PA:0.64)[251], Portuguese (FABQ-W:0.80 and FABQ-PA:0.90)[252], Norwegian (FABQ-W:0.90 & FABQ-PA:0.79)[253], Greek (FABQ-Work1:0.86; FABQ-Work2:0.90; & FABQ-PA:0.72)[254], Chinese (0.90)[255]and Spanish result (0.93)[256].

Test-retest reliability similar to the original scale was indicated by the highly significant correlation between the results obtained atbaseline and after 48 hours for the measure as a whole and both subscales. Once again, our findings are similar with the Swiss-German (FABQ-W:0.91 & FABQ-PA:0.83)[250], German (0.87)[251], French (FABQ-W:0.88 & FABQ-PA:0.72)[257], Portuguese (FABQ-W:0.91 & FABQ-PA:0.84)[252], Norwegian (FABQ-W:0.82 and FABQ-PA:0.66)[253], Greek (FABQ-Work1:0.93; FABQ-Work2: 0.94; & FABQ-PA:0.85)[254], Chinese (0.81)[255]and Spanish results (0.97)[256].

The FABQ-G was highly acceptable, easily understood, and was found suitable for self-administration. It required approximately 5-6 minutes filling up. Hence it seems to be appropriate in routine clinical practice. Avoidance behavior led by FABs in patients with CLBP leads to the development of chronic disability. In reality, fear-avoidance behavior was shown to be a significant risk factor for chronicity. Hence, encouraging patients to change their beliefs and behaviors has become more crucial in managing CLBP, especially in the early stage. It is important to focus on educating patients regarding pain along with gradual exposure to activities to help reduce pain-related fear; rather than allowing patients believing the imaging reports leading to the development of fear-avoidance behavior. The FABQ helps clinicians to detect patient's FABs and helps to establish an effective management plan to prevent CLBP.

This study has few limitations that should be pointed out. First, it was a cross-sectional design, and any significant correlations should not be confused with causal effects; it is possible that pain-related fear leads to increased activity avoidance and disability, but the reverse also may be possible. Longitudinal data may be superior because they could provide afar better understanding of the impact of baseline characteristics, management issues and expectations on FABs. Second, the associations between self-reported beliefs and physical tests were not taken into consideration. In future studies, this may be explored. Third, our study was limited to only CLBP, and it is doubtful whether our result can be generalized to acute or subacute LBP and other complaints of the musculoskeletal system. Hence, this may well be further investigated in future studies. Finally, the present study had the

limitation of not considering the divergent and factorial validity of the FABQ-G due to small sample size.

The exploratory factor analysis (EFA) was used to examine the structure of the FABQ-GR (German version) instead of a confirmatory factor analysis model since the number of possible factors expected was not predetermined from the literature and either a two or a three-factor model was anticipated [221, 251]. Principal component analysis (PCA) modeling identified three distinct factors with salient loadings of the items.

A serious concern in factorial models is the adequacy of sampling, resulting in desired samples consisting of 300 and more subjects [232]. Although in this study, only 128 subjects participated, the factors identified had more than four loadings above Eigenvalues>0.6 (Table-13), confirming a reliable model regardless of sample size[258]. Therefore, it can be argued that the 3-factor model, as established in this study, is statistically sound and acceptable for use.

The convergent validity of the FABQ was supported by the pattern of correlations with the RMDQ-G (r=0.514, p<0.000) and CSI-G (r=0.455, p<0.000) in our study. The divergent validity is seen by negative correlation with trunk flexors endurance (r= -0.266, p<0.002).

5.3.2 Conclusion of FABQ-G Questionnaire Study

Our results suggest that the FABQ-G has been successfully translated and cross-culturally adapted from English to Gujarati. The preliminary evidence generated by the psychometric testing showed that the FABQ-G shows psychometric properties similar to the English version. This study provides us with the evidence that the FABQ-G is a reliable and valid measure to assess ***'fear avoidance beliefs'*** in Gujarati-speaking CLBP patients and results of FABQ-G can be compared to international studies using other translated versions. The reasonable validity and reliability of the 3-factor FABQ-G shown in this study make it appropriate for clinical use with Gujarati CLBP patients. Responsiveness of the FABQ-G should be evaluated in further studies.

5.4 Comparison of 'McKenzie Exercise Program' and 'Conventional Physiotherapy Program' in CNSLBP with or without Central Sensitization

The study was done on128 subjects, 64 in each group. The mean age and BMI of the subjects in control group were 41.12±7.76 years and 24.72±2.76Kg/m^2 respectively, while in the experimental group were 41.33±7.27 years and 24.88±2.97 Kg/m^2 respectively. The gender distribution in control group was 44% males and 53.8% females; while in the experimental group were 56% males and 46.2% females. Also, the groups were similar at baseline for all outcome measures with p-value > 0.05 (Table-4.11).

The main objective of the study was to determine the efficacy of 'McKenzie exercise program' over 'conventional physiotherapy program' by using outcome measures NPRS for pain, CSI-G for central sensitization, PPT-IS& PPT-TA for pressure pain threshold, RMDQ-G for disability, FABQ-G for fear-avoidance beliefs and GROC for satisfaction from treatment.

Primary objectives were to find the presence of CS in CNSLBP patients in terms of, those who display higher CS scores on CSI-G; and those who display lower pressure pain thresholds (PPT) by pressure algometry and to identify the proportion of patients with CNSLBP experiencing central sensitization in terms of severity classification given by Neblett et al [(244)]by using CSI-G. Also literature was reviewed for description of presence of CS in chronic low back pain patients in previous studies. The secondary objectives were to find the relationship of CS with fear avoidance beliefs and disability.

The result of study which was done to test the central sensitization in CNSLBP population along with an objective to review the literature to examine the extent of sub-grouping and targeted treatment if anything previously revealed that there were subgroups of patients based on the severity of CSI scores according to Neblett et al [(244)]. In the present study, almost 90.6% and 75% patients in experimental group and control group respectively had mild to extreme level of CS severity (Table-4.12). When the pressure pain threshold (PPT) is examined in both the experimental and control group mean scores were low; and which is near to 5.03 Kg/cm^2 and 5.47 Kg/cm^2 respectively also indicated the presence of CS in CNSLBP.

The tenability of the hypotheses observed for all the outcome measures of the study are as follows:

5.4.1 Pain

The present study relates to the problem of CNSLBP in subjects and investigates the research question: ***Is McKenzie exercise program more effective for reduction of pain in CNSLBP patients in comparison to available conventional physiotherapy program?***

Table-4.13, Table-4.14, and Graph-4.8show the recovery patterns of NPRS scores of both the groups from baseline to 4th week and from 4th week to 8th week. The subjects in experimental group receiving McKenzie exercise program (blue line) showed better recovery at 4th week and 8th week compared to conventional physiotherapy program (red line). It is pertinent to note that recovery from pain was better during the4th week to 8th week in the experimental group than with from baseline to 4th week. Although control group also recovered on pain score; but it was significantly less than the experimental group.

Schnebel, Watkins, and Dillin[259] suggested that the positive results associated with McKenzie approach might be related to activation of the gate control mechanisms or relaxation and/or decompression of neural tissues. DeRosa and Porterfield[260] believed that the application of controlled forces to the spine through active exercise or manual techniques might temporarily reduce pain levels by altering the fluid dynamics of injured tissue. DeRosa and Porterfield [260] proposed that the stimulation of arterial, venous and lymphatic drainage or mechanoreceptors stimulation with subsequent increased afferent input to the central nervous system might result in pain modulation and inhibition of hypertonic muscles.

In a study by Petersen T et al [115] concluded that at the end of two months treatment there was no significant difference in pain scores of McKenzie group and intensive strength training group; but pain scores were consistently lower with McKenzie group, which indicates that McKenzie treatment method has potential to treat chronic back pain. Petersen T et al [115]had accepted that the high dropout rate of patients is adrawback of their study.

Mbada et al. [261]concluded that pain is the major problem of long-term LBP and it results in deconditioning of the musculoskeletal system leading to stiffness, loss of motion,cartilage degeneration, muscular inhibition, fear-avoidance behavior, and muscle atrophy[262]. Like a vicious cycle, the deconditioning syndrome may also precipitate and perpetuate pain which results in recurrent or acute-on-chronic LBP. Pain leads to muscle guarding of all movements in the affected region, disuse leads to muscular atrophy, which in turn results in weakness[262]. The weakness, therefore, may be secondary to inhibition caused by the noxious stimuli caused by pain[262]. The movement component of McKenzie exercise program as used in this study may have resulted in reconditioning of the patients by making them expand the limits to their physical functioning, and enhance their pain control ability.

On the basis of above discussion, it can be stated that **H1: McKenzie exercise program is more effective for reduction of pain in CNSLBP patients in comparison to available conventional physiotherapy program.**

5.4.2 Central sensitization

The present study relates to the problem of CNSLBP in subjects and investigates the research question: ***Is McKenzie exercise program more effective for reduction of central sensitization in CNSLBP patients in comparison to available conventional physiotherapy program?***

Table-4.13, Table-4.14, and Graph-4.7show the recovery patterns of central sensitization scores of both the groups from baseline to 4th week and from 4th week to 8th week. The subjects in experimental group receiving McKenzie exercise program (blue line) showed better recovery at 4th week and 8th week compared to conventional physiotherapy program (red line). The control group also recovered on central sensitization score, but it was significantly less than the experimental group. This central sensitization score was measured by validated Gujarati version of central sensitization inventory (CSI-G). The original CSI was developed and validated by Mayer Tom G. et al [247] on fibromyalgia, chronic widespread pain, regional CLBP, and a normative control group of patients. The psychometric strength of CSI to detect the CS related symptoms was excellent in above-mentioned patient groups. Hence in our study, we translated and validated the CSI in the Gujarati

language to use with Gujarati population. In our study, in experimental group 78.1% patients have detected with central sensitization of varying severity and in control group, it was 64.1% patients, who had symptoms of CS. As CSI is inexpensive, it can very well be used to detect the presence of CS in chronic low back pain cases and patients can be sent towards more appropriate non-pharmacological treatments like manual therapy (e.g. McKenzie therapy) and pharmacological treatments like use of dual reuptake inhibitors which targets descending central pathways by enhancing serotonin and nor-epinephrine levels, resulting in decreased CS-related pain[263].

In our study, we were successful to establish the existence of CS among CNSLBP patients to varying degrees by means of CSI-G scores and low-pressure pain threshold among CLBP patients who are having CSI-G scores above 40. Similarly, Giesecke T et al. [24] have reported that patients with CLBP having CS experienced significantly more pain and showed more extensive, common patterns of neuronal activation in pain-related cortical areas. This may explain why some CLBP patients are having disproportionate pain irrespective of their actual pathology has already healed. The reason is probably the occurrence of augmented central pain processing in patients with CLBP.

There is not enough literature available regarding the use of this CSI, especially in the chronic low back pain cases. In future when more studies are conducted with this CS inventory, we might get a deeper insight into the functioning of CSI.

On the basis of above discussion, it can be stated that **H1: McKenzie exercise program is more effective for reduction of central sensitization scores on CSI-G in CNSLBP patients in comparison to available conventional physiotherapy program.**

5.4.3 Pressure Pain Threshold (Segmental and Extra-segmental)

The present study relates to the problem of CNSLBP in subjects and investigates the research question: ***Is McKenzie exercise program more effective for increasing pressure pain threshold over infraspinatus (extra-segmental) and tibialis***

anterior (segmental) in CNSLBP patients in comparison to available conventional physiotherapy program?

Table-4.13, Table-4.14,Graph-4.9 (PPT-IS) and Graph-4.10 (PPT-TA)show the recovery patterns of pressure pain threshold scores of both the groups from baseline to 4th week and from 4th week to 8th week. The subjects in experimental group receiving McKenzie exercise program (blue line) showed better recovery at 4th week and 8th week compared to conventional physiotherapy program (red line). The control group also recovered on central sensitization score, but it was significantly less than the experimental group. Here, it is pertinent to note that recovery pattern of PPT was better during the4th week to 8th week in the experimental group than with from baseline to 4th week for both PPT-IS and PPT-TA. This indicates that PPT recovers slowly over a period of two months to reach their normal or near normal level of sensitivity in CNSLBP patients.

Imamura M et al [264] showed that individuals with CLBP have lower PPT values than healthy individuals in almost all assessed structures and they proposedan approach that can differentiate patients with CLBP whose CS in the painful area should be further examined. However, Meeus M et al[174] did not find lower PPT values in CLBP patients in their study (n=21CLBP patients). This could be due to small sample size off CLBP patients. Imamura M, Alfieri FM, Filippo TR, and Battistella LR [265]in their study showed that most PPT values are correlated to the VAS and the Roland Morris Disability Questionnaire for LBP.

Şenay Özdolap, Selda Sarikaya, and Fürüzan Köktürk[266] in their study showed that patients with CLBP have significantly lower PPT values at every individual site compared with healthy controls and their result suggests that widespread pain should be taken into account in the evaluation of patients with CLBP.

O'Neill S, Manniche C, Graven-Nielsen T, and Arendt-Nielsen L [173]in their study with a group of patients with CLBP (n=12) with intervertebral disc herniation demonstrated that PPT was lower in the anterior tibialis muscle compared to controls (n=12) and hence concluded that these patients should be investigated for generalized deep-tissue hyperalgesia suggesting presence of CS.

Farasyn A and Meeusen R [267] investigated the PPTs with respect to the Erector spinae and the hip muscles in 87 patients with subacute non-specific LBP. They found that the mean PPT values of the Erector spinae and the hip at all examined points of the LBP group were a significantly lower in comparison to the PPT values of the healthy group.

There was a paucity of literature which directly shows the effect of physiotherapy or manual therapy methods to deal with reduced PPT. In this study, an attempt is made to demonstrate the effect of McKenzie exercise program to deal with CS in terms of changes in PPT.

On the basis of above discussion, it can be stated that **H1: McKenzie exercise program is more effective for increasing both PPT-IS and PPT-TA scores in CNSLBP patients in comparison to available conventional physiotherapy program.**

5.4.4 Roland Morris Disability Questionnaire for Low Back Pain

The present study relates to the problem of CNSLBP in subjects and investigates the research question: ***Is McKenzie exercise program more effective for reduction of disability in terms of RMDQ-G in CNSLBP patients in comparison to available conventional physiotherapy program?***

Table-4.13, Table-4.14,and Graph-4.11show the recovery patterns of RMDQ-G scores of both the groups from baseline to 4th week and from 4th week to 8th week. The subjects in experimental group receiving McKenzie exercise program (blue line) showed better recovery at 4th week and 8th week compared to conventional physiotherapy program (red line). The control group also recovered on central sensitization score, but it was significantly less than the experimental group. It is pertinent to note that recovery from disability was better during the4th week to 8th week in the experimental group than with from baseline to 4th week.

The Roland-Morris Disability Questionnaire[219, 220] is most sensitive to patients with mild to moderate disability due to acute, sub-acute or chronic low back pain. There are different questionnaires available, which differ from each other in the number of

statements: 24-, 18- and 11-item questionnaire. The score ranges from 0 (no disability) to 11, 18 or 24 (maximum disability) depending on the questionnaire that is used.

Miller E.R.[127] in their RCT compared a specific spine stabilization program with the McKenzie approach for CLBP patients and found that McKenzie group improved only in short form McGill Questionnaire and stabilization group improved on pain scores and straight leg raise range. In between group comparison, the functional status questionnaire (FSQ) revealed no statistical difference. But in our study pain scores, RMDQ-G scores (disability) were better with McKenzie exercise program. The difference in results can be attributed to small sample size and very wide age range (19-87) of patients in Miller's study could be termed as confounding factors.

Paatelma M et al. [268]examined the effects of orthopedic manual therapy (OMT)and McKenzie method compared with one counseling session with a physiotherapist with "advice-only to stay active" for treating LBP/leg pain and disability. Paatelma M et al.[268]concluded that the OMT and McKenzie methods seemed to be only slightly more effective than was one session of assessment and advice-only. This conclusion was based on one year follow up and it is natural that at one-yearfollow-up the difference between treatments groups is expected to be minimal. However, our study is significantly favoring McKenzie exercise at 1-month and 2-month follow-up i.e. at the short term.

On the basis of above discussion, it can be stated that **H1: McKenzie exercise program is more effective for reducing disability scores on RMDQ-G questionnaire in CNSLBP patients in comparison to available conventional physiotherapy program.**

5.4.5 Fear-avoidance Beliefs Questionnaire-Gujarati for Low Back Pain

The present study relates to the problem of CNSLBP in subjects and investigates the research question: ***Is McKenzie exercise program more effective for reduction of fear-avoidance beliefs in terms of FABQ-G in CNSLBP patients in comparison to available conventional physiotherapy program?***

Table-4.13, Table-4.14,and Graph-4.12show the recovery patterns of FABQ-G scores of both the groups from baseline to 4th week and from 4th week to 8th week. The subjects in experimental group receiving McKenzie exercise program (blue line) showed better recovery at 4th week and 8th week compared to conventional physiotherapy program (red line). The control group also recovered on central sensitization score, but it was significantly less than the experimental group. It is pertinent to note that recovery from disability was better during the4th week to 8th week in the experimental group than with from baseline to 4th week.

Al-Obaidi SM, Al-Sayegh NA, Ben Nakhi H, and Al-Mandeel M[269] in their study showed that McKenzie intervention reduced pain and related fear and disability beliefs and improved physical performances in individuals with CLBP. George SZ, Bialosky J E, and Donald D A [270] predicted that higher the fear avoidance beliefs about work and absence of centralization phenomenon leads to higher level of disability in acute low back pain patients after 6-months.Mbada CE, Ayanniyi O and Ogunlade SO [271] found in their study that McKenzie Protocol alone, or in combination with static or dynamic back extensors endurance exercise reduces Fear avoidance beliefs (FAB) in patients with LBP.

On the basis of above discussion, it can be stated that **H1:McKenzie exercise program is more effective for reducing fear-avoidance beliefs on the FABQ-G questionnaire in CNSLBP patients in comparison to available conventional physiotherapy program.**

5.4.6 Trunk Flexors and Extensor Endurance

The present study relates to the problem of CNSLBP in subjects and investigates the research question: ***Is McKenzie exercise program more effective for improving 'trunk flexors endurance' and 'trunk extensors endurance' scores in CNSLBP patients in comparison to available conventional physiotherapy program?***

Table-4.13, Table-4.14,Graph-4.15 and Graph-4.16show the recovery patterns of *'trunk flexors endurance' and 'trunk extensors endurance' scores* of both the groups from baseline to 4th week and from 4th week to 8th week. The subjects in

experimental group receiving McKenzie exercise program (blue line) showed less recovery at 4th week and 8th week compared to conventional physiotherapy program (red line). The experimental group also recovered on flexors and extensors endurance score, but it was significantly less than the control group. It is pertinent to note that recovery for flexors and extensors endurance was better during the4th week to 8th week in the control group than with from baseline to 4th week.

Browder DA et al [272] in their multicenter RCT examined the effectiveness of an extension-oriented treatment approach (n=26) or a strengthening exercise program (n=22) in a subgroup of LBP whose pain was centralizing with extension movements. Their study showed that the extension-oriented treatment approach is more effective than the strengthening exercise program for reducing disability and pain. The weakness of this study may be small sample size and they did not take an outcome measure which accounts for trunk strength.

In our study, we measured trunk flexors and extensors endurance and found that it improves better in the control group, which is in accordance with 'Specific adaptation to imposed demands principle'.

On the basis of above discussion, it can be stated that ***H1:McKenzie exercise program is less effective for improving 'trunk flexors endurance' and 'trunk extensors endurance' scores in CNSLBP patients in comparison to available conventional physiotherapy program.***

5.4.7 Global Rating of Change Scale

The present study relates to the problem of CNSLBP in subjects and investigates the research question: ***Is McKenzie exercise program more effective for demonstrating the global rate of change score in CNSLBP patients in comparison to available conventional physiotherapy program?***

*In our study, theexperimental group showed more positive changes in GROC scores than the experimental group (Table-4.18).*GROC is a 15-point scale is used as described by Jaeschke R, Singer J, and Guyatt GH [273], and this scale requires the

patient to rate the degree of change in his or her condition or to rate their own perception of improved function from the beginning of treatment to the present. The midpoint of the scale is no change (0). Ratings from -1 to -7 represent varying degrees of a worsening of the patient's condition, whereas rating from +1 to +7 represent varying degrees of improvement.

At the end of 8th-weekevaluation, the experimental group had significantly (t=12.05, p<0.000) greater improvements based on the GROC measure (mean ± SD, +6.63±0.58) as compared to the control group (+4.5±1.21). A cut-off score of +4 indicates significant improvement on GROC score in both the groups but experimental group fared significantly better.

In a study by Halliday MH et al [274]subjects reported a little better sense of perceived recovery with the McKenzie method than with the motor control method. Machado LAC et al [275] concluded in their study of acute LBP treated with McKenzie method does not produce appreciable additional short-term improvements in *global perceived effect*. But our study showed better outcome on GROC when treated with McKenzie exercise program.

On the basis of above discussion, it can be stated that **H1:McKenzie exercise program is more effective for improving the global rating of change scores in CNSLBP patients in comparison to available conventional physiotherapy program.**

5.4.8 Efficacy of McKenzie Exercise Program

The minimum detectable change for CSI-G was 5.09 points on a total of 100 points scale. Considering this, a calculation of the percentage of patients benefitted for 5, 10, 15 and 20 points as the difference on a scale of a total of 100 points for CSI-G (Table-4.20). The number needed to treat (NNT- for benefit) calculation revealed that for a small difference (5 points) 30 patients would be treated to produce an effect in one patient for McKenzie exercise program and that for a large difference (20 points), it was only 2 patients. The efficacy of McKenzie program was also more than 82% for any of the difference ranging from 5-20 points. The study result also revealed that CSI-G had a moderate positive correlation with fear-avoidance beliefs

and disability scores, which indicates that the CSI-G questionnaire would reflect the convergence of the symptoms of CNSLBP patients along with these scales [235].

5.4.9 How does McKenzie exercise program work to reduce CS?

Hypothetically exercise may activate the endogenous analgesia in the process of managing central sensitization [276]. Hence the clinicians prefer the contingent approach in treating patients with OA and central sensitization. Even though the pain does not cease and the patient adheres to the predetermined exercise modalities may interpret pain increases as non-threatening[277]. A pilot RCT by Sterling M et al [278] concluded that lateral glide applied to the cervical spine as manual therapy may be effective in reducing sensory hyperexcitability (nociceptive flexion reflex). However, the short-term analgesic effects of manual therapy limit its use for desensitizing the CNS. But increasing the frequency manual therapy sessions may result in long-term activation of descending anti-nociceptive pathways. In our study, McKenzie exercise is a patient-operated manual therapy which may explain its effects on CS on the line of activation of descending anti-nociceptive pathways. Bialosky J. E. et al[279] in their study demonstrated that inhibition of Aδ fiber–mediated pain perception was similar for all thesubgroups of LBP patients. However, inhibition of temporal summation was observed only in participants receiving manipulative therapy.

Jo Nijs et al (280) in their professional article described central sensitization as the development of more excitatory synapses. Such brain mechanisms are identical to those seen in learning and memory. To treat this altered brain mechanisms in pain problem they suggested *cognition-targeted exercise therapy*; the goal is to replace the old and maladaptive movement-related pain memories (systematic desensitization). The graded approaches of McKenzie exercise program may work as a systemic technique. Moreover, the anti-CS effect is by influencing neurotrophic factors. A habitual and regular exercise, in contrast to temporary exercise, increases Brain-derived neurotrophic factor (BDNF)in blood levels [281]. A study in humans with osteoarthritis, a chronic pain disorder characterized by central sensitization, provides preliminary evidence that manual joint mobilization provides widespread analgesia

[282]. Hence, the reduction in pain and disability in the McKenzie group of CNSLBP patients might have been enhanced.

Nijs J. et al [276] in their narrative review stated that exercise activates endogenous analgesia in healthy subjects. The increased pain threshold following exercise is due to the liberation of endogenous opioids and activation of supraspinal nociceptive inhibitory mechanisms directed by the brain. But, many musculoskeletal conditions have shown the disturbed functioning of endogenous analgesia system in response to exercise in chronic pain patients. Generally, muscle contractions activate generalized endogenous analgesia in healthy, pain-free subjects and patients with rheumatoid arthritis or osteoarthritis, but in fibromyalgia patients, it results in increased pain sensitivity. Hence, it may be prudent not to exercise at high intensity but rather at a mild or low intensity which is comfortable to CS patients.
Smith Ashley et al [283]in their study showed increases in PPT at exercising (leg) and non-exercising (neck) body parts in subjects with whiplash associated disorders and pain-free controls after the isometric exercise condition, but not after the aerobic bicycling exercise. This may explain how the how repetitive isometric hold of lower back in flexion or extension is useful in reducing CS in our study.

It is well known that strength training is important for protecting and stabilizing joints and other body tissues, it is also well known that exercise has analgesic effects, particularly isometric exercise. With isometric contraction, the significant decrease in sensitivity to noxious stimulus occurs after low-intensity contractions (25–50% MVC) held for a longer duration[284]. This may be the reason that in our study control group also showed improvement in CS and PPT scores after treatment. It is recommended that strength training should be progressed slowly in a very graded manner.

5.4.10 Precautions in applying Manual Therapy and Therapeutic exercise

It is observed that manual therapy and therapeutic exercise, in general, exert hypoalgesia by activating descending inhibitory pain mechanisms [285, 286]. But in subjects with central sensitization, the reverse may also occur; exercise [287] and potentially manual therapy may induce hyperalgesia if not well controlled. In reality, aggressive exercise or manual therapy in an ‘acute on chronic’ stage of CNSLBP may be detrimental if excessive or forceful movements trigger sensitize peripheral

nociceptors and cause increased or prolonged pain. This flare response may happen through mechanisms of neurogenic inflammation where inflammatory mediators such as Substance P and calcitonin gene-related peptide (CGRP) are released into the periphery and promote pain and chronic inflammation [288]. Further, patients of CNSLBP with CS may experience greater exercise-induced hypoalgesia with lower intensity exercise. Physiotherapists must be skilled enough at discriminating and interpreting patient symptoms during treatment programs through consecutive reassessment.

5.4.11 Clinical Application

The present study may have important clinical implications because it provides preliminary support for using McKenzie exercise program that may work well with conventional physiotherapy program. Specifically, the present study strongly suggests that clinicians who aim to reduce CS, pain, reduce disability and fear avoidance beliefs during the treatment of non-specific chronic low back pain should consider McKenzie exercise program along with conventional physiotherapy program.

Central sensitization inventory - Gujarati version and Fear-avoidance beliefs questionnaire - Gujarati version is recommended in future research to detect the presence of CS and fear avoidance beliefs in musculoskeletal pain patients. As the usage of these questionnaires increases in musculoskeletal pain research in future may lead to its further refinement.

5.5 LIMITATIONS

Every research work is subjected to certain limitations and this study is also not different. Though the present study supported the hypotheses formulated in the Chapter-2, still there are some limitations observed in the study, which should be highlighted to help the researchers planning similar studies in future. Despite our best efforts, the present study has the following limitations:

(a) Data collection by an independent observer was not used.

(b) Patients may have answered questionnaires to please the researcher.

(c) Gender wise patient's distribution in both groups was not equal. A greater number of females were assigned to the study compared with males in both the treatment groups. This gender imbalance may have biased the outcomes.

(d) The sample of the study covers only subjects from Surat, the southern part of Gujarat. For the sake of generalization of results, it would be more appropriate if the sample includes subjects from various parts of the country.

(e) As the elderly participants were not present in the sample, thus, the results cannot be generalized.

(f) One limitation of our study was not blinding the therapists and patients to the treatment allocation and this could be considered as a limitation of the study because of the risk of a possible preference bias due to differing in expertise.

(g) Moreover, we did not include a non-treatment or placebo control group in our study, which also can be considered as a limitation. The rationale for not including a non-treatment group in our study is based on a Cochrane review that investigated the effect of exercise therapy in patients with CLBP[79] which concluded that exercise therapy is at least 10 points(on a scale of 0–100 points) more effective than no treatment.

(h) Although we used precisely translated and validated questionnaires we suspect that the population from Gujarat may have a different understanding of pain concepts and to what degree this would influence our study is not clear.

5.6 FURTHER RECOMMENDATIONS

(a) The long-term benefits of this treatment protocol could be established.

(b) This study can be done with other sub-populations of chronic low back pain.

(c) McKenzie exercise program along with trunk flexors and extensors endurance exercises can be evaluated by comparing with conventional physiotherapy program.

(d) The future study may include heterogeneous samples from larger populations and different zones of the country.

(e) Elderly subjects could be included in future research, for generalization of outcome.

(f) It is further suggested that only two groups should form the future study, one receiving McKenzie exercise program (experimental group) and the other only placebo (control group).

(g) The algometer used in the present study was manually operated. Using digital algometer could be an important improvement for recording PPT and minimizing the human error.

(h) A long-term follow-up (more than one year) study can be done in order to illustrate which treatment approach is more effective in long-term.

6

CONCLUSION

"Having excluded the impossible, whatever remains

and unlikely it may be, that must be the truth."

- Arthur Conan Doyle

6.1 CONCLUSION

The conclusion is described here under two headings:

6.1.1 Primary Conclusion

The findings of this study suggest that 'McKenzie exercise program' can be used as a therapyin reducing pain, ***central sensitization***, minimizing functional disability and fear-avoidance beliefs; in subjects with CNSLBP. However, 'McKenzie exercise program' does not improve trunk flexors and extensors endurance in subjects with CNSLBP.

6.1.2 Secondary Conclusion

Our results suggest that the CSI-G has been successfully translated and cross-culturally adapted from English to Gujarati. The preliminary evidence generated by the psychometric testing showed that the CSI-G demonstrates psychometric properties similar to the English version. This study provides us with the evidence that the CSI-G is a reliable and valid measure to assess CS in Gujarati speaking CLBP patients.

Our results suggest that the FABQ-G has been successfully translated and cross-culturally adapted from English to Gujarati. The preliminary evidence generated by the psychometric testing showed that the FABQ-G shows psychometric properties similar to the English version. This study provides us with the evidence that the FABQ-G is a reliable and valid measure to assess 'fear avoidance beliefs' in Gujarati-speaking CLBP patients and results of FABQ-G can be compared to international studies using other translated versions.

6.1.3 Contribution to Knowledge

This study provided two successful cross-cultural translation and validation of two questionnaires namely, 'Central Sensitization Inventory' and 'Fear-Avoidance Beliefs Questionnaire' into the Gujarati language.

This study proves that McKenzie exercise program has a significant role in reducing central sensitization in CNSLBP patients.

REFERENCES

1. Airaksinen O, Brox JI, Cedraschi C, Hildebrandt J, Klaber-Moffett J, Kovacs F, et al. Chapter 4. European guidelines for the management of chronic nonspecific low back pain. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2006;15 Suppl 2:S192-300.
2. Gordon W. The Back Pain Revolution. 2 ed: Churchill-Livingstone; 2004.
3. Burton AK, Balague F, Cardon G, Eriksen HR, Henrotin Y, Lahad A, et al. Chapter 2. European guidelines for prevention in low back pain : November 2004. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2006;15 Suppl 2:S136-68.
4. Borkan J, Van Tulder M, Reis S, Schoene ML, Croft P, Hermoni D. Advances in the field of low back pain in primary care: a report from the fourth international forum. Spine. 2002;27(5):E128-32.
5. Waddell G. The back pain revolution. London: Churchill Livingstone; 2004.
6. Cherkin D, Kovacs FM, Croft P, Borkan J, Foster NE, Oberg B, et al. The Ninth International Forum for Primary Care Research on Low Back Pain. Spine. 2009;34(3):304-7.
7. Pain terms: a list with definitions and notes on usage. Recommended by the IASP Subcommittee on Taxonomy. Pain. 1979;6(3):249.
8. Melzack R, Casey K. Sensory, motivational, and central control determinants of pain: a new conceptual model in pain. In: Kenshalo D, editor. The skin senses: Proceedings. Springfield (Illinois): Charles C. Thomas; 1968. p. p-63.
9. Jensen MP, Karoly P. Self-Report Scales and Procedures for Assessing Pain in Adults. In: Turk DC, Melzack R, editors. Handbook of Pain Assessment New York: Guilford Publication; 2001.
10. Turk DC MR. Handbook of Pain Assessment. 2 ed: The Guilford Press; 2001.
11. Wade JB, Dougherty LM, Archer CR, Price DD. Assessing the stages of pain processing: a multivariate analytical approach. Pain. 1996;68(1):157-67.
12. Melzack R, Wall P. The challenge of pain. 2 ed. London: Penguin Books; 1996.
13. de CWAC, Davies HT, Chadury Y. Simple pain rating scales hide complex idiosyncratic meanings. Pain. 2000;85(3):457-63.
14. Craig AD. A new view of pain as a homeostatic emotion. Trends in neurosciences. 2003;26(6):303-7.
15. Craig AD. Pain mechanisms: labeled lines versus convergence in central processing. Annual review of neuroscience. 2003;26:1-30.
16. Marchand S. The physiology of pain mechanisms: from the periphery to the brain. Rheumatic diseases clinics of North America. 2008;34(2):285-309.

17. Nicholson B. Differential diagnosis: nociceptive and neuropathic pain. The American journal of managed care. 2006;12(9 Suppl):S256-62.
18. Costigan M, Scholz J, Woolf CJ. Neuropathic pain: a maladaptive response of the nervous system to damage. Annual review of neuroscience. 2009;32:1-32.
19. Finnerup NB, Sindrup SH, Jensen TS. Chronic neuropathic pain: mechanisms, drug targets and measurement. Fundamental & clinical pharmacology. 2007;21(2):129-36.
20. Butler DS, Moseley GL. Explain Pain. Adelaide, Australia: Noigroup Publications 2003.
21. Moseley GL. A pain neuromatrix approach to patients with chronic pain. Manual therapy. 2003;8(3):130-40.
22. Wand BM, Parkitny L, O'Connell NE, Luomajoki H, McAuley JH, Thacker M, et al. Cortical changes in chronic low back pain: current state of the art and implications for clinical practice. Manual therapy. 2011;16(1):15-20.
23. Bolay H, Moskowitz MA. Mechanisms of pain modulation in chronic syndromes. Neurology. 2002;59(5 Suppl 2):S2-7.
24. Giesecke T, Gracely RH, Grant MA, Nachemson A, Petzke F, Williams DA, et al. Evidence of augmented central pain processing in idiopathic chronic low back pain. Arthritis and rheumatism. 2004;50(2):613-23.
25. Clauw DJ, Williams D, Lauerman W, Dahlman M, Aslami A, Nachemson AL, et al. Pain sensitivity as a correlate of clinical status in individuals with chronic low back pain. Spine. 1999;24(19):2035-41.
26. Giesbrecht RJ, Battie MC. A comparison of pressure pain detection thresholds in people with chronic low back pain and volunteers without pain. Physical therapy. 2005;85(10):1085-92.
27. Laursen BS, Bajaj P, Olesen AS, Delmar C, Arendt-Nielsen L. Health related quality of life and quantitative pain measurement in females with chronic non-malignant pain. European journal of pain. 2005;9(3):267-75.
28. Flor H, Braun C, Elbert T, Birbaumer N. Extensive reorganization of primary somatosensory cortex in chronic back pain patients. Neuroscience letters. 1997;224(1):5-8.
29. Apkarian AV, Sosa Y, Sonty S, Levy RM, Harden RN, Parrish TB, et al. Chronic back pain is associated with decreased prefrontal and thalamic gray matter density. The Journal of neuroscience : the official journal of the Society for Neuroscience. 2004;24(46):10410-5.
30. Schmidt-Wilcke T, Leinisch E, Ganssbauer S, Draganski B, Bogdahn U, Altmeppen J, et al. Affective components and intensity of pain correlate with structural differences in gray matter in chronic back pain patients. Pain. 2006;125(1-2):89-97.
31. Meyer K, Tschopp A, Sprott H, Mannion AF. Association between catastrophizing and self-rated pain and disability in patients with chronic low back pain. Journal of rehabilitation medicine. 2009;41(8):620-5.
32. Waxman SE, Tripp DA, Flamenbaum R. The mediating role of depression and negative partner responses in chronic low back pain and relationship satisfaction. The journal of pain : official journal of the American Pain Society. 2008;9(5):434-42.

33. Vlaeyen JW, Kole-Snijders AM, Boeren RG, van Eek H. Fear of movement/(re)injury in chronic low back pain and its relation to behavioral performance. Pain. 1995;62(3):363-72.
34. Crombez G, Vlaeyen JW, Heuts PH, Lysens R. Pain-related fear is more disabling than pain itself: evidence on the role of pain-related fear in chronic back pain disability. Pain. 1999;80(1-2):329-39.
35. Gheldof EL, Crombez G, Van den Bussche E, Vinck J, Van Nieuwenhuyse A, Moens G, et al. Pain-related fear predicts disability, but not pain severity: a path analytic approach of the fear-avoidance model. European journal of pain. 2010;14(8):870.e1-9.
36. Andersson GB. Epidemiology of low back pain. Acta orthopaedica Scandinavica Supplementum. 1998;281:28-31.
37. Dionne CE, Dunn KM, Croft PR. Does back pain prevalence really decrease with increasing age? A systematic review. Age and ageing. 2006;35(3):229-34.
38. Rapoport J, Jacobs P, Bell NR, Klarenbach S. Refining the measurement of the economic burden of chronic diseases in Canada. Chronic diseases in Canada. 2004;25(1):13-21.
39. Deyo RA, Cherkin D, Conrad D, Volinn E. Cost, controversy, crisis: low back pain and the health of the public. Annual review of public health. 1991;12:141-56.
40. Lidgren L. The bone and joint decade 2000-2010. Bulletin of the World Health Organization. 2003;81(9):629.
41. Steenstra I, Verbeek J, Heymans M, Bongers P. Prognostic factors for duration of sick leave in patients sick listed with acute low back pain: a systematic review of the literature. Occupational and environmental medicine. 2005;62(12):851-60.
42. Kent PM, Keating JL. The epidemiology of low back pain in primary care. Chiropractic & Osteopathy. 2005;13:13-.
43. Thelin A, Holmberg S, Thelin N. Functioning in neck and low back pain from a 12-year perspective: a prospective population-based study. Journal of rehabilitation medicine. 2008;40(7):555-61.
44. Volinn E. The epidemiology of low back pain in the rest of the world. A review of surveys in low- and middle-income countries. Spine. 1997;22(15):1747-54.
45. Chaiamnuay P, Darmawan J, Muirden KD, Assawatanabodee P. Epidemiology of rheumatic disease in rural Thailand: a WHO-ILAR COPCORD study. Community Oriented Programme for the Control of Rheumatic Disease. The Journal of rheumatology. 1998;25(7):1382-7.
46. Hoy D, Toole MJ, Morgan D, Morgan C. Low back pain in rural Tibet. Lancet (London, England). 2003;361(9353):225-6.
47. Jin K, Sorock GS, Courtney TK. Prevalence of low back pain in three occupational groups in Shanghai, People's Republic of China. Journal of safety research. 2004;35(1):23-8.
48. Ory FG, Rahman FU, Katagade V, Shukla A, Burdorf A. Respiratory disorders, skin complaints, and low-back trouble among tannery workers in Kanpur, India. American Industrial Hygiene Association journal. 1997;58(10):740-6.
49. Bindra S, Sinha AGK, Benjamin AI. Epidemiology of low back pain in Indian population: A review. International Journal of Basic and Applied Medical Sciences. 2015;5(1):166-79.

50. Ahdhi G, Subramanian R, Saya G, Yamuna T. Prevalence of low back pain and its relation to quality of life and disability among women in rural area of Puducherry, India. Indian Journal of Pain. 2016;30(2):111-5.
51. Hameed PS. Prevalance Of Work Related Low Back Pain Among The Information Technology Professionals In India – A Cross Sectional Study. International Journal of Scientific & Technology Research. 2013;2(7):80-5.
52. Meucci RD, Fassa AG, Faria NMX. Prevalence of chronic low back pain: systematic review. Revista de Saúde Pública. 2015;49:1-.
53. Freburger JK, Holmes GM, Agans RP, Jackman AM, Darter JD, Wallace AS, et al. The Rising Prevalence of Chronic Low Back Pain(). Archives of internal medicine. 2009;169(3):251-8.
54. Hoy D, Bain C, Williams G, March L, Brooks P, Blyth F, et al. A systematic review of the global prevalence of low back pain. Arthritis and rheumatism. 2012;64(6):2028-37.
55. Nachemson AL, Waddell G, Norlund AL. Epidemiology of neck and low back pain. In: Nachemson AL, Jonsson E, editors. Neck and back pain: the scientific evidence of causes, diagnosis and treatment. Philadelphia: Lippincott Williams and Wilkins; 2000.
56. Holloway I, Sofaer-Bennett B, Walker J. The stigmatisation of people with chronic back pain. Disability and rehabilitation. 2007;29(18):1456-64.
57. Drake R, Vogl AW, Mitchell AWM. Gray's Anatomy for Students. 2 ed: Churchill Livingstone; 2009.
58. Lovejoy CO. Evolution of the human lumbopelvic region and its relationship to some clinical deficits of the spine and pelvis. In: Vleeming A, Mooney V, Stoeckart R, editors. Movement, Stability and Lumbopelvic Pain- Integration of Research and Therapy. New York: Churchill Livingstone; 2007. p. 141 – 58.
59. Kishner S, Moradian M, Morello JK. Lumbar Spine Anatomy: Medscape; 2015 [cited 2017 1/4/2017]. Available from: http://emedicine.medscape.com/article/1899031-overview.
60. Adams MA, Stefanakis M, Dolan P. Healing of a painful intervertebral disc should not be confused with reversing disc degeneration: implications for physical therapies for discogenic back pain. Clinical biomechanics (Bristol, Avon). 2010;25(10):961-71.
61. Bogduk N, Twomey LT. Clinical Anatomy of the Lumbar Spine. Edinburgh: Churchill Livingstone; 1987.
62. Cholewicki J, Panjabi MM, Khachatryan A. Stabilizing function of trunk flexor-extensor muscles around a neutral spine posture. Spine. 1997;22(19):2207-12.
63. Rosatelli AL, Ravichandiran K, Agur AM. Three-dimensional study of the musculotendinous architecture of lumbar multifidus and its functional implications. Clinical anatomy (New York, NY). 2008;21(6):539-46.
64. Willard FH, Vleeming A, Schuenke MD, Danneels L, Schleip R. The thoracolumbar fascia: anatomy, function and clinical considerations. Journal of anatomy. 2012;221(6):507-36.
65. Deyo RA. Measuring the functional status of patients with low back pain. Archives of physical medicine and rehabilitation. 1988;69(12):1044-53.

66. van Tulder M, Becker A, Bekkering T, Breen A, del Real MT, Hutchinson A, et al. Chapter 3. European guidelines for the management of acute nonspecific low back pain in primary care. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2006;15 Suppl 2:S169-91.
67. McCarthy CJ, Arnall FA, Strimpakos N, Freemont A, Oldham JA. The biopsychosocial classification of nonspecific loe back pain: A systematic review. Physical Therapy Reviews. 2004;9:17-30.
68. Wiesel SW, Tsourmas N, Feffer HL, Citrin CM, Patronas N. A study of computer-assisted tomography. I. The incidence of positive CAT scans in an asymptomatic group of patients. Spine. 1984;9(6):549-51.
69. Kent P, Keating J. Do primary-care clinicians think that nonspecific low back pain is one condition? Spine. 2004;29(9):1022-31.
70. Frymoyer JW. An international challenge to the diagnosis and treatment of disorders of the lumbar spine. Spine. 1993;18(15):2147-52.
71. Evans G, Richards SH. Low Back Pain: An Evaluation of Therapeutic Interventions: University of Bristol, Department of Social Medici 1996.
72. Croft PR, Macfarlane GJ, Papageorgiou AC, Thomas E, Silman AJ. Outcome of low back pain in general practice: a prospective study. BMJ. 1998;316(7141):1356.
73. Waddell G, Main CJ. Assessment of severity of low back disorders. Acta orthopaedica Belgica. 1987;53(2):269-71.
74. Materson RS. The AHCPR practice guidelines for low back pain. Bulletin on the rheumatic diseases. 1996;45(2):6-8.
75. White AA, 3rd, Gordon SL. Synopsis: workshop on idiopathic low-back pain. Spine. 1982;7(2):141-9.
76. Koes BW, van Tulder MW, Thomas S. Diagnosis and treatment of low back pain. BMJ. 2006;332(7555):1430-4.
77. van Tulder MW, Waddell G. Evidence-based medicine for non-specific low back pain. Best Practice & Research Clinical Rheumatology.19(4):vii-ix.
78. Assendelft W, Morton S, Yu E, Suttorp M, Shekelle P. Spinal manipulative therapy for low-back pain. Cochrane Database of Systematic Reviews. 2004(1).
79. Hayden JA, van Tulder MW, Malmivaara A, Koes BW. Exercise therapy for treatment of non-specific low back pain. The Cochrane database of systematic reviews. 2005(3):Cd000335.
80. Karjalainen K, Malmivaara A, van Tulder M, Roine R, Jauhiainen M, Hurri H, et al. Multidisciplinary biopsychosocial rehabilitation for subacute low back pain among working age adults. The Cochrane database of systematic reviews. 2003(2):Cd002193.
81. Ostelo RW, van Tulder MW, Vlaeyen JW, Linton SJ, Morley SJ, Assendelft WJ. Behavioural treatment for chronic low-back pain. The Cochrane database of systematic reviews. 2005(1):Cd002014.

82. Dankaerts W, O'Sullivan P, Burnett A, Straker L. Differences in sitting postures are associated with nonspecific chronic low back pain disorders when patients are subclassified. Spine. 2006;31(6):698-704.
83. Riddle DL. Classification and low back pain: a review of the literature and critical analysis of selected systems. Physical therapy. 1998;78(7):708-37.
84. Rose SJ. Physical therapy diagnosis: role and function. Physical therapy. 1989;69(7):535-7.
85. Arena JG, Sherman RA, Bruno GM, Young TR. Electromyographic recordings of 5 types of low back pain subjects and non-pain controls in different positions. Pain. 1989;37(1):57-65.

86. Delitto A, Erhard RE, Bowling RW. A treatment-based classification approach to low back syndrome: identifying and staging patients for conservative treatment. Physical therapy. 1995;75(6):470-85; discussion 85-9.
87. O'Sullivan PB. Lumbar segmental 'instability': clinical presentation and specific stabilizing exercise management. Manual therapy. 2000;5(1):2-12.
88. Fritz JM. Use of a classification approach to the treatment of 3 patients with low back syndrome. Physical therapy. 1998;78(7):766-77.
89. O'Sullivan P. Classification of lumbopelvic pain disorders--why is it essential for management? Manual therapy. 2006;11(3):169-70.
90. Dankaerts W, O'Sullivan PB, Burnett AF, Straker LM. The use of a mechanism-based classification system to evaluate and direct management of a patient with non-specific chronic low back pain and motor control impairment--a case report. Manual therapy. 2007;12(2):181-91.
91. O'Sullivan PB, Phyty GD, Twomey LT, Allison GT. Evaluation of specific stabilizing exercise in the treatment of chronic low back pain with radiologic diagnosis of spondylolysis or spondylolisbook. Spine. 1997;22(24):2959-67.
92. O'Sullivan PB, Beales DJ, Beetham JA, Cripps J, Graf F, Lin IB, et al. Altered motor control strategies in subjects with sacroiliac joint pain during the active straight-leg-raise test. Spine. 2002;27(1):E1-8.
93. Stuge B, Laerum E, Kirkesola G, Vollestad N. The efficacy of a treatment program focusing on specific stabilizing exercises for pelvic girdle pain after pregnancy: a randomized controlled trial. Spine. 2004;29(4):351-9.
94. Stuge B, Veierod MB, Laerum E, Vollestad N. The efficacy of a treatment program focusing on specific stabilizing exercises for pelvic girdle pain after pregnancy: a two-year follow-up of a randomized clinical trial. Spine. 2004;29(10):E197-203.
95. Stuge B, Holm I, Vollestad N. To treat or not to treat postpartum pelvic girdle pain with stabilizing exercises? Manual therapy. 2006;11(4):337-43.
96. Fritz JM, Delitto A, Erhard RE. Comparison of Classification-Based Physical Therapy With Therapy Based on Clinical Practice Guidelines for Patients with Acute Low Back Pain: A Randomized Clinical Trial. Spine. 2003;28(13):1363-71.

97. Mooney V VJ, Morris C. Clinical management of chronic, disabling low back syndromes. C M, editor. New York: McGraw-Hill; 2006.
98. McKenzie R, May S. The lumbar spine: Mechanical Diagnosis & Therapy, vol 1. New Zealand: Spinal Publications; 2003.
99. McKenzie R, May S. The lumbar spine: Mechanical Diagnosis & Therapy, vol 2. New Zealand: Spinal Publications; 2003.
100. Moffett JK, Torgerson D, Bell-Syer S, Jackson D, Llewlyn-Phillips H, Farrin A, et al. Randomised controlled trial of exercise for low back pain: clinical outcomes, costs, and preferences. BMJ (Clinical research ed). 1999;319(7205):279-83.
101. Seferlis T, Lindholm L, Nemeth G. Cost-minimisation analysis of three conservative treatment programmes in 180 patients sick-listed for acute low-back pain. Scandinavian journal of primary health care. 2000;18(1):53-7.
102. Long A, Donelson R, Fung T. Does it matter which exercise? A randomized control trial of exercise for low back pain. Spine. 2004;29(23):2593-602.
103. Wetzel FT, Donelson R. The role of repeated end-range/pain response assessment in the management of symptomatic lumbar discs. The spine journal : official journal of the North American Spine Society. 2003;3(2):146-54.
104. Stankovic R, Johnell O. Conservative treatment of acute low-back pain. A prospective randomized trial: McKenzie method of treatment versus patient education in "mini back school". Spine. 1990;15(2):120-3.
105. Boissonnault W, Fabio RP. Pain profile of patients with low back pain referred to physical therapy. The Journal of orthopaedic and sports physical therapy. 1996;24(4):180-91.
106. Pengel LH, Refshauge KM, Maher CG. Responsiveness of pain, disability, and physical impairment outcomes in patients with low back pain. Spine. 2004;29(8):879-83.
107. van Deursen LL, Patijn J, Durinck JR, Brouwer R, van Erven-Sommers JR, Vortman BJ. Sitting and low back pain: the positive effect of rotary dynamic stimuli during prolonged sitting. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 1999;8(3):187-93.
108. Donelson R, Silva G, Murphy K. Centralization phenomenon. Its usefulness in evaluating and treating referred pain. Spine. 1990;15(3):211-3.
109. Long AL. The centralization phenomenon. Its usefulness as a predictor or outcome in conservative treatment of chronic law back pain (a pilot study). Spine. 1995;20(23):2513-20; discussion 21.
110. Karas R, McIntosh G, Hall H, Wilson L, Melles T. The relationship between nonorganic signs and centralization of symptoms in the prediction of return to work for patients with low back pain. Physical therapy. 1997;77(4):354-60; discussion 61-9.
111. Sufka A, Hauger B, Trenary M, Bishop B, Hagen A, Lozon R, et al. Centralization of low back pain and perceived functional outcome. The Journal of orthopaedic and sports physical therapy. 1998;27(3):205-12.

112. Werneke M, Hart DL, Cook D. A descriptive study of the centralization phenomenon. A prospective analysis. Spine. 1999;24(7):676-83.
113. Werneke M, Hart DL. Centralization phenomenon as a prognostic factor for chronic low back pain and disability. Spine. 2001;26(7):758-64; discussion 65.
114. Aina A, May S, Clare H. The centralization phenomenon of spinal symptoms--a systematic review. Manual therapy. 2004;9(3):134-43.
115. Petersen T, Kryger P, Ekdahl C, Olsen S, Jacobsen S. The effect of McKenzie therapy as compared with that of intensive strengthening training for the treatment of patients with subacute or chronic low back pain: A randomized controlled trial. Spine. 2002;27(16):1702-9.
116. Cherkin DC, Deyo RA, Battie M, Street J, Barlow W. A comparison of physical therapy, chiropractic manipulation, and provision of an educational booklet for the treatment of patients with low back pain. The New England journal of medicine. 1998;339(15):1021-9.
117. Delitto A, Cibulka MT, Erhard RE, Bowling RW, Tenhula JA. Evidence for use of an extension-mobilization category in acute low back syndrome: a prescriptive validation pilot study. Physical therapy. 1993;73(4):216-22; discussion 23-8.
118. Chou R, Huffman LH, American Pain S, American College of P. Nonpharmacologic therapies for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. Annals of internal medicine. 2007;147(7):492-504.
119. Clare HA, Adams R, Maher CG. A systematic review of efficacy of McKenzie therapy for spinal pain. The Australian journal of physiotherapy. 2004;50(4):209-16.
120. Machado LA, de Souza M, Ferreira PH, Ferreira ML. The McKenzie method for low back pain: a systematic review of the literature with a meta-analysis approach. Spine. 2006;31(9):E254-62.
121. Gillan MG, Ross JC, McLean IP, Porter RW. The natural history of trunk list, its associated disability and the influence of McKenzie management. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 1998;7(6):480-3.
122. Kjellman G, Oberg B. A randomized clinical trial comparing general exercise, McKenzie treatment and a control group in patients with neck pain. Journal of rehabilitation medicine. 2002;34(4):183-90.
123. Schenk RJ, Jozefczyk C, Kopf A. A Randomized Trial Comparing Interventions in Patients with Lumbar Posterior Derangement. Journal of Manual & Manipulative Therapy. 2003;11(2):95-102.
124. Elnaggar IM, Nordin M, Sheikhzadeh A, Parnianpour M, Kahanovitz N. Effects of spinal flexion and extension exercises on low-back pain and spinal mobility in chronic mechanical low-back pain patients. Spine. 1991;16(8):967-72.

125. Cook C, Hegedus EJ, Ramey K. Physical Therapy Exercise Intervention Based on Classification Using the Patient Response Method: A Systematic Review of the Literature. Journal of Manual & Manipulative Therapy. 2005;13(3):152-62.
126. Slade SC, Keating JL. Unloaded movement facilitation exercise compared to no exercise or alternative therapy on outcomes for people with nonspecific chronic low back pain: a systematic review. Journal of manipulative and physiological therapeutics. 2007;30(4):301-11.
127. Miller ER, Schenk RJ, Karnes JL, Rousselle JG. A Comparison of the McKenzie Approach to a Specific Spine Stabilization Program for Chronic Low Back Pain. Journal of Manual & Manipulative Therapy. 2005;13(2):103-12.
128. Nijs J, Apeldoorn A, Hallegraeff H, Clark J, Smeets R, Malfliet A, et al. Low back pain: guidelines for the clinical classification of predominant neuropathic, nociceptive, or central sensitization pain. Pain physician. 2015;18(3):E333-46.
129. Neblett R, Hartzell MM, Cohen H, Mayer TG, Williams M, Choi Y, et al. Ability of the central sensitization inventory to identify central sensitivity syndromes in an outpatient chronic pain sample. The Clinical journal of pain. 2015;31(4):323-32.
130. Hoy D, March L, Brooks P, Blyth F, Woolf A, Bain C, et al. The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. Annals of the Rheumatic Diseases. 2014;73(6):968-74.
131. Ekman M, Johnell O, Lidgren L. The economic cost of low back pain in sweden in 2001. Acta Orthopaedica. 2005;76(2):275-84.
132. Manchikanti L. Epidemiology of low back pain. Pain physician. 2000;3(2):167-92.
133. Hoy D, Toole MJ, Morgan D, Morgan C. Low back pain in rural Tibet. The Lancet.361(9353):225-6.
134. Cakmak A, Yucel B, Ozyalcn SN, Bayraktar B, Ural HI, Duruoz MT, et al. The frequency and associated factors of low back pain among a younger population in Turkey. Spine. 2004;29(14):1567-72.
135. Gilgil E, Kacar C, Butun B, Tuncer T, Urhan S, Yildirim C, et al. Prevalence of low back pain in a developing urban setting. Spine. 2005;30(9):1093-8.
136. Barrero LH, Hsu YH, Terwedow H, Perry MJ, Dennerlein JT, Brain JD, et al. Prevalence and physical determinants of low back pain in a rural Chinese population. Spine. 2006;31(23):2728-34.
137. Andersson GBJ. Epidemiological features of chronic low-back pain. The Lancet.354(9178):581-5.
138. Airaksinen O, Brox JI, Cedraschi C, Hildebrandt J, Klaber-Moffett J, Kovacs F, et al. Chapter 4 European guidelines for the management of chronic nonspecific low back pain. European Spine Journal. 2006;15(Suppl 2):s192-s300.
139. Kovacs FM, Arana E. Degenerative disease of the lumbar spine. Radiologia. 2016.
140. Steffens D, Hancock MJ, Pereira LS, Kent PM, Latimer J, Maher CG. Do MRI findings identify patients with low back pain or sciatica who respond better to particular interventions? A systematic review. European spine journal : official publication of the European Spine Society,

the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2015.

141. Peters ML, Vlaeyen JW, Weber WE. The joint contribution of physical pathology, pain-related fear and catastrophizing to chronic back pain disability. Pain. 2005;113(1-2):45-50.
142. Baranauskas G, Nistri A. Sensitization of pain pathways in the spinal cord: cellular mechanisms. Progress in neurobiology. 1998;54(3):349-65.
143. Staud R. Evidence of involvement of central neural mechanisms in generating fibromyalgia pain. Current rheumatology reports. 2002;4(4):299-305.
144. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. Pain. 2011;152(3 Suppl):S2-15.
145. Sorensen J, Graven-Nielsen T, Henriksson KG, Bengtsson M, Arendt-Nielsen L. Hyperexcitability in fibromyalgia. The Journal of rheumatology. 1998;25(1):152-5.
146. Leffler AS, Hansson P, Kosek E. Somatosensory perception in a remote pain-free area and function of diffuse noxious inhibitory controls (DNIC) in patients suffering from long-term trapezius myalgia. European journal of pain. 2002;6(2):149-59.
147. Banic B, Petersen-Felix S, Andersen OK, Radanov BP, Villiger PM, Arendt-Nielsen L, et al. Evidence for spinal cord hypersensitivity in chronic pain after whiplash injury and in fibromyalgia. Pain. 2004;107(1-2):7-15.
148. Meeus M, Nijs J, Huybrechts S, Truijen S. Evidence for generalized hyperalgesia in chronic fatigue syndrome: a case control study. Clinical rheumatology. 2010;29(4):393-8.
149. Loeser JD, Treede RD. The Kyoto protocol of IASP Basic Pain Terminology. Pain. 2008;137(3):473-7.
150. Meyer RA, Campbell JN, Raja SN. Peripheral neural mechanisms of nociception. 3 ed. Wall PD, Melzack R, editors. Edinburgh: Churchill Livingstone; 1995.
151. Staud R, Craggs JG, Robinson ME, Perlstein WM, Price DD. Brain activity related to temporal summation of C-fiber evoked pain. Pain. 2007;129(1-2):130-42.
152. Meeus M, Nijs J, Van de Wauwer N, Toeback L, Truijen S. Diffuse noxious inhibitory control is delayed in chronic fatigue syndrome: an experimental study. Pain. 2008;139(2):439-48.
153. Meeus M, Nijs J. Central sensitization: a biopsychosocial explanation for chronic widespread pain in patients with fibromyalgia and chronic fatigue syndrome. Clinical rheumatology. 2007;26(4):465-73.
154. Zhuo M. A synaptic model for pain: long-term potentiation in the anterior cingulate cortex. Molecules and cells. 2007;23(3):259-71.
155. Maier SF, Watkins LR. Cytokines for psychologists: implications of bidirectional immune-to-brain communication for understanding behavior, mood, and cognition. Psychological review. 1998;105(1):83-107.
156. Watkins LR, Maier SF. Implications of immune-to-brain communication for sickness and pain. Proceedings of the National Academy of Sciences. 1999;96(14):7710-3.
157. Bazan NG. COX-2 as a multifunctional neuronal modulator. Nat Med. 2001;7(4):414-5.

158. Samad TA, Moore KA, Sapirstein A, Billet S, Allchorne A, Poole S, et al. Interleukin-1beta-mediated induction of Cox-2 in the CNS contributes to inflammatory pain hypersensitivity. Nature. 2001;410(6827):471-5.
159. Gracely RH, Grant MA, Giesecke T. Evoked pain measures in fibromyalgia. Best practice & research Clinical rheumatology. 2003;17(4):593-609.
160. Nijs J, Van Houdenhove B. From acute musculoskeletal pain to chronic widespread pain and fibromyalgia: application of pain neurophysiology in manual therapy practice. Manual therapy. 2009;14(1):3-12.
161. Woolf CJ, Salter MW. Neuronal plasticity: increasing the gain in pain. Science (New York, NY). 2000;288(5472):1765-9.
162. Zusman M. Forebrain-mediated sensitization of central pain pathways: 'non-specific' pain and a new image for MT. Manual therapy. 2002;7(2):80-8.
163. Lorenz J, Minoshima S, Casey KL. Keeping pain out of mind: the role of the dorsolateral prefrontal cortex in pain modulation. Brain : a journal of neurology. 2003;126(Pt 5):1079-91.
164. Rygh LJ, Tjolsen A, Hole K, Svendsen F. Cellular memory in spinal nociceptive circuitry. Scandinavian journal of psychology. 2002;43(2):153-9.
165. Brosschot JF. Cognitive-emotional sensitization and somatic health complaints. Scandinavian journal of psychology. 2002;43(2):113-21.
166. Seminowicz DA, Davis KD. Cortical responses to pain in healthy individuals depends on pain catastrophizing. Pain. 2006;120(3):297-306.
167. Ploghaus A, Becerra L, Borras C, Borsook D. Neural circuitry underlying pain modulation: expectation, hypnosis, placebo. Trends in cognitive sciences. 2003;7(5):197-200.
168. Seifert F, Maihofner C. Central mechanisms of experimental and chronic neuropathic pain: findings from functional imaging studies. Cellular and molecular life sciences : CMLS. 2009;66(3):375-90.
169. W. W. Hyperalgesia and Allodynia. New York: Raven Press; 1992.
170. Nijs J, Van Houdenhove B, Oostendorp RA. Recognition of central sensitization in patients with musculoskeletal pain: Application of pain neurophysiology in manual therapy practice. Manual therapy. 2010;15(2):135-41.
171. Peters ML, Schmidt AJ. Differences in pain perception and sensory discrimination between chronic low back pain patients and healthy controls. Journal of psychosomatic research. 1992;36(1):47-53.
172. Burns PB, Rohrich RJ, Chung KC. The Levels of Evidence and their role in Evidence-Based Medicine. Plastic and reconstructive surgery. 2011;128(1):305-10.
173. O'Neill S, Manniche C, Graven-Nielsen T, Arendt-Nielsen L. Generalized deep-tissue hyperalgesia in patients with chronic low-back pain. European journal of pain. 2007;11(4):415-20.
174. Meeus M, Roussel NA, Truijen S, Nijs J. Reduced pressure pain thresholds in response to exercise in chronic fatigue syndrome but not in chronic low back pain: an experimental study. Journal of rehabilitation medicine. 2010;42(9):884-90.

175. Lautenbacher S, Galfe G, Karlbauer G, Moltner A, Strian F. Effects of chronic back pain on the perception of experimental heat pain. Perceptual and motor skills. 1990;71(3 Pt 2):1283-92.
176. Derbyshire SW, Jones AK, Creed F, Starz T, Meltzer CC, Townsend DW, et al. Cerebral responses to noxious thermal stimulation in chronic low back pain patients and normal controls. NeuroImage. 2002;16(1):158-68.
177. Arntz A, Merckelbach H, Peters M, Schmidt AJ. Chronic low back pain, response specificity and habituation to painful stimuli. Journal of Psychophysiology. 1991;5:177-88.
178. Kleinbohl D, Holzl R, Moltner A, Rommel C, Weber C, Osswald PM. Psychophysical measures of sensitization to tonic heat discriminate chronic pain patients. Pain. 1999;81(1-2):35-43.
179. Flor H, Knost B, Birbaumer N. The role of operant conditioning in chronic pain: an experimental investigation. Pain. 2002;95(1-2):111-8.
180. Diers M, Koeppe C, Diesch E, Stolle AM, Holzl R, Schiltenwolf M, et al. Central processing of acute muscle pain in chronic low back pain patients: an EEG mapping study. Journal of clinical neurophysiology : official publication of the American Electroencephalographic Society. 2007;24(1):76-83.
181. Julien N, Goffaux P, Arsenault P, Marchand S. Widespread pain in fibromyalgia is related to a deficit of endogenous pain inhibition. Pain. 2005;114(1-2):295-302.
182. Hoffman MD, Shepanski MA, Mackenzie SP, Clifford PS. Experimentally induced pain perception is acutely reduced by aerobic exercise in people with chronic low back pain. Journal of rehabilitation research and development. 2005;42(2):183-90.
183. Peters ML, Schmidt AJ, Van den Hout MA, Koopmans R, Sluijter ME. Chronic back pain, acute postoperative pain and the activation of diffuse noxious inhibitory controls (DNIC). Pain. 1992;50(2):177-87.
184. Kosek E, Ordeberg G. Lack of pressure pain modulation by heterotopic noxious conditioning stimulation in patients with painful osteoarthritis before, but not following, surgical pain relief. Pain. 2000;88(1):69-78.
185. Pielsticker A, Haag G, Zaudig M, Lautenbacher S. Impairment of pain inhibition in chronic tension-type headache. Pain. 2005;118(1-2):215-23.
186. Le Bars D. The whole body receptive field of dorsal horn multireceptive neurones. Brain research Brain research reviews. 2002;40(1-3):29-44.
187. Le Bars D, Willer JC, De Broucker T. Morphine blocks descending pain inhibitory controls in humans. Pain. 1992;48(1):13-20.
188. Chitour D, Dickenson AH, Le Bars D. Pharmacological evidence for the involvement of serotonergic mechanisms in diffuse noxious inhibitory controls (DNIC). Brain research. 1982;236(2):329-37.
189. Willer JC, Le Bars D, De Broucker T. Diffuse noxious inhibitory controls in man: involvement of an opioidergic link. European journal of pharmacology. 1990;182(2):347-55.

190. Koltyn KF, Arbogast RW. Perception of pain after resistance exercise. British Journal of Sports Medicine. 1998;32(1):20-4.
191. Millan MJ. Descending control of pain. Progress in neurobiology. 2002;66(6):355-474.
192. Hoffman MD, Shepanski MA, Ruble SB, Valic Z, Buckwalter JB, Clifford PS. Intensity and duration threshold for aerobic exercise-induced analgesia to pressure pain. Archives of physical medicine and rehabilitation. 2004;85(7):1183-7.
193. Sandrini G, Serrao M, Rossi P, Romaniello A, Cruccu G, Willer JC. The lower limb flexion reflex in humans. Progress in neurobiology. 2005;77(6):353-95.
194. Willer JC. Comparative study of perceived pain and nociceptive flexion reflex in man. Pain. 1977;3(1):69-80.
195. Lethem J, Slade PD, Troup JD, Bentley G. Outline of a Fear-Avoidance Model of exaggerated pain perception--I. Behaviour research and therapy. 1983;21(4):401-8.
196. Vlaeyen JW, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. Pain. 2000;85(3):317-32.
197. Arendt-Nielsen L, Graven-Nielsen T. Translational musculoskeletal pain research. Best practice & research Clinical rheumatology. 2011;25(2):209-26.
198. Sterling M, Jull G, Vicenzino B, Kenardy J. Sensory hypersensitivity occurs soon after whiplash injury and is associated with poor recovery. Pain. 2003;104(3):509-17.
199. Schliessbach J, Siegenthaler A, Streitberger K, Eichenberger U, Nuesch E, Juni P, et al. The prevalence of widespread central hypersensitivity in chronic pain patients. European journal of pain. 2013;17(10):1502-10.
200. Flor H. The modification of cortical reorganization and chronic pain by sensory feedback. Applied psychophysiology and biofeedback. 2002;27(3):215-27.
201. Lotze M, Moseley GL. Role of distorted body image in pain. Current rheumatology reports. 2007;9(6):488-96.
202. Peters ML, Schmidt AJ, Van den Hout MA. Chronic low back pain and the reaction to repeated acute pain stimulation. Pain. 1989;39(1):69-76.
203. Flor H. Cortical reorganisation and chronic pain: implications for rehabilitation. Journal of rehabilitation medicine. 2003(41 Suppl):66-72.
204. Flor H, Elbert T, Knecht S, Wienbruch C, Pantev C, Birbaumer N, et al. Phantom-limb pain as a perceptual correlate of cortical reorganization following arm amputation. Nature. 1995;375(6531):482-4.
205. Wand BM, O'Connell NE. Chronic non-specific low back pain - sub-groups or a single mechanism? BMC musculoskeletal disorders. 2008;9:11.
206. Sanzarello I, Merlini L, Rosa MA, Perrone M, Frugiuele J, Borghi R, et al. Central sensitization in chronic low back pain: A narrative review. Journal of back and musculoskeletal rehabilitation. 2016;29(4):625-33.
207. Graven-Nielsen T, Arendt-Nielsen L. Assessment of mechanisms in localized and widespread musculoskeletal pain. Nature reviews Rheumatology. 2010;6(10):599-606.

208. Neblett R, Cohen H, Choi Y, Hartzell M, Williams M, Mayer TG, et al. The Central Sensitization Inventory (CSI): Establishing Clinically-Significant Values For Identifying Central Sensitivity Syndromes In An Outpatient Chronic Pain Sample. The journal of pain : official journal of the American Pain Society. 2013;14(5):438-45.
209. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior research methods. 2007;39(2):175-91.
210. Garcia AN, Costa Lda C, da Silva TM, Gondo FL, Cyrillo FN, Costa RA, et al. Effectiveness of back school versus McKenzie exercises in patients with chronic nonspecific low back pain: a randomized controlled trial. Physical therapy. 2013;93(6):729-47.
211. Richardson C, Hodges PW, Hides J. Therapeutic Exercise for Lumbopelvic Stabilization-A Motor Control Approach for the Treatment and Prevention of Low Back Pain. 2 ed: CHURCHILL LIVINGSTONE; 2004.
212. Mayer TG, Neblett R, Cohen H, Howard KJ, Choi YH, Williams MJ, et al. The development and psychometric validation of the central sensitization inventory. Pain practice : the official journal of World Institute of Pain. 2012;12(4):276-85.
213. Neblett R, Cohen H, Choi Y, Hartzell MM, Williams M, Mayer TG, et al. The Central Sensitization Inventory (CSI): establishing clinically significant values for identifying central sensitivity syndromes in an outpatient chronic pain sample. The journal of pain : official journal of the American Pain Society. 2013;14(5):438-45.
214. Childs JD, Piva SR, Fritz JM. Responsiveness of the numeric pain rating scale in patients with low back pain. Spine. 2005;30(11):1331-4.
215. Geletka BJ, O'Hearn MA, Courtney CA. Quantitative sensory testing changes in the successful management of chronic low back pain. The Journal of manual & manipulative therapy. 2012;20(1):16-22.
216. Hogeweg JA, Kuis W, Huygen AC, de Jong-de vos van Steenwijk C, Bernards AT, Oostendorp RA, et al. The pain threshold in juvenile chronic arthritis. British journal of rheumatology. 1995;34(1):61-7.
217. Vanderweeen L, Oostendorp RA, Vaes P, Duquet W. Pressure algometry in manual therapy. Manual therapy. 1996;1(5):258-65.
218. Binderup AT, Arendt-Nielsen L, Madeleine P. Pressure pain sensitivity maps of the neck-shoulder and the low back regions in men and women. BMC musculoskeletal disorders. 2010;11:234.
219. Nambi GS. Reliability, validity, sensitivity and specificity of Guajarati version of the Roland-Morris Disability Questionnaire. Journal of Back & Musculoskeletal Rehabilitation. 2013;26(2):149-53.
220. Roland M, Fairbank J. The Roland-Morris Disability Questionnaire and the Oswestry Disability Questionnaire. Spine. 2000;25(24):3115-24.

221. Waddell G, Newton M, Henderson I, Somerville D, Main CJ. A Fear-Avoidance Beliefs Questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability. Pain. 1993;52(2):157-68.
222. Bid DD, Soni NC, Rathod PV, Ramalingam AT, Sinha RK. Cross Cultural Adaptation, Reliability and Validity of Gujarati Version of Fear Avoidance Belief Questionnaire in Chronic Low Back Pain. NJIRM. 2016;7(6):1-8.
223. Ito T, Shirado O, Suzuki H, Takahashi M, Kaneda K, Strax TE. Lumbar trunk muscle endurance testing: an inexpensive alternative to a machine for evaluation. Archives of physical medicine and rehabilitation. 1996;77(1):75-9.
224. Costa LO, Maher CG, Latimer J, Ferreira PH, Ferreira ML, Pozzi GC, et al. Clinimetric testing of three self-report outcome measures for low back pain patients in Brazil: which one is the best? Spine. 2008;33(22):2459-63.
225. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine. 2000;25(24):3186-91.
226. Guillemin F, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality of life measures: literature review and proposed guidelines. Journal of clinical epidemiology. 1993;46(12):1417-32.
227. McKenzie J, Wood ML, Kotecki JE, Clark JK, Brey RA. Establishing Content Validity: Using Qualitative and Quantitative Steps. American Journal of Health Behavior. 1999;23(4):311-8.
228. Joseph F. Hair RLT, Rolph E. Anderson, William Black. Multivariate Data Analysis. 5 ed: Prentice Hall; 1998.
229. Terwee CB, Bot SD, de Boer MR, van der Windt DA, Knol DL, Dekker J, et al. Quality criteria were proposed for measurement properties of health status questionnaires. Journal of clinical epidemiology. 2007;60(1):34-42.
230. Streiner D, Norman G. Health measurement scales-A practical guide to their development and use. 4 ed: Oxford University Press, 2008.
231. Fowler J, Chevannes M, Jarvis P. Practical statistics for nursing and health care. New York, Chichester: Wiley; 2002.
232. Tabachnick B, Fidell L. Using multivariate statistics 3ed. New York: Harper & Row; 1996.
233. Comery AL, Lee HB. A First Course in Factor Analysis. Hillsdale, NJ: Erlbaum; 1992.
234. Cronbach LJ. Coefficient alpha and the internal structure of tests. Psychometrika. 1951;16(3):297-334.
235. Portney L, Watkins M. Foundation of Clinical Research: Applications to practice. Upper Saddle River, NJ: Prentice-Hall; 2000.
236. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet (London, England). 1986;1(8476):307-10.
237. Hopkins WG. Measures of reliability in sports medicine and science. Sports medicine (Auckland, NZ). 2000;30(1):1-15.
238. Neblett R, Hartzell MM, Mayer TG, Cohen H, Gatchel RJ. Establishing Clinically Relevant Severity Levels for the Central Sensitization Inventory. Pain Practice. 2016:n/a-n/a.

239. George D, Mallery P. SPSS for Windows step by step: A simple Guide and Reference. 11.0 Update 4ed. Boston: Allyn & Bacon; 2003.
240. Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. Bmj. 1999;319(7211):670-4.
241. Cook RJ, Zeng L, Yi GY. Marginal Analysis of Incomplete Longitudinal Binary Data: A Cautionary Note on LOCF Imputation. Biometrics. 2004;60(3):820-8.
242. Gadbury GL, Coffey CS, Allison DB. Modern statistical methods for handling missing repeated measurements in obesity trial data: beyond LOCF. Obesity reviews : an official journal of the International Association for the Study of Obesity. 2003;4(3):175-84.
243. Sphericity: Laerd Statistics; 2017 [12/05/2017]. Available from: https://statistics.laerd.com/statistical-guides/sphericity-statistical-guide.php.
244. Neblett R, Hartzell MM, Mayer TG, Cohen H, Gatchel RJ. Establishing Clinically Relevant Severity Levels for the Central Sensitization Inventory. Pain Practice. 2017;17(2):166-75.
245. Pitance L, Piraux E, Lannoy B, Meeus M, Berquin A, Eeckhout C, et al. Cross cultural adaptation, reliability and validity of the French version of the central sensitization inventory. Manual therapy.25:e83-e4.
246. Kregel J, Vuijk PJ, Descheemaeker F, Keizer D, van der Noord R, Nijs J, et al. The Dutch Central Sensitization Inventory (CSI): Factor Analysis, Discriminative Power and Test-Retest Reliability. The Clinical journal of pain. 2015.
247. Mayer TG, Neblett R, Cohen H, Howard KJ, Choi YH, Williams MJ, et al. The Development and Psychometric Validation of the Central Sensitization Inventory (CSI). Pain Practice. 2012;12(4):276-85.
248. Keszei AP, Novak M, Streiner DL. Introduction to health measurement scales. Journal of psychosomatic research. 2010;68(4):319-23.
249. Cuesta-Vargas AI, Roldan-Jimenez C, Neblett R, Gatchel RJ. Cross-cultural adaptation and validity of the Spanish central sensitization inventory. SpringerPlus. 2016;5(1):1837.
250. Staerkle R, Mannion AF, Elfering A, Junge A, Semmer NK, Jacobshagen N, et al. Longitudinal validation of the fear-avoidance beliefs questionnaire (FABQ) in a Swiss-German sample of low back pain patients. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2004;13(4):332-40.
251. Pfingsten M, Kroner-Herwig B, Leibing E, Kronshage U, Hildebrandt J. Validation of the German version of the Fear-Avoidance Beliefs Questionnaire (FABQ). European journal of pain. 2000;4(3):259-66.
252. de Souza FS, Marinho Cda S, Siqueira FB, Maher CG, Costa LO. Psychometric testing confirms that the Brazilian-Portuguese adaptations, the original versions of the Fear-Avoidance Beliefs Questionnaire, and the Tampa Scale of Kinesiophobia have similar measurement properties. Spine. 2008;33(9):1028-33.

253. Grotle M, Brox JI, Vollestad NK. Reliability, validity and responsiveness of the fear-avoidance beliefs questionnaire: methodological aspects of the Norwegian version. Journal of rehabilitation medicine. 2006;38(6):346-53.
254. Georgoudis G, Papathanasiou G, Spiropoulos P, Katsoulakis K. Cognitive assessment of musculoskeletal pain with a newly validated Greek version of the Fear-Avoidance Beliefs Questionnaire (FABQ). European journal of pain. 2007;11(3):341-51.
255. Pei LB, Xia JJ, Yan JL. Cross-cultural adaptation, reliability and validity of the Chinese version of the Fear Avoidance Beliefs Questionnaire. The Journal of international medical research. 2010;38(6):1985-96.
256. Kovacs FM, Muriel A, Medina JM, Abraira V, Sanchez MD, Jauregui JO. Psychometric characteristics of the Spanish version of the FAB questionnaire. Spine. 2006;31(1):104-10.
257. Chaory K, Fayad F, Rannou F, Lefevre-Colau MM, Fermanian J, Revel M, et al. Validation of the French version of the fear avoidance belief questionnaire. Spine. 2004;29(8):908-13.
258. Guadagnoli E, Velicer WF. Relation of sample size to the stability of component patterns. Psychological bulletin. 1988;103(2):265-75.
259. Schnebel BE, Watkins RG, Dillin W. The role of spinal flexion and extension in changing nerve root compression in disc herniations. Spine. 1989;14(8):835-7.
260. Porterfield J, DeRosa C. Mechanical Low Back Pain. Perspectives in Functional Anatomy. 2 ed. Philadelphia, PA: WB Saunders Company; 1998.
261. Mbada CE, Ayanniyi O, Ogunlade SO. Effect of static and dynamic back extensor muscles endurance exercise on pain intensity, activity limitation and participation restriction in patients with Long-Term Mechanical Low-Back Pain. Rehabilitacja Medyczna. 2011;15(3):11-20.
262. Holmes B, Leggett S, Mooney V, Nichols J, Negri S, Hoeyberghs A. Comparison of Female Geriatric Lumbar-Extension Strength: Asymptotic Versus Chronic Low Back Pain Patients and Their Response to Active Rehabilitation. Clinical Spine Surgery. 1996;9(1):17-22.
263. Winfield JB. Fibromyalgia and related central sensitivity syndromes: twenty-five years of progress. Seminars in arthritis and rheumatism. 2007;36(6):335-8.
264. Imamura M, Chen J, Matsubayashi SR, Targino RA, Alfieri FM, Bueno DK, et al. Changes in pressure pain threshold in patients with chronic nonspecific low back pain. Spine. 2013;38(24):2098-107.
265. Imamura M, Alfieri FM, Filippo TR, Battistella LR. Pressure pain thresholds in patients with chronic nonspecific low back pain. Journal of back and musculoskeletal rehabilitation. 2016;29(2):327-36.
266. ÖZDOLAP Ş, SARIKAYA S, KÖKTÜRK F. Evaluation of Pain Pressure Threshold and Widespread Pain in Chronic Low Back Pain. Turkish Journal of Physical Medicine and Rehabilitation. 2014;60(1):32-6.
267. Farasyn A, Meeusen R. The influence of non-specific low back pain on pressure pain thresholds and disability. European journal of pain. 2005;9(4):375-81.

268. Paatelma M, Kilpikoski S, Simonen R, Heinonen A, Alen M, Videman T. Orthopaedic manual therapy, McKenzie method or advice only for low back pain in working adults: a randomized controlled trial with one year follow-up. Journal of rehabilitation medicine. 2008;40(10):858-63.
269. Al-Obaidi SM, Al-Sayegh NA, Ben Nakhi H, Al-Mandeel M. Evaluation of the McKenzie intervention for chronic low back pain by using selected physical and bio-behavioral outcome measures. PM & R : the journal of injury, function, and rehabilitation. 2011;3(7):637-46; quiz 46.
270. George SZ, Bialosky JE, Donald DA. The centralization phenomenon and fear-avoidance beliefs as prognostic factors for acute low back pain: a preliminary investigation involving patients classified for specific exercise. The Journal of orthopaedic and sports physical therapy. 2005;35(9):580-8.
271. Mbada CE, Ayanniyi O, Ogunlade SO. Comparative efficacy of three active treatment modules on psychosocial variables in patients with long-term mechanical low-back pain: a randomized-controlled trial. Archives of Physiotherapy. 2015;5(1):10.
272. Browder DA, Childs JD, Cleland JA, Fritz JM. Effectiveness of an extension-oriented treatment approach in a subgroup of subjects with low back pain: a randomized clinical trial. Physical therapy. 2007;87(12):1608-18; discussion 577-9.
273. Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. Controlled clinical trials. 1989;10(4):407-15.
274. Halliday MH, Pappas E, Hancock MJ, Clare HA, Pinto RZ, Robertson G, et al. A Randomized Controlled Trial Comparing the McKenzie Method to Motor Control Exercises in People With Chronic Low Back Pain and a Directional Preference. Journal of Orthopaedic & Sports Physical Therapy. 2016;46(7):514-22.
275. Machado LA, Maher CG, Herbert RD, Clare H, McAuley JH. The effectiveness of the McKenzie method in addition to first-line care for acute low back pain: a randomized controlled trial. BMC Medicine. 2010;8(1):10.
276. Nijs J, Kosek E, Van Oosterwijck J, Meeus M. Dysfunctional endogenous analgesia during exercise in patients with chronic pain: to exercise or not to exercise? Pain physician. 2012;15(3 Suppl):Es205-13.
277. Lluch Girbes E, Nijs J, Torres-Cueco R, Lopez Cubas C. Pain treatment for patients with osteoarthritis and central sensitization. Physical therapy. 2013;93(6):842-51.
278. Sterling M, Pedler A, Chan C, Puglisi M, Vuvan V, Vicenzino B. Cervical lateral glide increases nociceptive flexion reflex threshold but not pressure or thermal pain thresholds in chronic whiplash associated disorders: A pilot randomised controlled trial. Manual therapy. 2010;15(2):149-53.
279. Bialosky JE, Bishop MD, Robinson ME, Zeppieri G, Jr., George SZ. Spinal manipulative therapy has an immediate effect on thermal pain sensitivity in people with low back pain: a randomized controlled trial. Physical therapy. 2009;89(12):1292-303.

280. Nijs J, Lluch Girbes E, Lundberg M, Malfliet A, Sterling M. Exercise therapy for chronic musculoskeletal pain: Innovation by altering pain memories. Manual therapy. 2015;20(1):216-20.
281. Forsgren S, Grimsholm O, Dalén T, Rantapää-Dahlqvist S. Measurements in the Blood of BDNF for RA Patients and in Response to Anti-TNF Treatment Help Us to Clarify the Magnitude of Centrally Related Pain and to Explain the Relief of This Pain upon Treatment. International Journal of Inflammation. 2011;2011:7.
282. Moss P, Sluka K, Wright A. The initial effects of knee joint mobilization on osteoarthritic hyperalgesia. Manual therapy. 2007;12(2):109-18.
283. Smith A, Ritchie C, Pedler A, McCamley K, Roberts K, Sterling M. Exercise induced hypoalgesia is elicited by isometric, but not aerobic exercise in individuals with chronic whiplash associated disorders. Scandinavian Journal of Pain. 2017;15:14-21.
284. Hoeger Bement MK, Dicapo J, Rasiarmos R, Hunter SK. Dose response of isometric contractions on pain perception in healthy adults. Medicine and science in sports and exercise. 2008;40(11):1880-9.
285. Courtney CA, Steffen AD, Fernández-de-las-Pñas C, Kim J, Chmell SJ. Joint Mobilization Enhances Mechanisms of Conditioned Pain Modulation in Individuals With Osteoarthritis of the Knee. Journal of Orthopaedic & Sports Physical Therapy. 2016;46(3):168-76.
286. Koltyn KF, Brellenthin AG, Cook DB, Sehgal N, Hillard C. Mechanisms of exercise-induced hypoalgesia. The journal of pain : official journal of the American Pain Society. 2014;15(12):1294-304.
287. Staud R. Is it all central sensitization? Role of peripheral tissue nociception in chronic musculoskeletal pain. Current rheumatology reports. 2010;12(6):448-54.
288. Walsh DA, Mapp PI, Kelly S. Calcitonin gene-related peptide in the joint: contributions to pain and inflammation. British journal of clinical pharmacology. 2015;80(5):965-78.

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