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Objectives

- Compare patients with fibromyalgia syndrome and myofascial pain syndrome with each other and with healthy normal controls regarding their isokinetic and isometric muscle strength of the knee flexors and extensors.
- Discuss reasons for the different results in humans and animals for the use of dextromethorphan in conjunction with slow-release morphine.
- State the negative correlation between active mouth opening and trigger points in ankylosing spondylitis patients.
- Describe the proposed mechanism of action of the analgesic effect of tetrodotoxin.
- Discuss factors associated with severity of neck pain intensity in whiplash-associated disorders.
- Examine the effect of continuous low-level heatwrap therapy in acute low back pain patients.
- Examine severe respiratory depression following intrathecal morphine analgesia for lumbar surgery.
- Evaluate the prevalence of facet joint pain in patients with chronic low back pain after surgical intervention.
- State an important source of anxiety regarding movement by patients with sickle cell disorder.
- Evaluate the predictability of simple clinical tests to identify shoulder pain after stroke.

Isokinetic and isometric muscle strength of the knee flexors and extensors in patients with the fibromyalgia syndrome and chronic myofascial pain syndrome.

Cubukcu S et al

Journal: J Musculoskeletal Pain 15(3):49-55, 2007. 26 References
Reprint: Akdeniz University Faculty of Medicine, Department of Medical Education, 07059 Antalya, Turkey (MK Alimoglu, MD)
Faculty Disclosure: Abstracted by J. Joyce, who has nothing to disclose.

The fibromyalgia syndrome (FMS) is a non-inflammatory rheumatic syndrome characterized by widespread musculoskeletal pain and palpable points, muscle stiffness, fatigue, and sleep disturbances. Chronic myofascial pain syndrome (MPS) is a similar condition to FMS, but there is no requirement for the pain to be widespread. Impaired maximal isometric and isokinetic muscle strength have been reported in

FMS in several studies. The aim of this study was to compare FMS and MPS patients with each other and with healthy normal controls (HNCs) regarding their isokinetic and isometric muscle strength of the knee flexors and extensors.

The authors evaluated muscle function in a group of women with FMS and MPS compared to HNC subjects and searched for differences between FMS and MPS patients regarding muscle performances. They found that isokinetic and isometric peak torques and total work values in their FMS and MPS patients were decreased compared to the HNC group. Contrary to previous reports, these authors observed no difference between their patients and HNC groups regarding the endurance ratio possibly due to limited number of repetitions. The endurance ratio, an indicator of fatigue, may differ more significantly in patients and HNCs with more repetitions of flexion and extension. The reduction in endurance and strength was greater in FMS subjects than MPS subjects. The differences between muscular performances of FMS and MPS patients were significant only in particular movements and speeds in our study.

The differences between these results and previous literature may be related to different patient characteristics of the current and previous studies. These participants were younger and mean duration of the disease symptoms was shorter compared to previous studies. Perhaps, in earlier phases of the disease and at younger ages, FMS has a worse prognosis than MPS in isokinetic flexion abilities, whereas MPS shows a worse prognosis in isometric extension. In time, isokinetic strength differences between the two disorders may disappear, while isometric strength differences may be prominent in all movements.

The first limitation of this study was the lack of any data about the pain experienced by the patients during isokinetic measurements. Limited numbers of participants in patient groups was another limitation for the differentiation of the FMS and the MPS groups. Additionally, very large standard deviation of the MPS group may in part account for the lack of statistical significance in comparisons of the MPS and FMS groups. The final limitation is lack of any data on fatigue level and depressive symptoms of this study's participants.

A Phase III randomized, double-blind, placebo-controlled study evaluating dextromethorphan plus slow-release morphine in terminally ill patients.

Dudgeon DJ et al

Journal: J Pain Symptom Manage 33(4):365-371, 2007. 19 References
Reprint: Palliative Care Medicine, Queen's University, 34 Barrie Street, Kingston, Ontario, K7L 3J7 Canada (D Dudgeon, MD)
Faculty Disclosure: Abstracted by J. Joyce, who has nothing to disclose.

Pain is one of the most prevalent and feared symptoms of cancer patients. While opioid agonists remain the main approach to managing advanced cancer-related pain, approximately 10% of patients achieve only partial relief with current therapies. The *N*-methyl-D-aspartate (NMDA) receptor is implicated in pain

syndromes that respond poorly to opioids and in the development of opioid tolerance. Dextromethorphan (DM) is an antitussive that exhibits NMDA receptor antagonist properties. Animal studies suggest that the synergistic effects of DM and morphine have the potential to moderate opioid tolerance and improve pain management.

This multicenter, double-blind, randomized Phase III study had two phases. Phase A was to compare the analgesic efficacy of two different formulations of slow-release morphine products. Phase B was to evaluate the efficacy of DM as a moderator of opioid tolerance in cancer patients with pain by comparing the average pain score, total opioid consumption, the time to first breakthrough medication, and the response of different types of pain between the group of patients receiving slow-release morphine and DM and those receiving slow-release morphine and placebo.

The results offered in this study showed that DM, when added to morphine, resulted in a statistically nonsignificant enhancement of analgesia and perhaps modulation of opioid tolerance in cancer patients with pain. Contrary to what was predicted, there was no difference in the effect of DM on mean pain scores in patients with neuropathic pain or those taking higher doses of morphine. Participants in the DM arm also had more toxicity, particularly dizziness.

Pain syndromes that are poorly responsive to opioids and the development of opioid tolerance are thought to be consequences of the opening of the NMDA receptor in the dorsal horn of the spinal cord. Although in this study average pain scores, number of breakthrough doses, and change in total morphine consumption were less in the DM group than the placebo group, the differences were not statistically significant. The reasons for different results in animals and humans is not clear but may be related to the relatively small therapeutic doses of opioids used in humans and/or the differences in how pain is measured in animals and patients. Neuropathic pain syndromes are thought to be poorly responsive to opioids due to opening of the NMDA receptor. It is possible that further differentiation of the neuropathic pain syndromes in cancer would need to be made before a significant difference would be observed with the use of DM.

Trigger points in the masticatory muscles in subjects presenting with ankylosing spondylitis.

Fernández-de-las-Peñas C et al

Journal: J Musculoskel Pain 15(3):39-47, 2007. 35 References
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Faculty Disclosure: Abstracted by J. Joyce, who has nothing to disclose.

Ankylosing spondylitis (AS) is a chronic rheumatic disorder affecting mainly the axial skeleton, which progressively limits spinal mobility throughout the course of the disease. AS subjects have about a 50% increased risk of mortality. Early limitation of spinal mobility has been identified as one of the most important prognostic factors. Although it is uncommon for AS subjects to complain spontaneously about

temporomandibular disorder (TMD) symptoms, involvement of the stomatognathic system in these patients appears to be frequent and, in some cases, severe. Since cervical mobility is mainly affected by the natural course of the disease, these authors postulate that jaw motion could be affected in subjects with AS.

Forward head posture seen in AS subjects might also be a factor contributing to the alteration of the stomatognathic system in these subjects. These authors' aim was to describe differences in both the presence of TrPs in the masticatory muscles, and active mouth opening between subjects with AS and healthy normal controls (HNCs). In addition, the authors assessed the possible relationship between the presence of TrPs in the masticatory muscles, active mouth opening, cervical motion in flexion-extension, and forward head posture.

The present study is the first to provide preliminary evidence suggesting that TrPs in the masticatory muscles might constitute an important source of orofacial pain in subjects with AS. Subjects with AS showed a greater number of active TrPs than matched HNCs. Differences between tender points (TePs) and TrPs are very important since higher levels of algogenic substances, i.e. bradykinin, calcitonin gene-related peptide, substance P, tumor necrosis factor-α, interleukin-1β, serotonin, and norepinephrine, have been found in TrPs, but not in TePs. Finally, TrPs in both masseter and temporalis muscles were more conspicuous than TrPs in the lateral pterygoid. One possible reason is that both muscles are responsible for the gravitational balance of the jaw since both have a higher number of type I fibers.

These authors' results support the hypothesis that a greater forward head posture might generate a high stress in the masticatory muscles of the jaw. In addition, a negative correlation was found between active mouth opening and the number of TrPs: the lesser the active mouth opening, the greater the total number of TrPs. Cervical mobility in flexion-extension was also less in AS subjects as compared to HNCs. Intuitively, this makes sense as these patients have a limited spinal mobility. Since cervical extension occurs during jaw opening motion in normal subjects, the restricted cervical extension seen in AS subjects might be responsible for the restricted mouth opening. Further research is needed to clearly define the role of TrPs in the masticatory muscles and their repercussion in the stomatognathic system in subjects with AS.

An open-label, multi-dose efficacy and safety study of intramuscular tetrodotoxin in patients with severe cancer-related pain.

Hagen NA et al

Journal: J Pain Symptom Manage 34(2):171-182, 2007. 34 References
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Faculty Disclosure: Abstracted by J. Joyce, who has nothing to disclose.

Cancer pain is a highly prevalent and serious public health issue. It can usually be well controlled with oral opioids and other standard analgesic interventions, but for some patients with severe pain, high doses of

current therapies either fail to produce significant relief or result in side effects that significantly impair quality of life. Tetrodotoxin, a selective blocker of voltage-gated sodium channel (VGSC) subtypes, is a neurotoxin found in puffer fish and other marine animals. Early reports have identified tetrodotoxin as having a potential role in blocking pain and having an adequate safety profile. A Phase IIa clinical trial was developed to assess the effects of intramuscular tetrodotoxin in patients with severe cancer-related pain. The objectives were to determine the efficacy and safety of intramuscular tetrodotoxin; the duration of its analgesic effect; the minimal effective dose/dosing frequency; and to identify differential responses to treatment based on the inferred pathophysiology.

All patients enrolled in this study had severe, treatment-resistant cancer pain either due to the direct effects of cancer or its treatment. Results from this open-label, dose-escalation study provide evidence that intramuscular tetrodotoxin is generally well tolerated, and a tetrodotoxin regimen of up to 30 mcg b.i.d. for 4 days appears safe. Of all reported adverse effects (AEs) in the study, 98% were mild to moderate, with the most frequently reported AEs being oral hypesthesia and paresthesia, both of which are directly related to the pharmacology of the drug.

The observation that tetrodotoxin treatment can relieve pain in some patients, which persists after cessation of treatment, is particularly interesting. A pharmacodynamic effect of this nature is very different from the analgesic effect of opioids and other drugs used to manage pain, with the exception of sodium channel blockers such as lidocaine; systemic lidocaine has been shown to produce persistent analgesic effects in neuropathic pain.

Tetrodotoxin also has local anesthetic properties. The mechanism of action underlying the analgesic effect of tetrodotoxin is not fully understood. Injury in the periphery produces abnormal, repetitive discharges of primary afferent neurons and exaggerated responses of these neurons to sensory stimuli that are thought to medicate chronic inflammatory and neuropathic pain conditions. Changes in tetrodotoxin-sensitive and tetrodotoxin-resistant VGSC expression and/or function have been proposed, in part, to underlie the hyperactivity of peripheral and central nociceptive and sensory neurons following injury.

Factors influencing neck pain intensity in whiplash-associated disorders in Sweden.

Holm LW et al

Journal: Clin J Pain 23(7):591-597, 2007. 27 References
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Neck pain is the cardinal feature in whiplash injuries. Perception of pain is a multidimensional and complex concept involving sensory and affective aspects as well as cognitive abilities. Several studies of various pain populations have shown that age, educational level, and sex, are associated with level of pain intensity.

In the present study, the authors sought to confirm the findings from a previous study and thereby assess the associations between pre-injury factors and initial pain intensity in whiplash-associated disorders (WAD) after motor vehicle collision (MVC) in a Swedish setting. The authors considered prior health status, demographic, socioeconomic, and collision factors.

This is the second study to investigate the association between pre-injury factors and neck pain intensity in the early stage of WAD. The findings that socioeconomic status and prior health state, and not remembering head position at collision, are associated with initial neck pain intensity after MVC, confirm the findings of these authors' previous study. There was an association between low education and more severe pain intensity. There is also some evidence that better self-reported general health is associated with lower levels of passive pain coping strategies. The association between frequent neck pain before collision and collision-specific severe neck pain intensity may reflect difficulties in distinguishing prior neck pain from present neck pain. Also having poor or fair general health before collision and having frequent headache were risk factors for more intense neck pain. Those injured in rollover collisions were twice s likely as those in side collisions to report severe neck pain intensity. As in the previous study, having the head turned to the side at the time of collision or not remembering the head position, were associated with an increased risk for higher pain intensity.

The results of this study are important for the clinician in their judgment of the severity of the injury and when considering treatment options. The authors suggest that the case history should include socioeconomic status and detailed prior health state, because these may be of importance in understanding differences in pain and course of the injury. Also, it may be important to consider pain intensity as a potential mediator between pre-injury factors and recovery.

Impact of continuous low level heatwrap therapy in acute low back pain patients: subjective and objective measurements.

Kettenmann B et al

Journal: Clin J Pain 23(8):663-668, 2007. 29 References
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Faculty Disclosure: Abstracted by J. Joyce, who has nothing to disclose.

Low back pain (LBP) commonly occurs in the general population with an annual incidence of 5% and a lifetime prevalence of 60% to 90%. This study aims to broaden the range of collected data from LBP-patients, assessing an objective surrogate of CNS relaxation (spontaneous EEG-activity) in addition to subjective responses obtained from a Pain, Stress, and Sleep (PSS) Questionnaire. The authors hypothesize that a decrease in pain and muscle tension by continuous low level heatwrap therapy is accompanied by a decrease in arousal, measurable through a decrease of higher EEG frequencies. This study design aimed to look at an impact of the heatwrap therapy on pain-affected parameters in acute LBP-patients using a

combination of objective data and subjective data. The results indicated that the heatwrap therapy was more effective in reducing pain, decreasing stress at work, and increasing quality of sleep.

These findings are consistent with the view that topical heat increases the temperature of the skin surface and connective tissues resulting in stimulation of thermoreceptors. The psychophysical data were consistent with those coming from controlled clinical studies using the same heatwrap therapy.

The authors chose a "nonheatwrap" control group instead of a control group with a wrap without any heat producing elements. It would have been very difficult to properly assess the effect of a "cold" heatwrap, because of the logical contradiction in this approach. Because there was a possible bias during data analysis due to lack of blinding of the investigator evaluating the EEG data and the questionnaire results, some of the EEGs were checked by separate coinvestigators to try to detect any bias but none was found. Monitoring the amount of the oral analgesics taken during the study period in both groups provided an additional data point ensuring robustness of this approach.

This study investigated the impact of continuous low-level heatwrap therapy in acute LBP patients. In addition to typical assessment of pain-related parameters in psychophysical measurements of sleep performance, performance in daily life, etc, the authors were able to obtain objective measures (EEG) that suggested an acute therapeutic relaxation. The authors believe that this was due to a reduced nociceptive information load in LBP-patients after the use of heatwrap therapy.

Unconsciousness and severe respiratory depression following intrathecal morphine analgesia for lumbar surgery.

Law CJ, Visser EJ

Journal: Acute Pain 9(3):163-163, 2007. 14 References
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Faculty Disclosure: Abstracted by J. Joyce, who has nothing to disclose.

A 53-yr-old, 58 kg, ASA PS 2 female presented for laminectomy and spinal fusion with instrumentation. There was no significant past medical history except for a depressive disorder. Surgery proceeded for 5 hours without incident. At the end of the procedure the surgeon injected preservative free morphine 0.4 mg (6.89 mcg/kg) and bupivacaine HCl 5 mg (total volume of 1 mL) into the subarachnoid space. In the post anesthesia care unit (PACU) the patient was noted to be 'sleepy' but roused easily to gentle shaking. After being monitored for 1 hour in PACU, the patient was discharged to the ward with a patient-controlled analgesia (PCA) device. Six hours after the completion of surgery, the patient was found unconscious. She did not respond to vigorous shaking or painful stimuli.

A diagnosis of profound opioid-induced sedation and respiratory depression was made with severe hypercarbia and respiratory acidemia. 1.2 mg of naloxone was administered intravenously over 10 minutes

until there was clinical improvement in conscious state and respiratory depth. She was transferred to the ICU for further management and a naloxone infusion at 0.8 mg/hr. The naloxone infusion was stopped after 8 hours and the patient remained stable.

Intrathecal opioids are used for postoperative analgesia after a variety of procedures. The most feared complication of intrathecal opioid analgesia is respiratory depression, particularly with morphine, because of its hydrophilicity and potential for late rostral spread via the cerebrospinal fluid (CSF) circulation. The most likely cause of this patient's complication was opioid-induced sedation and respiratory depression due to rostral spread of the intrathecal morphine. The timing is consistent, with peak respiratory depression usually occurring between 3.5 and 12 hours post injection. There was no history of sleep-disordered breathing or evidence of residual anesthesia or muscle relaxation, electrolyte disturbance, hypoglycemia, neuroleptic malignant syndrome, serotonergic syndrome, stroke or post-ictal state to account for the patient's impaired state of consciousness.

The dose of intrathecal morphine may affect the incidence of sedation or respiratory depression. Care should be taken in drawing up the correct dose and volume of intrathecal morphine as errors may easily occur with such small doses. Doses should be calculated in terms of mcg/kg in smaller adults and certainly in children to avoid administering inadvertently high doses. Small dilution volumes are essential to limit the rostral spread of morphine and thus, unwanted side effects. The synergistic effects of supplemental parenteral opioid analgesia must be carefully considered, particularly in opioid-naïve patients and non-opioid multimodal analgesia used preferentially.

Prevalence of facet joint pain in chronic low back pain in postsurgical patients by controlled comparative local anesthetic blocks.

Manchikanti L et al

Journal: Arch Phys Med Rehabil 88(4):449-455, 2007. 68 References
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Zygapophyseal (facet) joints have been implicated as the source of chronic pain in 15-45% of patients with chronic low back pain (CLBP). The role of lumbar facet joints in CLBP after surgical intervention(s) has received very little attention with only a few publications discussing these joints as the source of pain production. Postlumbar laminectomy syndrome or pain after operative procedures of the lumbar spine is observed in a significant proportion of patients. It is even more difficult in postlumbar surgery syndrome to identify pain-generating structures. It is a general assumption that prevalence of facet joint pain in postlumbar surgery syndrome is insignificant. This study was undertaken to evaluate the prevalence of facet joint pain in patients who have undergone various surgical intervention(s), with chronic, persistent LBP presenting to an interventional pain-management practice for diagnosis and treatment.

This study showed that the prevalence was 16% in patients suspected of facet joint pain and was 8% in the overall population undergoing interventional techniques. False-positive rates were 49% following a single block with lidocaine. There were no significant differences noted based on radiologic findings, number of surgical interventions, or fusion in the prevalence of facet joint pain after surgical interventions.

Significant pain relief with the ability to perform maneuvers that were painful before facet joint nerve blocks are considered as the diagnostic criteria for facet joint pain. True positive responses are determined by performing controlled blocks, either in the form of placebo injections of normal saline or comparative local anesthetic blocks on two separate occasions. This implies that the same joint is anesthetized by using local anesthetics with different durations of action. If facet joints are determined to be causing radicular pain, treatment focused at facet joints will not be helpful.

This study shows the clinical relevance of diagnostic facet joint nerve blocks in diagnosing facet joint pain in patients suffering with chronic low back pain of postsurgery syndrome.

Fear of movement (kinesiophobia), pain, and psychopathology in patients with sickle cell disease.

Pells J et al

Journal: Clin J Pain 23(8):707-713, 2007. 43 References
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Fear of movement has emerged as a significant predictor of pain-related disability and distress across several painful conditions. Fear of movement, or kinesiophobia, refers to the anxiety that many individuals with persistent pain experience regarding engaging in activities or physical movements. The onset and development of kinesiophobia is typically in response to previous movement that produced significant pain or periods of disability. Although kinesiophobia was originally defined as the fear of movement/(re)injury, and examined in relation to musculoskeletal pain, more recent research, including studies of fibromyalgia and chronic fatigue syndrome have demonstrated its utility in nonmusculoskeletal pain disability. In a partial redefinition for these populations, and perhaps for diseases like sickle cell disease (SCD), "fear of movement" in the management of pain may be much more salient than the "fear of reinjury."

The current study examined the degree to which a sample of African American adults with SCD reported kinesiophobia, and whether its presence was associated with pain, psychological distress, or disability. The authors also examined associations between kinesiophobia and age, sex, and socioeconomic status in this population. The authors predicted that kinesiophobia would be moderately correlated with pain levels and strongly correlated with pain-related activity interference. They also hypothesized a significant and positive association between kinesiophobia and psychological distress. The authors found that, on average, patients with SCD reported moderate kinesiophobia, and did so at levels comparable to other persistent pain

populations, including patients with low back pain, fibromyalgia, and osteoarthritis.

These results show that higher levels of kinesiophobia are associated with greater pain and psychopathology. Individuals with SCD who worry that movement or activity will increase their pain, and who subsequently decrease their activities may have fewer resources for coping with stress, and thus, be at greater risk for psychological distress. Regarding clinical implications of these results, it will be important for healthcare providers and clinicians who work with SCD patients to recognize not only the prevalence of anxiety and depression in patients, but to recognize that one source of anxiety may be related to the patients' beliefs that movement and activity will exacerbate their pain. Reassurance that daily activities and even monitored aerobic exercise can be maintained without significant risk of harm may be important to reduce distress, particularly among males.

Education about kinesiophobia and activity avoidance, and exposure to fear-eliciting situations, have been shown to reduce pain-related fear, increase physical activity levels, and to decrease pain intensity ratings in studies with patients with persistent pain who report high levels of kinesiophobia.

Predictability of simple clinical tests to identify shoulder pain after stroke.

Rajaratnam BS et al

Journal: Arch Phys Med Rehabil 88(8):1016-1021, 2007. 51 References
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Faculty Disclosure: Abstracted by J. Joyce, who has nothing to disclose.

Hemiplegic shoulder pain is among the four most common, yet preventable, medical complications that patients may experience after stroke. It can appear as early as the first 2 weeks after stroke. Some authors attributed the early limitation in shoulder ranges of motion (ROMs) to soft tissue contractures because patients with hemiplegic shoulder pain showed synovial hypervascularization and cellular proliferation without inflammatory infiltration. The purpose of this study was to explore the association between early reporting of hemiplegic shoulder pain among patients who experienced an acute episode of stroke with differences in their shoulder ROMs, muscle strengths, muscle tones, and positive findings of musculoskeletal clinical tests to predict the likelihood of underlying shoulder dysfunction. The secondary aim of the study was to establish valid and simple diagnostic clinical tests that could predict those patients at risk for developing hemiplegic shoulder pain.

The current study found that the proposed model consisting of three simple bedside clinical tests allowed clinicians a 98% probability of provisional early diagnosis of hemiplegic shoulder pain after stroke. The clinical tests were positive Neer test (NRS score $\geq$5), moderate or greater shoulder pain during performance of the hand-behind-neck (HBN) maneuver, and a difference of greater than 10^{o} of passive external rotation at the shoulder joint.

This study's results confirmed reports of an association between shoulder pain at rest after stroke and decreased shoulder external rotation in the affected shoulder. Limitation of shoulder external rotation on the paretic upper limb also correlated with the time of onset. The current finding indicated that as early as a week after stroke, 93.9% of patients with hemiplegic shoulder pain at rest had a difference of more than 10º in range of shoulder external rotation between limbs.

Currently, there is no reliable criterion standard to accurately evaluate signs of acute shoulder pain. The present study found that complaints of moderate pain at rest and three positive clinical tests could act as a pseudo-valid standard to identify those who are at risk of hemiplegic shoulder pain. Chronic conditions such as complex regional pain syndrome have identified predictive symptoms and their critical levels, and these findings led to better understanding and management of this chronic condition. The current study could have used another pain intensity measuring tool to confirm reliability of the numeric rating scale, but this would have prolonged the assessment procedure and probably caused frustrated patients to respond inaccurately.