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Chronic Pain in Persons With Myotonic Dystrophy and Facioscapulohumeral Dystrophy

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Abstract

Objective—To determine the nature and scope of pain in working-aged adults with myotonic muscular dystrophy (MMD) and facioscapulohumeral muscular dystrophy (FSHD).

Design—Retrospective, cross-sectional survey.

Setting—Community-based survey.

Participants—Convenience sample of subjects with MMD and FSHD.

Interventions—Not applicable.

Main Outcome Measures—Overall intensity and duration of pain, pain inference, pain sites, pain treatments, and relief provided by pain treatments.

Results—More subjects with FSHD (82%) than with MMD (64%) reported pain. The most frequently reported pain sites for both diagnostic groups were lower back (66% MMD, 74% FSHD) and legs (60% MMD, 72% FSHD). Significant differences in pain intensity were found between the diagnostic groups in the hands, legs, knees, ankles, and feet, with patients with MMD reporting greater pain intensity at these sites than patients with FSHD. Age was related to the onset of pain (participants reporting pain were younger than those not reporting pain in the FSHD sample), but pain severity was not significantly associated with age in those reporting pain. Respondents with both diagnoses that reported mobility limitations and used assistive devices (eg, wheelchair, cane) reported more pain severity than those with mobility limitations who did not use assistive devices, who, in turn, reported more pain severity than respondents who reported no mobility limitations at all. The treatments that were reported to provide the greatest pain relief were not necessarily those that were the most frequently tried or still used.

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Conclusions—The findings indicate that pain is a more common problem in persons with FSHD than in persons with MMD, although it is common in both populations. In addition, these pain problems are chronic, underscoring the need to identify and provide effective pain treatments for patients with these neuromuscular diseases.

Keywords

Facioscapulohumeral muscular dystrophy; Myotonic dystrophy; Pain; Rehabilitation

Recent research suggests that chronic pain may be a significant problem in many persons with chronic neuromuscular disease (NMD), including all forms of muscular dystrophy. Muscular dystrophy (MD) is a group of genetically distinct disorders characterized by progressive weakness and dystrophic changes in muscle with loss of normal muscle fibers and replacement with fat and connective tissue. Two of the most common forms of MD seen in adults are myotonic muscular dystrophy (MMD) and facioscapulohumeral muscular dystrophy (FSHD); they are the focus of this study.

There are 2 known forms of adult MMD. Type 2 MMD (MMD2 or DM2) is much less common than type 1 MMD and is also referred to as proximal myotonic myopathy. DM2 is caused by a mutation on chromosome 3 and is clinically less severe than either typical MMD (DM1) or congenital MMD, which is the childhood form of this disease.1 DM1, referred to as MMD hereafter, is an autosomal dominant, multisystem muscular dystrophy with an incidence of 1 per 8000.2‚3 All of the MMD participants in this study have DM1, which is a multisystem disorder affecting skeletal muscle, smooth muscle, myocardium, brain, and ocular structures. Associated findings include frontal pattern baldness and gonadal atrophy (in males), cataracts, and cardiac dysrhythmias. Because of insulin insensitivity, MMD patients have a high risk for developing type 2 diabetes mellitus. The gene has been localized to an unstable CTG trinucleotide repeat within the region of the DM protein kinase locus at 19q13.3.4‚5 MMD patients may have 50 to several thousand CTG repeats, with a tendency toward increased repeats with successive generations. The age of onset is inversely correlated by the size of the CTG repeats.4 Classic, young adult-onset MMD shows 100 to 1000 repeats. Several characteristic facial features of MMD may be seen, including frontal balding and temporal wasting. MMD is one of the few dystrophic myopathies with greater distal weakness than proximal weakness.6 Although neck flexors, shoulder girdle musculature, and pelvic girdle musculature can become significantly involved over decades, the weakness is initially most predominant in the ankle dorsiflexors, ankle everters and inverters, and hand muscles.[3] Significant muscle wasting can occur over time. MMD patients may experience painful muscle cramping because of myotonia, which is delayed relaxation or sustained contraction of the muscle fibers. Grip myotonia can be shown by delayed opening of the hand with difficulty extending the fingers after tight grip. Percussion myotonia can be elicited by striking the thenar eminence with a reflex hammer, producing adduction and flexion of the thumb with slow return. Needle electromyography shows myotonic discharges, which are spontaneous waxing and waning spikes that produce a characteristic “dive bomber” sound.[7] Cardiac abnormalities are present in 70% to 75% of patients with MMD.[3,8,9] Weakness in the respiratory muscles is a major cause of morbidity. Also, constipation is fairly common because of smooth muscle involvement. Adult-onset MMD patients frequently have a generally lower intelligence than normal, with full-scale intelligence quotient reported to be in the 86 to 92 range.[3] Cognitive functioning also appears to be directly related to the size of the CTG expansion at the MMD gene locus.

FSHD, also referred to as Landouzy-Déjérine disease, is a slowly progressive dystrophic myopathy with predominant involvement of facial and shoulder girdle musculature. FSHD has a worldwide prevalence estimated at 10 to 20 per million. [2,10] FSHD is caused by a deletion

on the chromosome 4q35 locus and is transmitted in an autosomal dominant fashion. [1,11–13] Prominent facial weakness is the hallmark of FSHD. These patients often have difficulty with eye closure and may appear expressionless. They have difficulty whistling, pursing the lips, drinking through a straw, or smiling. Oddly, masseter, temporalis, extraocular, and pharyngeal muscles characteristically are spared in FSHD. Weakness in the trapezius, rhomboids, latissimus dorsi, and serratus anterior muscles result in the scapula being positioned laterally and superiorly, with the shoulders forward sloped. This may produce posterior and lateral scapular winging. Unlike other dystrophies, the musculature involvement in FSHD may be quite asymmetric. Other comorbid problems seen in FSHD include a sensory neural hearing deficit and telangiectasia of the retina. Although limbjoint contractures are uncommon in FSHD, spinal deformity is common, usually hyperlordosis, alone or in combination with scoliosis. Cardiac and respiratory problems are rare in FSHD.

Recent preliminary research suggests that pain may be a significant problem for many persons with MMD and FSHD. For example, Bushby et al14 recently reported on 4 subjects with FSHD who identified pain as their most disabling symptom and complained of between 3 to 7 separate pain complaints. In addition, Abresch et al15 found that 83% of a sample of 811 subjects with various NMDs, including 64 persons with FSHD and 33 with MMD, reported at least some ongoing pain problems. Moreover, the frequency and severity of pain in their combined sample of patients with FSHD, MMD, and a sample of patients with limb-girdle syndrome was significantly greater than levels of pain reported by the general U.S. population. Finally, our group recently surveyed 193 subjects with a variety of NMDs, including 18 patients with FSHD and 26 patients with MMD, and found that 73% of the sample as a whole (89% of patients with FSHD, 69% of those with MMD) reported pain problems, with 27% of the overall sample reporting severe pain (19% of patients with FSHD, 50% of patients with MMD).[16] We found that pain was reported to interfere moderately with a number of activities of daily living across all of the NMD diagnostic groups (range of interference ratings, 2.6–4.63 on 0–10 interference ratings scales) and to occur all over the body (least common, abdomen, and/or pelvis at 16%; most common, back at 49%). Medications were the most common pain treatment used by these patients, with ibuprofen, aspirin, acetaminophen, opioids, gabapentin (Neurontin), and muscle relaxants the most common, and all used by 50% or more of the patients with pain. However, we were unable to examine pain interference, pain sites, and pain treatments as a function of diagnostic group because of the low sample sizes of the individual NMD diagnostic groups in our previous study.16

Although the preliminary findings from our group and others indicate that chronic pain can be a serious problem for many persons with FSHD and MMD, much remains unknown about the nature and scope of pain in these patient populations. Importantly, most of the research on pain that has been performed with patients with FSHD and MMD has reported findings from a mixed population of patients with limited sample sizes for particular diagnoses. This limits both the reliability and generalizability of the available findings. Descriptive analyses regarding pain with larger samples of patients with specific diagnoses would provide for greater reliability of the findings and would allow us to confirm (or question) previously published data concerning pain in patients with these conditions. Moreover, because both FSHD and MMD are progressive diseases, it is possible that the onset of pain and the severity of pain once it develops may be related to a patient's age or degree of mobility impairment. This study sought to address the need for more information about the nature and scope of pain in persons with FSHD and MMD.

METHODS

Participants

The research methodology and all the study protocols were approved by the University of Washington Human Subjects Committee. Participants were recruited from the following sources: the National Registry of Myotonic Dystrophy and Facioscapulohumeral Muscular Dystrophy Patients and Family Members (http://www.urmc.rochester.edu/nihregistry/) (n=296) funded by the National Institutes of Health, the University of Washington NMD Clinic list (n=87), the Quality of Life Pediatric Survey Study (n=8), and 4 participants who independently contacted study personnel. In total, 395 surveys were mailed out to persons living with NMD. Of those 395 surveys sent, 2 were returned because the participant no longer lived at the address on record, 6 were deceased, and 5 were returned as ineligible (no NMD diagnosis or <18 years of age). Of the remaining 382 surveys, 298 were returned, yielding a survey return rate of 78%. Data from 5 of these surveys could not be analyzed (because of insufficient data or ineligibility) and were consequently excluded from further analysis. The current sample includes only participants with MMD and FSHD (n=257). Because the majority of these participants were recruited through the National Registry, that protocol is as follows: individuals who have been diagnosed with FSHD or MMD by a neuromuscular specialist contact the Registry and provide the Registry with demographic information and permission to access their medical records. The Registry then abstracts and deidentifies the information in the medical records and assists with subject recruitment. Inclusion criteria for this study included the following: (1) primary diagnosis of MMD or FSHD, (2) chronologic age of 18 or older (ie, working-aged adults), and (3) ability to read and write English. On approval of the proposed study by the Scientific Advisory Committee of the Registry, the data manager extracted potentially eligible members from the database and wrote them a letter informing the prospective subjects about the study. Members of the Registry were instructed to call or e-mail research personnel if they were interested in participating. A total of 296 potential subjects with MMD or FSHD contacted us. Of these, 235 (93%) completed and returned a mail survey questionnaire on the nature and scope of their pain.

Approximately half (50.6%) of the sample was diagnosed with MMD and half (49.4%) with FSHD. Fifty-one percent of the sample reported having received a deoxyribonucleic acid (DNA) confirmation of NMD diagnosis.

Measures

The survey included questions asking about demographic information, NMD-related information, pain intensity, pain interference, pain location, and pain treatments.

Demographic characteristics and NMD-related information—All participants provided basic demographic information about their sex, age, race and ethnicity, educational level, and marital and employment status. They also provided information about their NMD diagnosis including approximate date of diagnosis; type of physician who made the diagnosis; whether or not they had received a DNA confirmation of diagnosis, presence, or absence of mobility limitations; and their use of assistive devices for ambulation. Basic demographic and descriptive information for the survey respondents (listed by diagnosis and for the sample as a whole) are listed in table 1.

Pain intensity and duration—Average pain intensity over the past week was assessed by using an 11-point numeric rating scale (range, 0 [no pain] to 10 [pain as bad as could be]) taken from the Grading of Chronic Pain scale.[17] Numeric rating scales of pain intensity have shown good evidence for their validity through their strong associations with other measures of pain intensity as well as through their ability to detect changes in pain with pain treatment.18

Reliability of a 0 to 10 pain rating scale of average pain has been shown by a strong (eg, *r*=.78) test-retest stability coefficient over a 2-day period.[19] Those participants who indicated that they had persistent, bothersome pain were also asked to give an approximate date that their pain began.

Pain interference—Pain interference with daily activities was assessed by using a 12-item interference scale adapted from the Brief Pain Inventory (BPI) pain interference scale.20 Participants were asked to rate the extent to which pain interferes with 12 specific activities during the preceding week on a 0 (does not interfere) to 10 (completely interferes) scale. The original BPI pain interference scale includes 7 items: general activity, mood, walking ability, normal work (including both work outside the home and housework), relations with other people, sleep, and enjoyment of life. We modified the original scale to make it more valid for persons with disabilities by changing the "walking ability" item to read "mobility (ability to get around)," because many persons with NMD are unable to walk, even when pain free. We also added 5 items (interference with self-care, recreational activities, social activities, communication with others, learning new information or skills) to obtain a broader-based sample of interference domains that both (1) are particularly important to persons with physical disabilities and (2) could potentially be impacted by pain. The original BPI pain interference scale has a great deal of data supporting its reliability and validity as a measure of pain interference in persons with cancer pain.19 Our modified version of this scale has shown high levels of internal consistency (Cronbach α range, .89 –.95) and validity through its strong association with pain intensity in samples of persons with limb loss21 and persons with cerebral palsy.22

Pain site(s) and intensity at specific site(s)—Participants were asked to indicate whether or not they experience bothersome pain in 1 or more of 17 specific body sites (head, neck, shoulders, upper back, lower back, arms, elbows, wrists, hands, buttocks, hips, chest, abdomen/pelvis, legs, knees, ankles, feet). If they did report pain in a specific location, they were asked to give the approximate date that the pain began and to rate average pain intensity in that location over the past week on a 0 (no pain) to 10 (pain as bad as could be) scale.

Pain treatments and relief provided by pain treatments—Participants were asked to indicate if they were currently using or had ever used any of 25 specific pain treatments (physical therapy, nerve blocks, biofeedback or relaxation training, acupuncture, magnets, massage, hypnosis, counseling or psychotherapy, mexiletine, gabapentin, tricyclic antidepressants, narcotics or opioids, acetaminophen, aspirin or ibuprofen, diazepam [Valium], carbamazepine [Tegretol], baclofen, transcutaneous electric nerve stimulation [TENS] units, anticonvulsants, chiropractic adjustments, heat, ice, marijuana, strengthening exercises, range of motion [ROM] exercises). They were also asked to indicate the amount of relief that each treatment they had tried provided on an 11-point scale (range, 0 [no relief] to 10 [complete relief]).

RESULTS

Differences Between Diagnostic Groups on Demographic and NMD-Related Variables

Comparisons between the 2 diagnostic groups were made on all demographic and NMD-related information by using *t* tests for continuous variables and chi-square analyses for dichotomous variables (see table 1). Differences were found in the age of participants, with FSHD participants being significantly older than MMD participants (t_{255}=–3.08, P<.01), and in employment status, with MMD participants more often unemployed than FSHD participants (χ^2_1 test=19.28, P<.001). Participants with MMD were more likely than participants with FSHD to report that they were unemployed due to disability (χ^2_1 test=15.64, P<.001). Furthermore,

FSHD participants were more likely to be working full-time (χ_1^2 test=14.21, P<.001) or retired than MMD participants (χ_1^2 test=8.19, P<.01), with 33.9% of FSHD participants working full-time versus 13.8% of MMD subjects. In terms of assistive devices, FSHD participants were more likely to report using an assistive device for help with mobility than were MMD participants (χ_1^2 test=6.78, P<.01), with 64.6% of FSHD participants using 1 or more assistive devices compared with 48.5% of MMD participants. With regard to use of specific assistive devices (canes and crutches, walker, scooter, manual wheelchair, electric wheelchair), only 1 significant difference between diagnostic groups was found: FSHD participants were more likely to report using an electric wheelchair compared with MMD participants (χ_1^2 test=5.47, P<.05). The percentage of FSHD participants using an electric wheelchair was more than twice that of MMD participants (17.3% vs 7.7%).

Frequency and Severity of Pain

Table 2 lists the percent of the sample that reported experiencing pain in the past 3 months for the sample as a whole (71%) and for each of the 2 diagnostic groups. More individuals with FSHD (82%) reported experiencing pain than those with MMD (60%). For those participants who reported pain, the average pain intensity was in the moderate range overall (4.45), on average, and did not differ significantly between diagnostic groups. Approximately one quarter of all those respondents in both groups with pain reported experiencing severe average pain (rated 7 or higher on the 0–10 scale). The duration of pain averaged 12.49 years for the sample as a whole.

Pain Interference

Table 3 lists the average ratings of pain interference with the 12 activities of the modified BPI pain interference scale. Pain interfered most with recreational activities (3.82) and mobility or ability to get around (3.79). Pain interference with each activity was also moderately to strongly associated with pain intensity (correlation range, .32–.63; median=.51).

Analyses performed by using *t* tests examined differences in the extent to which pain interferes with daily activities between the diagnostic groups. The only significant differences were in communication and learning new information and/or skills, with participants with MMD reporting more interference than participants with FSHD (mean ± standard deviation [SD], 2.22±3.01; mean, 2.33±3.14 vs mean, 1.15±2.00; mean, 1.14±2.02; t_{180}=2.87, t_{176}=3.09; P<.01, P<.01, respectively).

Pain Location

The percentages of participants with pain who reported pain at each location are presented in table 4. The most frequent pain sites for both diagnostic groups were lower back (66% MMD, 74% FSHD) and legs (64% MMD, 72% FSHD). Significant differences between diagnostic groups in frequency of pain at specific sites were found in shoulders, hips, and feet, with participants with FSHD reporting pain more often in their shoulders and hips and participants with MMD reporting pain more often in their feet (χ_2^2 test=9.12, χ_2^2test=7.50, χ_1^2 test=6.62, respectively; all P<.05). Significant differences in average pain intensity were found in hands for MMD and FSHD (mean, 5.22±2.83 vs 3.85±2.31; t_{68}=2.2; P=.031), legs (mean, 5.92±2.37 vs 4.85±2.45; t_{123}=2.41; P=.017), knees (mean, 5.84±2.49 vs 4.59±2.66; t_{84}=2.16; P=.034), ankles (mean, 6.00±2.72 vs 4.56±2.45; t_{57}=2.13; P=.038), and feet (mean, 6.59±2.78 vs 3.93 ±2.35; t_{65}=4.17; P=.0), respectively. Furthermore, participants with FSHD reported significantly older age at which pain began in their hands and their ankles than participants with MMD did (mean, 46.89±15.89 vs 38.32±15.85; t_{66}=−2.22; P=.030; mean, 43.91±12.58 vs 35.03±15.42; t_{54}=−2.37; P=.021).

Pain Treatments and Treatment-Related Pain Relief

Table 5 lists the percentage of patients with pain who had tried each pain treatment at least once previously and the percentage of those who are currently using the treatment and the average amount of pain relief produced by the treatment. Because it is likely that many patients with only mild or even moderate pain may not seek out pain treatments, the percentages of patients with severe pain (average pain ≥7 on a 0–10 scale) who have tried and currently use the pain treatments listed are also presented in table 5. Ibuprofen or aspirin (78% of all respondents with pain, 84% of those with severe pain) is the treatment most often tried for pain management, and the application of heat is the second most common treatment (71% of all subjects, 79% with severe pain). Acetaminophen follows close behind (70%, 80%) along with strengthening exercise (64%, 29%), and physical therapy (57%, 58%).

The treatments that provided the greatest pain relief were not necessarily those that were the ones most frequently tried or still used. The highest average relief rating (8.29 on a 0–10 scale) came from severe pain patients reporting using marijuana for pain relief, with 11% of the entire sample and 21% of those with severe pain reporting having ever tried marijuana for pain relief. Other pain treatments that were reported as relatively more effective included opioids (6.49 average relief for all patients, 6.70 average relief for patients reporting severe pain), nerve blocks (5.38 average relief rating for all patients, 5.33 for those with severe pain), massage (5.16 average relief for all patients, 6.05 average relief for patients reporting severe pain), and chiropractic manipulation (5.32 average relief for all patients, 5.53 average relief for patients reporting severe pain). Although opioids, massage, and chiropractic manipulation were all tried by at least 30% or more of all participants, only 9% had received nerve blocks. Most of the other treatments, including hypnosis (2.00 relief for all patients, 2.00 for severe pain patients), magnets (2.50 for all patients, 1.14 for severe pain patients), and counseling (3.00 for all patients, 2.78 for severe pain patients), were tried infrequently. These latter treatments were also reported to provide little relief by the participants in this sample.

Association Between Age and the Onset and Severity of Pain

To test the hypothesized relationship between age and the onset of pain, we performed 2 *t* tests comparing the ages between those participants with and without pain in both samples. There was no difference in age in MMD participants with (mean, 46.74±11.63y) and without (mean, 47.15±11.52y) pain. However, among the FSHD participants, the patients reporting pain (mean, 50.53±12.83y) were significantly younger than those not reporting pain (mean, 57.43 ±16.54y; t_{125}=2.21, P<.05). For those reporting pain, the association between pain severity and age was weak and nonsignificant in both samples (FSHD r=.17, MMD r=.20, both not significant).

Association Between Pain Severity and Mobility Status

To test whether the mobility limitations and use of assistive devices are associated with pain severity, we performed a 2-way analysis of variance comparing the severity of pain from subjects that fit into 1 of 3 categories: (1) subjects without mobility limitations, (2) subjects who reported mobility limitations but do not use an assistive device, and (3) subjects who had mobility limitations and use an assistive device (another person, cane, crutches, wheelchair, scooter, etc) to help them with their mobility. The results indicated that the average pain severity was significantly (P<.001) higher for the group that used assistive devices (mean ± standard error, 5.49±0.30) than the group that had mobility limitations but did not use assistive devices (mean, 4.10±0.33). The group that had mobility limitations but did not use assistive devices, in turn, reported significantly more pain than the group without mobility limitations (mean, 2.23±0.51). There were no significant main effects or interactions in these analyses as a function of disease type (MMD or FSHD).

DISCUSSION

In our samples, 82% and 60% of patients with FSHD and MMD, respectively, reported pain. These percentages largely replicate those of a previous study (89% and 69%, respectively), 16 which used much smaller samples, and indicate that pain is very common in these patient populations. The findings also replicate previously reported findings that pain is more common in patients with FSHD than in patients with MMD. Moreover, the average pain severity reported in patients with FSHD in our sample (4.4/10 in the current sample) and percent age of patients with FSHD who report severe pain (23% in the current sample) also replicate previous findings.16 However, in the previous study (with smaller samples), patients with MMD reported more severe pain (average, 6.28/10; percentage reporting severe pain, 50%) than patients with MMD in the current sample (average, 4.5/10; percentage reporting severe pain, 24%). Given the larger sample size of the current study, the current estimates of pain severity are more likely to reflect those found in the population of patients with MMD. However, additional research would be needed to confirm this.

This study reports, for the first time, the duration of pain problems in samples of patients with MMD and FSHD. Although patients with FSHD reported somewhat longer duration of pain than patients with MMD (13.44y vs 11.19y; this difference was not statistically significant), perhaps related to the fact that the FSHD patients in the current study were significantly older than the MMD patients, both samples reported pain of significant duration. Thus, patients with these NMDs can be expected to experience pain for many years. This finding, when considered in light of both the high frequency of pain in general and the existence of subgroups of patients (≈25% in both samples) who report severe pain, underscores the need to identify and provide effective pain treatments for patients with these NMDs.

The 2 samples of patients endorsed generally similar levels of interference of pain with functioning, although there was a slight trend for patients with MMD (range of interference ratings, 2.14–4.17 out of 10) to report higher levels of interference with some activities than patients with FSHD (range, 1.14 –3.65 out of 10). Perhaps not surprisingly, pain tended to interfere less with basic activities common to all people in all situations (eg, communication with others, relations with other people, learning new skills, self-care) and more with activities that require the use of muscles (eg, mobility, normal work, recreational activities). However, in both samples, pain was reported to have a moderate degree (3.73 and 3.53 out of 10) of interference with enjoyment of life. Moreover, the strength of the associations found between pain severity and interference with the life activities tended to be strong (correlation coefficients >.50 for 6 of the 12 activities; the correlation coefficient was never less than .3). Modern biopsychosocial pain-rehabilitation treatments focus not only on the pain itself but also on the extent to which pain interferes with function.[23–25] The significant pain interference reported by the patients in this study, when considered in light of the multidomain focus of contemporary pain treatments, raises the possibility that patients with NMD and chronic pain might benefit from pain rehabilitation approaches. Investigations to explore this possibility are clearly warranted.

Overall, the sites of pain reported by these patients reflect the body areas that are commonly affected by these MDs (eg, low back and legs as most common, chest, buttocks, and head as relatively less common). The most frequent pain site for both diagnostic groups was the low back. This probably reflects the fact that low back pain is a common site of pain in the able-bodied adult population. In both FSHD and MMD, the degree of back pain may be exacerbated by the fact that the trunk and neck flexors are among the weakest muscle groups in both of these disorders.[3,10] Moreover, in both diseases, there is a significant imbalance between the extensors and flexors of the neck and the trunk. This weakness in neck and trunk flexion may contribute to the high incidence of kyphosis and lordosis seen in FSHD and the overall high

degree of back pain seen in both MMD and FSHD. Muscle imbalance is also thought to contribute to spinal pain generation in patients with muscular dystrophy.[14,15] The muscle weakness and imbalance of strength in the contralateral muscles increases the amount of biomechanic stress that MMD and FSHD patients place on their musculoskeletal system. As the individuals become weaker, the biomechanic stresses are increased and pain can become even more pronounced. This conclusion is consistent with the finding that subjects with FSHD reported a significantly older age at which pain began in their hands and ankles compared to the subjects with MMD. MMD is a distal myopathy, unlike FSHD, and can involve both the hands and ankles early in the disease course. Thus, fitting with the overwork weakness model of disability in muscular dystrophy, the MMD patients would theoretically have problems with pain and physical performance at an earlier age than patients with FSHD.

Although the frequency of current use of the various pain treatments rated by the participants in the current survey study was generally lower across all treatments than that reported by participants in an earlier study (only a subset of whom had MMD or FSHD, however),[16] the amount of relief provided by these treatments was similar across the 2 studies. No treatment was currently used by more than 46% of all of the patients reporting pain or by more than 42% of the patients reporting severe pain. The most common treatments still being used were ibuprofen or aspirin (used by 46% of patients with pain), acetaminophen (used by 34%), and strengthening and ROM exercises (both used by 29%).

Similar to the findings from the previous study with fewer subjects with MMD and FSHD, of those treatments that had been tried, the most effective (rated as providing at least 5/10 relief) were ibuprofen and aspirin, opioids, massage, chiropractic manipulation, nerve blocks, heat, and marijuana. However, it should also be noted that many of these treatments also have significant drawbacks. For example, opioids, which were rated as the most effective (6.49/10) in this sample, had been tried by 33% of the sample but were only currently being used by 8%. Clearly, there must be a substantial downside to opioids for so many patients to stop using them, despite their reported effectiveness. Our clinical experience suggests that this downside is primarily related to the side effects, especially feelings of grogginess and constipation, associated with opioids that are taken at the doses required to provide substantial relief. Similarly, marijuana, although reported to be highly effective (6/10), was only still used by less than half of the patients who had tried it (4% of the sample using, 11% had tried). The significant side effects (such as decreased motivation) and significant problems with access may decrease the desirability of this treatment. Concerning problems with access, there are now only 11 states that allow for the medicinal use of marijuana.

The other treatments that were rated as being relatively highly effective tend in our experience to only be short lasting. This may explain the fact that many of the patients who had ever tried massage, chiropractic manipulation, and nerve blocks no longer receive these treatments. The only treatment that was relatively highly effective and was still being used by a substantial number of patients (26%) was heat. Perhaps this is because heat is an extremely accessible treatment (most people own a hot water bottle or heating pad) that has few, if any, negative side effects. Overall, the findings suggest that that there remain too few options for pain relief for patients with MMD and FSHD and chronic pain. There is a substantial need for the development of effective and long-lasting pain treatments for persons with NMD and FSHD that can be made easily available and that have few negative side effects.

We hypothesized that participant age would be significantly related to both the onset and severity of reported pain, based on the fact that both FSHD and MMD are progressive conditions. However, this hypothesis was not supported by our analyses. If anything, younger participants (at least in the FSHD sample) were more likely to report pain. However, the lack of a significant association between pain severity (in those reporting pain) and age in both

samples suggests that age is not strongly related to pain in persons with FSHD and MMD. The lack of support for our hypothesis concerning age effects on pain may be related to the relative youth of the participants in this study (average age of both samples combined, ≈50y); stronger relationships might have emerged had there been a greater number of older participants. Moreover, it is possible that the effects of pain on functioning might differ among older participants (or those with more dysfunction) than younger participants (ie, older patients with fewer physical resources may have a more difficult time coping with pain and its impact on functioning than younger patients with more resources and less disability).

Although pain severity did not correlate significantly with age, it was associated with mobility status and use of assistive devices. Subjects who had no mobility limitations had the least amount of pain; as the degree of disability increased, so did levels of reported pain in both FSHD and MMD subjects. This increase in levels of reported pain may be a consequence of the greater biomechanic stress placed on the musculoskeletal system as weakness became more pronounced. This suggests the possibility that rehabilitative modalities, such as appropriate, low-intensity, graded exercise, in conjunction with judicious use of orthotics and other assistive devices, may be effective strategies to treat some of the pain problems in this population. Furthermore, novel pharmacologic modalities and gene-based therapies that facilitate muscle growth and function may also help treat pain. It is also possible that the converse is true (ie, that effective pain treatment may help offset some weakness that may be caused directly by disuse atrophy as a consequence of immobility). Although detailed analyses of the interactions between age, physical functioning, pain, and pain interference are beyond the scope of this study, future investigators should consider examining these relationships more closely.

Study Limitations

This study improved on similar previous studies by evaluating larger samples of patients with MMD and FSHD. However, this study also has important limitations. First, all of the data were obtained through self-report. We did not have independent verification of the participant's diagnoses, so it is possible that some of the participants did not actually have an MMD or FSHD diagnosis. In addition, because all of the data came from the same source (the patient), the analyses showing significant associations among variables may have provided findings that overestimate those associations to some extent because of shared method variance (ie, associations between variables due to similarity of assessment methods in the sample rather than because of real associations between domains in the population). Including variables from other sources (eg, spouse or family member observations of patient behavior) can provide a method of confirming the strength of the associations found. Finally, because the data came from only 1 time point and are correlational, no conclusions regarding causal relationships among the variables can be made. It cannot be determined, for example, from these data, the extent to which the significant associations found between pain intensity and pain interference reflect a causal impact of pain on functioning or may simply reflect the causal impact of some uncontrolled third variable (eg, general negative view) that influences reports of both pain intensity and interference. True experiments and longitudinal studies would help to better clarify possible causal associations among the variables. However, despite this study's limitations, the findings confirm the significance of pain problems in persons with MMD and FSHD and underscore the need to identify more effective treatments for these pain problems. To the extent that treatments can be developed that decrease MMD- and FSHD-related pain or at least help these patients minimize the negative impact of pain, people with these NMDs would have more opportunities to experience improvements in their quality of life.

Pain is likely related, at least in part, to fatigue. Our results are consistent with a recent study[25] of NMD patients that included 139 subjects with FSHD and 322 subjects with MMD. Severe fatigue was reported by 61% to 74% of these patients, and the severity of the fatigue

was correlated with an increase in the number of problems with physical functioning, mental health, and bodily pain. Although the causal relationship is not clear, it is likely that physical disability leads to both pain and fatigue conjointly, but chronic pain would certainly worsen fatigue symptoms.[26]

CONCLUSIONS

The findings from this study indicate that pain is a common problem in both FSHD and MMD, with the majority of adults with these conditions reporting pain. The most frequent pain sites for both diagnostic groups were lower back and legs. Significant differences between diagnostic groups in frequency of pain at specific sites were found in shoulders, hips, and feet, with participants with FSHD reporting pain more often in their shoulders and hips and participants with MMD reporting pain more often in their feet and hands. In addition, these pain problems are chronic, with a mean duration of pain of 11 to 13 years in our samples. These findings highlight the need to identify and provide effective pain treatments for patients with FSHD and MMD. Future work needs to address chronic pain in a variety of other NMDs.

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Table 1

Study Sample Characteristics (N=257)

Characteristics	All Subjects	MMD Subjects	FSHD Subjects
Sex (% male/female)	44.7/55.3	41.5/58.5	48.0/52.0
Mean age ± SD (range), y	49.32±12.90 (19–88)	46.91±11.55†	51.78±13.77‡
Ethnic group (%)*			
White	95.3	95.4	95.3
Native American	1.6	1.5	1.6
Black	0.0	0.0	0.0
Hispanic	2.7	1.5	3.9
Asian/Pacific Islander	0.4	0.8	0.0
Other	0.4	0.8	0.0
Marital status (%)			
Married	65.4	60.8	70.1
Never married	16.3	16.9	15.7
Divorced	7.8	7.7	7.9
Living with partner	6.2	10.8	1.6
Widowed	2.3	2.3	2.4
Separated	1.9	1.5	2.4
Highest education level (%)			
Grade 11 or lower	0.4	0.8	0.0
High school/GED	19.5	21.5	17.3
Vocational/technical/business school	6.2	6.9	5.5
Some college	23.7	24.6	22.8
College graduate	30.7	30.8	30.7
Graduate/professional school	19.5	15.4	23.6
Employment (%)*			
Employed full time	23.7	13.8†	33.9‡
Employed part time	12.1	13.1	11.0
School/vocational training	4.3	4.6	3.9
Retired	24.5	16.9†	32.3‡
Homemaker	10.5	13.8	7.1
Unemployed	47.5	58.5†	36.2‡
Assistive device use			
None	43.6	51.5†	35.4‡
One or more	56.4	48.5†	64.6‡
Cane/crutches	30.0	27.7	32.3
Walker	14.8	12.3	17.3
Scooter	15.2	12.3	18.1
Manual wheelchair	14.4	17.7	11.0
Electric wheelchair	12.5	7.7†	17.3‡

Abbreviations: GED, Graduate Education Diploma; SD, standard deviation.

[*] Total sums to greater than 100% because respondents were allowed to select more than 1 option.

[†,‡] Means or percentages of the MMD and FSHD subjects with different superscripts are significantly different from one another.

Table 2

Pain Frequency and Severity for All Subjects and by NMD Diagnostic Group

Pain Measure	All subjects (N=257)	MMD (n=130)	FSHD (n=127)	Difference Between Groups
Subjects reporting pain	182 (71)	78 (60)	104 (82)	χ^2=14.90[§]
Average pain[*]	4.45±2.58	4.50±2.82	4.40±2.40	*t*=.248
Subjects reporting severe pain[†]	43 (24)	19 (24)	24 (23)	χ^2=.041
Duration of pain[‡] mean years	12.50±10.44	11.19±10.44	13.44±10.40	*t*=−1.42

NOTE. Values are n (%) or mean ± SD.

[*] Assessed by using a 0 (no pain) to 10 (pain as bad as can be) scale for those subjects with pain.

[†] Severe pain is pain rated as 7 or greater on a 0 to 10 scale.

[‡] N values for these statistics are slightly less because not all participants provided information on date pain began (n=177 for all subjects; n=74 for MMD, n=103 for FSHD).

[§] *P*<.001.

Table 3

Pain Interference for All Subjects (n±182) and by NMD Diagnostic Group

Interference Measure	All Subjects	MMD (n=78)	FSHD (n=104)	Correlation With Average Pain Intensity
General activity	2.89±2.76	2.88±2.90	2.89±2.67	.58*
Mood	3.50±2.87	3.94±3.06	3.17±2.70	.56*
Mobility (ability to get around)	3.79±3.20	3.97±3.52	3.65±2.94	.63*
Normal work (including housework)	3.64±3.13	3.91±3.46	3.44±2.86	.59*
Relations with other people	2.30±2.69	2.67±3.11	2.02±2.31	.51*
Sleep	3.40±3.13	3.26±3.36	3.50±2.95	.42*
Enjoyment of life	3.62±3.14	3.73±3.29	3.53±3.04	.52*
Self-care	2.22±2.81	2.14±3.04	2.28±2.63	.41*
Recreational activities	3.82±3.53	4.17±3.80	3.57±3.32	.50*
Social activities	3.03±3.16	3.38±3.48	2.76±2.89	.50*
Communication with others	1.61±2.53	2.22±3.01†	1.15±2.00‡	.43*
Learning new skills	1.64±2.61	2.33±3.14†	1.14±2.02‡	.32*
Total BPI score	2.93±2.43	3.20±2.68	2.74±2.23	.62*

NOTE: Values are mean ± SD. Not all participants responded to each BPI item, so the sample size differs slightly for each group (MMD range, 74–78; FSHD range, 103–104).

*P<.001.

†,‡Means with different superscripts are significantly different between the 2 samples.

Table 4

Pain Locations, Average Pain Intensity, and Approximate Average Age at Which Pain Began by NMD Diagnostic Group

	MMD (n=77)				FSHD (n=102)			
Pain Location	**n**	**%**	**Average Pain Intensity***	**Approximate Average Age (y) Pain Began†**	**n**	**%**	**Average Pain Intensity***	**Approximate Average Age (y) Pain Began†**
Head	13	17	4.85±3.18	39.47±14.38	15	14	4.87±2.83	40.94±13.68
Neck	34	44	4.79±2.72	41.56±15.24	59	57	4.14±2.26	41.85±13.17
Shoulder	38	49	4.39±2.24	41.93±13.39	72	69	4.72±2.25	39.43±14.93
Upper back	24	31	5.29±2.35	39.74±14.14	43	41	4.14±2.37	38.41±16.06
Lower back	51	66	5.45±2.44	38.10±15.08	77	74	5.53±2.49	39.72±13.85
Arms	27	35	5.26±2.46	40.15±13.99	42	40	4.43±2.45	38.23±14.56
Elbows	9	12	3.89±2.15	43.39±15.07	20	19	4.75±2.15	44.64±13.64
Wrists	20	26	5.00±2.97	40.74±18.18	26	25	3.92±2.30	45.63±15.82
Hands	37	47	5.22±2.83	38.32±15.85‡	33	32	3.85±2.31§	46.89±15.89§
Buttocks	13	17	4.69±2.10	42.11±13.86	21	20	5.00±2.32	48.05±15.08
Hips	28	36	4.82±2.16	42.81±14.74	57	55	4.60±2.30	45.17±12.99
Chest	10	13	5.00±2.31	43.37±8.28	10	10	4.78±2.28	47.18±16.53
Abdomen/pelvis	15	21	5.40±2.61	33.10±15.80	20	19	5.35±2.35	38.21±18.48
Legs	50	64	5.92±2.37‡	37.15±12.24	75	72	4.85±2.45§	41.52±13.42
Knees	32	43	5.84±2.49‡	40.05±14.93	54	52	4.59±2.66§	40.76±12.37
Ankles	25	32	6.00±2.72‡	35.03±15.42‡	34	33	4.56±2.45§	43.91±12.58§
Feet	37	48	6.59±2.78‡	40.27±11.91	30	29	3.93±2.35§	41.06±11.14

NOTE. Values are n, percent, or mean ± SD.

*Rated on a 0 (no pain) to 10 (pain as bad as could be) scale.

†Sample sizes for these statistics are slightly less because not all participants provided information on date pain began.

‡,§Means with different superscripts are significantly different between the 2 samples.

Table 5

Percentage of Participants With Pain Who Had Tried Each Treatment and the Percentage of Participants Who Still Used the Treatment, and Average Relief Rating Associated With Each Treatment

	All Subjects With Pain (n=182)		Subjects With Severe Pain (n=43)	
Pain Treatment	**% Tried/% Still Use**	**Average Relief ± SD***	**% Tried/% Still Use**	**Average Relief ± SD***
Ibuprofen, aspirin	78/46	5.30±2.71	84/42	4.33±2.64
Acetaminophen	70/34	4.92±2.64	80/40	4.24±2.84
Physical therapy	57/7	3.60±3.20	58/9	3.17±2.89
Opioids	33/8	6.49±2.41	46/16	6.70±2.18
Massage	46/16	5.16±2.55	44/16	6.05±2.27
Neurontin	11/4	3.10±2.83	21/9	3.00±2.83
Tricyclic antidepressants	15/4	3.67±2.79	26/7	3.10±2.73
Acupuncture	8/1	3.77±2.56	12/0	4.80±1.48
Magnets	11/3	2.50±3.40	16/2	1.14±1.57
Biofeedback/relaxation training	11/1	3.00±2.57	16/2	3.43±1.40
Counseling	14/3	3.00±2.59	23/7	2.78±2.44
Chiropractic manipulation	34/6	5.32±3.05	35/0	5.53±3.29
Nerve blocks	9/1	5.38±3.45	16/2	5.33±3.20
Hypnosis	3/1	2.00±1.58	5/0	2.00±1.41
Mexiletine	6/2	3.91±3.30	2/0	0.00±0.00
Diazepam	12/5	3.82±2.83	17/12	4.67±1.86
Carbamazepine	3/1	2.40±2.88	2/0	3.00±0.00
Baclofen	6/1	2.89±2.21	9/0	2.25±2.63
TENS unit	14/2	3.92±2.80	28/5	4.17±2.25
Phenytoin (Dilantin)	10/2	2.94±3.24	21/5	2.89±3.37
Heat	71/26	5.15±2.29	79/35	4.97±1.72
Ice	49/13	4.33±2.60	51/16	2.57±2.62
Marijuana	11/4	6.00±2.94	21/9	8.29±0.76
Strengthening exercise	64/29	3.04±2.90	61/21	2.48±2.80
ROM	44/29	3.75±2.96	52/33	2.25±2.25

* Subjects who had used the treatment rated the amount of relief provided by each on a 0 (no relief) to 10 (complete relief) scale.