Physical Activity and Exercise in FSHD: A Physician's and a Patients Perspectives

Craig M. McDonald, MD

Department of Physical Medicine & Rehabilitation

Department of Pediatrics

Director, NIDRR RRTC in Neuromuscular Diseases

University of California, Davis

Facial Weakness in FSHD

- Initial manifestation: Often
- Frequency: 95% at age 30
- May be asymmetric
- Especially orbicularis oris
- Clinical test: Opposition of lips, Ask patient to pucker lips
- Functional changes

  Sleeping with eyes open

  Bulbar dysfunction

  Using straws

  Blowing up balloons

  Dysarthria

  Especially labial consonants

  Transverse smile
- Some 4q35 linked patients have no facial weakness

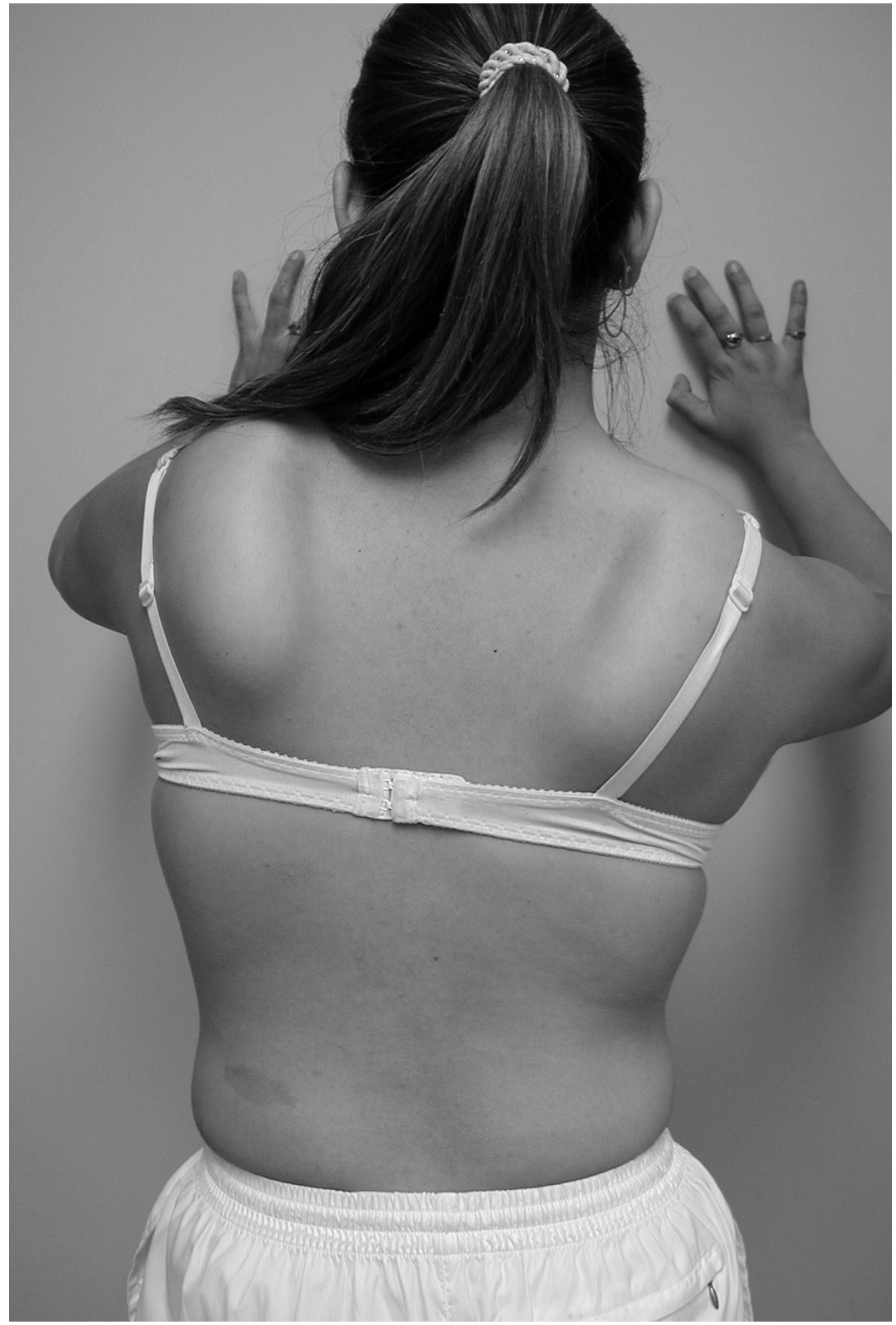
Upper Extremity Earliest Disabling Feature

- Scapular:
  - Latissimus dorsi;
  - Lower Trapezius;
  - Rhomboids;
  - Serratus anterior
  - Sh. Ext. Rotators
- Humeral:
  - Especially biceps

- Arm abduction:
  - Weak 2° poor scapular fixation; Deltoids normal
- Distal: Wrist extensors involved later in course

FSHD Scapular Instability

- Profound winging of the medial border of the scapula
- Pain due to scapular instability common



Asymmetry of Weakness Common in FSHD

- Dominant side statistically weaker

- ? Overwork weakness (controversial)


Lower Extremity Weakness in FSHD

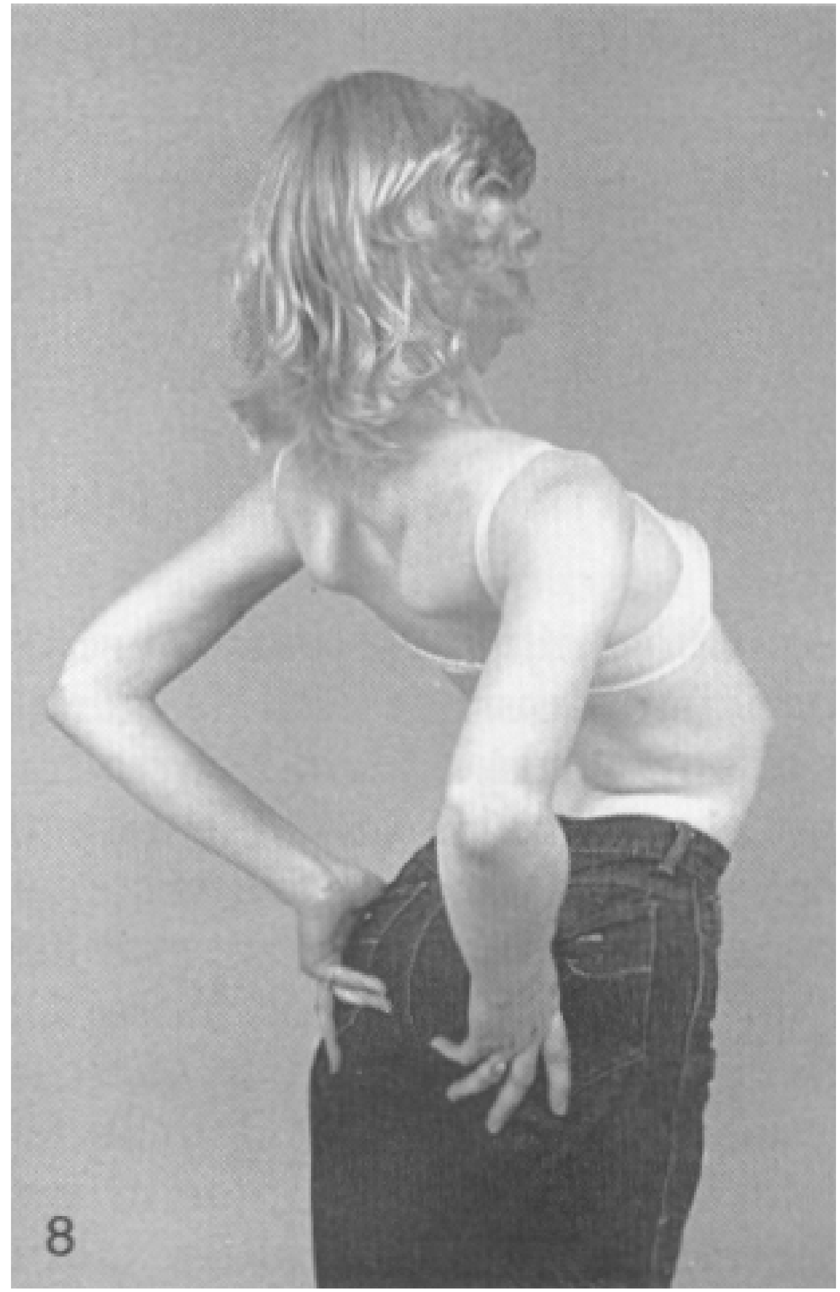
- Lower extremity
  - Peroneal
  - Ankle dorsiflexion weaker than toe extension (AFOs helpful)
  - Rare in absence of face weakness
- Proximal muscles
  - Pelvic Girdle
  - Involved with disease progression
  - 50% of gene carriers

Trunk Weakness in FSHD

- Pectoral (Clavicular head)

- Lower abdominal:
  - Abdominal Protrusion
  - Positive Beevor's sign

- Late Progressive Hyperlordosis



Cardiac Involvement in FSHD

- Cardiac complications rare,

- There are patients with cardiac fibrosis and cardiac conduction defects.

Pulmonary Involvement

- Mild restrictive lung disease is present in nearly half of patients

- Expiratory muscles affected to a greater extent than inspiratory muscles

- In the absence of significant bulbar or respiratory involvement, the life expectancy of FSHD patients is normal.

Chronic pain in persons with myotonic dystrophy and facioscapulohumeral dystrophy. Jensen et al. 2008

- 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).
- Pain severity was not significantly associated with age in those reporting pain.

Quality of life and pain in patients with facioscapulohumeral muscular dystrophy. Padua et al. 2009

- QoL was statistically significantly reduced mainly in physical domains.
- More than half of the patients complained of at least moderate pain.
- Women complained of slightly higher levels of deterioration in the emotional aspects of QoL than men.
- The higher the clinical involvement, the more severe the physical QoL deterioration.

Pain Locations in FSHD

- Locations with muscle Imbalances

- Upper back and shoulders
- Low back
- Hips

Pain in FSHD

- Weak muscles will lengthen or “stretch” over time if they are opposed by muscles that are stronger.
- For example muscles in the front of the chest (the pectoral muscles) may also be weak, but usually are stronger than the shoulder stabilizer muscles and will tend to pull the shoulders forward.
- Pectoral muscles are stronger, they will become tight or shortened.

Abnormal resting Length leads to Pain in FSHD

- Some muscles are chronically in a lengthened or shortened position,
- Nerve fibers within the muscle will send out signals that something is not right – a request, if you will, for the individual to fix the problem by changing the muscle position.
- If the lengthened or stretched muscle cannot be readjusted, chronic pain will occur.

Weakened over-used muscles develop pain / inflammation

- Weak muscles are asked to perform tasks that are beyond their contractile capability.
- These muscles struggle to contract (shorten) over and over again and are over-active because they unable to contract sufficiently.
- Over time, the muscle tissue and associated connective tissue will become inflamed and painful.

Pain / Overuse Weakness with Exercise in FSHD

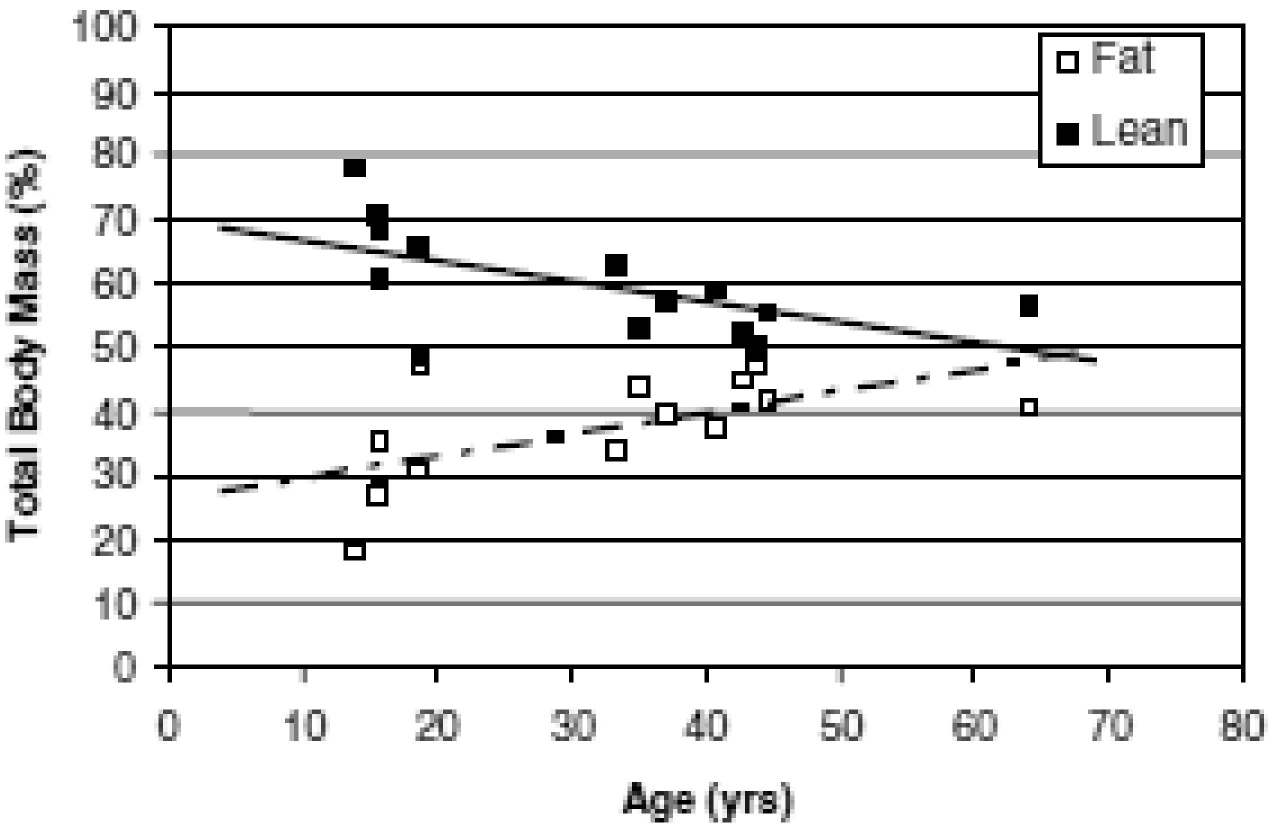
- Muscles may be working (exercising) to their maximum just to perform ADLs against the force of gravity.
- A weak scapular (shoulder blade) stabilizer muscle such as the serratus anterior or middle trapezius for example, will be challenged to complete daily showering, hair washing, and hair combing tasks.
- These specific muscles may need to rest and not perform additional resistive exercises.

Abdominal binder in FSHD

- Abdominal muscles are too weak for an exercise program
- Soft orthosis (brace) can assist in keeping the stomach muscles nearer to their normal length.
- In addition, such a support will help protect the low back muscles, which are strained and at risk of injury

The relationship between regional body composition and quantitative strength in facioscapulohumeral muscular dystrophy (FSHD)

Skalsky et al. Neuromuscular Disorders 2008



Regional Lean Tissue Mass

Table 2
Lean tissue mass by regional DEXA (kg)

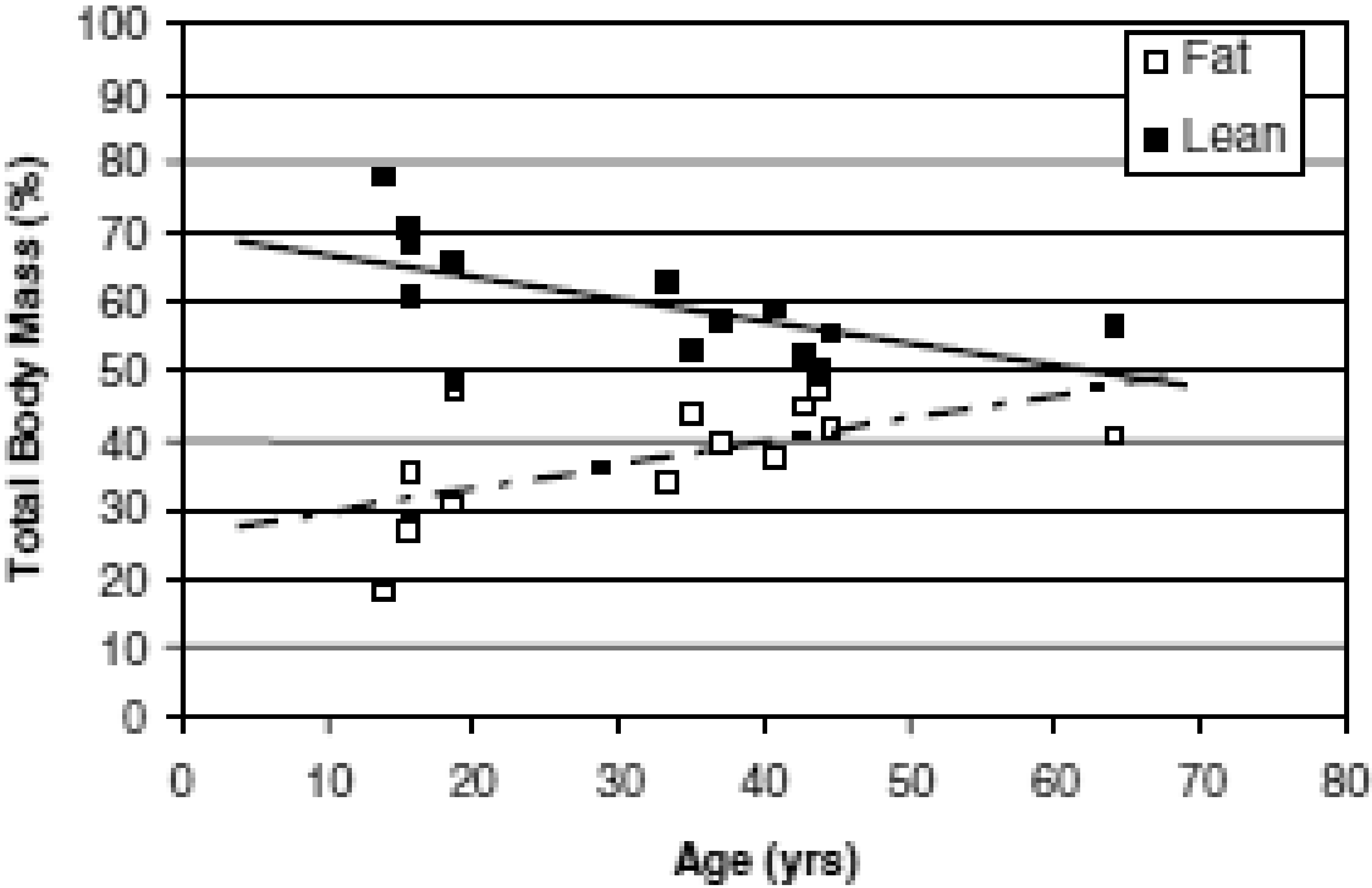
	Mean (±SD)		p-Value
	FSHD ($n = 14$)	Control ($n = 14$)	
Whole-body	40.44 (±11.07)	48.76 (±12.33)	0.001
Trunk	20.30 (±4.73)	23.68 (±5.69)	<0.001
Arm	1.25 (±0.50)	1.72 (±0.75)	0.015
Forearm	0.94 (±0.31)	1.09 (±0.33)	0.061
Thigh	4.01 (±1.96)	5.36 (±1.52)	0.009
Leg	1.64 (±0.60)	2.12 (±0.52)	0.005

Regional Fat Tissue Mass

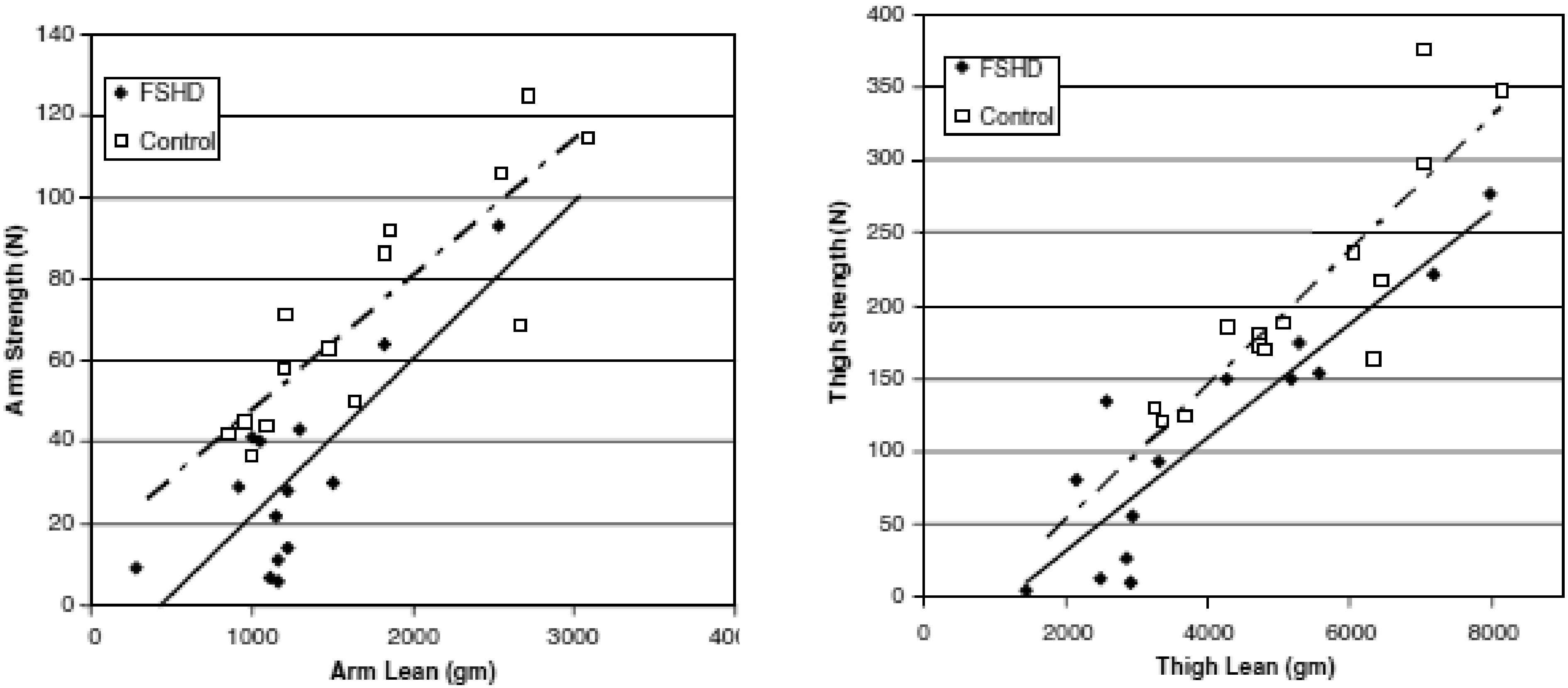
Table 3
Body fat mass by regional DEXA (kg)

	Mean (±SD)		p-Value
	FSHD ($n = 14$)	Control ($n = 14$)	
Whole-body	25.41 (±8.33)	17.98 (±6.65)	0.001
Trunk	11.45 (±4.59)	7.65 (±3.64)	0.004
Arm	1.03 (±0.38)	0.68 (±0.32)	0.001
Forearm	0.41 (±0.24)	0.36 (±0.16)	0.466
Thigh	3.49 (±1.19)	2.61 (±1.07)	<0.001
Leg	1.25 (±0.43)	0.91(±0.32)	0.014

Age-related Progression



Correlation between Strength and Lean Tissue



Strength per Lean Tissue mass

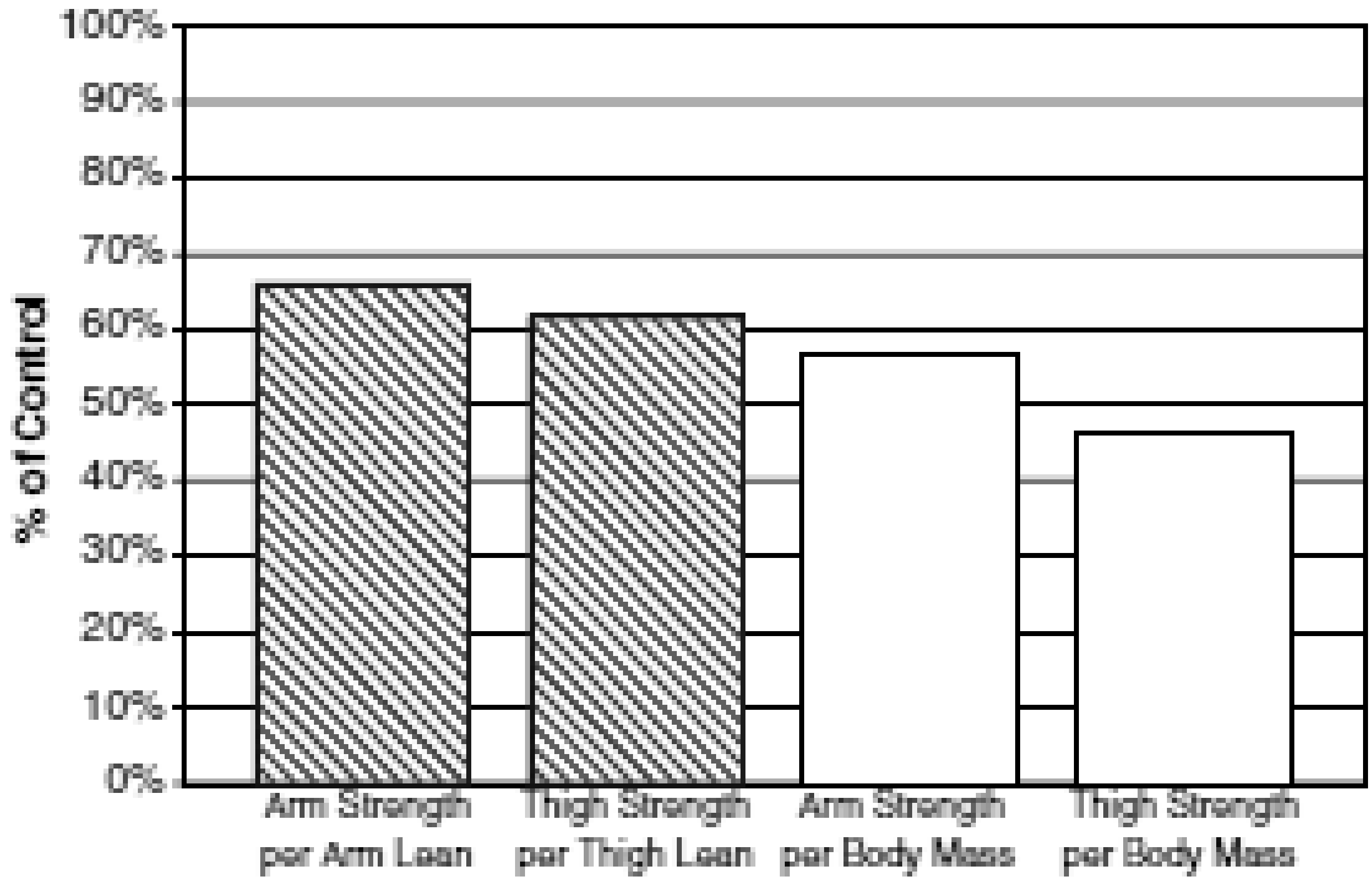
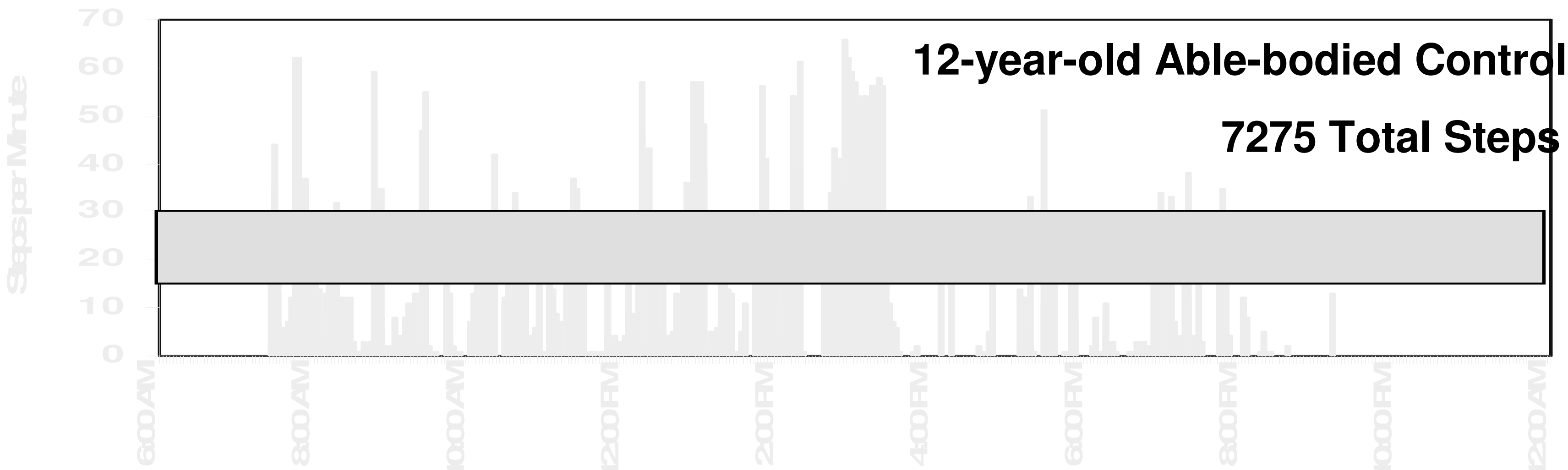
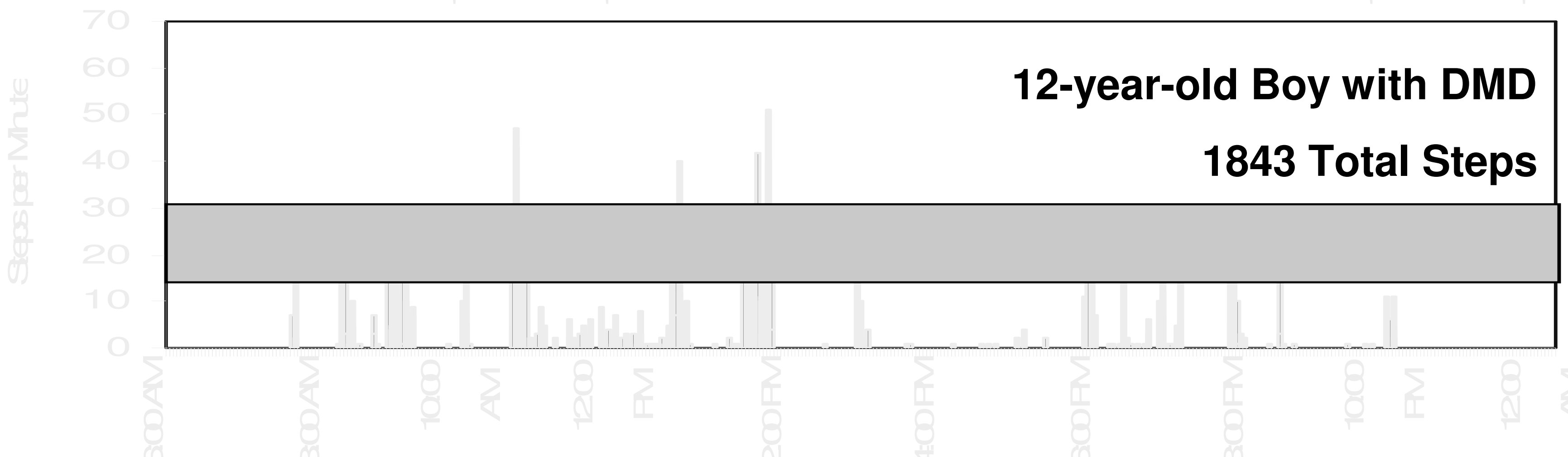


Fig. 6. FSHD values expressed as percent of control. Limb strength per limb lean tissue mass and limb strength per total body mass.

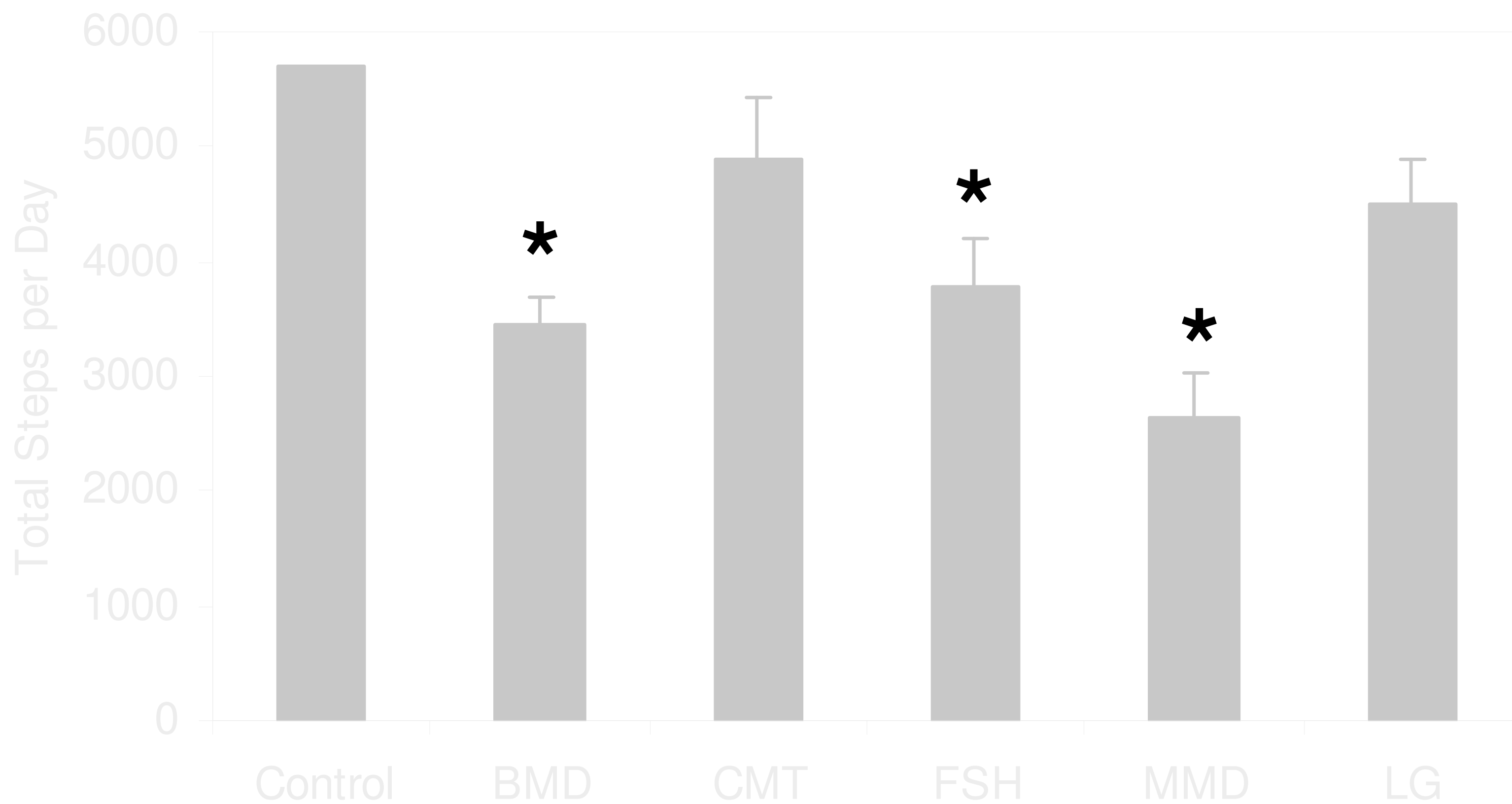
StepWatch™ Activity Monitor (SAM)

Minute by Minute Step Activity

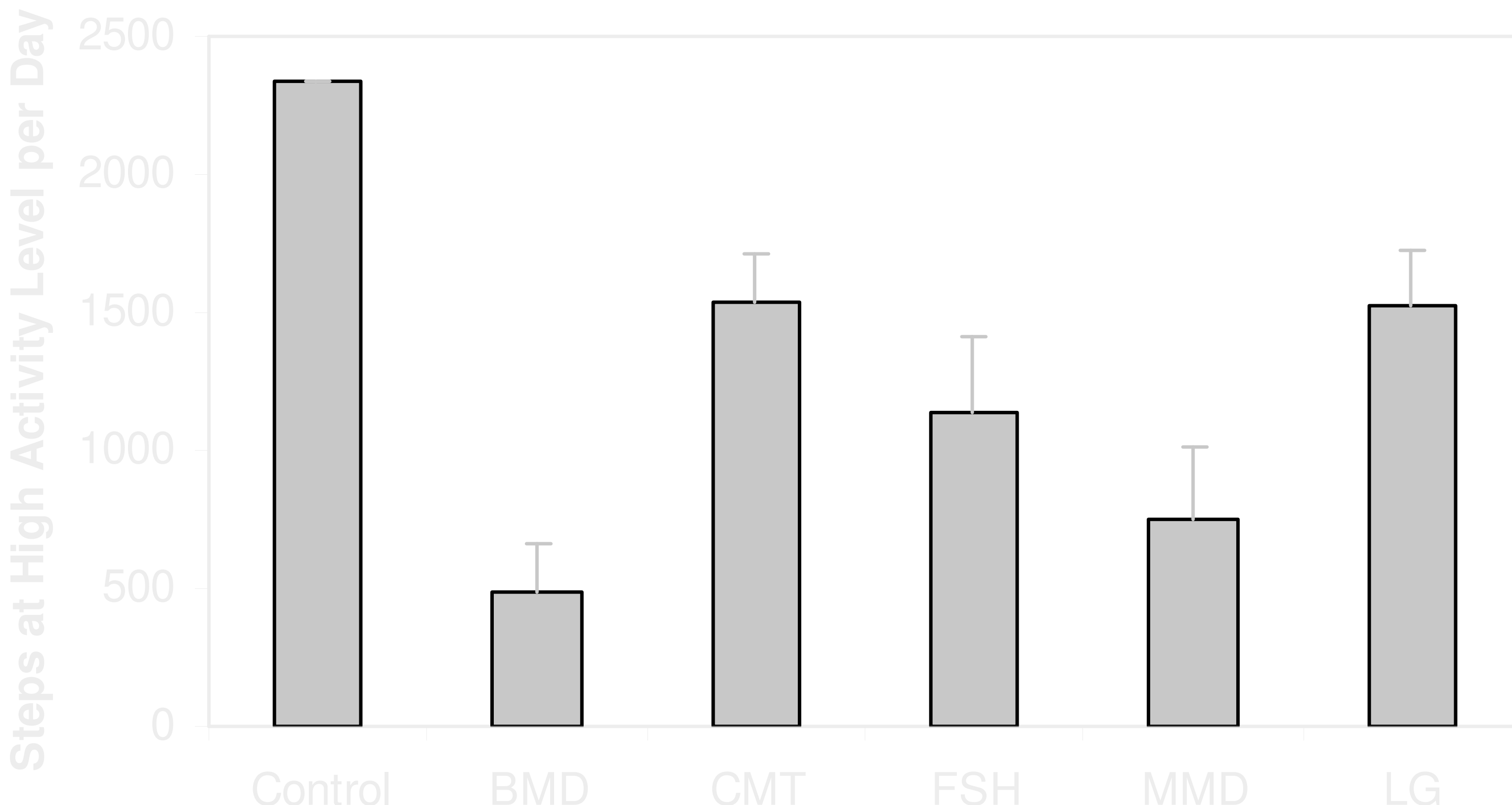




Total Steps per Day
Adult NMD



Steps at High Activity Level
(>30 steps/min)



All NMD groups are significantly different from control group.

Hydrotherapy in FSHD

No controlled trials studying the effects of hydrotherapy and FSHD.

Advantages of Water-based therapy in MD

- Buoyancy of the acts to assist mobility.
- Hydrotherapy can efficient means of exercise, working many muscles at the same time.
- Aerobic activity (Increased HR)

The Issue of Exercise in FSHD

- Patients with FSHD and other muscular dystrophies are concerned about everyday issues such as participation in sports, work and recreation.

- There is limited evidence-based advice about these concerns because we do not know how physical exertion affects the diseased neuromuscular system.

QUESTIONS OFTEN ASKED

- Will exercise help my disease?
- Will exercise make me stronger?
- Is there any harm in exercising?
- How much should I exercise?
- What type of exercise would be best for me?

Active Exercise in MD
The Basic Question

- Does exercise training (strength or aerobic):
- Improve muscle strength, and/or
- Benefit cardio-respiratory function, and/or
- Prevent disuse atrophy, and/or
- Improve overall well-being (QOL)

OR

- ***Accelerate*** muscle breakdown, disease progression and weakness?
  - ? Overuse syndrome

Exercise in Dytrophinopathy
mdx mouse

- > 20 studies
- Mechanical stress may *accelerate* disease
    - Esp. when eccentric
    - Inc IC calcium; necrosis
    - Irreversible force loss
- Treadmill training - decreased strength ~20%
    - Inc. muscle lesions

? Different size, posture, mechanical forces, and course of disease *may* dictate caution in interpretation

Is exercise potentially harmful?

- Contraction-induced muscle fiber injury in non-diseased muscle
- Over-exerting muscles might accelerate disease progression
  - (Brouwer 1992; Fowler 1982; Fowler 1984; Johnson 1971).

Musculoskeletal Pain associated with Exercise in FSHD

- It is difficult to safely exercise a strong or only mildly weakened muscle without risking overuse or stretch injury to a much weaker muscle that is also involved in performing the exercise.

Issues in FSHD

- No Sarcolemmal membrane suseptibility to injury
- Primary deficits
- Focal muscle wasting
- Weakness
- Impaired cardiorespiratory function

- Secondary Deficits
- Disuse atrophy due to sedentary activity
- Musculoskeletal pain
- Metabolic syndrome

Training of muscle

- In healthy subjects the best intervention to improve strength and cardiorespiratory function is training.
  - Strength training
  - Comprehensive aerobic exercise programs

- In muscular dystrohy:
- Goal is to maximize muscle and cardiorespiratory function and prevent additional disuse atrophy (Vignos 1983).

Problems with many studies

- Most published studies have grouped patients with different neuromuscular disorders together

- Pathophysiology of these disorders differs, so their reaction to an intervention might be different.

Problems with many studies

- Conclusions on the effect of training derived from these mixed populations cannot be extrapolated to patients with specific neuromuscular disorders such as FSHD.

Cochrane Collaboration ®

- **Strength training and aerobic exercise training for muscle disease (Review)**

- **Voet NB, van der Kooi EL, Riphagen II, Lindeman E, van Engelen BG, Geurts ACh.**
- Cochrane Database Syst Rev. 2010 Jan 20;(1):CD003907.
- http://www.thecochranelibrary.com

Cochrane Collaboration ®

- **Objectives:** To examine the efficacy and safety of strength training and aerobic exercise training in patients with muscle diseases.
- **Selection criteria:** Randomized or quasi-randomised controlled trials comparing strength training and/or aerobic exercise programmes lasting at least 10 weeks.

Search Strategy

- Cochrane Neuromuscular Disease Group register
- The Cochrane Collaboration Rehabilitation and Related Therapies Field
- MEDLINE (January 1966 toDecember 2002), EMBASE (January 1973 to July 2009),
- CINAHL (January 1982 to July 2009) for randomised trials.
- Reviewed the bibliographies of trials and identified and reviews covering the subject.

Exercise Interventions

- Training, or physical fitness training:
- Planned, structured regimen of regular physical exercise deliberately performed to improve one or more of the following components of:
  - physical fitness,
  - cardiorespiratory fitness,
  - body composition,
  - muscle strength and endurance,
  - flexibility (ACSM1998; USDHHS 1996)

Exercise Interventions

- Strength Training:
- Training performed primarily to improve muscle strength and endurance.

- It is typically carried out making repeated muscle contractions against resistance.

Resistive Strength Training

- At least one set of eight to ten exercises should condition the major muscle groups two to three days per week.
- Most persons should complete eight to twelve repetitions of each exercise
- Older or weaker persons should do 10 to 15 repetitions with lower resistance.

Resistive Strength Training

- Type:
  - (isometric) or
  - dynamic (concentric, excentric, isokinetic)

- Duration: should not exceed 60 minutes, in order not to interfere too much with other required daily activities.

Exercise Interventions

- Aerobic exercise training or cardiorespiratory fitness training:
- Training that consists of an activity or combination of activities that use large muscle groups, that can be maintained continuously, and are rhythmical and aerobic in nature, e.g. walking-hiking, running-jogging, cycling-bicycling, aerobic dance exercise or swimming

(ACSM 1998)

Aerobic Training

- The optimal frequency of training is three
- to five days per week.
- Intensity of training should be at 55 to 90% of maximum heart rate, or 40 to 85% of maximum oxygen uptake reserve or maximum heart rate reserve.
- The duration of training should be 20 to 60 min continuous or intermittent in bouts of at least 10 minutes.

Adaptations of Strength Training

- The entire program duration should be at least ten weeks to be able to detect training effects based on :

- Neural adaptation (which has its maximum contribution in first four to six weeks) and

- Muscle hypertrophy (which has its main contribution after six weeks).

Regular Supervision of Training

- Optimizes the effect of training, and improves safety and compliance.

- Does not need to be a physical therapist

Three Randomized Trials

- Myotonic dystrophy: trial compared the effect of strength training versus no training in 36 patients with myotonic dystrophy.

- FSHD: compared strength training versus no training combined with albuterol or placebo in 65 patients with FSHD.

- Mitochondrial Myopathy (combined training in 18 subjects)

FSHD Strength Trial
(van der Kooi 2004)

- Patients were randomly assigned to one of the four treatment groups:

  - training plus albuterol,
  - training plus placebo,
  - non-training plus albuterol,
  - or non-training plus placebo

FSHD Strength Trial
(van der Kooi 2004)

- Training or non-training was the first intervention, starting just after the baseline visit until after the final visit at 52 weeks.

- After 26 weeks participants started using the blinded trial medication.

Strength training Protocol

- Dynamic and isometric exercises for elbow flexors and ankle dorsiflexors
- Frequency: 3x/week for 52 week
- weeks 1-8: 2 sets of 5-10 repetitions with 10-RM weights, interspersed with 30s isometric exercise with 10-RM;
- weeks 9-17: sets of 8 reps with 8-RM weights;
- from week 18: 5 reps of 5-RM.

Effect of Strength Training

- Isometric strength of the elbow flexors did not differ significantly between the training and non-training group

- Dynamic strength (1 RM) of elbow flexors showed a significant larger increase in the training group compared to the non-training group (mean difference right side
- 1.2 kg, 95% CI 0.2 to 2.1).

Effect of Strength Training

- Both strength measures of the ankle dorsiflexors decreased significantly and markedly in all treatment groups.

Effect on Endurance

- In the FSHD trial muscle endurance was expressed as a Force-Time Integral (FTI30) of a sustained 30 seconds maximal isometric contraction.

- The FTI30 of the elbow flexors did not differ significantly between the training and non-training group (trend in favor for the training group).

Effect of Strength Training

- Functional upper extremity grade
- Functional lower extremity grade
- Timed standing from lying supine
- Timed standing from sitting
- Timed walking 30 feet (9.14 m)
- Timed climbing three standard stairs
- None of the outcomes demonstrated relevant or significant changes between treatment groups in either trial.

Effect of Strength Training on Pain

- Number of neck-shoulder and elbow complaints by the Mc-Gill Pain Questionnaire did not differ between treatment groups

- Number of neck-shoulder and elbow complaints slightly decreased in both groups.
-
- Participants experienced no notable muscle soreness after training.

Effect of Strength Training on Fatigue

- Participants experienced no notable general fatigue, and

- Training-induced muscle fatigue lasted less than an hour.

Conclusions: Strength Training in FSHD

- Most mean differences in muscle strength outcomes (isometric, dynamic and endurance) between groups showed small, non-significant positive effects in favor of the training groups.

Conclusions: Strength Training in FSHD

- In neuromuscular patients it is assumed that absolute gain in muscle strength resulting from strength training is probably related to pre-exercise muscle strength,

- Severely weak muscles (<10% of normal strength) may not improve.

Conclusions: Strength Training in FSHD

- Lack of functional benefits may be due to
  - the small number of muscle groups trained,
  - the absent or limited effects on muscle strength,
  - and the specificity of the training stimuli applied.

- Best appoach to improve walking capacity is to walk

Aerobic Exercise in FSHD

- Olsen DB, Orngreen MC & Vissing J. (2005) Aerobic training improves exercise performance in facioscapulohumeral muscular dystrophy. Neurology 64:1064–1066.
- N = 8 subjects with FSHD

Aerobic Exercise in FSHD

- Low intensity aerobic cycling at a HR corresponding to a work intensity of 65% of VO_2max for 35 min, 5 times a week for 12 wk

- Significantly increased their maximal oxygen uptake and workload, with no signs of muscle damage.

Conclusions: Exercise Training in FSHD

- ’Normal’ participation in sports and work appears not to harm their muscles but there is insufficient evidence to establish that it offers benefit.

- There is insufficient evidence for general prescription of exercise programs in FSHD.

Exercise Training in BMD
Sveen et al; Brain, 2008

Endurance training improves fitness and strength in patients with Becker muscular dystrophy

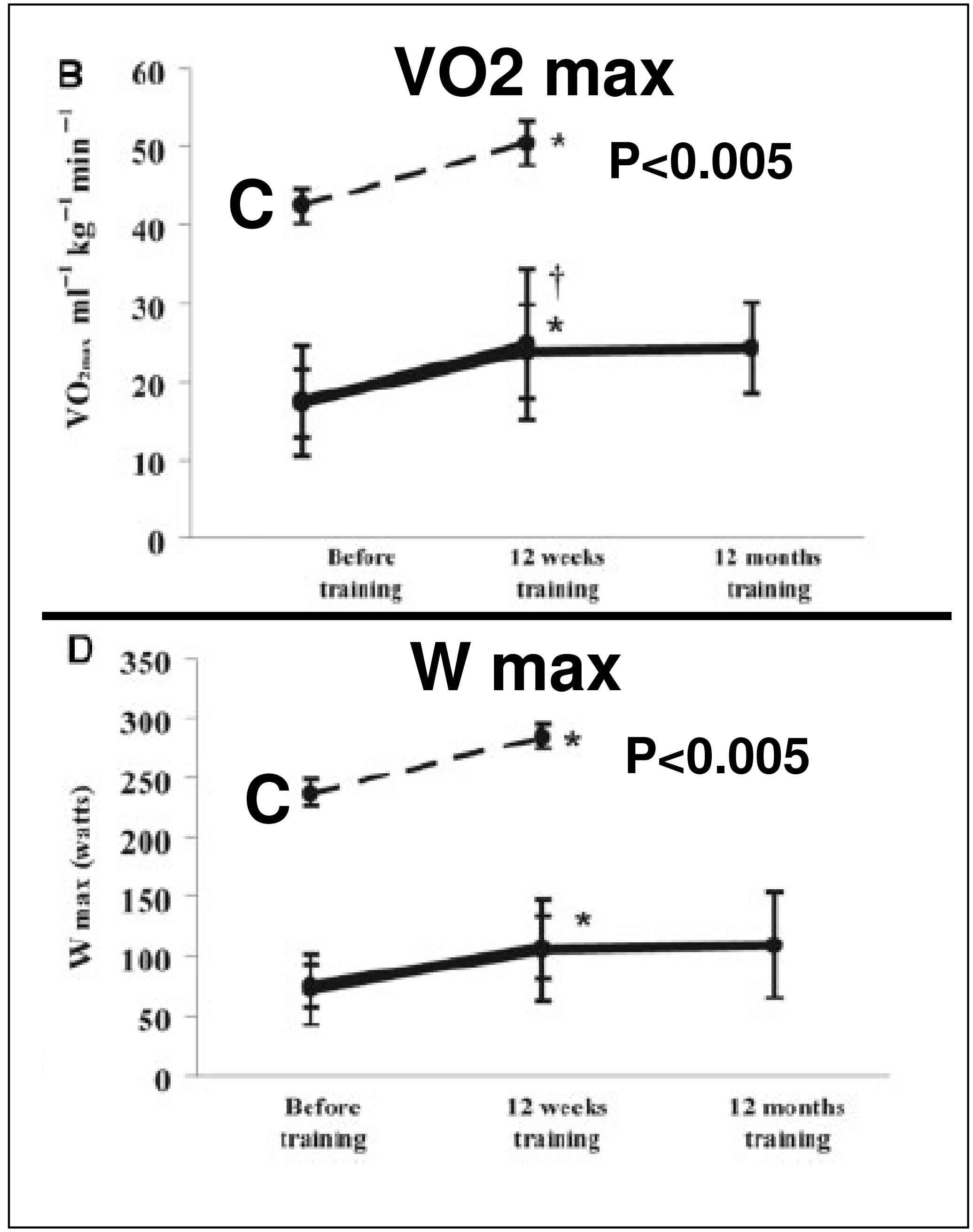
Marie Louise Sveen,[1] Tina D. Jeppesen,[1] Simon Hauerslev,[1] Lars Køber,[2] Thomas O. Krag[1] and John Vissing[1]

[1]Department of Neurology, Neuromuscular Research Unit, The Copenhagen Muscle Research Centre and
[2]Department of Cardiology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

- 11 gene + BMD patients age 18-55; 7 nl controls
- 12 weeks of 65% VO2 max aerobic exercise on bicycle ergometer; 30 min; 5x per week (50 sessions)
  - 6 pts continued protocol for **12 months** at 3x/week
- Muscle biopsies done pre/post-exercise in 6
- CK, QOL, monitored

Exercise in BMD
Sveen et al, 2008

- VO2 max up by 47 $\pm$ 11%
  - 16% in normals
- W max work up 80$\pm$ 19%
- Strength up by 13-40%
- Most "showed improvement" in QOL
- No change in HR, CK, histology, central nuclei
- Improvements maintained at one year in six patients
- "Our studies support a more active approach to …patients with BMD."



Conclusion: Overwork weakness in FSHD?

- Unlike subjects with sarcolemmal abnormalities, there are no studies that show that FSHD muscle fibers are more predisposed to mechanical injury than control subjects in the short-term.
- Caution:
- Eccentric workload? Unknown
- Weakened muscles overstretched
- Dominant extremity weakness?

Neuromuscular Electrical Stimulation Training: A Safe and Effective Treatment for Facioscapulohumeral Muscular Dystrophy Patients

- Colson et al. 2010 Arch Phys Med Rehabil

- FSHD patients (N=9; 3 women, 6 men; age
- 55.2□10.4y)
- Clinically characterized by shoulder girdle and quadriceps femoris muscle weakness.

NMES in FSHD

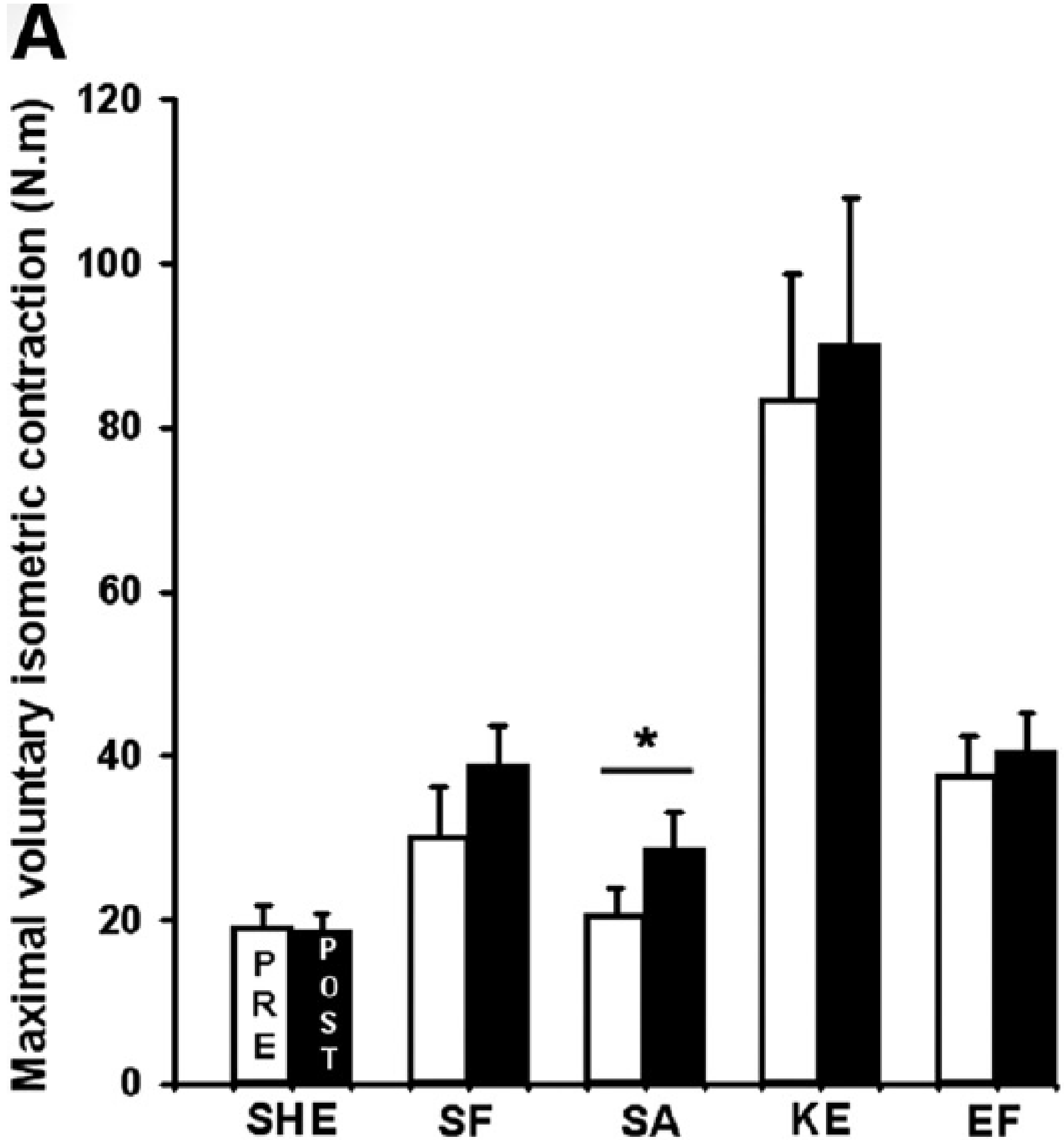
- Interventions: Patients underwent 5 months of strength training with

- NMES bilaterally applied to the deltoideus, trapezius, transversalis, vastus lateralis, and vastus medialis muscles

- five 20-minute sessions per week.

NMES in FSHD

- NMES strength training was well tolerated (CK activity and pain and fatigue scores on VAS were not modified).
- Most of the muscle functions (shoulder flexion and extension and knee extension) assessed by MMT were significantly
- increased.
- MVIC of shoulder flexion and abduction and the 6MWT distance were also improved.


A
Maximal voluntary isometric contraction (N.m)
120
100
80
60
40
20
0
PRE
POST
*
SHE
SF
SA
KE
EF

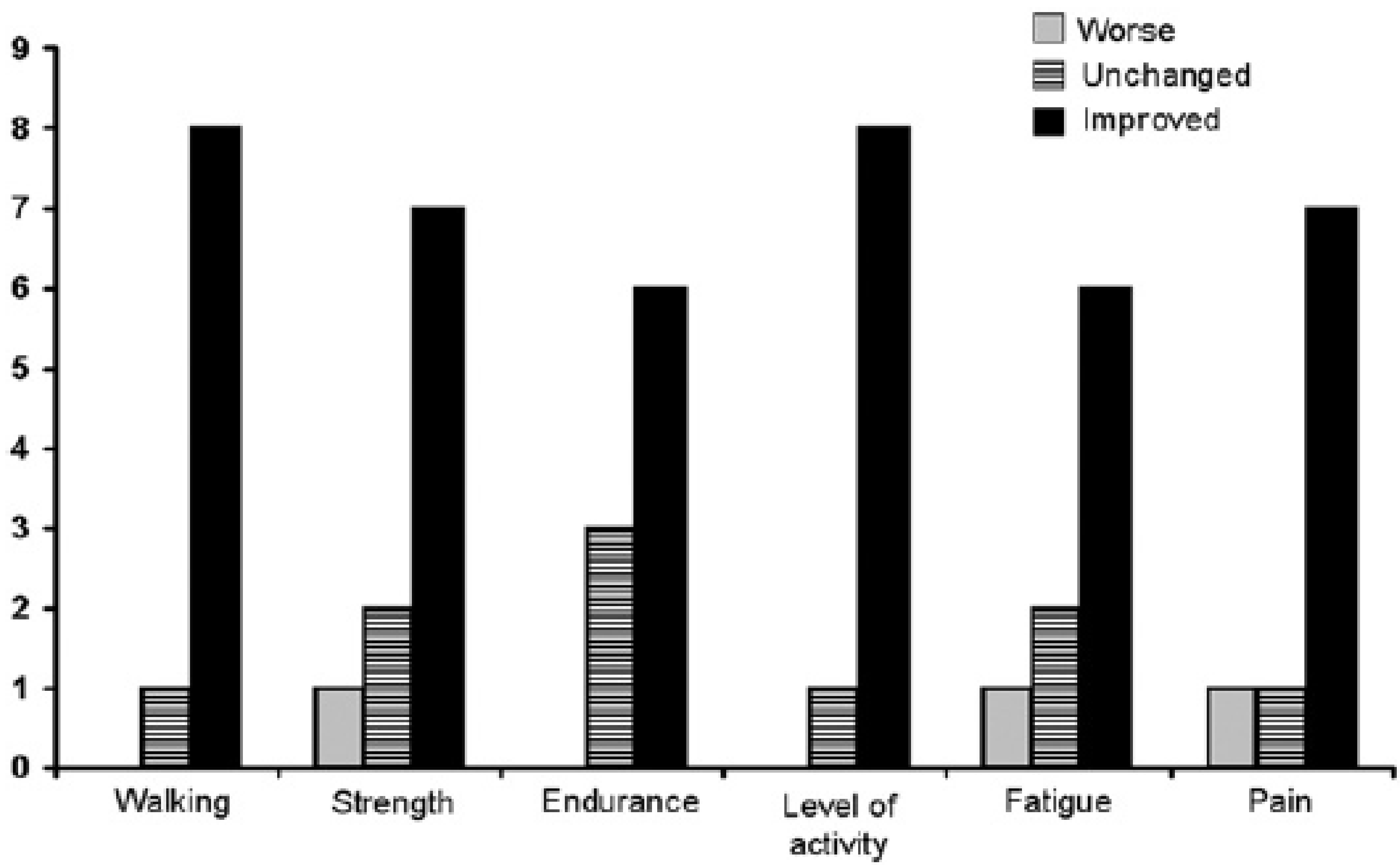


Fig 3. Self-reported changes in activities related to daily living in 9 FSHD patients after 5 months of NMES strength training. The y-axis represents the number of subjects.

RT-300 FES System (RTI - Restorative Therapies)

Standard of Care?

- Aerobic activity 3-5 times per week
- Regular sub-maximal active exercise

---Pool exercise

---Community recreation-based exercise

---Low resistance strength training

NO high resistance strength training

STRETCHING EXERCISE

- Maintenance of good ROM / flexability is important to prevent pain, maintain ambulation & prevent fixed deformity

Static positioning leads to contractures in Muscular Dystrophies

STRETCHING EXERCISE

- Active, active-assistive, passive stretching
- Minimum of 4-6 times/week to any specific joint
- Home, school, clinic setting
- Evidence? (not available)

Summary: Exercise Approach to FSHD

- Should obtain baseline strength measurements prior to beginning an exercise program.

- Once baseline muscle strength data has been gathered, then the individual should return periodically for follow☐up evaluations”

Summary: Exercise Approach to FSHD

- Maintain a daily log of his/her ADL, specific exercises erformed and the duration, and symptoms experienced on the following day

- Physical Activity should emphasize enjoyable activities; recreation and aerobic activity emphasized

Summary:
Exercise Approach to FSHD

- High resistance exercise avoided

  (>30% 1 rep max)
- Eccentric contractions avoided
- Persistent Pain / cramping (>24 hrs) after an activity or exercise indicates the patient has overdone it and risk of contraction-induced injury / "overwork weakness"

Summary: Exercise Approach to FSHD

- Non-weight bearing, endurance/aerobic exercise is optimal ---> swimming

  Flexability, gentle strengthening

  improvement in aerobic capacity
- Swimming encouraged (both recreationally and aquatic therapy)
- Inspiratory / Expiratory exercises
  - IS / IMT/ PEP
- ? Electrical stimulation (chronic, low freq)
- ? Vibration

Implications for Research

- More research is needed to determine whether strengthening &/or aerobic exercise is of benefit or harm to individuals with FSHD and other MDs.
- Well-controlled studies are needed to determine ideal exercise prescription in FSHD
- Which exercise protocols are most beneficial or cause undue risk
- Whether there is a subset of people who respond more positively both physically & psychologically.

A Patient’s Perspective: Nils Hakansson, Ph.D.

- Historical Background
- Concepts concerning concentric / eccentric muscle contractions
  - Examples:
    - Stair climbing (assent versus descent)
    - Weight training (eccentric vs. concentric)

A Patient's Perspective: Nils Hakansson, Ph.D.

- Previous experience with exercise
  - Specific activities
  - Experience with swimming
  - Fatigue issues

- Hindsight: What I would do differently

A Patient’s Perspective: Nils Hakansson, Ph.D.

- Current Activity / Exercise Program
  - Scapular squeezes
  - Putty hand exercises
  - Elastic band for rowing exercise
  - Daily ADLs (dressing, showering, foot tapping during day etc.)
  - Passive and Active ROM
  - Physical Therapy (creative approaches)