Exercise in Neuromuscular Diseases

R. Ted Abresch, MS*, Gregory T. Carter, MD, MS, Jay J. Han, MD, Craig M. McDonald, MD

KEYWORDS

• Neuromuscular disease • Exercise therapy • Randomized controlled trials
• Muscular dystrophies

KEY POINTS

- An accurate diagnosis of a specific neuromuscular disease (NMD) is essential to better understand the potential benefits and contraindications that may result from a potential exercise therapy program.
- There is inadequate evidence from randomized controlled trials with sufficient sample size to document the optimal prescriptions regarding the type, intensity, duration, frequency, and mode of delivery of exercise programs for individuals with NMDs.
- In general, there is a potential for moderate-intensity aerobic training and physical activity to improve the cardiopulmonary condition of individuals with NMD, but the level and type of training depends on the diagnosis, stage, and severity of the disease.
- Moderate aerobic exercise may reverse some of the effects of deconditioning and provide positive health benefits in terms of reduced adiposity, improved cardiorespiratory status, improved sense of well-being, and increased bone mass for individuals with NMDs.
- Low-intensity resistance exercise may be beneficial for individuals with NMDs who have antigravity strength or better.
- High-resistance exercise has not been shown to offer any advantage over a moderate-resistance training program in NMDs, and should be avoided because it may cause overwork injury.

Tremendous advances have occurred in the past decade in our understanding of the molecular genetic basis and pathophysiology of neuromuscular diseases (NMDs). These advances have led to the development of a host of promising pharmaceutical therapies for NMDs, including antisense oligonucleotide (AON) exon-skipping

Funding: This work was supported by Grant #H133B0900001 from the National Institute of Disability and Rehabilitation Research. The authors take full responsibility for the contents of this article, which do not represent the views of the National Institute of Disability and Rehabilitation Research or the United States Government.
Conflict of Interest: The authors have nothing to disclose.
Department of Rehabilitation Medicine, University of California, Davis, 4860 Y Street Suite, 3850, Sacramento, CA 95817, USA
* Corresponding author. 4860 Y Street, Suite 3850, Sacramento, CA 95817.
E-mail address: rtabresch@ucdavis.edu

Phys Med Rehabil Clin N Am 23 (2012) 653–673
http://dx.doi.org/10.1016/j.pmr.2012.06.001 **pmr.theclinics.com**
1047-9651/12/$ – see front matter

therapies, gene-therapy strategies, stem-cell therapies, and a host of small-molecule therapies (eg, compounds that induce read-through of premature stop-codon mutations, promotion of muscle growth via myostatin inhibition, utrophin upregulation, and steroid analogues with improved side-effect profiles).[1] While it is recognized that these therapeutic approaches will not be curative, there is significant hope that new therapies on the horizon will significantly alter disease progression, improve function, and improve quality of life. As these therapies have various biochemical targets, clinicians may need to give combinations of drugs to minimize secondary medical comorbidity, prevent or limit physical deformity, and allow the patient to integrate into society.

In addition to pharmaceutical interventions, comprehensive rehabilitation program modalities such as resistance training, aerobic exercise training, range-of-motion activities, and bracing, may prolong ambulation, increase strength, and reduce the progression of many NMDs.[2,3] These interventions may be made at various points in the natural evolution of the disease to increase strength, reduce pain, prevent or reduce the development of contractures, and maintain function for as long as possible.[3,4] Unfortunately there is not enough evidence-based information available to make an informed assessment of the potential risks and benefits of exercise for individuals with NMDs. We do not know what types of exercise programs are most appropriate for people with NMDs, nor are there randomized clinical trials, in most instances, to justify the proper intensity, duration, and frequency of those exercise regimens that should be ideally included in a prescription for an individual with an NMD.

GENERAL BENEFITS OF EXERCISE

As everyone knows, there are many potential benefits to increased physical activity and strength-training exercise in healthy subjects. Physical activity and exercise lowers mortality and prevents morbidity by reducing the development of chronic diseases, by reduction of disease-related complications and by restoration of function.[5] Increased physical activity has been shown to reduce blood pressure, help prevent obesity, and reduce the risk of osteoporosis, heart disease, arthritis, and type 2 diabetes. Exercise also decreases anxiety, depression, and pain. It enhances a feeling of well-being, promotes sleep, and increases vitality with age. Comprehensive guidelines have been developed to combat physical inactivity,[6] which is the fourth leading independent risk factor for death caused by noncommunicable diseases.

Strength Training (Progressive Resistive Exercise)

Strength training (progressive resistive exercise) increases lean body mass, muscle protein mass, contractile force, and power, and improves physical function.[7–9] Lifting of weights during concentric (muscle shortens during contraction) or eccentric (muscle lengthens during contraction) exercise produces microinjuries to the sarcolemma and initiates transcriptional and splice mechanisms, protein turnover, and signaling pathways from hormone and cytokine receptors.[10] This process involves several proteins that shuttle between sarcomeric and nonsarcomeric localizations and convey signals to the nucleus. Satellite cells, mononuclear cells, and myogenic progenitor cells that typically exist in a state of quiescence under the basal lamina are activated and fuse to the existing fiber, leading to proliferation of nuclei in the muscle, which provides the machinery for additional contractile proteins. Resistance exercise increases the DNA content in the myofibrils, which in turn increases the number of muscle proteins, especially actin and myosin.[11]