Management of Muscle Wasting in NMD
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Progressive muscle wasting is common to all progressive neuromuscular diseases (NMD) and may arise from both muscle degeneration due to the disease itself and disuse that is secondary to a sedentary lifestyle. Muscle wasting is an important factor that contributes to the reduced strength, increased fatigue, diminished mobility, respiratory insufficiency and decreased quality of life experienced by those with progressive neuromuscular diseases. These muscular disorders may have their origin in the muscle itself (muscular atrophies) such as myotonic muscular dystrophy (MMD), fascioscapulohumeral muscular dystrophy (FSH), limb girdle muscular dystrophy (LGMD), Duchenne muscular dystrophy (DMD), or Becker muscular dystrophy (BMD) or they may arise in the nerves that reach the muscles (neurogenic muscular atrophy), such as spinal muscular atrophy (SMA), amyotrophic lateral sclerosis (ALS), or Charcot Marie Tooth neuropathy (CMT). Another difference in these progressive neuromuscular diseases is that they may affect only a specific group of muscles (focal), such as FSH, or they may be more generalized, such as SMA. Evaluation of the effect of therapies on these diseases requires the ability to reliably measure the progression of the disease. Unfortunately, there has been no accepted method by which focal and generalized muscle wasting could be reliably determined and there have been no good methods to quantitatively evaluate the daily minute-by-minute activity of this group with neuromuscular diseases.

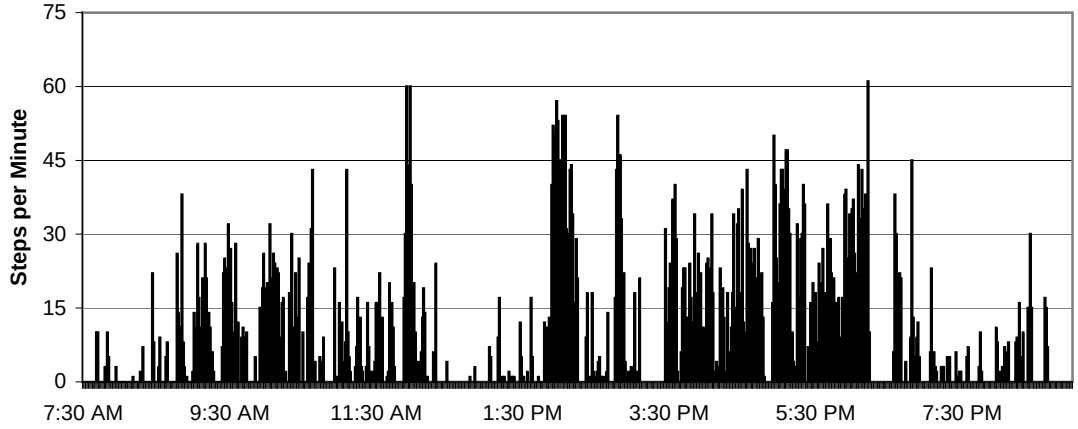
Evaluation and application of new technologies to individuals with neuromuscular diseases is a main goal of this project. The ability to measure activity and energy expenditure will provide a basis for the evaluation of therapies and interventions that may improve their quality of life.

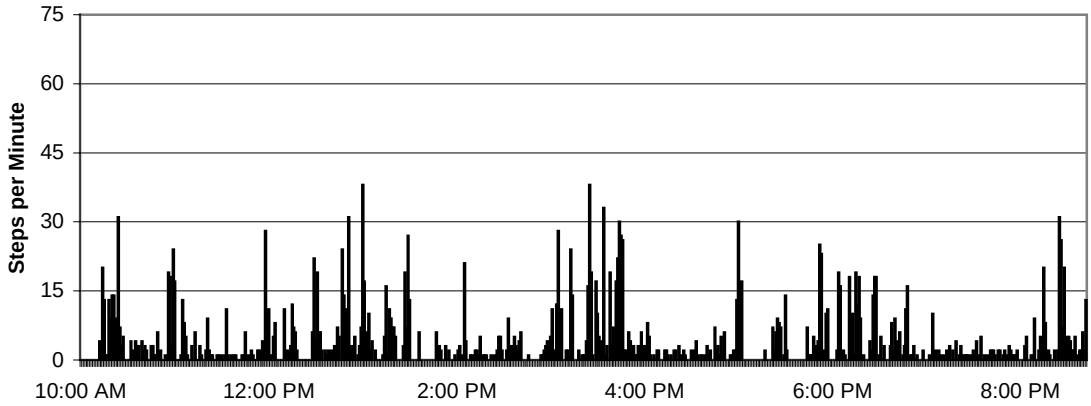
Minute-by-minute Step Rate

The first phase of our study addressed the issue of measuring the minute-by-minute step activity using the step activity monitor (SAM). The SAM is a small, unobtrusive device that is worn on the ankle. It is individually programmed by computer to define the length of time of data collection, the intervals at which data is collected and adjustments for different gait styles. The first groups studied were non-disabled control children and ambulatory boys with Duchenne muscular dystrophy. Each of the participants in these groups wore the SAM for three days while going about his ordinary daily routine. Figures below show one day of minute-by-minute activity for a representative non-disabled boy and for a boy with Duchenne muscular dystrophy.

Our results demonstrated that, when awake during the 3 days of activity, the DMD subjects spent 32% more time inactive than the non-disabled boys as recorded by the SAM. When active, the DMD boys spent fewer minutes and took significantly fewer steps at moderate and high step rates than the non-disabled boys. As would be expected, the non-disabled boys took 42% more total steps each day than the boys with DMD.

These results were not surprising, but the importance of the study is the demonstration of the usefulness of the SAM in assessing the activity of disabled children. This method of analyzing minute-by-minute step activity can be utilized in future studies to evaluate the effectiveness of interventions that may improve the mobility of disabled and non-disabled children. By comparing a baseline assessment of daily activity before an intervention to daily activity following an intervention, the value of the intervention can be determined.



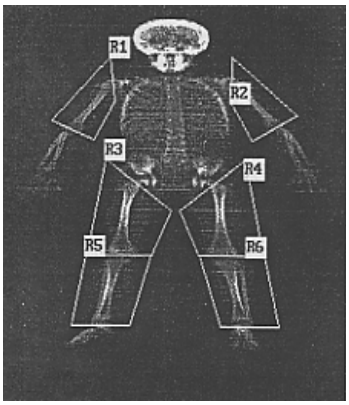


Heart Rate

In addition to measurement of the step activity, the heart rate of these two groups of boys was recorded during the three days. An interesting observation was that, when inactive, the boys with DMD had a higher heart rate than the non-disabled boys. Although the resting heart rate was higher, the maximum heart rate of the DMD boys was lower than that of the non-disabled boys. As the step rate increased, the heart rate of the boys with DMD increased, but at a slower rate than the rate of increase seen in the non-disabled boys. At the highest step rate the heart rate of the non-disabled boys was higher than the heart rate of the boys with DMD. It is known that as the dystrophy progresses, there is involvement of the heart. Further work is needed to understand the meaning of these preliminary results.

Body Composition

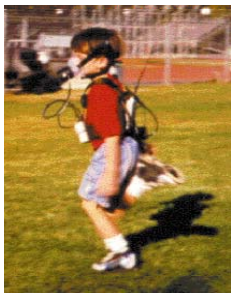
To evaluate the body composition of the groups of boys DEXA (Dual Energy X-ray Absorptiometry) was used. This method allowed the evaluation of both total body composition and the composition of regional areas of the body (upper arms, trunk, thighs, etc).



Determinations were made of bone, fat and lean tissue (muscle). Results demonstrated that the percent body fat, as determined by DEXA, was negatively correlated with total step activity in the DMD group; the higher the percent body fat, the fewer the total steps taken each day. The amount of muscle in the thigh was positively correlated with knee extension strength in DMD group. In the control group there was no relationship between either the body composition or the strength of the thigh and steps taken per day. Therefore, the activity of the non-disabled boys is apparently not affected by their muscularity, while, not surprisingly, those boys with muscles affected by DMD demonstrate an effect of the disease on their daily activities.

Energy Expenditure

We also examined the energy expenditure of the two groups of boys while they walked for 10-minutes at a comfortable rate and while they sprinted (fast walking) for 100 meters. For this laboratory part of the study we used a small, portable device (COSMED K4b^2 breath-by-breath ambulatory metabolic measurement system) to determine oxygen consumption during these two exercises.



The boys with DMD had a significantly higher oxygen cost during both the 10-minute walk and the sprint; it took them more energy to perform tasks similar to those performed by the non-disabled boys. Although their oxygen cost was higher, the boys with DMD walked only 48% as far as the non-disabled boys in 10 minutes and their sprinting speed was 37% of that of the non-disabled boys. The results of the analysis of the daily minute-by-minute step activity of the two groups of boys are reflected in their ability as demonstrated in this laboratory study. On the average day the boys with DMD spend more time inactive and when they are active, their activity is less intense than the non-disabled boys. It

takes more energy for the DMD boys to perform a level of activity similar to the non-disabled boys.

Summary

In summary, these preliminary studies demonstrate that the Step Activity Monitor, the DEXA analysis of body composition and the COSMED K4b^2 are instruments that can be used to provide meaningful information in examining activities in both the disabled and non-disabled populations. We have data currently under analysis using these techniques to evaluate adult subjects with neuromuscular diseases. These methods will provide an excellent means of evaluating interventions designed to improve mobility or to increase the efficiency of energy expenditure during daily activities in the disabled population.