MEASURING HABITUAL PHYSICAL ACTIVITY IN DUCHENNE MUSCULAR DYSTROPHY

Genevieve Wilson[1]; Trisha Sundaram[2]; Benjamin Siegel, MD[3]; Matthew Alexander, PhD[4]; Han C. Phan, MD[1,4]

[1]Rare Disease Research, LLC; [2]Emory University Department of Biology; [3]Emory University School of Medicine, Department of Pediatrics ; [4]University of Alabama School of Medicine, Department of Pediatrics

INTRODUCTION

Duchenne Muscular Dystrophy (DMD)

- Characterized by progressive degeneration of muscle cells leading to the loss of ambulation and cardiopulmonary compromise.

Functional Measures in DMD Research

- Often dependent on a limited number of primary and secondary efficacy functional assessments
  - These often serve as the main endpoints
    - 6-Minute Walk Test (6MWT)
    - Brooke Upper Extremity Scale
    - 9-Hole Peg Test
  - External factors and disease complications can greatly affect subject performance on these measures in clinic
    - anxiety
    - meal schedule
    - travel to the study site

Actigraphy

- Allows for remote, noninvasive assessment of habitual, free-living activity
- May offer insights not observed during in-clinic assessments
- Potential for use in decentralized trials

OBJECTIVES

- To study the habitual physical activity of DMD patients at different stages of disease progression using actigraphy
- To characterize activity patterns, activity magnitude, and patient compliance

STUDY DESIGN

Design: Observational, longitudinal study

Setting: MDA Clinic at UAB; remote monitoring through wearable device

Procedure: Nonambulatory male subjects with DMD (n=22) between the ages of 9 and 27 wore wrist ActiGraph activity monitors for between 15 to 60 days and nights, with a minimum daily wear of 5 hours.

Analysis: ActiGraph software (CentrePoint and ActiLife) for data characteristics and visual inspection. R computing software package nparACT for non-parametic actigraphy measures.[1]

PRELIMINARY RESULTS

Table 1 - Average Sample Characteristics (n=22)

Demographics *(nonambulatory, male)*	
Age (years)	14.1
Weight (kg)	56.1
Activity Data	
Daily calorie expenditure (kcal)	325.2
Daily Y axis counts	474832
Total days with ≥5 hours of data	379
Compliance	
Days worn	21.1
Wear compliance (%)	75.8

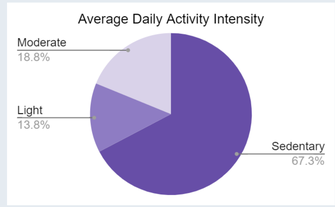

Figure 1 – Average Daily Activity Intensity. For all subjects, 67.3 percent of total activity is classified as sedentary.

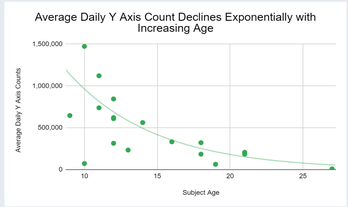

Figure 2 – Average Daily Y Axis Count Declines Exponentially with Increasing Age. Y axis count reflects amount of activity. This data supports known decline in functional ability with disease progression

Figure 3 - Representative Actigraphy Data

A three-day sample of actigraphy data shown as "counts" (calculated triaxial accelerometry data) per minute

Table 2 – Average Sleep Characteristics

Sleep duration (hrs)	5.52
Sleep efficiency (%)	89.33

Red blocks indicate sleep periods, as automatically detected by ActiLife software. Visual inspection of all data suggests a delayed sleep onset.

Table 3 – Non-Parametric Actigraphy Measure Definitions

Interdaily stability (IS) – Measures how similar activity patterns are between days

$$IS = \frac{n\sum_{h=1}^{p}(\bar{X}_h - \bar{X})^2}{p\sum_{i=1}^{n}(X_i - \bar{X})^2}$$

Intradaily variability (IV) – Measures how fragmented the activity pattern is within each day

$$IV = \frac{n\sum_{i=2}^{n}(X_i - X_{i-1})^2}{(n-1)\sum_{i=1}^{n}(X_i - \bar{X})^2}$$

Most active 10 hours (M10) – Average activity count during most active 10 hours each day, calculated on a minute-wise level across days

Least active 5 hours (L5) – Average activity count during the least active 5 hours of the day, calculated on a minute-wise level across days

Table 4 – Preliminary Non-Parametric Actigraphy Results

IS	0.23
IV	0.58
M10	55792.54
L5	1438.72

Non-parametric actigraphy measures were calculated with the formulas shown to the left. IS values range from 0 to 1, with a greater value representing greater stability between days. IV values range from 0 to 1, with a greater value representing greater variability within each day.

SUMMARY

- Decreasing functional ability is a key component of disease progression in DMD
- Measures of free-living, habitual physical activity may present a pragmatic method of directly assessing status and disease progression among non-ambulatory DMD patients
  - Through this research, we hope to contribute to the development of improved outcome measures and more accurate assessment of patient status
- High wear compliance (75.8%) suggests that wearable actigraphy devices are agreeable to patients
  - Implementation in clinical trials may reduce patient burden related to functional assessments performed in clinic
- To further study the use of actigraphy among this patient population, additional research is needed to evaluate the barriers to and practicality of this method

REFERENCES

1. Blume, C., Santhi, N., & Schabus, M. (2016). 'nparACT' package for R: A free software tool for the non-parametric analysis of actigraphy data. *MethodsX*, *3*, 430–435. https://doi.org/10.1016/j.mex.2016.05.006
2. Siegel, B. I., Cakmak, A., Reinertsen, E., Benoit, M., Figueroa, J., Clifford, G. D., & Phan, H. C. (2020). Use of a wearable device to assess sleep and motor function in Duchenne muscular dystrophy. *Muscle & nerve*, *61*(2), 198–204. https://doi.org/10.1002/mus.26759

CONTACT US

Communicate with us directly:

- Genevieve Wilson: genevieve.wilson@rarediseaseresearch.com
- Dr. Han Phan: hphan@rarediseaseresearch.com