



Exercise Training in Kennedy's Disease

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Benefits of exercise

- Increase muscle size
- Promote cardiovascular health
 - Disease modification- Hypertension, Heart disease, Obesity, Diabetes
- Improve sleep hygiene
- Mood benefits

Exercise in SBMA

Work by Preisler et al.¹ showed that frequent, moderate-intensity aerobic exercise is of little benefit in Kennedy's disease.

- Studied the effects of 12 weeks of cycling exercises in a group of 8 subjects with Kennedy's disease.
- Subjects were involved in up to four 30 minute sessions per week.
- No training induced increases in CK level.
- 89% compliance rate
- No significant change in maximal oxygen uptake.
- No significant changes in EMG data.
- No changes in muscle strength, lean body tissue, or lung function.

However...

- 18% increase in the maximal work capacity.

NIH Exercise Study-Functional exercises

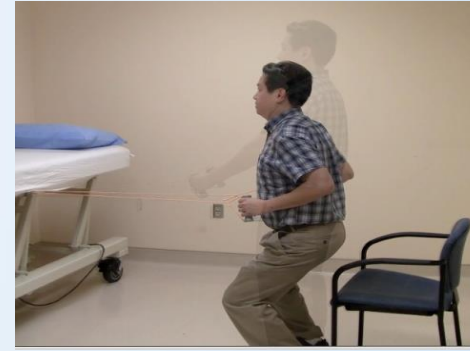
Sit Backs



Sit to Stand



Standing rows



Standing punch



Heel Rise



Wall Pushup

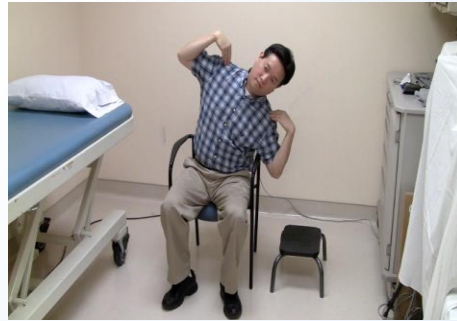


NIH Exercise Study- Stretching exercises

Neck Rotation



Trunk side bending



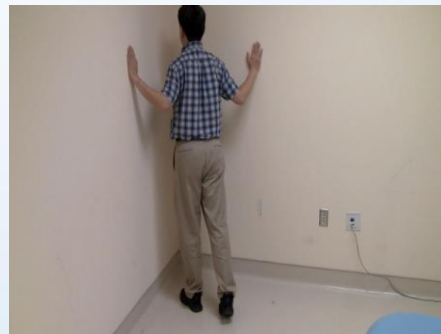
Hamstring stretch



Calf stretch



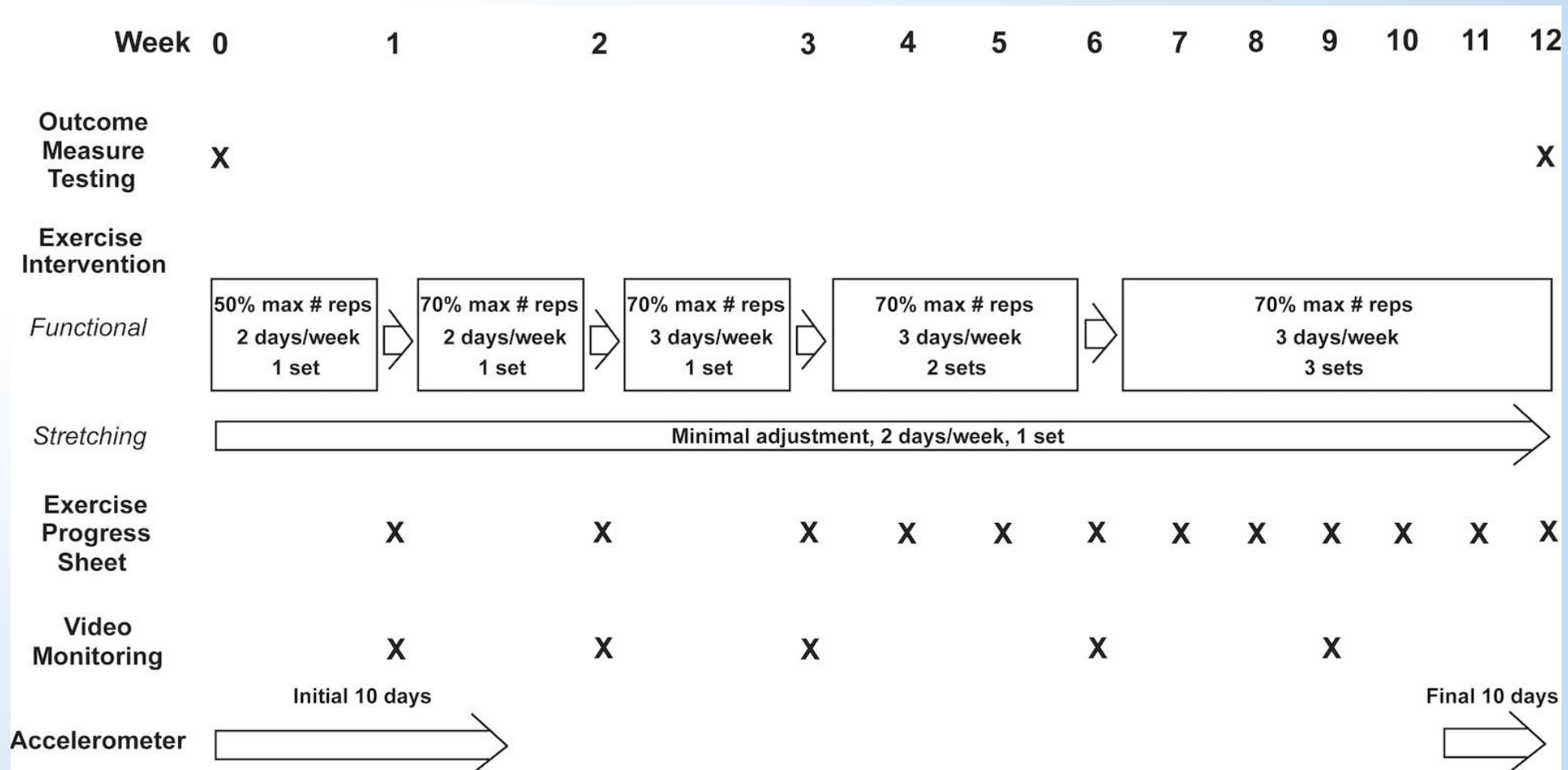
Corner stretch



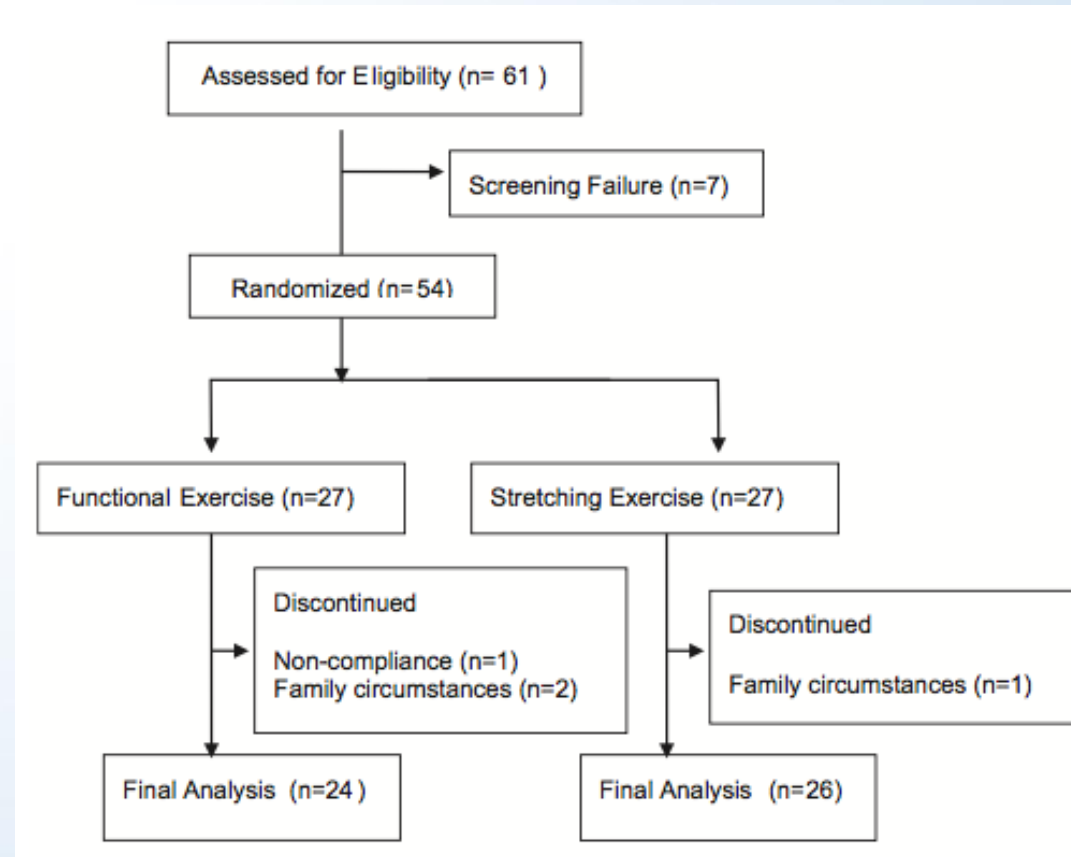
Hip rotator stretch



12 weeks of exercise



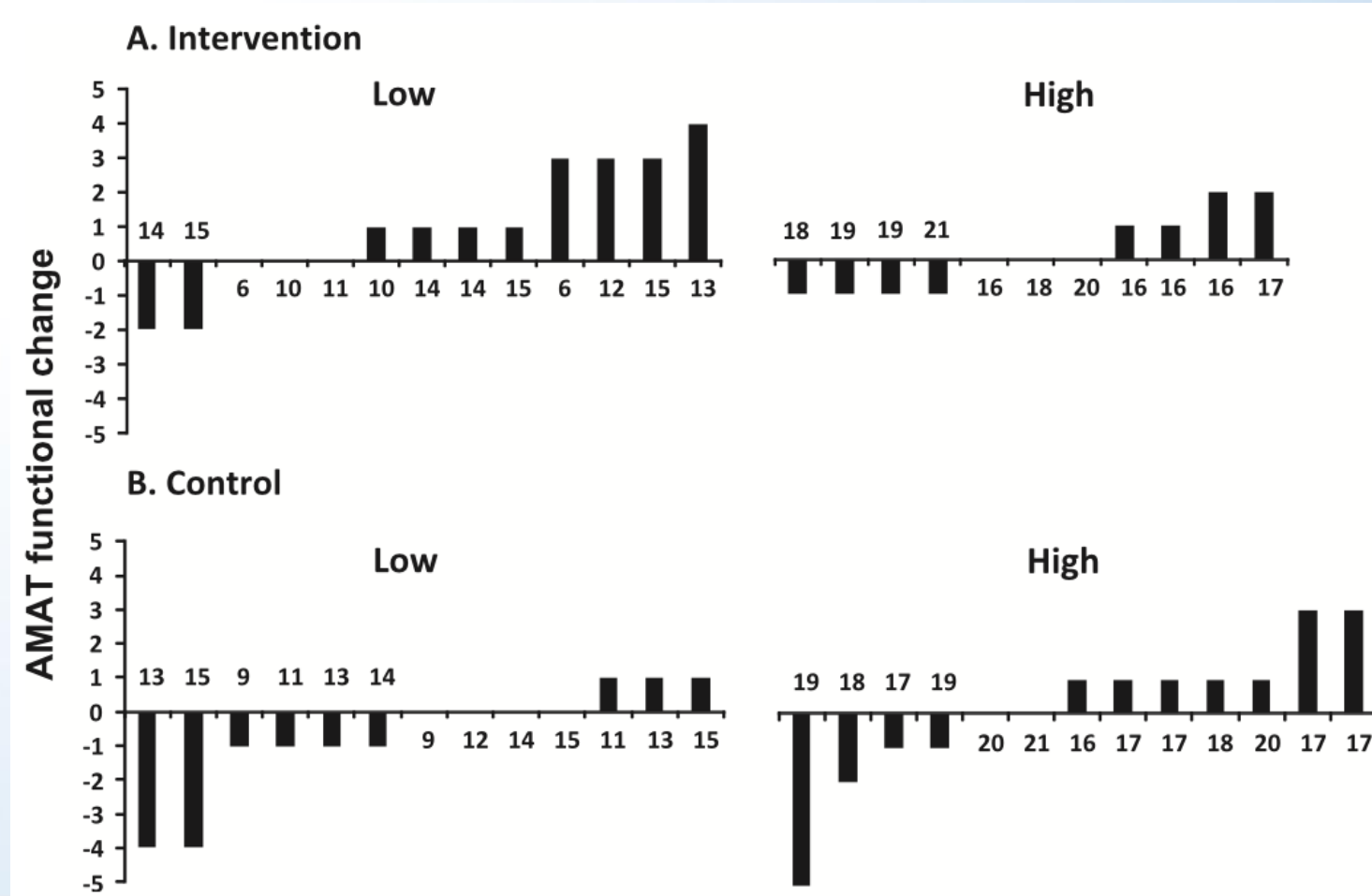
Flowchart of the trial



No significant improvement in primary outcome measure

	Intervention group				Control group				<i>P</i> -value
	Pretest	Posttest	Change	<i>N</i>	Pretest	Posttest	Change	<i>N</i>	
Mobility									
AMAT total ¹ (0–45)	29.3 (6.8)	29.9 (6.6)	0.6	24	28.9 (6.7)	29.0 (7.7)	0.2	26	0.60
AMAT functional ¹ (0–21)	14.6 (4.0)	15.3 (3.7)	0.6	24	15.4 (3.4)	15.1 (4.0)	−0.3	26	0.08
AMAT endurance ¹ (0–24)	14.7 (3.3)	14.7 (3.6)	0.0	24	13.5 (3.7)	13.9 (4.0)	0.4	26	0.29
STS scale ¹ (% of knee height)	103.3 (22)	103.8 (24.3)	0.4	24	102.3 (22.5)	103.1 (23.5)	0.8	26	0.86
TUG (sec) ¹	10.8 (6.5)	11.0 (6.5)	0.2	24	9.5 (3.2)	9.6 (3.7)	0.1	26	0.93
Actical total activity (average count per day) ^{1, 2}	53,949 (42,610)	61,797 (48,383)	7848	20	69,326 (51,539)	70,498 (50,508)	1171	23	0.19

Post hoc analysis- improvement for low functioning subjects?



NIH Exercise Study Summary

- 12 weeks of light functional exercise had no significant effect on muscle function.
- Functional exercises had a favorable safety profile.
- Post-hoc analysis indicates that functional exercise may improve task performance in those with low baseline function.

What about other types of exercise
intervention?



Patient History- Case #1

- 50-year-old working 50 hours per week
- Reports gait instability, balance issues, muscle weakness
- 2008 – Decompressive Spine Surgery for radiculopathy
- 2013 – Diagnosed with Kennedy's Disease





Patient's Symptoms

- Inability to run for several years
- Approximately 1 fall per week
- Choking on eating, approximately 10% of attempts
- Chronic Sleep disturbance due to muscle cramping that wakes him at night
- Less steady on feet while hunting and ascending stairs
- Leg weakness that prevents running, jumping, and stair use
- Difficulty donning socks and shoes
- Worsening facial muscle fasciculations





Patient's Goals

“I want to know if a physical lifestyle is compatible with this disease...
My hope is to build and work a farm over the next decade”



- Desires to transition from office work to an active outdoor lifestyle after retirement in one year
- Wants to maintain strength and functional abilities, but is uncertain of optimal and/or safe exercise intensity

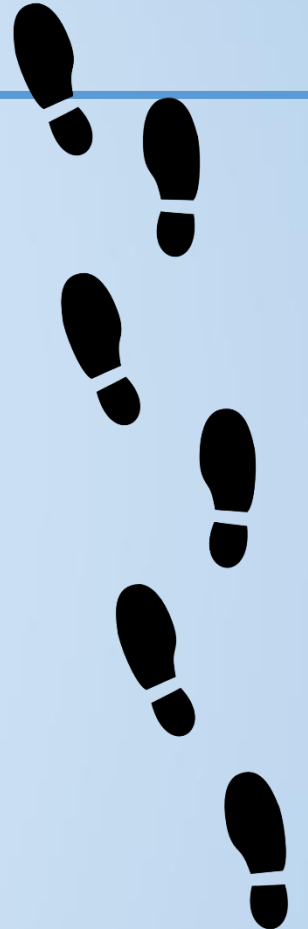
Examination



- Strength & Balance
 - Manual Muscle Testing was 5/5
 - Ankle dorsiflexion asymmetry due to left radiculopathy with partial resolution of weakness following surgical decompression.
- Range of Motion and Edema
 - no joint motion limitations
 - no swelling
- Fatigue
 - Self-reported fatigue; Fatigue Severity Scale: 28/63
 - Scores above 36 indicate need for medical evaluation

Functional Tests and Measures

- Full functional mobility with independent community ambulation, self-care abilities, instrumental activities of daily living, and vocational skills.
- Gait: minimal deviation; wearing supportive shoes, left ankle foot orthosis used for community distance ambulation
- 6 Minute Walk Test resulted in 615 meters placing him at 90% of his predicted result based on age, gender, and height.
- Adult Myopathy Assessment Tool score was 45/45.
 - 13 Performance based functional and muscle endurance tasks
 - The patient was excluded from a recent exercise trial due to hitting AMAT ceiling



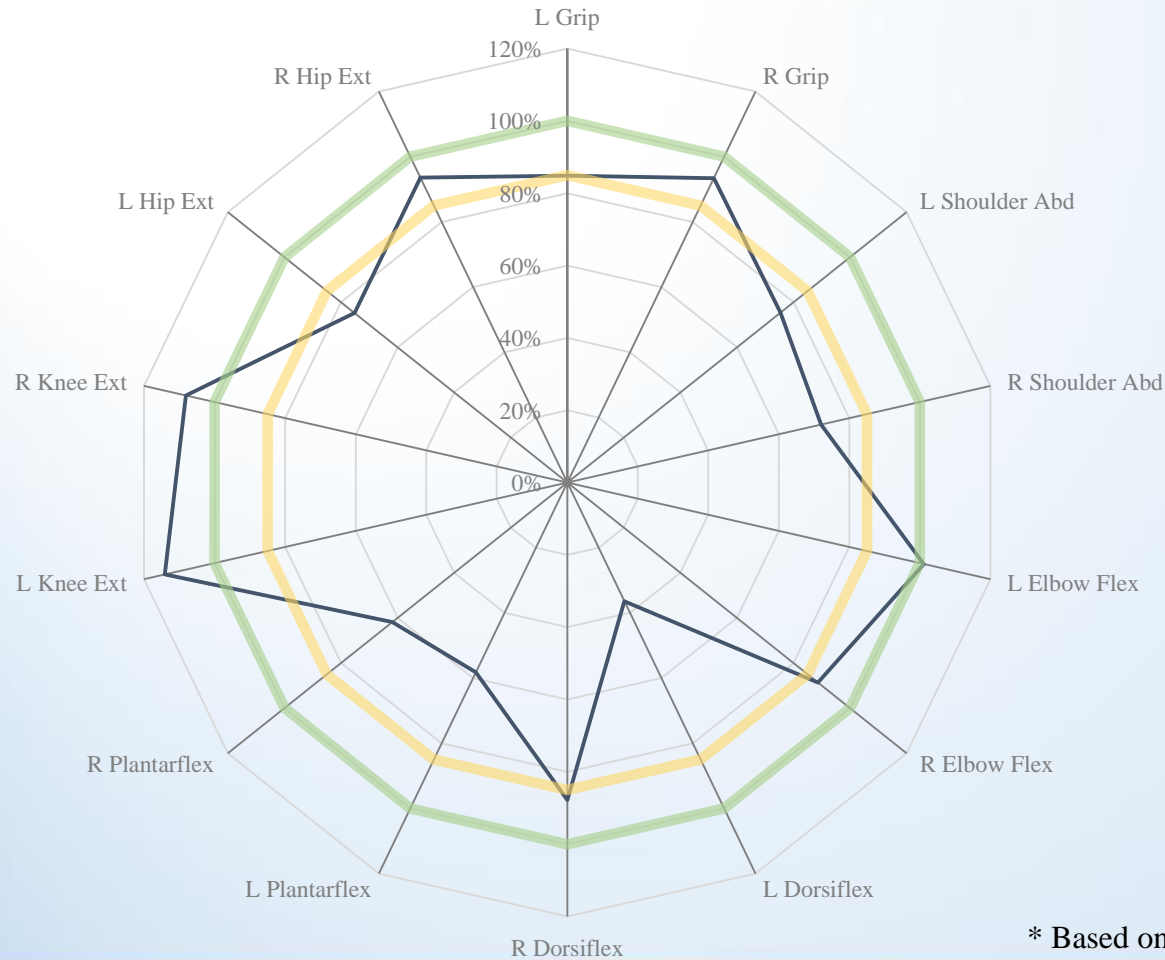
Clinical Impression – *Mild disease...*



- Patient does not appear to be weak based on the MMT results
- Patient revealed to have normal function and the ability to sustain task performance by AMAT, classifying him as high functioning compared to SBMA patients
- He walks without gait aid and only requires AFO for community distances
- *Patient reports considerable changes in his strength and cannot lift weights like he used to*
- *Patient has difficulty ascending or descending multiple flights of stairs, raking the yard, and hiking or walking long distances like he previously was able to*
- *He cannot run, jump or play sports with previous coordination and confidence*



Further Examination - *Strength*

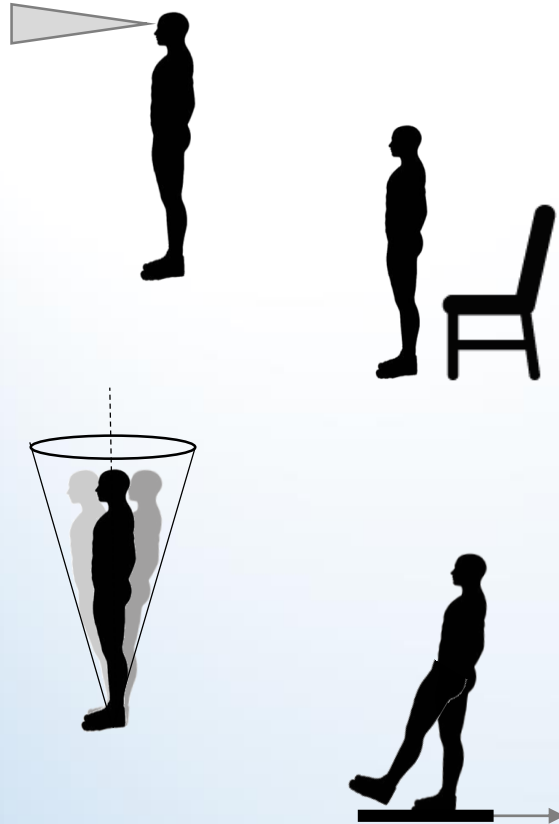


- Overall body was 84% of predicted strength
- Eight LE and UE muscles were in the healthy predicted range (85-114%)
- The following six muscles are identified to be weak compared to predicted healthy values:

Muscle	Percent Predicted*	
	Right	Left
Deltoid	72%	75%
Gluteus Maximus	94%	75%
Calf	62%	58%
Anterior Tibialis	88%	36%

* Based on Andrews 1996, NIMS 1996, Stoll 2000, and Turnquist et al normative database prediction equations

Further Examination - *Balance*



Neurocom Tests

Outcome and Evaluation

- | Neurocom Tests | Outcome and Evaluation |
|-----------------------|---|
| ▫ MCTSIB | Normal balance control via sensory system;
No falls during 30 second quiet standing test |
| ▫ Sit to Stand | Normal task performance speed and stability;
No falls and appropriate sway velocity |
| ▫ Forward Lunge | Normal impact and force tolerance;
Lost balance during 2 of 3 trials |
| ▫ Limits of Stability | Low endpoint composite scores;
Difficulty controlling and leaning anterior and posterior via ankle movements |
| ▫ Motor Control Test | Slow response to sudden floor shifting;
Delayed automatic postural correction |



Further Examination - *Gait*

Gait Rite	Predicted*	Measured
Step Length (statures) – fast pace		
Right	.47	.48
Left	.47	.46
Step Length Asymmetry (cm)	-	4.7
Velocity (stature/s) – fast pace	.92	.92
ΔVelocity (%) – self selected to fast pace		
with orthotics	-	32
without orthotics	21	18
Cadence (steps per minute) – fast pace	118	118

- Patient's step length as a ratio to stature is normal, but is asymmetrical
 - Right step is 4.7 cm longer
- Patient walks at the average velocity
- Patient can increase walking speed even more with the support of the ankle foot orthosis
- Patient's cadence is normal

* Based on 92 healthy males volunteers aged 40-62 (56.3 ± 6.5) (Himann 1987)



Clinical Findings– *quantifying the disease*

- QMA testing identified muscle weakness undetected by MMT. Three muscle groups at the ankle, two at shoulders, and one at hip are weak based on healthy prediction equations
- Although basic clinical balance tests were normal, Neurocom tests detected problems in his ability to react to unexpected postural disturbances and difficulty using his ankle muscles to make active backward postural shifts
- Gait evaluation is generally good, but reveals stride length asymmetry. With ankle foot orthosis he increased his walking speed 40% more compared with no AFO use.
- Functional deficits of both lower and upper extremities in dynamic activity are reflected in the self-reported functional scales.



How can rehab medicine help?

- Patient potentially can tolerate and benefit from weight training
 - An upper extremity training module may help prepare him to pass his work Physical Exam
 - A lower extremity strengthening and balance training module may improve his strength and upright mobility functional capacity
- He will require close monitoring of soreness, cramps, pain, falls, etc. during training sessions
 - Can we help him determine safe and optimal exercise intensity?
 - Due to lack of research evidence substantiating weight training in neuromuscular diseases we recommended training in our clinic

Interventions



- Physical therapist supervised strength training combining free weights, machine weights, and functional exercises utilizing body weight
- Swedish style, light weight, left Ankle Foot Orthosis fitted for management of mild foot drop symptoms
- Instruction in balance exercises
- Regular rhythmic walking program



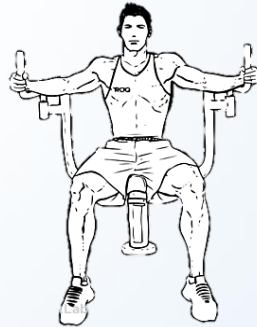
Approach – *Strength training*



- 15 week supervised strength training program in RMD. One exercise session with a therapist and another unsupervised at health club per week



Bent Over Row



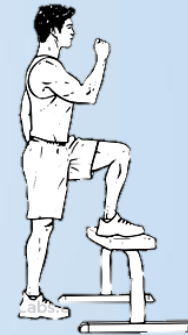
Arm Flies



Plank



Lunge



Step Ups



Overhead Press



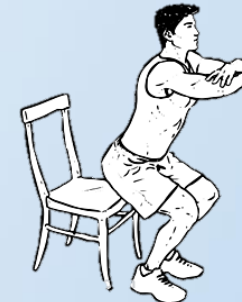
Chest Press



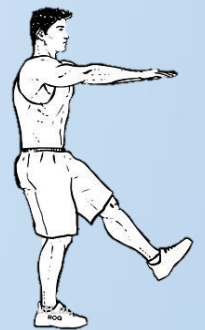
Lateral Pull Down



Knee Extensions



Squat



Single Leg Stand

Approach - *continued*



- Patient completed a symptom progress sheet every time he exercised that was reviewed prior to supervised session.
- Program periodization with increases in intensity, duration, and/or frequency implemented gradually over time based on exercise recovery
- Session rating of perceived exertion and responses to weight training recovery, including soreness, fatigue, cramps, loss of performance, falls, or shortness of breath, dizziness, or chest pain
- Regular monitoring of blood work (CPK, LDH, IGF1)



Outcome Measures – *understanding the effects of weight training*

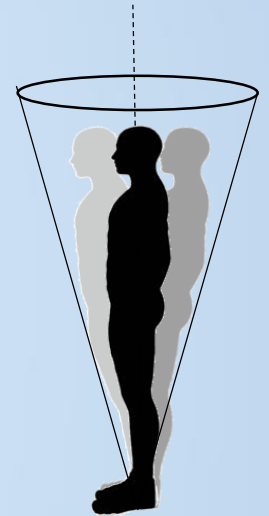


- Primary Outcome Measures (Strength, Balance, Gait)

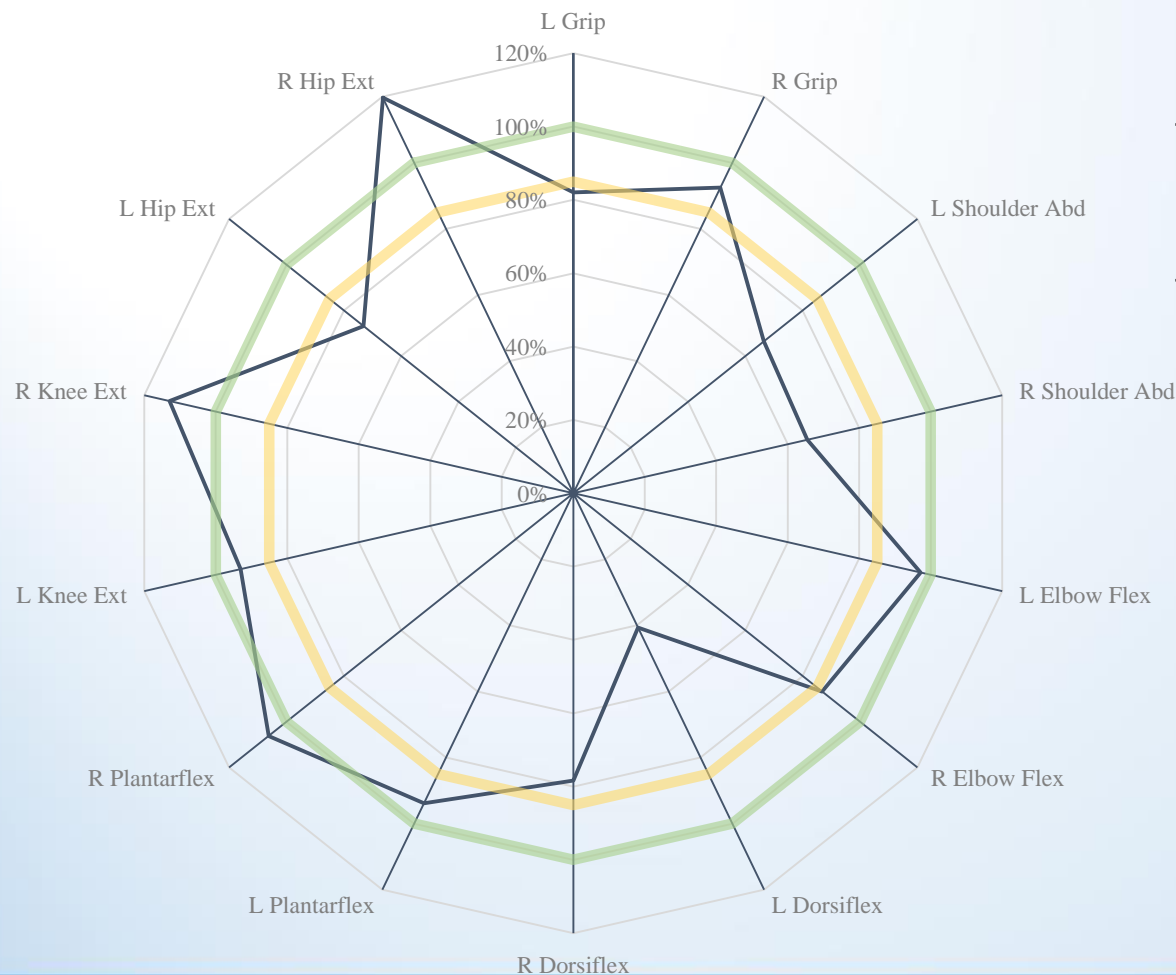
- Quantitative Muscle Assessment (QMA)
- Neurocom
- Gaitrite

- Secondary Outcome Measures

- Blood Work
- Adult Myopathy Assessment Tool (AMAT)
- Six Minute Walk Test (6MWT)
- Fatigue Severity Scale (FSS)



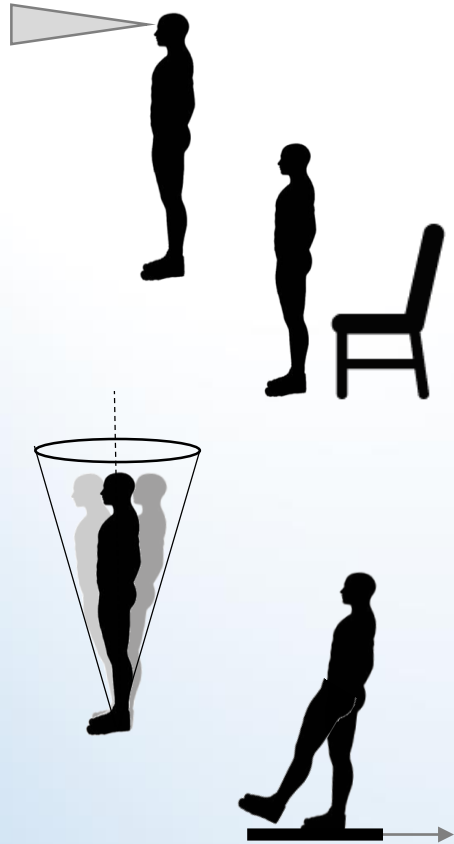
Results - *Strength*



Strength (QMA)	Baseline	Follow-up
Upper Extremity	166 kg (87% predicted)	159 kg (83% predicted)
Lower Extremity	319 kg (83% predicted)	360 kg (94% predicted)
Total	485 kg (84% predicted)	519 kg (90% predicted)

Muscle	Percent Predicted Baseline		Percent Predicted Follow-up	
	Right	Left	Right	Left
Deltoid Muscle	72%	75%	65%	66%
Gluteus	94%	75%	120%	73%
Calf Muscle	62%	58%	106%	94%
Anterior Tibialis	88%	36%	78%	40%

Results - *Balance*



Neurocom Tests

Outcome and Evaluation

- | Neurocom Tests | Outcome and Evaluation |
|-----------------------|---|
| ▫ MCTSIB | Normal and improved balance control via sensory system;
Decreased sway velocity, especially eyes closed from 2.2 to 1.4 deg/sec |
| ▫ Sit to Stand | Normal and improved task performance speed and stability;
Increased weight symmetry from 8% to 2% skew and decreased sway velocity from 4.8 to 3.8 deg/sec |
| ▫ Forward Lunge | Normal and improved impact and force tolerance;
Did not fall. Completed lunge trials with less effort and time |
| ▫ Limits of Stability | Improved from low to almost-healthy endpoint composite scores;
Increased backwards excursion 30% and right side directional control 4% |
| ▫ Motor Control Test | Response to sudden floor shifting is slow with no improvement;
Delayed automatic postural correction |

Results - *Gait*

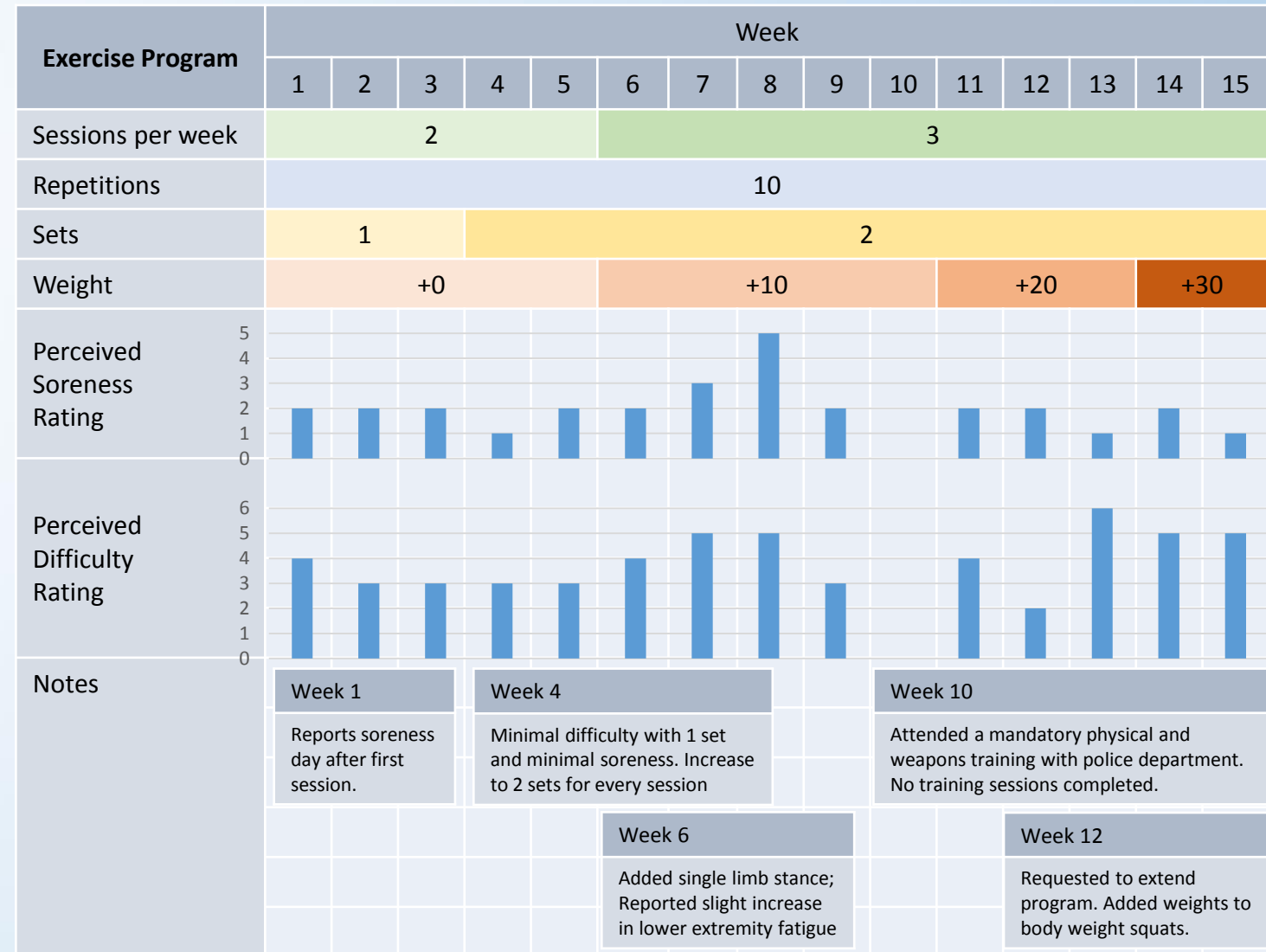


Gait Rite	Baseline	Follow-up	
Step Length (stature) – fast pace			
Right	.48	.49	□ Patient achieved consistently longer stride lengths <ul style="list-style-type: none">□ Step length more symmetrical by 1.9 cm□ Velocity becomes 7.1 cm/s (.04 stature/s) faster□ Cadence not improved significantly
Left	.46	.48	
Step Length Asymmetry (cm)	4.7	2.8	
Velocity (stature/s) – fast pace	.92	.96	□ Patient can achieve a similar fast pace with or without orthotics <ul style="list-style-type: none">□ Ankle Foot Orthosis now has less of a supportive role for the patient for short distance walking
ΔVelocity (%) – self selected to fast pace			
with orthotics	32	28	
without orthotics	18	26	
Cadence (steps per minute) – fast pace	118.4	119.0	

Results

- *Blood Work*
- *Perceived Exertion*

- During 15 week exercise program, LDH and CK were in a normal range.
- The program was adjusted weekly so that soreness was below 3/10 and perceived exertion was 5 - 6/10
- Close monitoring by physical therapists allowed for appropriate modification of program intensity



Patient Response

- Functional, gait, and balance improvements were detected through objective assessments, performance tests, and self-report questionnaires
 - Patient increased peak muscle strength in LE by 11% but lost 4% at UE
 - Patient increased 30 second chair stands from 10 to 15 repetitions
 - Patient improved balance excursion and directional control of his limits of stability
 - Patient walks with longer and more symmetrical step lengths
 - Patient reports no fatigue during the past 2 weeks at conclusion of the intervention
- He tolerated moderate intensity weight training with self-reported exertion of 5-6/10 accompanied by low soreness ratings of 2-3/10 and was able to double almost all weight levels over 15 weeks
- The patient reported high satisfaction with the training program and was confident he could safely continue at the present training intensity to maintain his desired activity level and functional profile as he planned for retirement and an active farming lifestyle

Discussion- case #1

- Patients with Kennedy's Disease or other neuromuscular diseases are frequently told to avoid weight lifting or exercise
 - There is little evidence to help substantiate or refute this recommendation
 - Based on this case, some patients with Kennedy's disease may respond positively to weight training under medical supervision
- Even though our patient initially scored at or near maximum on walking (T6MWT) and functional performance tests (AMAT), other objective and self report tests detected subclinical problems and allowed us to see improvements in strength and function with intervention.
- Our previous work showed that high functioning men with Kennedy's disease did not benefit from the functional exercise intervention as much as those who were low functioning at baseline evaluation.

Exercise intervention- Case #2

- 60 year old male
- Hyperlipidemia
- Diabetes Mellitus type 2
- Depression
- Has difficulty climbing stairs , washing hair, brushing teeth, and suffers from various falls.
- Recently retired, although upon starting treatment was still employed.
- Had previously declined exercise because of weakness.

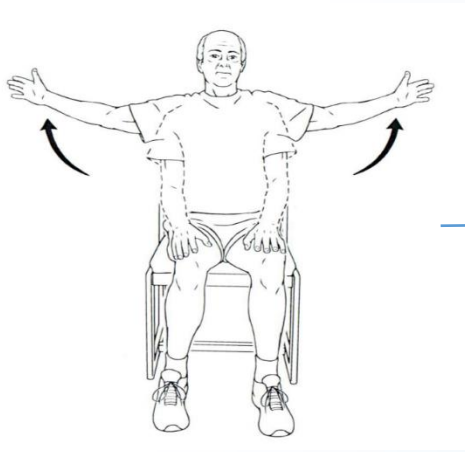
Initial Examination

- He has difficulty climbing stairs, washing hair, brushing teeth.
- Experiences significant falls.
- He was very fatigued, the alarming concern was his very low dorsiflexion strength
- In need of better shoes, gate aid
- AMAT – 24/45
- Berg Balance scale – 34 (maximum score is 56, higher- better)

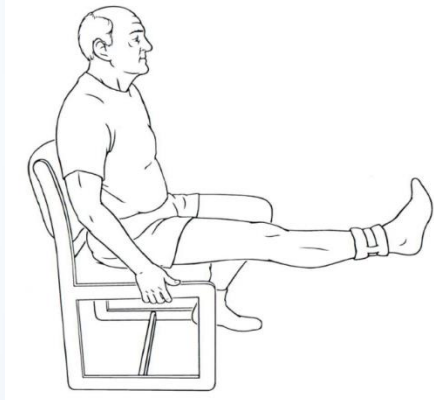
Exercises- Strategy

- The patient was initially given 9 exercises and gradually worked up to a program of 25 exercises over 5 months.
- Main concern was his high risk for falling so the exercises needed to be done in a safe zone
- During this period, several rehab measures taken; Gait aid, better quality shoes, vocational counseling for retirement.

Interventions



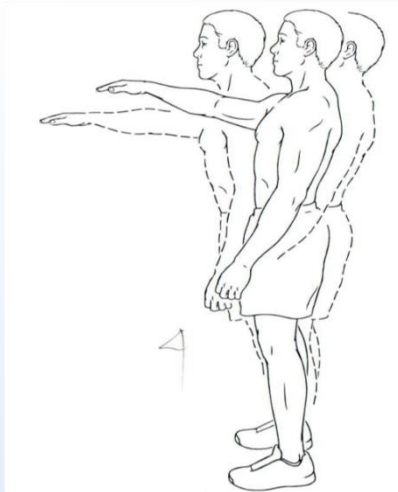
Breathing & posture



Seated muscle strengthening



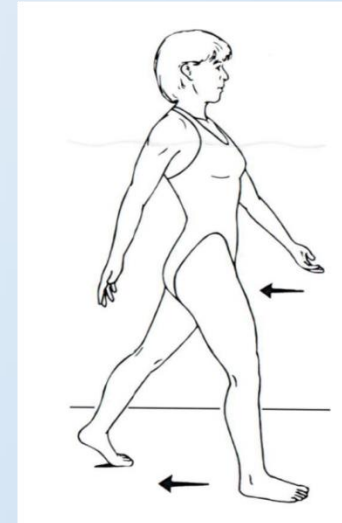
Endurance



Improvement of stability

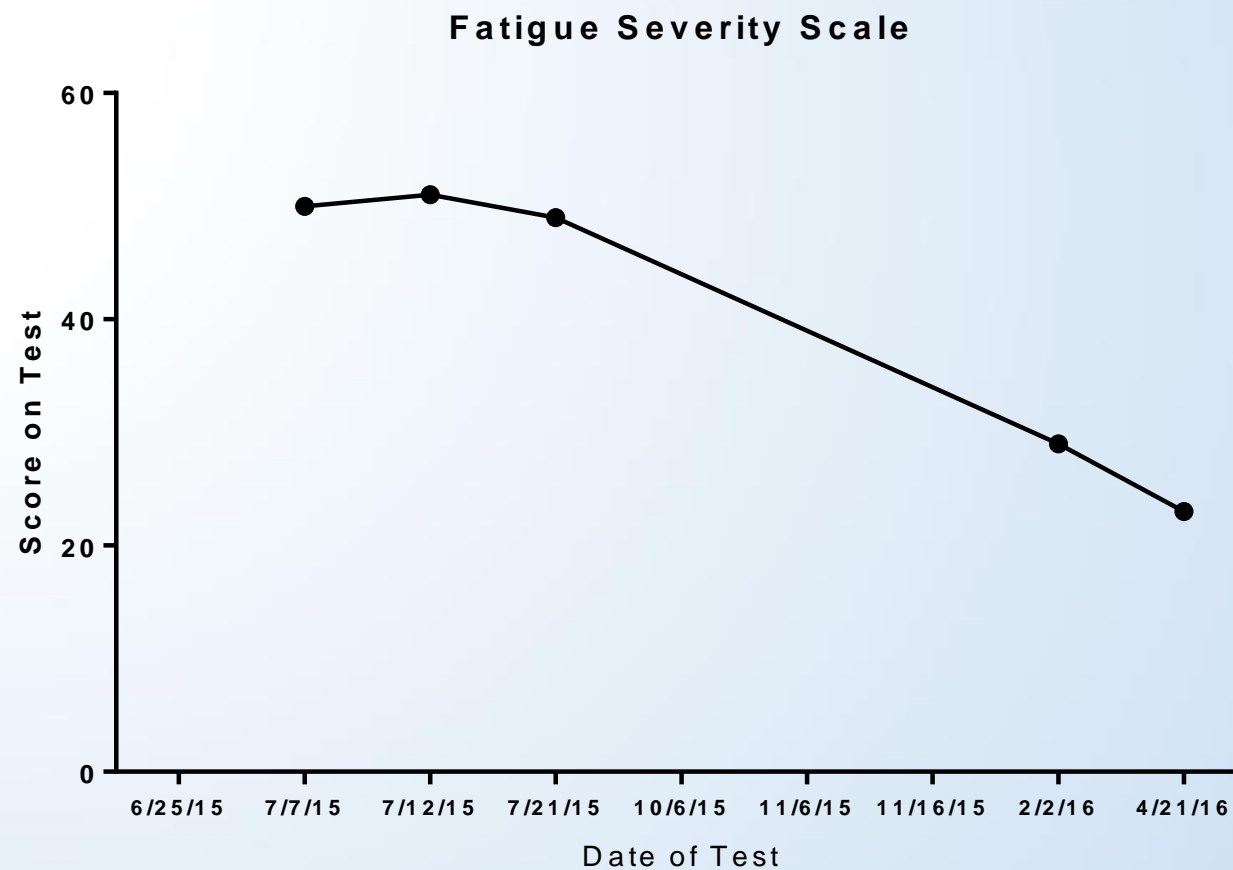


Muscle strengthening:
walking and standing

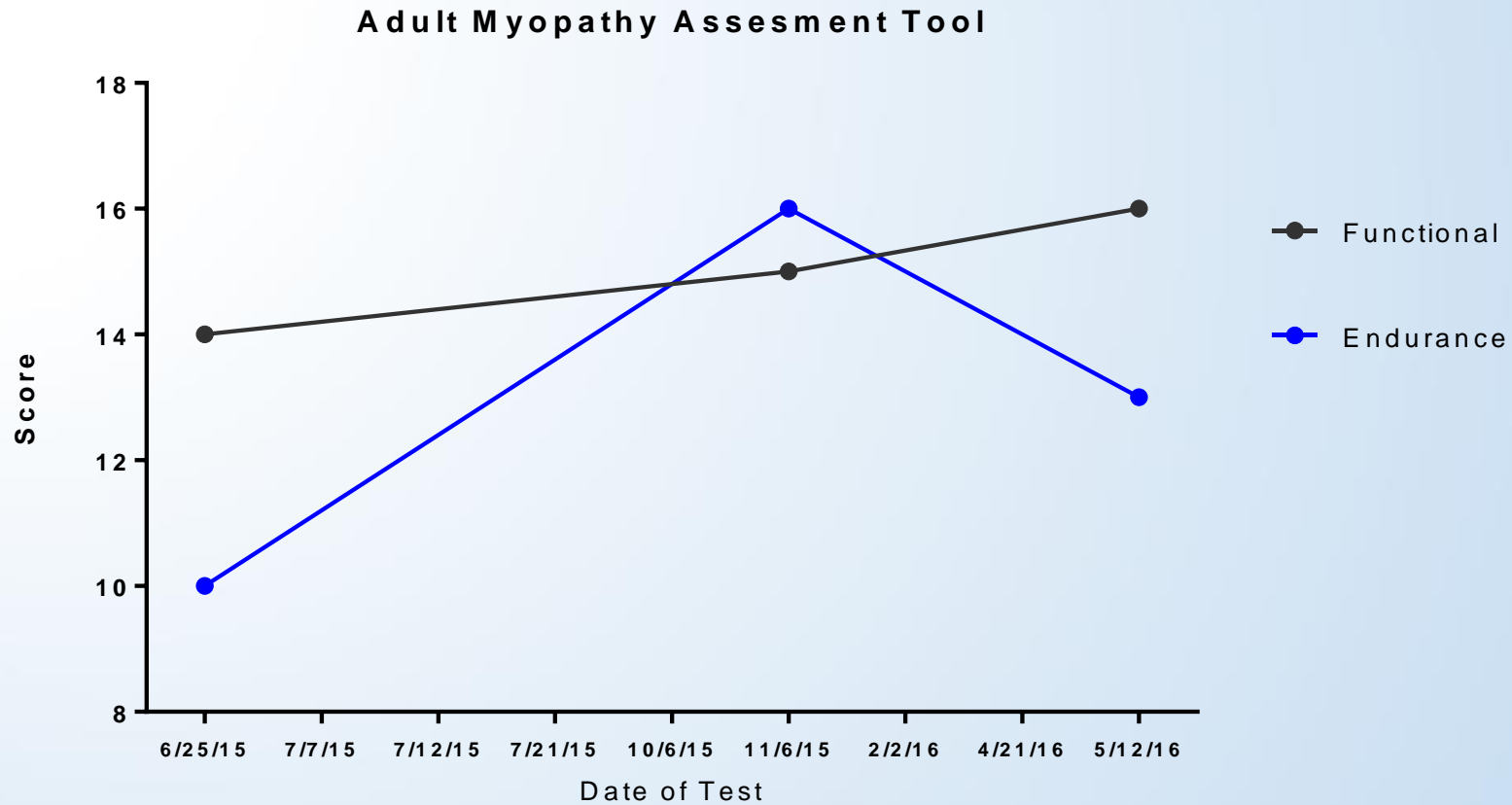


Balance/strength training

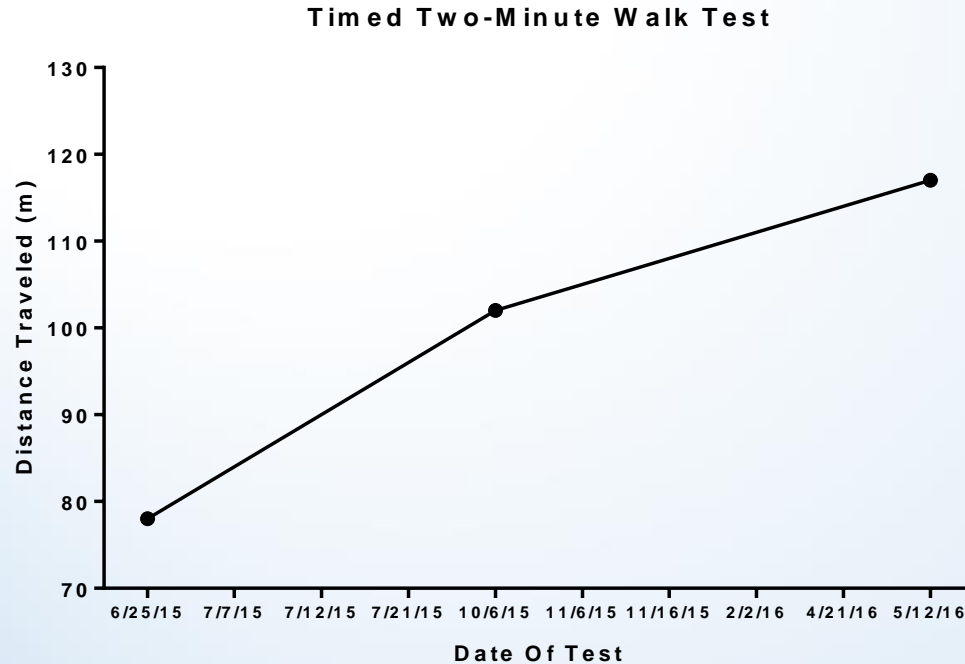
Fatigue:



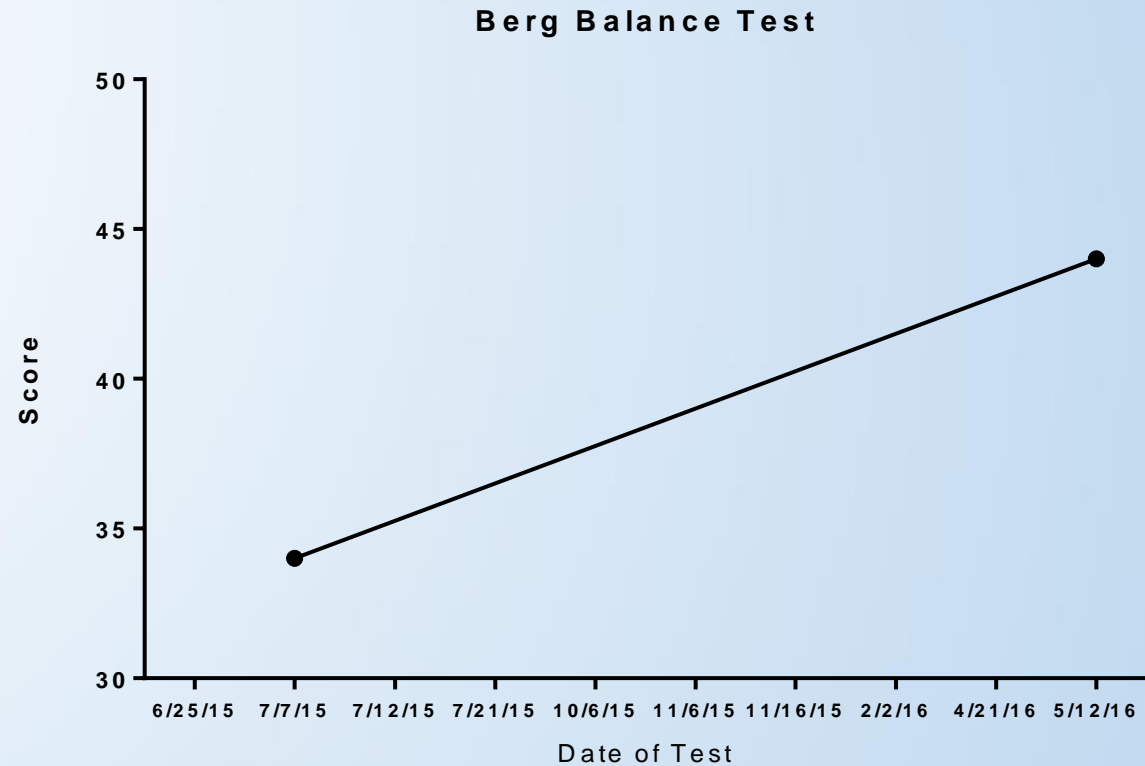
AMAT testing:



Two-minute walk



Balance Function



Conclusions



- While we cannot conclude cause/effect relationships from case reports, however, patient #1 showed that a patient with spinal and bulbar muscular atrophy tolerated supervised, moderate intensity progressive strength training with weights over a 3 month period.
- Patient #2 saw significant improvement in AMAT= 7 points in 5 months. Intervention improved function, balance, strength, fatigue in the setting of gait aids and outfitting with better quality shoes.
- We suggest ratings of perceived exertion and muscle soreness be closely monitored by clinicians to ensure safety and efficacy of a strength training program on a case by case basis.



Future Directions

- Clinical study design to test utility of similar exercise interventions in SBMA.
 - Denmark Study- Dr. John Vissing (U. of Copenhagen).
- Utilize appropriate study measures for detecting benefit.
- Appropriate “prescription” of exercise regimen given limitations/baseline function.

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