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New Approaches for Exercise Training in Advanced Multiple Sclerosis

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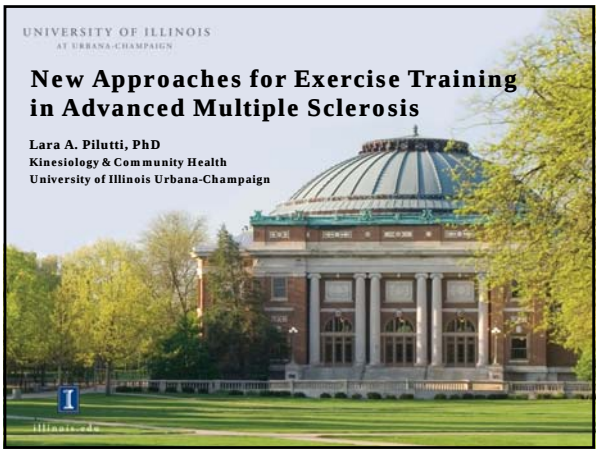

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Outline

- Advanced MS
- Exercise & MS: Problems & solutions
- Potential approaches for exercise training in advanced MS
  - Approach
  - Current Evidence
  - Long-term potential
- Conclusions

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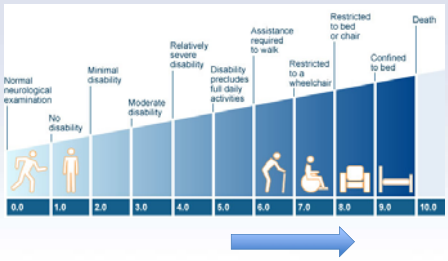
Advanced MS



Expanded Disability Status Scale (EDSS)

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Advanced MS: Limitations

- Walking impairment
- Loss of physical fitness
  - Strength, aerobic capacity, balance, body composition
- Symptoms
  - Fatigue, depression, pain
- Quality of life
- Participation in daily activities

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Exercise Training in MS

- Potential benefits:
  - Walking performance & gait
  - Aerobic and muscular fitness
  - Balance
  - Body composition
  - Symptoms
  - Quality of life

- Current evidence based on patients with mild-moderate MS, <u>not</u> advanced MS disability

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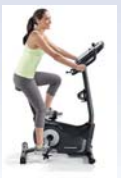
Latimer-Cheung et al 2013

Why Limited Research?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Other Limitations

- Barriers to exercise in advanced MS:
  - Availability of facilities/programs
  - Transportation
  - Financial burden
  - Lack of support
  - Limited information

Why Exercise for Advanced MS?

- Importance
  - Limited options for therapy
  - DMT not effective long-term
  - Need alternative approaches to restore and maintain function and independence

Solution: Adapted Exercise

- Adapted exercise approaches:
  - Modified exercises, training approaches and/or equipment that is accessible for individuals with advanced MS

Potential Approaches for Exercise

1. Body-weight supported treadmill
2. Recumbent stepper
3. Adapted home-based resistance exercise
4. Functional electrical stimulation cycling

Body-Weight Supported Treadmill Training

- Approach:
  - Partial or complete body weight support via overhead harness
  - Repetitive, task-oriented gait training
  - Therapist or robotic assistance

Body-Weight Supported Treadmill Training

- Evidence:
  - Some trials in advanced MS
    - Benefits: walking performance, gait, strength, MS symptoms, QOL
    - Benefits generally not maintained when training discontinued

Effects of 12 Weeks of Supported Treadmill Training on Functional Ability and Quality of Life in Progressive Multiple Sclerosis: A Pilot Study

Lara A. Pilutti, BSc, BPHE, Danny A. Lelli, MD, John E. Paulseth, MD, Maria Crome, BKin, Shucai Jiang, MD, PhD, Michel P. Rathbone, MD, PhD, Audrey L. Hicks, PhD

Beer et al 2008; Lo & Triche 2008; Giesser et al 2007; Schwartz et al 2011; Wier et al 2011

Body-Weight Supported Treadmill Training

- Long-term potential:
  - Limited to specialized training centers
  - High costs
  - Therapist-assisted training inefficient and may limit patient contribution to training
  - Potential as short-term gait rehabilitation tool to regain mobility and function

Potential Approaches for Exercise

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Recumbent Stepper Training

- Approach:
  - Bilateral, reciprocal arm and leg pedals – coupled action
  - Large foot pedals, rotating seat, arm and leg strapping
  - Provides full body aerobic exercise in seated position

Recumbent Stepper Training

- Evidence:
  - No published training studies in MS
  - Improved fitness in healthy sedentary
  - Benefits reported in older adults, stroke and PD patients
    - Improved blood pressure, strength, walking, & balance

Hass et al 2001; Johnson et al 2002; Page et al 2008; Sage & Almeida 2009

Recumbent Stepper Training

- Pilot study:
  - 12 participants progressive, advanced MS (EDSS=6.0-8.0)
  - 6 recumbent stepper/6 BWSTT
  - Intervention: 3x/wk, 12-weeks
  - Outcomes:
    1. Safety, compliance & patient experience
    2. Efficacy vs BWSTT

Recumbent Stepper Training

- Primary outcomes:
  - Safety: stepper 2 AEs; BWSTT 5 AEs
  - Compliance: ~89% for both groups
  - Equipment preferred: recumbent stepper
- Secondary outcomes:
  - Improved fatigue and QOL in both groups
  - No change in function both groups
  - Higher training heart rate in stepper group

Recumbent Stepper Training

- **Long-term potential:**
  - Relatively cost-effective
  - Simple to use
  - Self-driven training
  - Available in many community settings
  - Potential for home use, although large piece of equipment

Potential Approaches for Exercise

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Home-Based Resistance Training

- **Approach:**
  - Adapted, resistance training exercises suitable for home setting
  - Resistance = bands, free weights, body weight
  - Target strength loss



Home-Based Resistance Training

- **Evidence:**
  - One previous study in mod-advanced MS
  - Benefits in mild-mod MS and general population
  - Project RETRO:
    - Design: 6-month, home-based resistance training program, using elastic bands (vs no exercise control)
    - Goals:
      1. Safety and efficacy
      2. Secondary benefits

DeBolt & McCubbin 2004

RETRO Intervention

- **Home-based PRT:**
  - 10 exercises, 2x/wk, 1-2 sets, 8-12 reps
  - Provided log book, training manual, equipment
- **Behavioral Component:**
  - Theory-based strategies
- **In-person visits**
  - Training progression
  - Behavioral strategies

RETRO Exercise Program

- **Group-based training sessions:**


Behavioral Strategies

- Tools to help maximize program adherence and the potential benefits from exercise
- E.g., self-monitoring, goal setting
- Part of group-based sessions

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GOAL SETTING

S.M.A.A.R.T. goals
- Specific
- Measurable
- Adjustable
- Action-Oriented
- Realistic
- Time-Based

RETRO: Results

- Participants:
  - 12 completed (5 exercise/7 control)
  - Age = 59.1 ± 8.2 years
  - Disease duration = 19.1 ± 10.1 years
  - EDSS = 6.5 (i.e., constant bilateral assistance)
- Safety:
  - 1 shoulder injury, 1 fall, 2 relapses
- Compliance:
  - ~45 sessions over 24 weeks

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Strength & Lean Mass

Outcome	Control	Exercise	*P*	n_p^2	*d*
Grip strength, kg	27.8 (0.5)	27.7 (0.6)	.92	.001	-.01
Knee extensors, Nm	85.8 (6.7)	85.7 (8.1)	.99	<.001	<-.001
Knee flexors, Nm	29.2 (2.1)	31.4 (2.3)	.50	.06	.38
Shoulder extensors, Nm	35.4 (2.0)	34.0 (2.4)	.66	.02	-.12
Shoulder flexors, Nm	38.5 (3.6)	47.5 (4.2)	.13	.23	.46
Ankle dorsiflexors, Nm	17.8 (1.4)	17.5 (1.5)	.88	.003	-.09
Ankle plantarflexors, Nm	52.0 (7.9)	66.6 (8.7)	.27	.15	.52
Whole body lean mass, g	42188.0 (952.5)	43093.5 (1127.1)	.55	.04	.08
Skeletal muscle mass, g	18475.7 (461.8)	18906.7 (546.44)	.56	.04	.08

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Values are estimated marginal means (SE)

Secondary Outcomes

Outcome	Control	Exercise	*P*	n_p^2	*d*
Upper body function – 9HPT, seconds	73.8 (3.2)	75.9 (3.9)	.70	.02	-.05
Cognition – SDMT	39.8 (3.6)	42.0 (4.3)	.72	.02	.38
Fatigue – MFIS	42.9 (3.6)	39.9 (4.3)	.61	.03	.05
Pain – MPQ	5.3 (1.6)	8.4 (1.9)	.25	.14	-.83
Physical QOL	59.4 (2.5)	62.7 (3.0)	.42	.08	.23
Mental QOL	21.7 (1.5)	17.5 (1.75)	.10	.27	.53

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Values are estimated marginal means (SE)

Home-Based Resistance Training

- Long-term potential:
  - Cost effective
  - Easily implemented in home/community settings
  - Strategies for promoting compliance and home-monitoring should be considered

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Potential Approaches for Exercise

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Functional Electrical Simulation (FES) Cycling

- Approach:
  - Surface electrodes placed over leg muscles
  - Mild electrical stimulation results in muscle contraction and leg cycling


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FES Cycling

- Evidence:
  - Benefits largely established in SCI and stroke
    - Improved walking, gait, strength, spasticity, bone & skin health, metabolism, cardiovascular function
  - MS studies (n=4)
    - Preliminary benefits: walking, gait, strength, muscle mass and metabolism, quality of life
    - Limitations: Small samples (8-12 people), no control condition, short-term training

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Fornusek & Hoang 2014; Ratchford et al 2010; Reynolds et al 2015; Szecsi et al 2009

Next Steps: Pilot FES Study

- 6-month trial of supervised FES cycling
- 16 participants with advanced MS
- 2 interventions: FES and passive leg cycling

- Primary outcomes:
  - Safety, feasibility, walking, & fitness
- Secondary outcomes:
  - MS symptoms, cognition, eye & brain imaging
- Assessments: baseline, 3 months, 6 months

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FES Cycling

- Long-term potential:
  - FDA approved for home use
  - Ability to track progress and provide feedback through Internet monitoring
  - Potential to achieve higher exercise training stimulus
  - Need to first establish benefits in MS

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Other Rehabilitation Considerations

- New approaches can be combined with other strategies:
  - Physical and occupational therapy
  - Assistive devices and orthoses
  - Medical and surgical therapies

Conclusions

- Need for new exercise approaches in advanced MS
- Adapted exercise requires rigorous evaluation in advanced MS for establishing safety, feasibility, and efficacy
- Ultimate goal to develop effective home- and community-based exercise programs for the long-term management of advanced MS

Thank You

- Participants
- Research team:
  - Clinical Exercise Physiology Lab
- Collaborators
  - Rob Motl & Exercise Neuroscience Research Lab

Questions?

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