Exercise and MS: History, Research Evidence, and Clinical Considerations

Eduard Gappmaier, PT, PhD
Clinical Neuromuscular Research Laboratory
Department of Physical Therapy, University of Utah
UU Rehab & Wellness Program
Overview

1) MS & exercise - History

2) (Very, very quick) Summary of Research Evidence
   • MS & Exercise

3) Special clinical management considerations and precautions in regards to exercise training for PwMS

4) Safety of Exercise – Relapse and Adverse Event Rates
Strenuous physical activity may enhance progression of MS! →Avoid Exercise!
Current scientific evidence on the effects of **aerobic exercise** on fitness and function of persons with MS
Subjects: 69; duration: 2-8 yrs

Intervention: rest-exercise therapy (REP)
- Following 20 min of rest - “press-ups” or UE weightlifting exercises with maximal effort to fatigue to cause flushing of the face (goal: hyperemic response in the blood circulation of the upper spinal cord and brain stem)

Outcome Measures
- Comparison of level of compliance with the REP with change in disability grade (scale 1-6)

Conclusion:
- “for those who have the persistence and enthusiasm necessary to carry out the programme advised, the future course of their disseminated sclerosis is likely to become benign”
Role of Cardiovascular Fitness in Multiple Sclerosis: A Pilot Study

• Matched-control pre/post-test design (n=48)
• Intervention:
  – Schwinn Air-Dyne ergometer (16 wk, 4-5/wk, 15-30 min, 65-85% HR_{peak})
• Conclusions
  – No increase in disability after 16 wks training
  – Modest improvement in fitness (peak workload)
Impact of aerobic training on fitness and quality of life in MSP

• Randomized, controlled repeated measures design

• Subjects: (n=46, EX=21, CG=25)
  – EDSS 3.3 (1.0-6.0)
  – 15 M, 31 F; 40.1 a (23-56)

• Intervention:
  – UE/LE cycle ergometry (Schwinn-AirDyne)
    • 40 min @ 60% VO₂max
    • TIW, 15 wks
Impact of aerobic training on fitness and quality of life in MSP

• Outcome Measures/Results
  – Training compliance 97% (91-100%)
  – Neurological Status
    • EDSS – no change
    • FS (no change except ↑ bowel and bladder function (p<0.05)
    • ISS (EX 9.0 to 6.8; CG 8.1-8.3; ns)
  – VO$_2$$_{max}$: +22% EX (+1% CG) (p<0.01)
  – WL$_{max}$: +48% EX (+12% CG) (p<0.01)
    • Magnitude of improvement not related to level of neurological impairment - EDSS ≤ 3.5 (n=14) ≈ EDSS > 3.5 (n=7)
Outcome Measures/Results –cont.
- Blood Lipid Profile
  - serum triglycerides -17% EX -1% CG (p<0.05)
  - HDL, LDL (ns)
- Body Composition
  - skinfold thickness -9% EX +3 CG (p<0.05)
  - % body fat (p=0.068)
- POMS, SIP, FSS
  - improvements of several subscales by wk 5 and 10 no longer significant at wk 15
- Strength (MIVC)
  - UE: +17% EX (-2% CG) (p<0.05)
  - LE: +11% EX (+3% CG) (p<0.05)
  - sig training effect on shoulder flexion, shoulder extension, elbow flexion and knee extension (p<0.05)
Impact of aerobic training on fitness and quality of life in MSP

• Conclusions
  – Aerobic training had no negative impact on neurological status
  – MS patients may reap similar benefits from aerobic conditioning as individuals without MS
    • increased aerobic capacity
    • increase in muscle strength
    • favorable changes in body composition and lipid profile
Aerobic Training Studies
Summary of Research Evidence

• 21 “aerobic” training studies
• 9 “RCT” (only 6 with n ≥ 10/grp; only 3 of those measured max exercise capacity)
• Not a “ton of research” BUT ....
Aerobic Training Studies
Summary of Research Evidence

No evidence of detrimental effects on neurological status or disease activity

- AT may improve fitness: ↑↑↑↑↑↑↑↑↑↑↑
- AT may improve fatigue: ↑↑↑↑↑↑↑
- AT may improve strength: ↑
- AT may improve functional mobility: ↑↑↑↑↑↑↑↑↑
- AT may improve some aspects of psychosocial function and HRQOL: ↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑
Current scientific evidence on the effects of **resistance exercise** on fitness and function of persons with MS
Resistance Training Studies
Summary of Research Evidence

• 20 peer-reviewed papers (9 RCT, variable quality)

• No evidence of detrimental effects on muscle, neurological status, disease activity

• RT may improve strength: ↑↑↑↑↑↑↑↑↑↑↑↑↑↑

• RT may increase mm mass: ↑↑

• RT may improve functional mobility: ↑↑↑↑↑↑↑↑

• RT may improve fatigue: ↑↑↑↑↑↑↑↑↑

• RT may improve some aspects of psychosocial function and HRQOL: ↑↑↑↑↑
Resistance Training Studies

Critics may rightfully argue:

- **Few studies!**
- **Many limitations!**
  - Lack of controls
  - Small n
  - Inconsistent results limit conclusions
  - Short-term interventions
    - Need long-term studies with repeated evaluations
      - Reversal of disuse atrophy $\approx$ adaptive capacity $\approx$ overuse
  - Studies to unspecific
    - Need to explore relationship of
      - Degree of impairment $\approx$ intensity of training stimulus $\approx$ training adaptation
    - Nature of adaptations - neural vs. peripheral (metabolic vs. structural)
- Insufficient evidence to exclude possibility of detrimental effects!

Show me the evidence!
Figure 1. Peak torque changes (%) of maximal isometric knee extensor (A) and knee flexor (B) strength at a knee angle of 45° and 90° following 10 (MID) and 20 (POST) weeks of control conditions (CON) or resistance training either in combination with (RES_e) or without (RES_o) simultaneous electro-stimulation. †p < 0.05 compared with the corresponding baseline value and *p < 0.05 compared with the corresponding CON value. See Methods for further details.
Current scientific evidence on the effects of **aquatic exercise** on fitness and function of persons with MS

MSAA 2013. Salem, Csiza, Harrison & See
Aquatic Training Studies
Summary of Research Evidence

• 12 peer-reviewed papers (3 RCT, variable quality)

• AQT may improve strength: ↑↑↑↑↑

• AQT may improve functional mobility: ↑↑↑↑↑

• AQT may improve fatigue: ↑↑↑

• AQT may improve some aspects of psychosocial function and HRQOL: ↑↑↑↑↑
Questions for Future Research: Long-Term Effects of Exercise?

- **Disease Prevention – Wellness?**
  - Light to moderate leisure time activity highly correlated to risk factor profile (Slawta, MSSE 2002; 34:905-12)
  - Physical Inactivity associated with CVD symptoms in PwMS (Motl et al, Neuroepidemiology 2011; 36:183-91)

- **Disease Modulation?**
  - Effect on Immune function? (Schulz, J Neurol Sci 2004)
  - Effect on MS progression? (Dalgas & Stenager, Ther Adv Neurol Disord 2012; 5(2):81-95; Castellano, J Neurol Sci 2008)

- **Effects on Progression of MS Disability?**
  - Functional Mobility – balance, gait (Snook, Neurorehabil Neural Repair 2009; 23:108; Motl, Neuropsychiatr Dis Treat 2010; 6:767)
  - Cognitive Function (Motl, Gappmaier et al; J Sport Exerc Psychol 2011)
Exercise & MS
Clinical Mgmt. Considerations
Exercise & MS ??

- physical exertion – relapse?
- increased temperature sensitivity
- autonomic dysfunction
- fatigue
- muscle impairments
Exercise & MS?

physcial exertion - relapse
Multiple Sclerosis Relapses are not associated with Exercise.

Sport Index – Baecke Questionnaire
(Retrospective Analysis, N=625)
Multiple Sclerosis Relapses are not associated with Exercise.

<table>
<thead>
<tr>
<th></th>
<th>Active (n=21)</th>
<th>Inactive (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapses</td>
<td>0.95</td>
<td>1.6</td>
</tr>
<tr>
<td>Sport Index</td>
<td>3.6</td>
<td>2.33</td>
</tr>
<tr>
<td>VO2peak</td>
<td>3.47</td>
<td>2.73</td>
</tr>
<tr>
<td>Watts/100</td>
<td>2.04</td>
<td>1.5</td>
</tr>
</tbody>
</table>
The Safety of Exercise Training in MS: A Systematic Review (in press)

N=1295 from 26 RCTs of exercise training in MS
physical exertion - relapse

No Evidence of Link!

Confirming Our Experience:

400 + Max Ex Tests
400 + Ext. Ex Tests
15 wks vigorous training
Up to 14 yrs MSEP participation

NO RELAPSES
NO LONGTERM ↑ SX
DUE TO ExTestg or Training
Exercise - Exacerbations

• in case of exacerbation
  - program modification/temporary discontinuation
  - residual deficits → program modification, PT
Symptom Modification

• A transient worsening of symptoms was reported by 22 MSP (n=54).

<table>
<thead>
<tr>
<th>Type of Symptom</th>
<th>Number of Occurrences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated muscle weakness</td>
<td>14</td>
</tr>
<tr>
<td>Blurring of vision</td>
<td>3</td>
</tr>
<tr>
<td>Lower extremity clonus</td>
<td>3</td>
</tr>
<tr>
<td>Sensory changes</td>
<td>2</td>
</tr>
<tr>
<td>Muscle cramping</td>
<td>2</td>
</tr>
</tbody>
</table>

• All resolved within 30 min or less
Symptom Modification

Gappmaier et al. MSSE 2001; 32:S264

- Reported by 50% of participants (n=20)

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<thead>
<tr>
<th></th>
<th>LTR-A</th>
<th>LTR-B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensation</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Vision</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Neuromuscular</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>

- All resolved within 30 min or less

Smith et al. Symptom Change with Exercise is a Temporary Phenomenon for PwMS. Arch Phys Med Rehabil 2006;87:723-7
Symptom Change with Exercise is a Temporary Phenomenon for PwMS.
Smith et al. Arch Phys Med Rehabil 2006;87:723-7

- 34 MSP – initial exercise session at “commencement level” – 5-45 min (mean 17.4)
- Immediate post-exercise
  - 40% experienced ↑ number of sensory Sx
  - 44% experienced ↑ severity of sensory Sx
  - 29% experienced ↑ in both no. and severity of Sx
  - No sig. Δ in fatigue and function
- Return to baseline within 30 min (mean 18.6) in 85% of subjects
Uhthoff’s Phenomenon

• A transient visual impairment provoked by physical exertion (Uhthoff, *Arch Psychiatr Nervenkr* 1889).

• Experienced by approximately 1/3 of MS patients [McAlpine & Compston (1952), Nikoskelainen (1975), Perkin & Rose (1979)].

• Most likely caused by temperature induced changes in impulse conduction in the CNS (Davis 2010).

• Changes are temporary - Return to baseline within 30 minutes after cessation of exercise.
Symptom Modification

• Frequently underreported
  - Pilutti (in press) – only 5 of the 26 studies commented on symptom changes – only 1 reported symptom modification.

Clinical/Research Recommendation:
Standardized monitoring and reporting of
• Relapses
• Adverse Events
• Drop-outs
• Temporary Symptom Changes
  In all clinical/exercise studies!
increased temperature sensitivity

Exercise & MS ??
Temperature & MS

- MSP are very sensitive to increases in body core temperature
- Symptom magnification or new Sx with induced hyperthermia → Hot bath test
- Reversible conduction block in experimentally demyelinated nerve fibres with 0.5°C increase in temperature (Rasminsky, 1973; Schauf & Davis, 1974).
- Temperature regulation impaired by sweating dysfunction (Davis, 2010)
Increased Core Temperature
→ Temporary Symptom Modification

→ cool environment
  AC, early AM, water exercise

→ pre-exercise cooling
  20-30 min of lower body immersion
  → "cool storage" in mm → avoid overheating
  (White, Mult Scler 2000; Wilson, Eur J Appl Physiol 2002)

→ cooling during exercise
  cooling vests, evaporative cooling
Exercise & MS ??

autonomic dysfunction
Autonomic Dysfunction in MS

- Manifested by bladder-, sexual-, and sudomotor dysfunction.
- Blunted HR and BP response to noninvasive perturbations such as sustained Valsalva maneuver, rhythmic deep breathing, or sustained isometric handgrip (Pepin et al. 1996)

→ Cardiovascular adjustments during exercise may be inadequate to support the metabolic demands.
Achieved vs. predicted HR$_{\text{max}}$ (n=200+ GXT-MS)

![Graph showing achieved vs. predicted HR$_{\text{max}}$. The graph compares "True-max" and All Tests.

- "True-max": Achieved = 187 bpm, Predicted = 183 bpm
- All Tests: Achieved = 179 bpm, Predicted = 182 bpm]
Case Example KM
69 y/o F, MS (17 yrs, EDSS=4.0)

- RHR 60 - 62
- RPE 4/10-4/10
Autonomic dysfunction - MS

• Abnormal cardiovascular response, risk of syncopal episodes
  → evaluate/monitor hemodynamic response, appropriately adjust exercise prescription

• Thermoregulation, Hypohidrosis
  → cooling strategies
HR_{max} = 220 - AGE
Exercise & MS ??

fatigue
Fatigue in MS

- One of top two reasons for unemployment
- 83%/33% report worsening after exercise
- Worsened by heat
- Frequently follows a diurnal cycle
- Causes temporary increase in disability
- No direct relationship between fatigue severity and neurologic impairment
### Aerobic Ex - Improvement in FATIGUE

<table>
<thead>
<tr>
<th>Group x Time Effect</th>
<th>Time Effect</th>
</tr>
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<tbody>
<tr>
<td>McCullagh 2008 (MFIS)</td>
<td>Petajan 1996 (FSS)</td>
</tr>
<tr>
<td>Rasova 2006 (MFIS)</td>
<td></td>
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<tr>
<td>Huisinger 2011 (FSS, MFIS)</td>
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<tr>
<td>Sabapathy 2011 (MFIS)</td>
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<tr>
<td>Wier 2011 (FSS, MFIS)</td>
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- **“Success Stories”**

Exercise ~ Fatigue

- Increased fatigue, weakness or pain → decrease exercise intensity and duration
- Complete recovery after night’s sleep
Exercise Evaluations in the Physical Therapy Clinic

The Submaximal Clinical Exercise Tolerance Test (SXTT) to Establish Safe Exercise Prescription Parameters for Patients with Chronic Disease and Disability

Eduard Gappmaier, PT, PhD

University of Utah, Department of Physical Therapy, Salt Lake City, UT
Rx ➔ Cardiovascular Conditioning

• **Intensity:**
  - 60-85% \( HR_{peak} \)
  - 50-70% \( VO_{2peak} \)

• **Duration:** 30 min

• **Frequency:**
  - 3-5 d/wk

• **Multiple, shorter bouts for persons with low work capacity**

ACSM CDMgmt 2009 (3rd ed)
Adapted Modes of Exercise
Equipment Modifications
Exercise & MS ??

muscle impairments
• Resistance training:
  4-10 exercises
  1-2 sets, 8-15 reps
  50-70% MVC
  [“light”/“low-mod” intensity]
  2-3 days/wk
• Protect severely weak muscles
• Carefully monitor strength changes in at risk patients
Monitor Strength Changes
QUESTIONS

“ed.gappmaier@hsc.utah.edu”