WEBINAR & TELELEARNING SERIES

The Mind Can Benefit From Muscle Activation, Too!
The Relationship Between Exercise and Cognition

Robert Motl, Ph.D and Mandy Rohrig, PT, DPT

January 12, 2016

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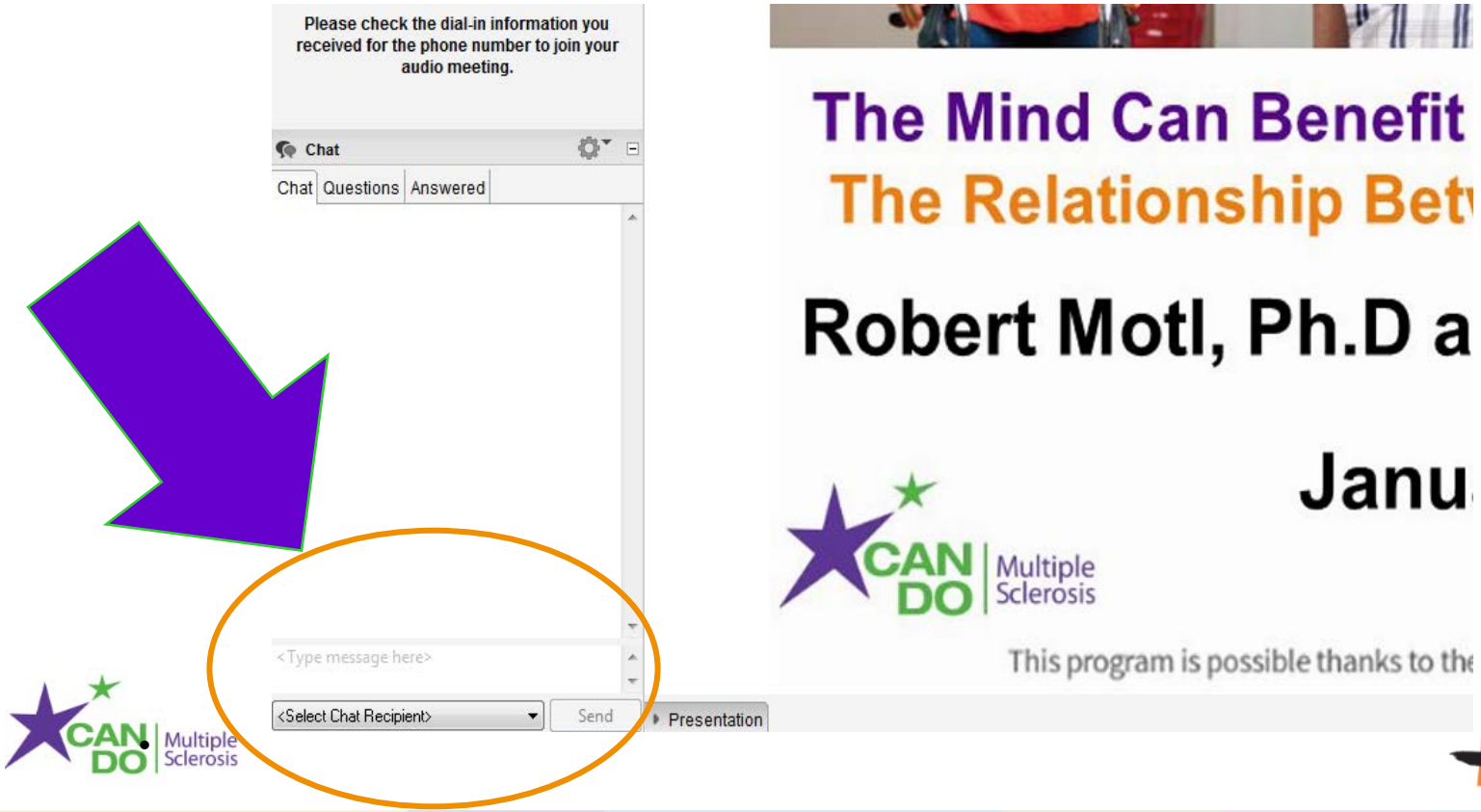
How to Ask Questions During the Webinar:

- **Chat Feature** – Type in your questions using the chat box on the lower left hand side of your screen.



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Objectives

- **Identify the causes and effects of cognitive challenges and understand how they are impacted by multiple sclerosis**
- **Recognize how physical activity affects cognition**
- **Implement exercises that address cognitive symptoms and improve overall brain health**
- **Connect research related to exercise and cognition with practical, “real life” applications**

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Common Cognitive Challenges

- **What it is**.....(www.nationalmssociety.org)
  - Impaired “processing speed”
  - Impaired “working memory”
  - Impaired “learning and memory”
  - Impaired “executive function”
  - Impaired “visual/spacial processing”
- **What it is not…..**
  - Forgetfulness
- **What are your challenges?**

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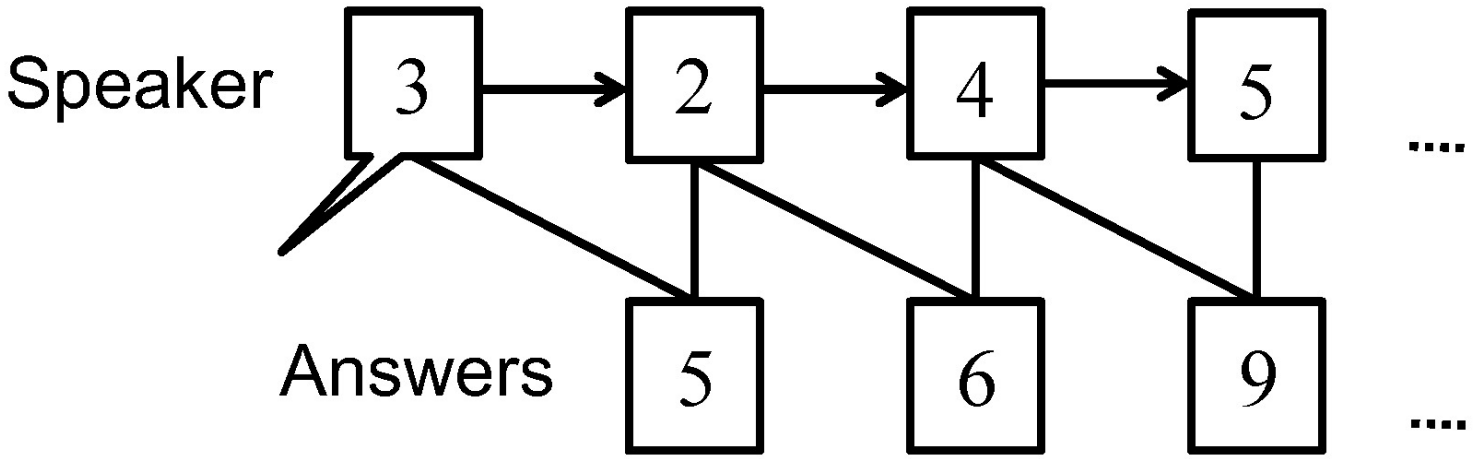
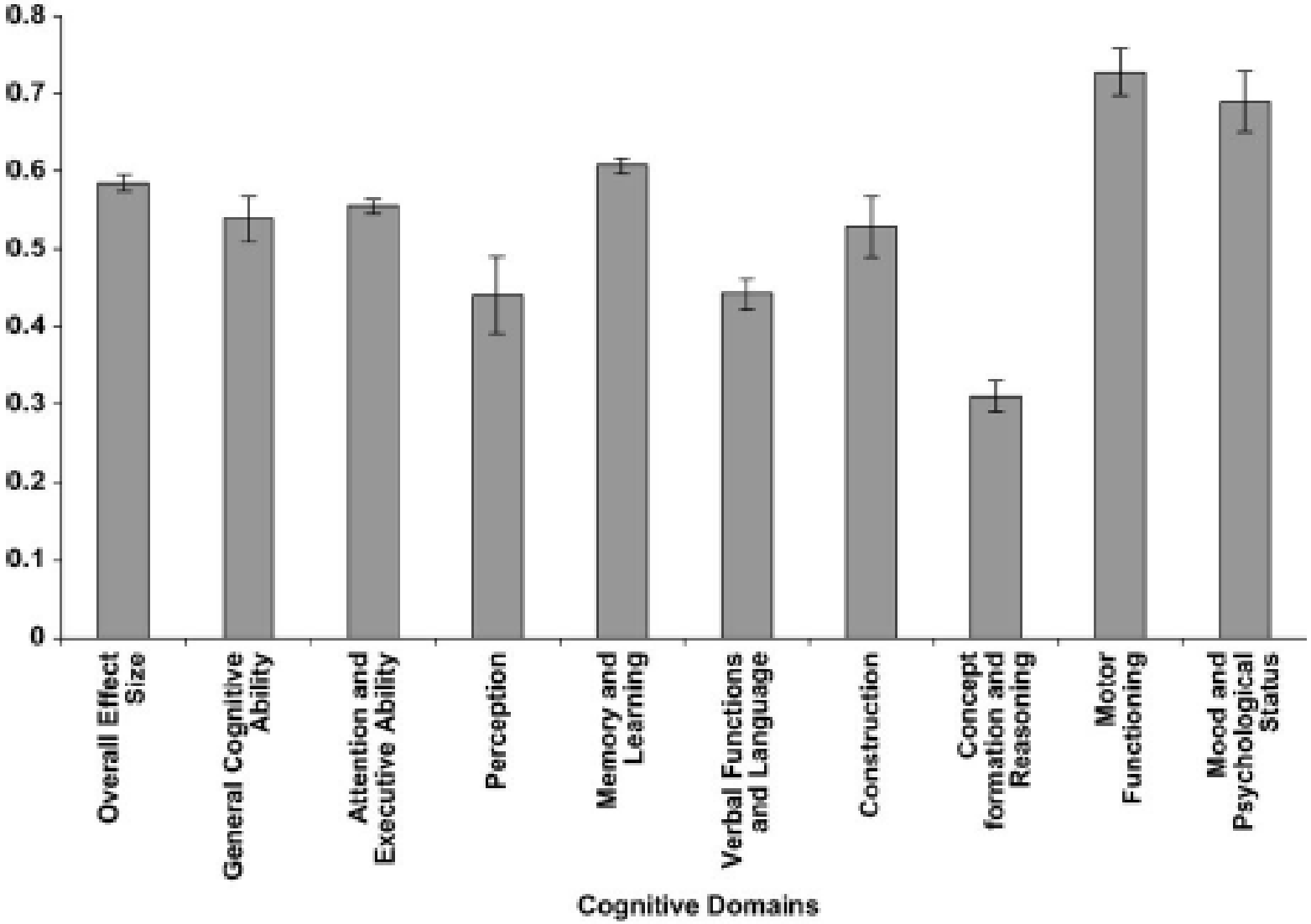
Paced Auditory Serial Addition Test – An Example

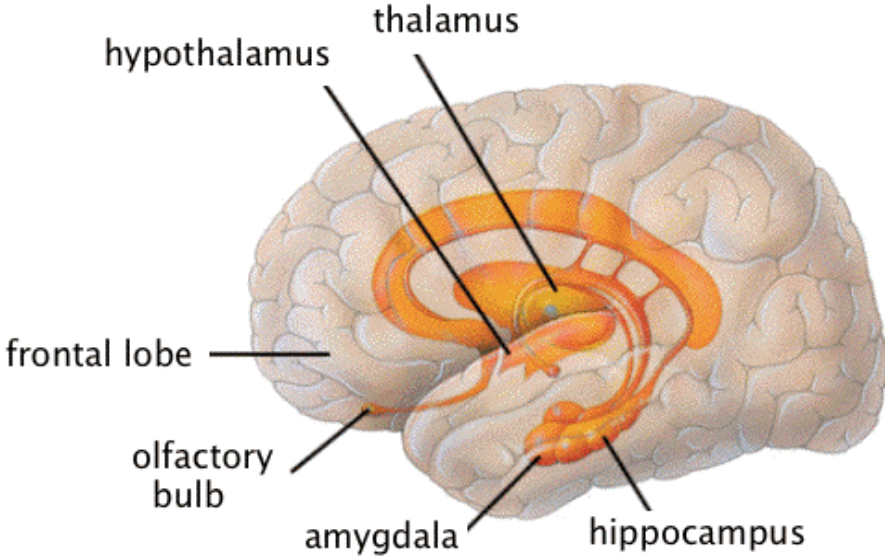


www.figshare.com



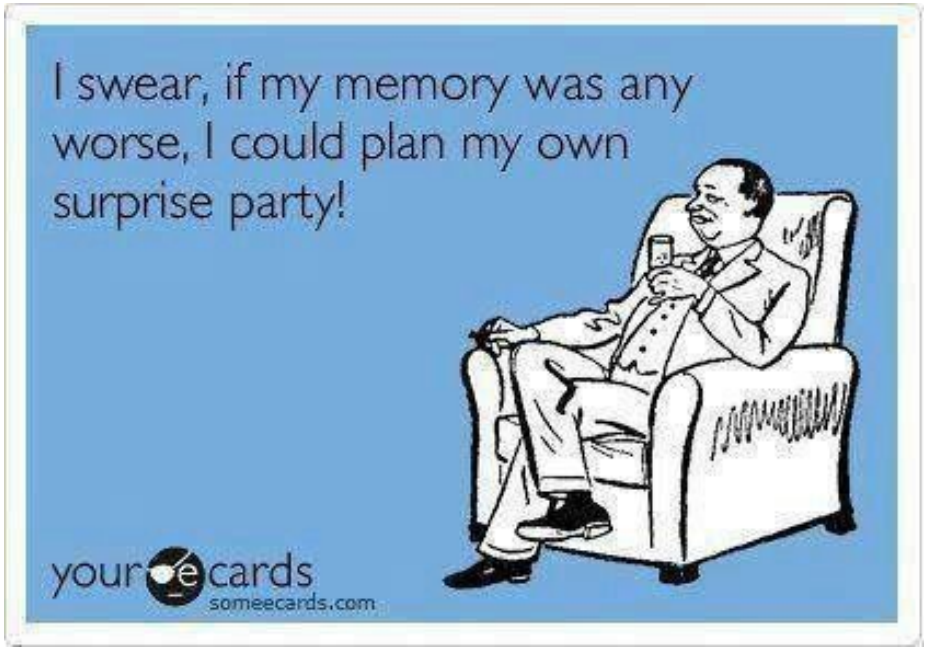
Brain Areas Associated with Cognitive Problems in MS

- **Thalamus**
- **Hippocampus**
- **Pre-frontal/frontal cortex**
- **Connectivity**



Challenges of Poor Cognition in Life

- **Employment**
- **ADLs**
- **Walking**
- **Driving**
- **Communication**
- **Others you may have?**



www.pinterest.com

Cognitive Remediation?

- **Treatment Strategies**
  - **Medications**
  - **Cognitive Rehabilitation: Occupational Therapy or Speech/Language Pathologist**
  - **Physical therapy…..**
- Exercise!!

www.neuropsychdoc.com

Many Benefits of Exercise in MS

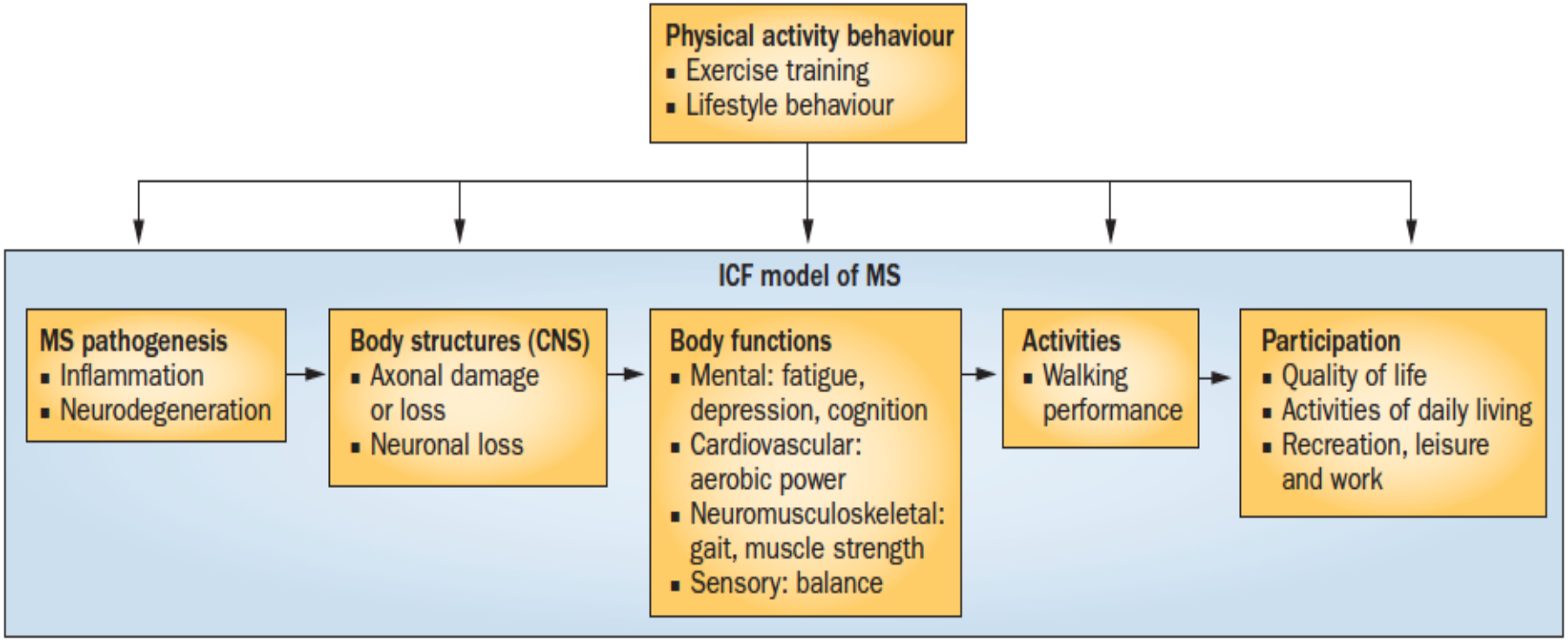


Figure 1 | Interactions between exercise and the ICF model of MS pathogenesis. The ICF model outlines the consequences of MS pathogenesis, including effects on structure and function of the body, and on patient activities and participation. Exercise could have beneficial effects at each of these stages, from influences on cellular processes, such as reduction of inflammation, to improved patient participation in the community. Abbreviations: ICF, International Classification of Functioning, Disability and Health; MS, multiple sclerosis.

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An Initial Proposal!

Review

MULTIPLE SCLEROSIS JOURNAL | MSJ

Multiple Sclerosis Journal
17(9) 1034–1040

DOI: 10.1177/1352458511409612
msj.sagepub.com
SAGE

Cognitive dysfunction and multiple sclerosis: developing a rationale for considering the efficacy of exercise training

Robert W Motl[1], Brian M Sandroff[1] and Ralph HB Benedict[2]

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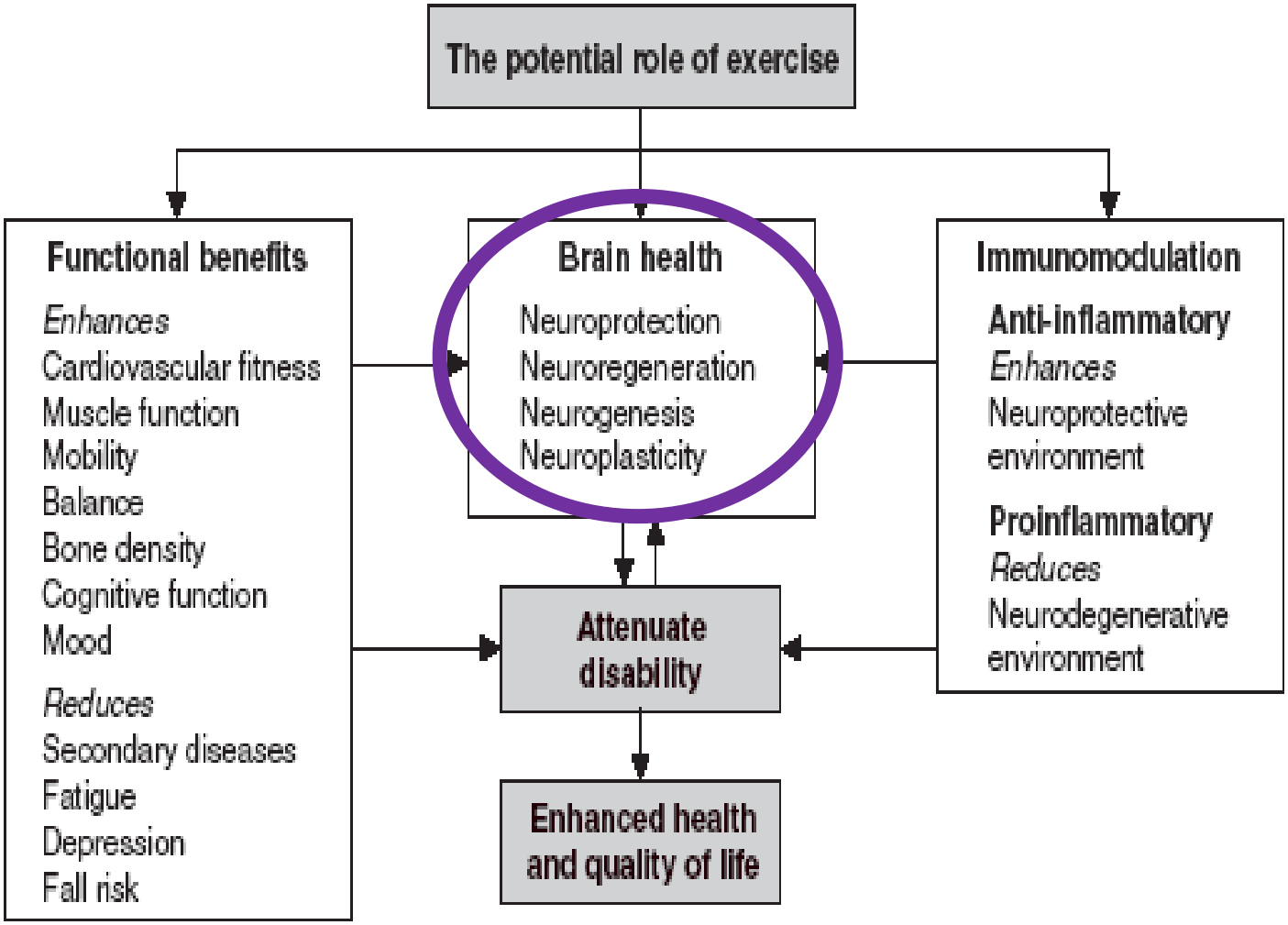

Fig. 1. A conceptual model highlighting the hypothetical effects of exercise in improving health, mobility and modulating disease activity in multiple sclerosis.

White, L. J. and Castellano, V. **Exercise and Brain Health – Implications for Multiple Sclerosis Part 1 – Neuronal Growth Factors**. 2008 Sports Med: 38 (2); 91-100.

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Neuro….. What?

- **Neuroprotection**
- **Neuroregeneration**
- **Neurogenesis**
- **Neuroplasticity**

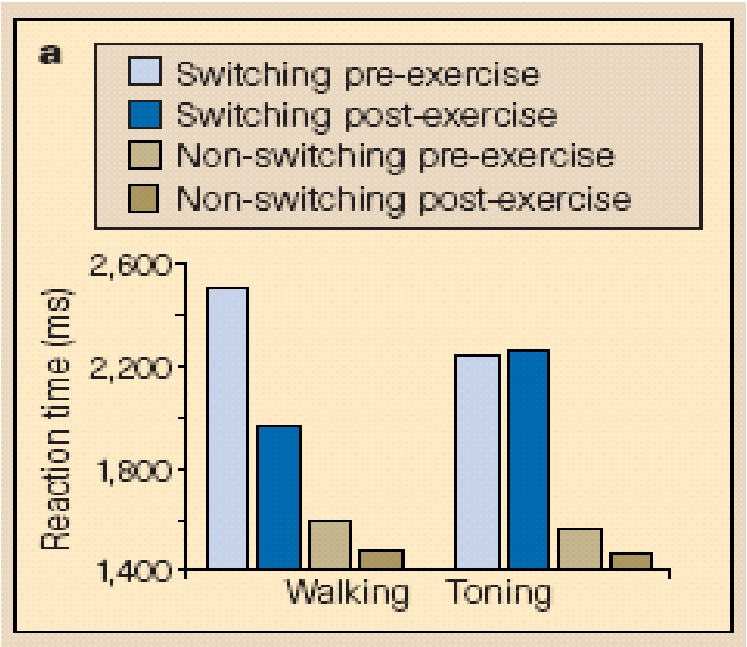
www.fitnessmash.com

Exercise and Brain Health

comments.bmartin.cc-

Example Study in Aging

- **Who: 124 previously sedentary adults, 60-75 yrs old**
- **What: Randomly assigned to 6 months of either aerobic (walking) or non-aerobic (stretching/strengthening) exercise**
- **Cognitive tasks:**
  - **Task switching – RT difference when performing same task or switching between tasks**
- **Fitness: 5.1% increase in walking; 2.8% decrease in stretching/strengthening**



Kramer et al. (1999). Aging, fitness, and neurocognitive function. *Nature, 400,* 418-419.

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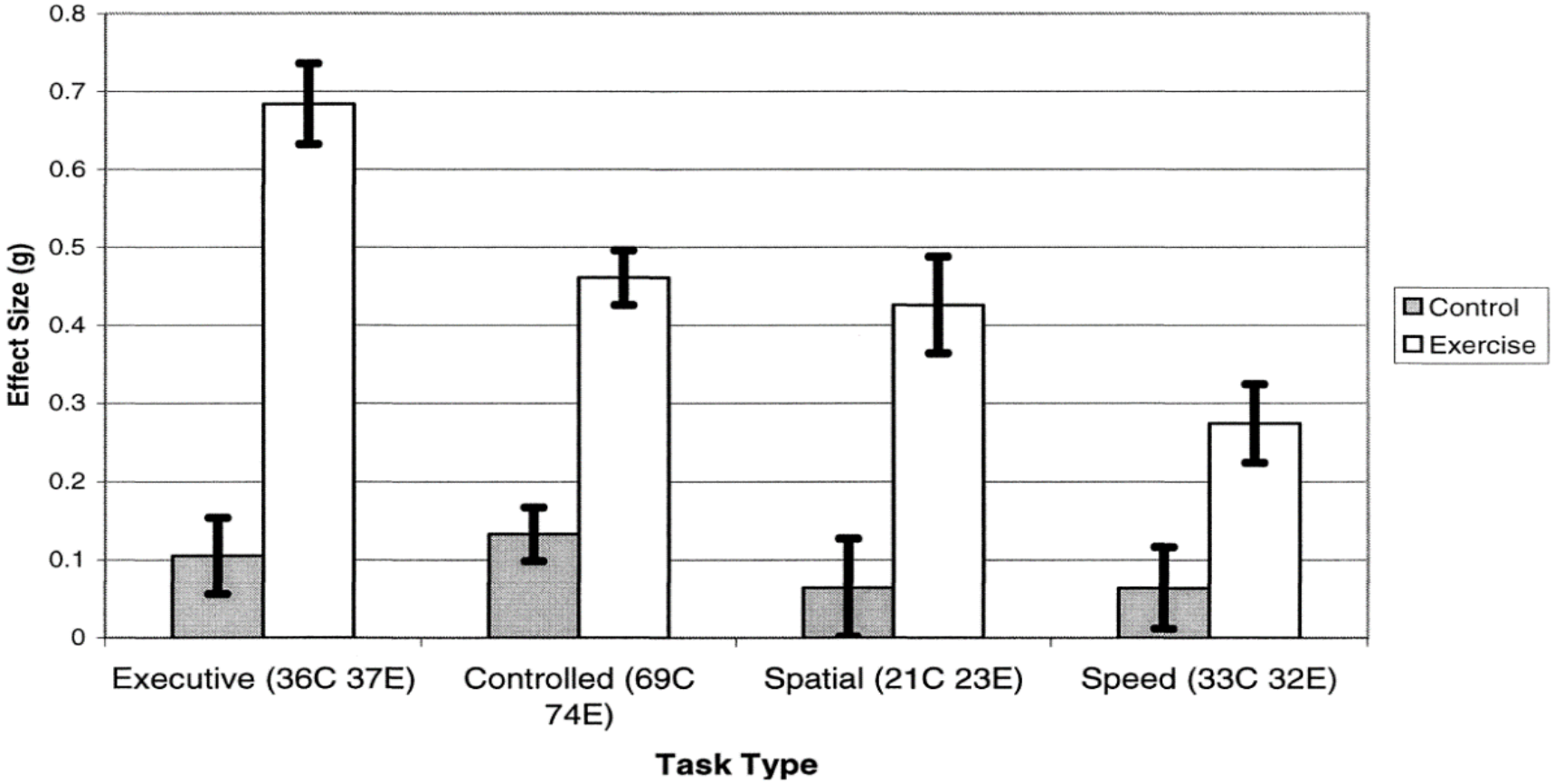
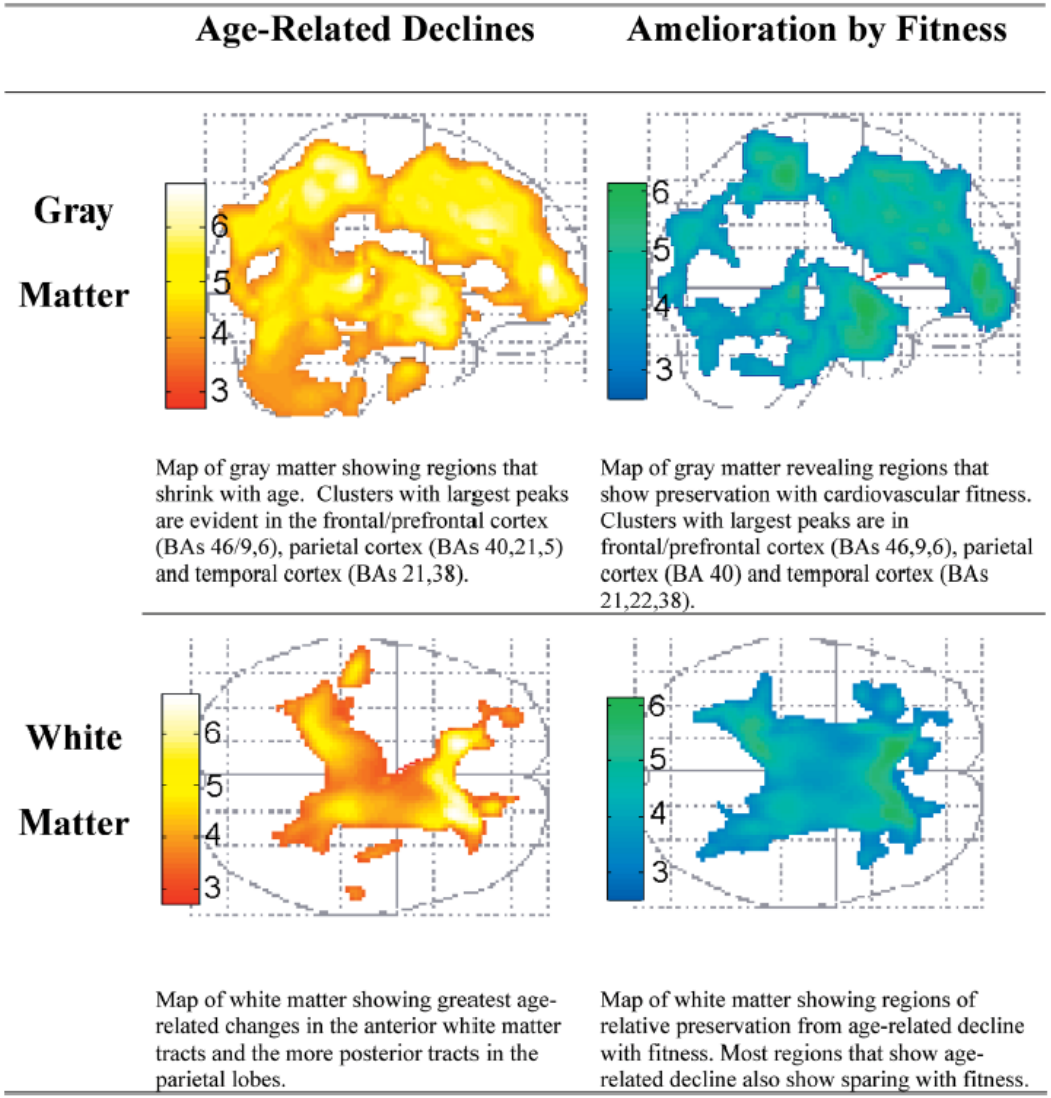
Very Robust Effect



Colcombe & Kramer (2003). Fitness effects on the cognitive function of older adults: A meta-analytic study. *Psychol Sci, 14,* 125-130.

How does this occur?

- **Slowing of brain tissue loss/ neurogenesis**
- **New cell growth**
  - **Brained-derived neurotrophic factors (BDNF)**



Colcombe et al. (2003). Aerobic fitness reduces brain tissue loss in aging humans. *J Gerontol A Biol Sci Med Sci, 58,* 176-180.

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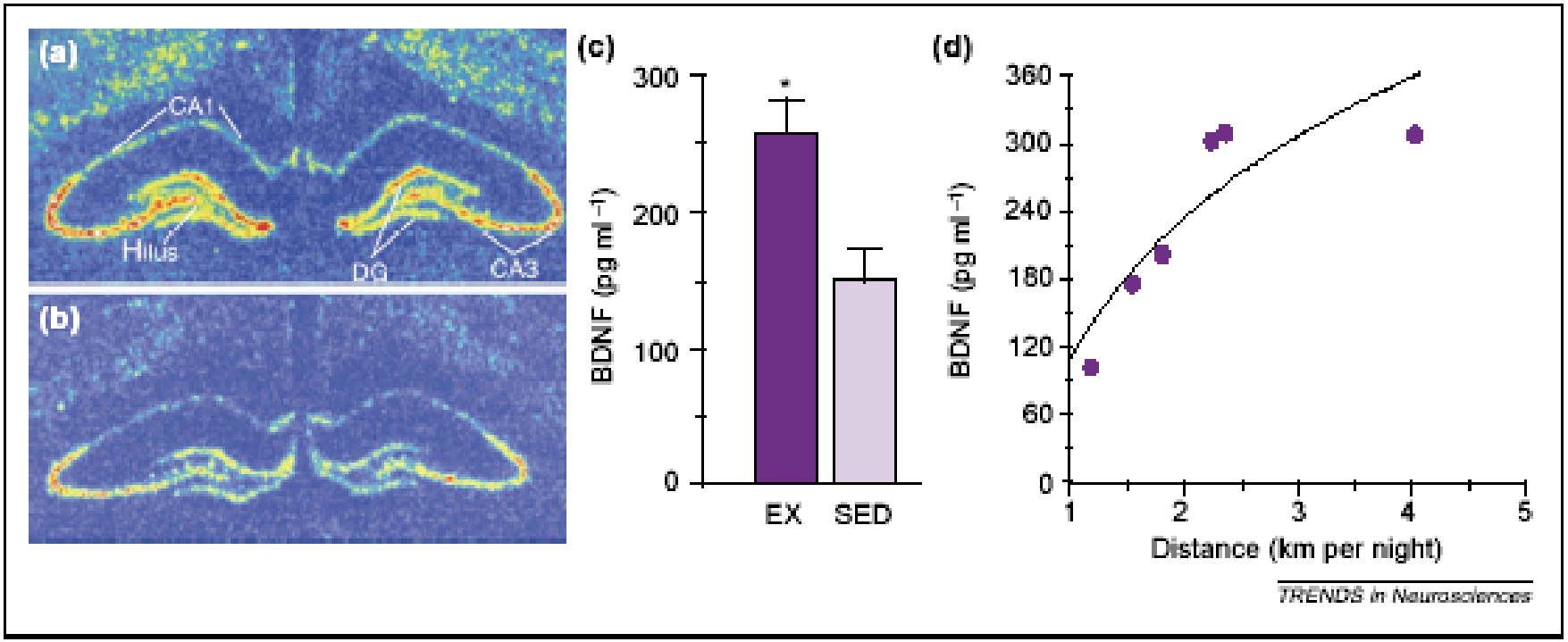
How in the World Does this Work?



Cotman & Berchtold (2002). Exercise: A behavioral intervention to enhance brain health and plasticity. *Trends Neurosci, 25,* 295-301.

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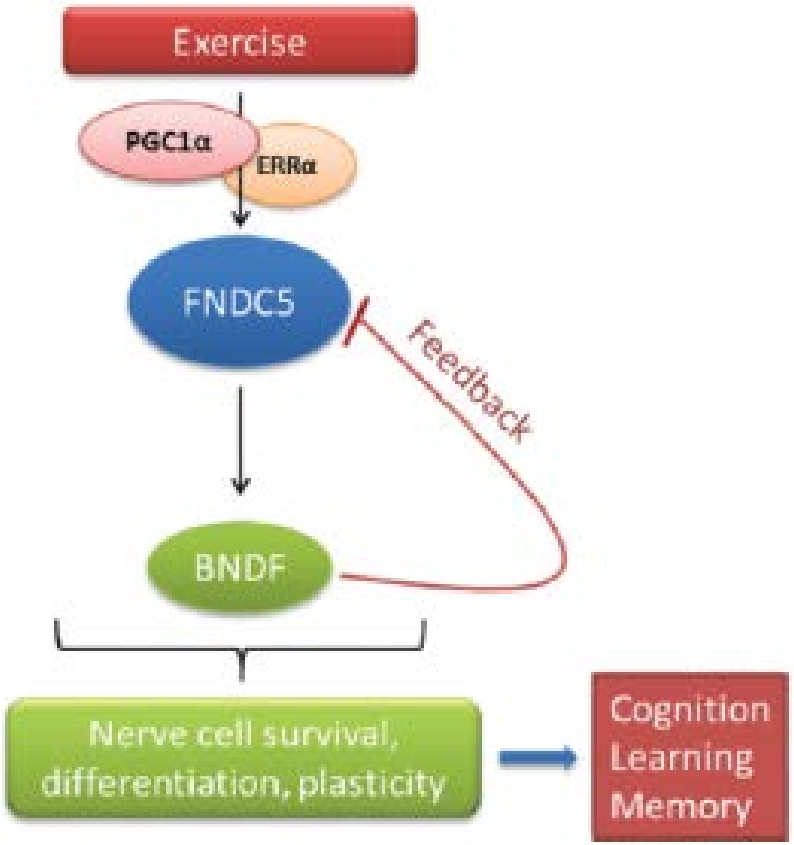
What? How? Wow!

- **Protein (FNDC5) is produced by muscle contraction (PGC-1α regulatory molecule) and released into the blood.**
- **FNDC5 increased expression of BDNF in hippocampus.**
- **FNDC5 delivered via a virus in bloodstream increases BDNF, w/o exercise.**



Wrann et al. (in press). Exercise induces hippocampal BDNF through a PGC-1a/FNDC5 pathway. *Cell Metabolism*.

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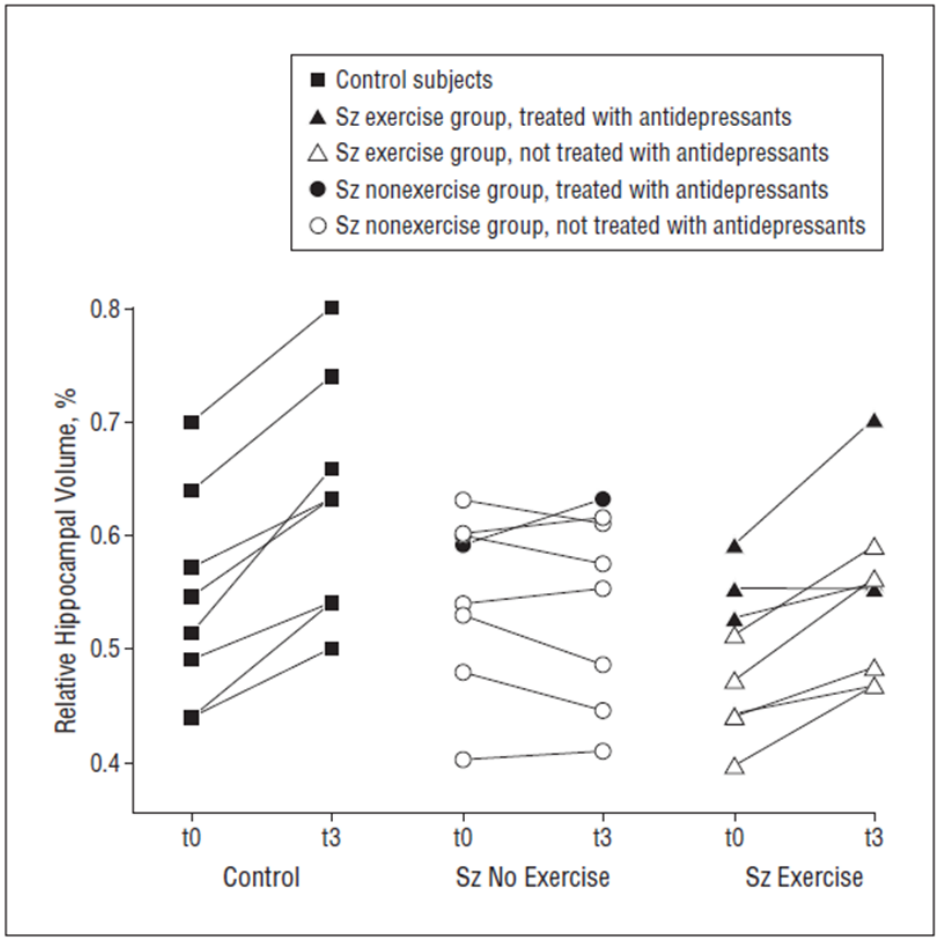


Figure 2. The changes in hippocampal volume in control subjects, schizophrenic (Sz) patients participating in aerobic exercise, and Sz patients with no aerobic exercise intervention. The data points present the relative hippocampal volume of each subject as a percentage of the total brain volume at baseline (t0) and 3 months later at end point (t3).

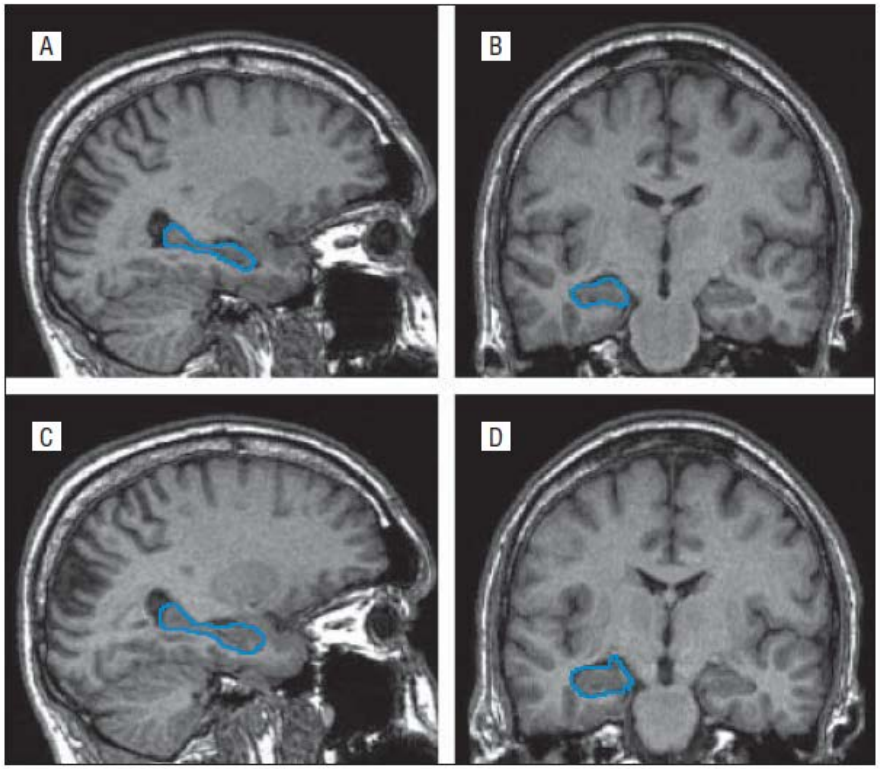
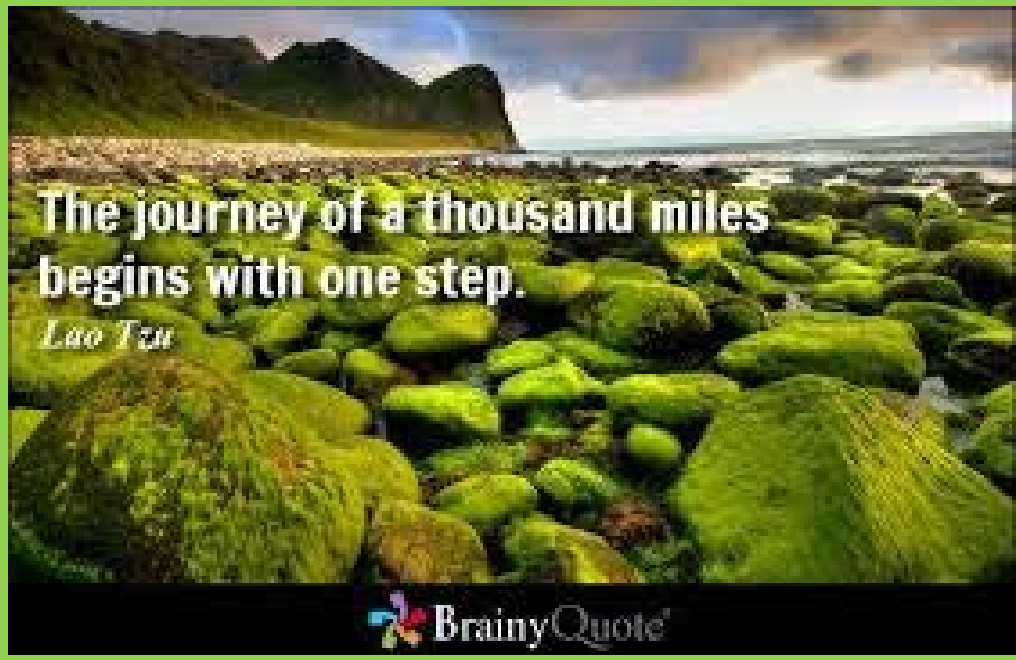


Figure 3. T1-weighted magnetic resonance images in the sagittal and coronal plane, with the right hippocampus marked in blue, comparing baseline (A and B) and end point (C and D) of the patient in the schizophrenia exercise group with the largest increase in hippocampal volume (from 3.898 cm^3 to 4.667 cm^3; +19.7%).

What is Known about Exercise and MS

- **Step 1: Exercise and Fitness Associated with Better Cognition**
- **Step 2: Fitness Associated with Better Brain Health**



LETS GET *MOVING*!

Does Fitness/Physical Activity improve CPS in MS?

Variable	VO_{2peak}	KE_{max}	KF_{max}
VO_{2peak}	—		
KE_{max}	.622*	—	
KF_{max}	.686*	.842*	—
KE_{a}	−.390*	−.346*	−.445*
KF_{a}	−.120	−.157	−245*
SDMT	.410*	.352*	.393*
CVLT-2	.193	.067	.132
BVMT-R	.184	.090	.075

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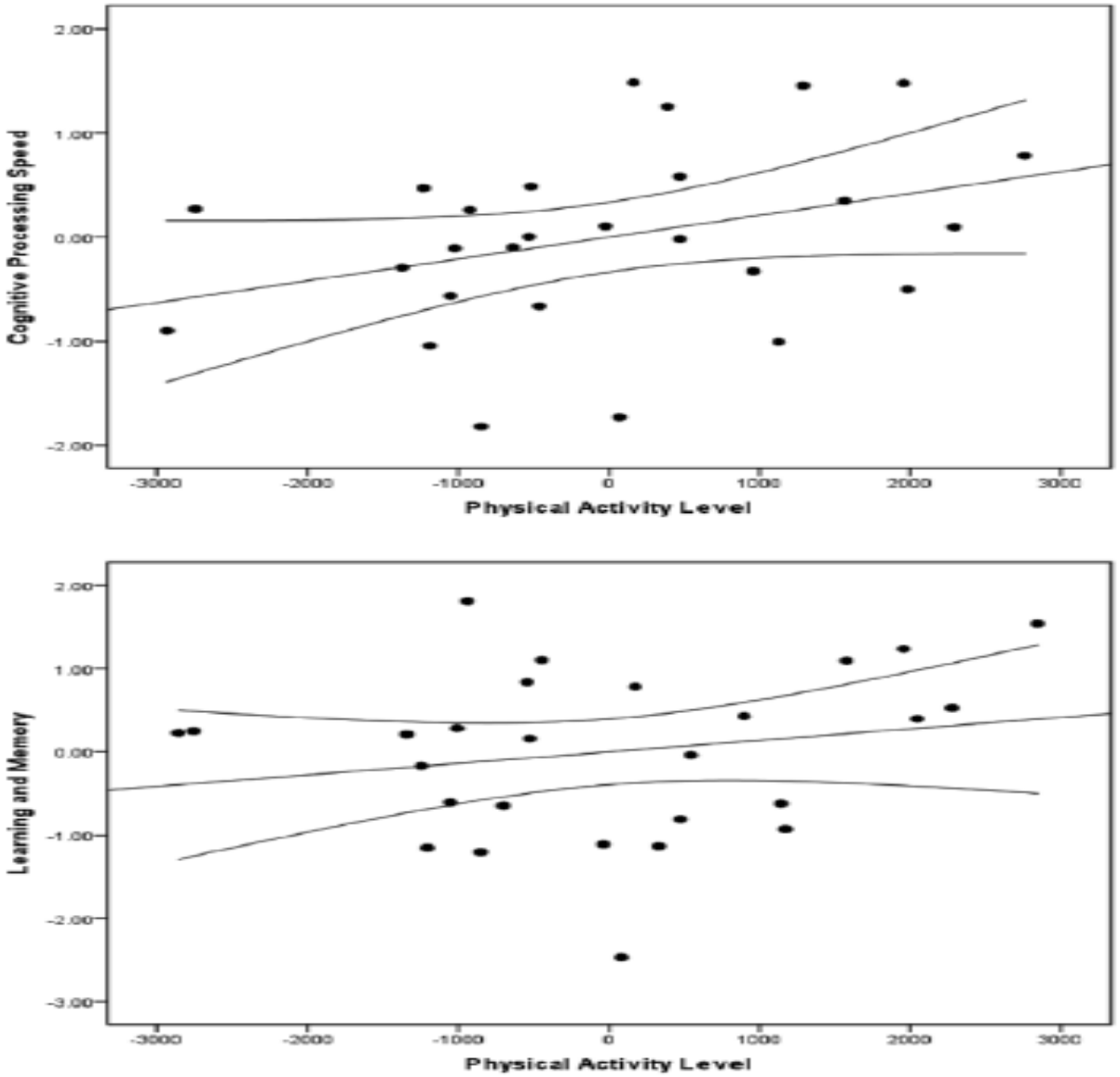

Figure 1 — Partial regression plots, along with the line of best fit and 95% confidence interval, for the associations among physical activity and cognitive processing speed and learning and memory, controlling for sex, age, and education.

Fitness/Physical Activity and Brain Health

TABLE 2: Correlations between levels of physical activity and scaled composite volumes of normalized brain volume measures in 39 persons with MS.

Variable	Model 1			Model 2			Model 3		
	MVPA (min/day)	Light physical activity (min/day)	Sedentary behavior (min/day)	MVPA (min/day)	Light physical activity (min/day)	Sedentary behavior (min/day)	MVPA (min/day)	Light physical activity (min/day)	Sedentary behavior (min/day)
NGMV (mm^3)	.304	.215	−.099	.297	.167	−.156	.370*	.219	.059
NWMV (mm^3)	.418**	.235	.124	.359*	.126	−.029	.433**	.171	.281
Hippocampus (mm^3)	.325*	.140	−.046	.284	.065	−.151	.499**	.018	.164
Thalamus (mm^3)	.404*	.163	.078	.352*	.065	−.058	.380*	.024	.228
Caudate (mm^3)	.418*	.267	−.065	.405**	.227	−.123	.539**	.198	.099
Putamen (mm^3)	.341*	.218	.015	.303	.144	−.072	.369*	.168	.125
Pallidum (mm^3)	.454**	.198	.162	.407**	.074	.027	.498**	.145	.253

Note: Model 1 = Pearson product-moment correlations (*r*); Model 2 = partial Pearson product-moment correlations (*pr*), controlling for days of valid accelerometer data and accelerometer wear time; Model 3 = partial Pearson product-moment correlations (*pr*), controlling for sex, age, clinical course of MS, and EDSS; ** correlation is significant at the 0.01 level (2-tailed); * correlation is significant at the 0.05 level (2-tailed); MS = multiple sclerosis; MVPA = moderate-to-vigorous physical activity; NGMV = normalized gray matter volume; NWMV = normalized white matter volume.

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Exercise and Cognition

Randomized controlled trial of yoga and exercise in multiple sclerosis

B.S. Oken, MD; S. Kishiyama, MA; D. Zajdel; D. Bourdette, MD; J. Carlsen, AB; M. Haas, DC, MA; C. Hugos, MS, PT; D.F. Kraemer, PhD; J. Lawrence, BS; M. Mass, MD

Abstract—*Objective:* To determine the effect of yoga and of aerobic exercise on cognitive function, fatigue, mood, and quality of life in multiple sclerosis (MS). *Methods:* Subjects with clinically definite MS and Expanded Disability Status Score less than or equal to 6.0 were randomly assigned to one of three groups lasting 6 months: weekly Iyengar yoga class along with home practice, weekly exercise class using a stationary bicycle along with home exercise, or a waiting-list control group. Outcome assessments performed at baseline and at the end of the 6-month period included a battery of cognitive measures focused on attention, physiologic measures of alertness, Profile of Mood States, State-Trait Anxiety Inventory, Multi-Dimensional Fatigue Inventory (MFI), and Short Form (SF)-36 health-related quality of life. *Results:* Sixty-nine subjects were recruited and randomized. Twelve subjects did not finish the 6-month intervention. There were no adverse events related to the intervention. There were no effects from either of the active interventions on either of the primary outcome measures of attention or alertness. Both active interventions produced improvement in secondary measures of fatigue compared to the control group: Energy and Fatigue (Vitality) on the SF-36 and general fatigue on the MFI. There were no clear changes in mood related to yoga or exercise. *Conclusion:* Subjects with MS participating in either a 6-month yoga class or exercise class showed significant improvement in measures of fatigue compared to a waiting-list control group. There was no relative improvement of cognitive function in either of the intervention groups.

NEUROLOGY 2004;62:2058–2064

Research Paper

MULTIPLE SCLEROSIS JOURNAL | MSJ

Effects of exercise on fitness and cognition in progressive MS: a randomized, controlled pilot trial

Multiple Sclerosis Journal
2014, Vol. 20(3) 382–390

DOI: 10.1177/1352458513507358
msj.sagepub.com
SAGE

S Briken[1,2], SM Gold[1], S Patra[3], E Vettorazzi[4], D Harbs[3], A Tallner[5], G Ketels[6], KH Schulz[3,7] and C Heesen[1,2]

Abstract

Background: Exercise may have beneficial effects on both well-being and walking ability in multiple sclerosis (MS). Exercise is shown to be neuroprotective in rodents and may also enhance cognitive function in humans. It may, therefore, be particularly useful for MS patients with pronounced neurodegeneration.

Objective: To investigate the potential of standardized exercise as a therapeutic intervention for progressive MS, in a randomized-controlled pilot trial.

Methods: Patients with progressive MS and moderate disability (Expanded Disability Status Scale (EDSS) of 4–6) were randomized to one of three exercise interventions (arm ergometry, rowing, bicycle ergometry) for 8–10 weeks or a waitlist control group. We analyzed the drop-out rate as a measure of feasibility. The primary endpoint of the study was aerobic fitness. Secondary endpoints were walking ability, cognitive function as measured by a neuropsychological test battery, depression and fatigue.

Results: A total of 42 patients completed the trial (10.6% drop-out rate). Significant improvements were seen in aerobic fitness. In addition, exercise improved walking ability, depressive symptoms, fatigue and several domains of cognitive function.

Conclusion: This study indicated that aerobic training is feasible and could be beneficial for patients with progressive MS. Larger exercise studies are needed to confirm the effect on cognition.

Trial Registration: ISRCTN (trial number 76467492) http://isrctn.org

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Very Exciting Case Study…..

Aerobic Exercise → **Hippocampus Volume** → **Memory in People with MS!!**

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Research

(Rob – Researcher)

www.movieweb.com

YOU

“Real Life”

(Mandy – Physical Therapist)

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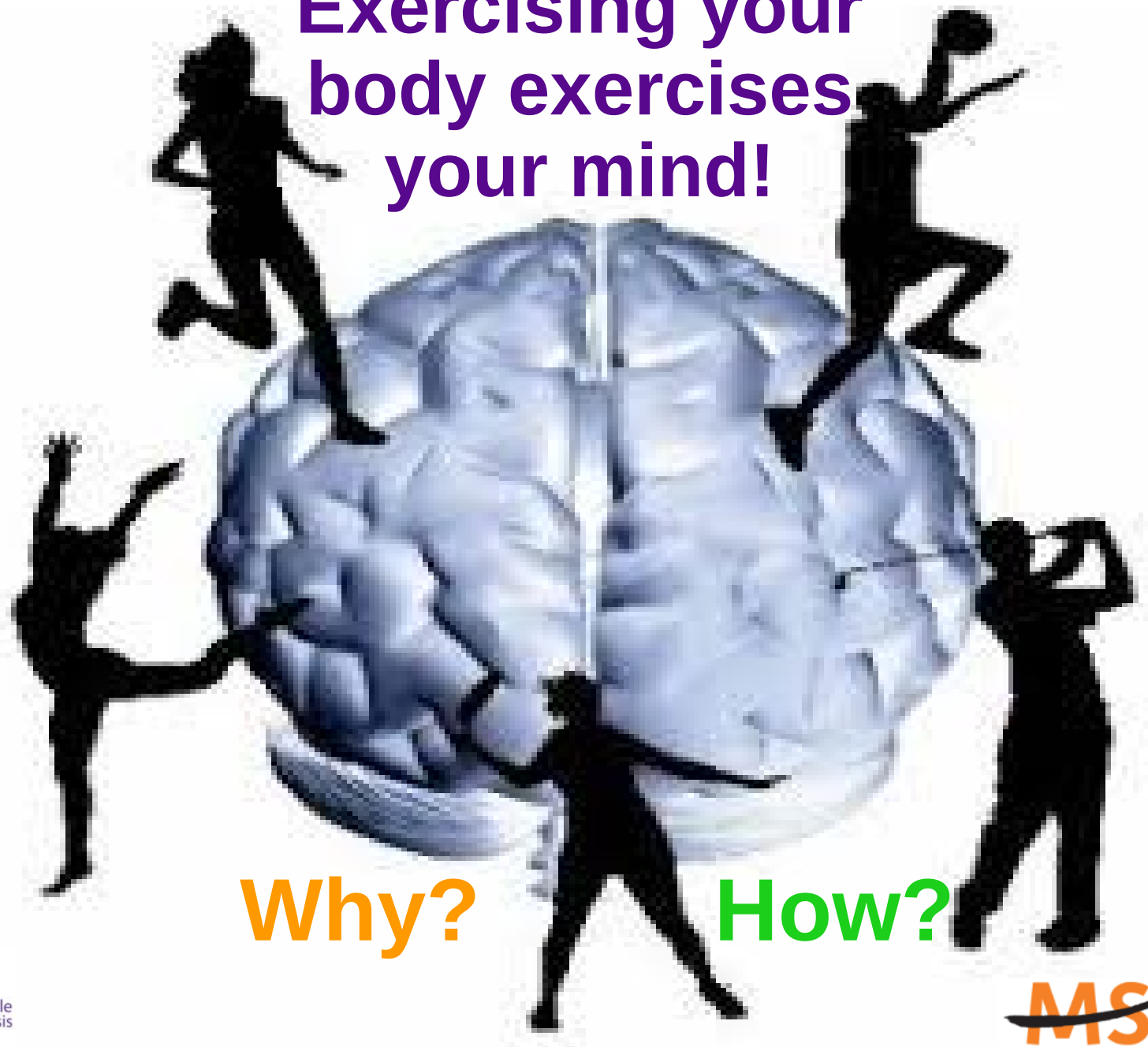
Exercising your body exercises your mind!



Why? **How?**

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Components of an Exercise Program

Components of an Exercise Program

- **Flexibility**
  - **Examples: Yoga, Stretching Program**

Components of an Exercise Program

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  - **Examples: Yoga, Stretching Program**
- **Strength/Endurance**
  - **Examples: Weightlifting (machines or free weights), Resistance Bands, Pilates**

Components of an Exercise Program

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- **Balance/Coordination**
  - **Examples: Tai Chi, Yoga, Vestibular Exercises**

Components of an Exercise Program

- **Flexibility**
  - **Examples: Yoga, Stretching Program**
- **Strength/Endurance**
  - **Examples: Weightlifting (machines or free weights), Resistance Bands, Pilates**
- **Balance/Coordination**
  - **Examples: Tai Chi, Yoga, Vestibular Exercises**
- **Cardiopulmonary Endurance/ Aerobic Exercise**
  - **Examples: Walking, Cycling, Rowing**

Guidelines

- **FITT** Principle

Guidelines

- **FITT** Principle
  - *Frequency*
    - How often should you exercise?

Guidelines

- **FITT** Principle
  - *Frequency*
    - How often should you exercise?
  - *Intensity*
    - How hard should you exercise?

Guidelines

- **FITT** Principle
  - *Frequency*
    - How often should you exercise?
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    - How hard should you exercise?
  - *Time/Duration*
    - How long should you exercise?

Guidelines

- **FITT** Principle
  - *Frequency*
    - How often should you exercise?
  - *Intensity*
    - How hard should you exercise?
  - *Time/Duration*
    - How long should you exercise?
  - *Type/Specificity*
    - What type of exercise is most appropriate?

Guidelines

- **FITT** Principle
  - *Frequency*
    - How often should you exercise?
  - *Intensity*
    - How hard should you exercise?
  - *Time/Duration*
    - How long should you exercise?
  - *Type/Specificity*
    - What type of exercise is most appropriate?

Functional/“Real Life” Application

Flexibility Exercise

Research

- Yoga 20 minutes may be helpful, but not as much as walking
- Yoga has minimal effect cognition, but seems to improve fatigue
- Yoga may influence attention performance

Real Life

- Frequency
  - Daily
- Intensity
  - 2-3 repetitions
- Time/Duration
  - Hold each repetition 20-60 seconds

Research

(Rob – Researcher)

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YOU

“Real Life”

(Mandy – Physical Therapist)

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Flexibility Exercise Ideas

- www.nationalmssociety
  - Stretching for people with MS manual
  - Stretching with a partner manual
- www.nchpad.org
  - Videos/online images
- www.mstrust.org.uk
  - Videos/online images

- Online yoga videos
- Consult PT for specific needs
- Your idea?

www.cartoonstock.com

Strength Training Exercise

Research

- 1-2x/week high intensity free weights and machine weightlifting improved cognition in elderly women
- 2 year MRI follow up same ladies indicated less brain atrophy in resistance training group
- No known research supporting resistance training to treat cognition for people with MS

Real Life

- 2-3 sessions/week
- 1-3 sets, 8-15 repetitions
- 1 session or multiple smaller sessions/day to minimize fatigue
- Alternate arms/legs
- Rest 1-5 minutes as needed between sets
- Exercise for function

Research

(Rob – Researcher)

www.movieweb.com

YOU

“Real Life”

(Mandy – Physical Therapist)

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Strength Training Ideas

www.bodybuilding-wizard.com

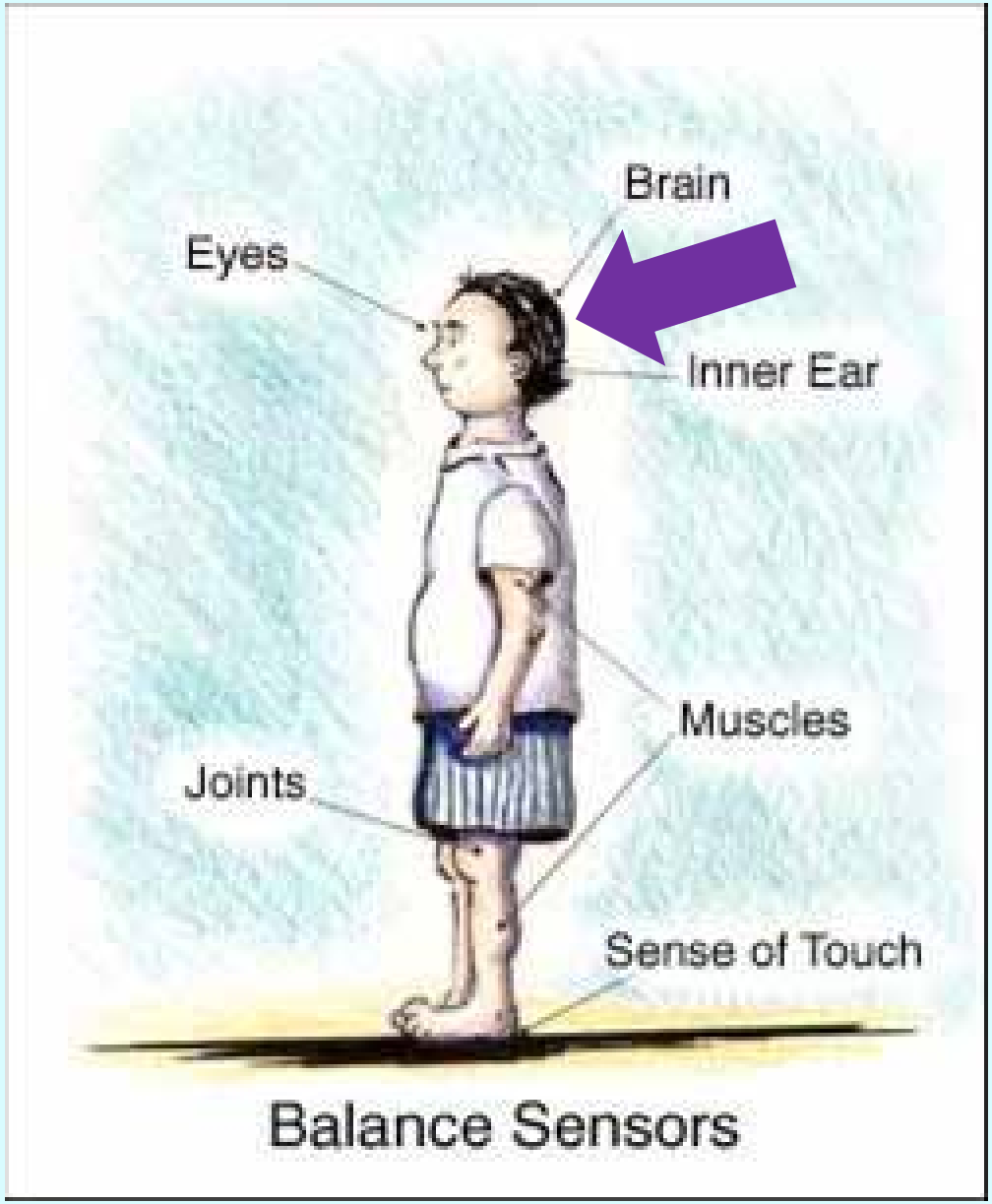
www.themusclediary.com

www.thoroughlyreviewed.com

www.build-muscle-101.com

BALANCE:

The Sixth Sense



Balance Exercise

Research

- Personalized balance program demonstrates greater improvement than traditional for people with MS
- Vestibular exercises improve walking, standing balance, and reduce fatigue
- No research in people with MS on the effect of balance training on improving cognition
- Balance function is associated with cognition

Real Life

- HIGHLY Individualized
  - Depends on systems of balance most involved

Complexity of Balance:

- Standing
  - Still/Statically – Concentration – No distractions
  - Multi-tasking
- Walking
  - Concentration – No distractions
  - Multi-tasking
- Influence on Falls
- Others?

www.robinsnestky.com

Dual Task/Multi Task Standing/Walking Research

Standing Research

- Increased sway during dual task present in early disease and/or clinically isolated syndrome
- Increased sway during standing dual task noted with increased disability
- RRMS/SPMS decline in cognitive performance during dual task standing – less reserve

Walking Research

- Compromised in early disease and/or clinically isolated syndrome
  - Slower walking and changes to walking biomechanics noted
- Dual task walking ability worsens with increased disability
- Dual task walking ability decline closely associated with worsening fatigue

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Fall Risk Considerations

- **Falls NOT occurring when concentrating on balance**
- **Common fall situations:**
  - **Dark/dim light**
  - **Uneven surface**
  - **Quick turns/changes of direction**
  - **Walking and talking**
- **Yours?**

www.nursetogether.com

Research

(Rob – Researcher)

www.movieweb.com

YOU

“Real Life”

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Balance Exercise Ideas

- **Identify and explain to PT situations when balance is compromised or falls have occurred**
- **Dual Task Training Ideas: (while performing appropriate balance task)**
  - **Counting**
  - **Reading**
  - **Doing a crossword or jigsaw puzzle**
  - **Turning head**
  - **Your ideas?**

FUNCTIONAL APPLICATION!!

Balance Exercise Ideas

www.exerciseforbalance.com

www.functionalaginginstitute.com

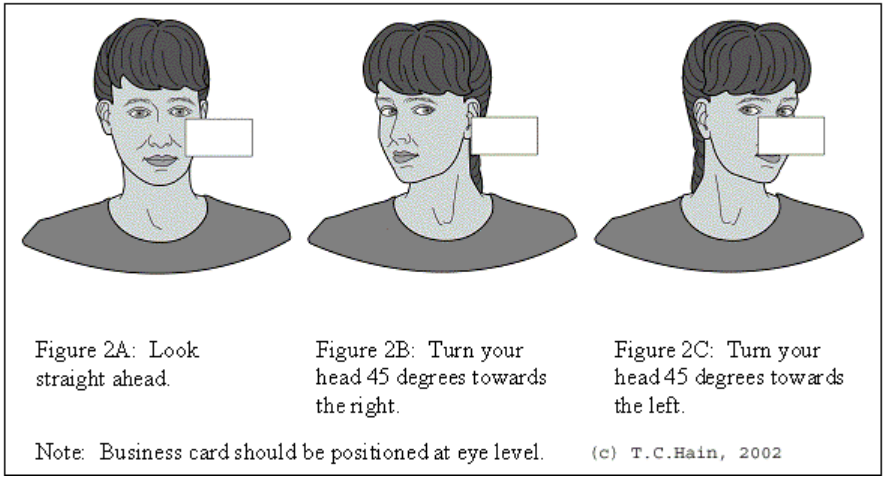

Figure 2A: Look straight ahead.

Figure 2B: Turn your head 45 degrees towards the right.

Figure 2C: Turn your head 45 degrees towards the left.

Note: Business card should be positioned at eye level. (c) T.C.Hain, 2002

www.dizziness-and-balance.com

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Cardiopulmonary/Aerobic Exercise

Research

- Aerobic exercise may improve cognition in 8-10 weeks among progressive MS
- Increased brain volume in motor and cognitive areas, as per MRI, with aerobic exercise

Real Life

- Frequency
  - 3-4 sessions/week (minimal)
- Intensity
  - Percentage of (MHR) Maximum Heart Rate
    - MHR=220-age
    - 60-85% of Maximum Heart Rate
  - Rate of Perceived Exertion
    - 1-2/10 Warm Up/Cool Down
    - 3-5/10 Exercise Zone
- Duration
  - 20-30 minutes; 2 10-15 minute sessions

Rate of Perceived Exertion

- 0 - Nothing
- 1 - Very, Very Light
- 2 - Very Light
- 3 - Moderate
- 4 - Somewhat Hard
- 5 - Hard
- 6
- 7 - Very Hard
- 8
- 9 - Very, Very Hard
- 10 - Maximal

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Research

(Rob – Researcher)

www.movieweb.com

YOU

“Real Life”

(Mandy – Physical Therapist)

www.dailyfit.ru

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Aerobic Training Ideas

www.nustep.com

www.amazon.com

www.Walmart.com

You don’t know what you don’t know

The Quest Has Just Begun!

Review

Exercise Training and Cognitive Rehabilitation: A Symbiotic Approach for Rehabilitating Walking and Cognitive Functions in Multiple Sclerosis?

Neurorehabilitation and
Neural Repair
1–13

DOI: 10.1177/1545968315606993
nnr.sagepub.com
SAGE

Robert W. Motl, PhD[1], Brian M. Sandroff, PhD[1], and John DeLuca, PhD[2,3]

Abstract

The current review develops a rationale and framework for examining the independent and combined effects of exercise training and cognitive rehabilitation on walking and cognitive functions in persons with multiple sclerosis (MS). To do so, we first review evidence for improvements in walking and cognitive outcomes with exercise training and cognitive rehabilitation in MS. We then review evidence regarding cognitive–motor coupling and possible cross-modality transfer effects of exercise training and cognitive rehabilitation. We lastly present a macro-level framework for considering mechanisms that might explain improvements in walking and cognitive dysfunction with exercise and cognitive rehabilitation individually and combined in MS. We conclude that researchers should consider examining the effects of exercise training and cognitive rehabilitation on walking, cognition, and cognitive–motor interactions in MS and the possible physiological and central mechanisms for improving these functions.

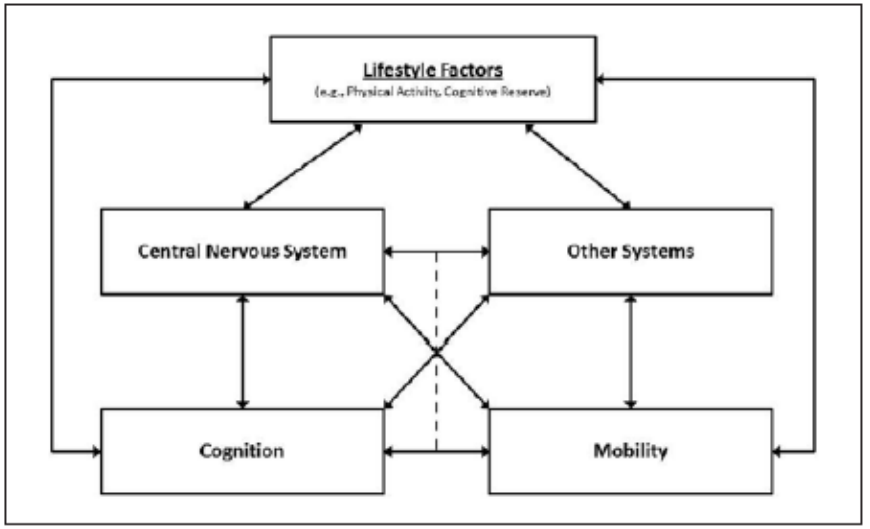

Figure 1. Model for possible cognitive and exercise rehabilitation effects on cognition and walking in multiple sclerosis.

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Questions that remain…..

- What type of exercise is ideal to encourage positive changes in the brain and cognition?
- How much exercise is enough for lasting change? Duration? Frequency?
- When is the ideal time to intervene with exercise to help with cognition?
- Individual disease….individual challenges…..individualized exercise program?

Final Thoughts…..

- **Aerobic exercise is associated with improved brain health and cognition in people with multiple sclerosis**
- **You can exercise to improve brain health**
- **Stay tuned!**

Thank You!

Questions?

Comments?

Can Do MS Resources

e|NEWS
your best life update

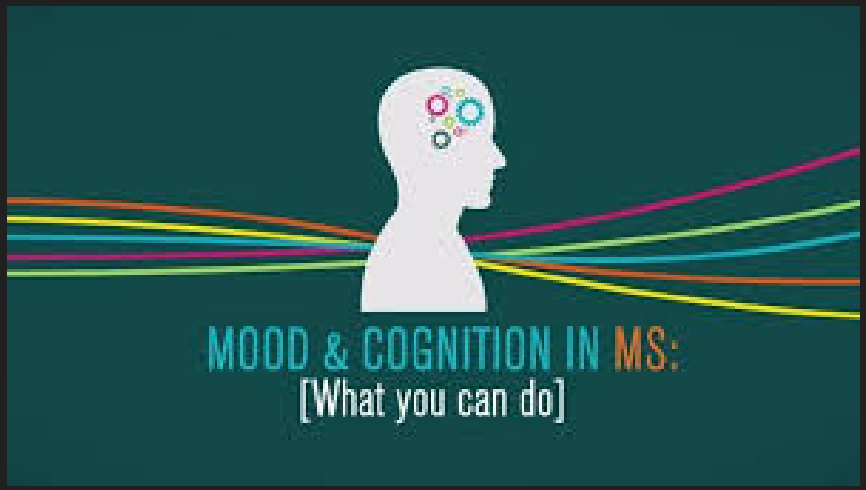
Q&A

Can Do Library

Find these resources at www.MSCanDo.org.

National MS Society Resources

NationalMSSociety.org/brochures



NationalMSSociety.org/videos

SKI OR RIDE FOR MS 2016

CAN DO Multiple Sclerosis | VERTICAL EXPRESS

SKI OR RIDE TO MAKE A DIFFERENCE

2016 EVENT DATES

Loon Mountain, NH - Feb. 6

Norway Mountain, MI - Feb. 13

Hunter Mountain, NY - Feb. 20

Crystal Mountain, WA - Feb 26 & 27

Vail Mountain, CO - Feb. 27

Squaw Valley, CA - Feb. 27

Schweitzer Mountain, ID - Mar. 5

7 MOUNTAINS. 1 CAUSE.

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February 9, 2016

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This program is possible thanks to the generous support of Biogen and EMD Serono.

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