Top 5 Research Articles

Exercise and Brain Health in Community-Dwelling Older Adults

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Research to Action Conference

June 20th, 2014

Outline

- Introduction
- **Top 5 Research Articles**
- Multi-Modality, Mind-Motor (M4) Research Program
  - Parkwood Case Series
  - CCAA pilot RCT
  - Woodstock RCT
- Take-Home Message

Introduction

The Problem – AD & Dementia

- **Dementia:** overall term for diseases and conditions characterized by declines in memory or thinking skills that affect everyday activities
  - **Alzheimer's disease** (AD) accounts for 60-80% of cases

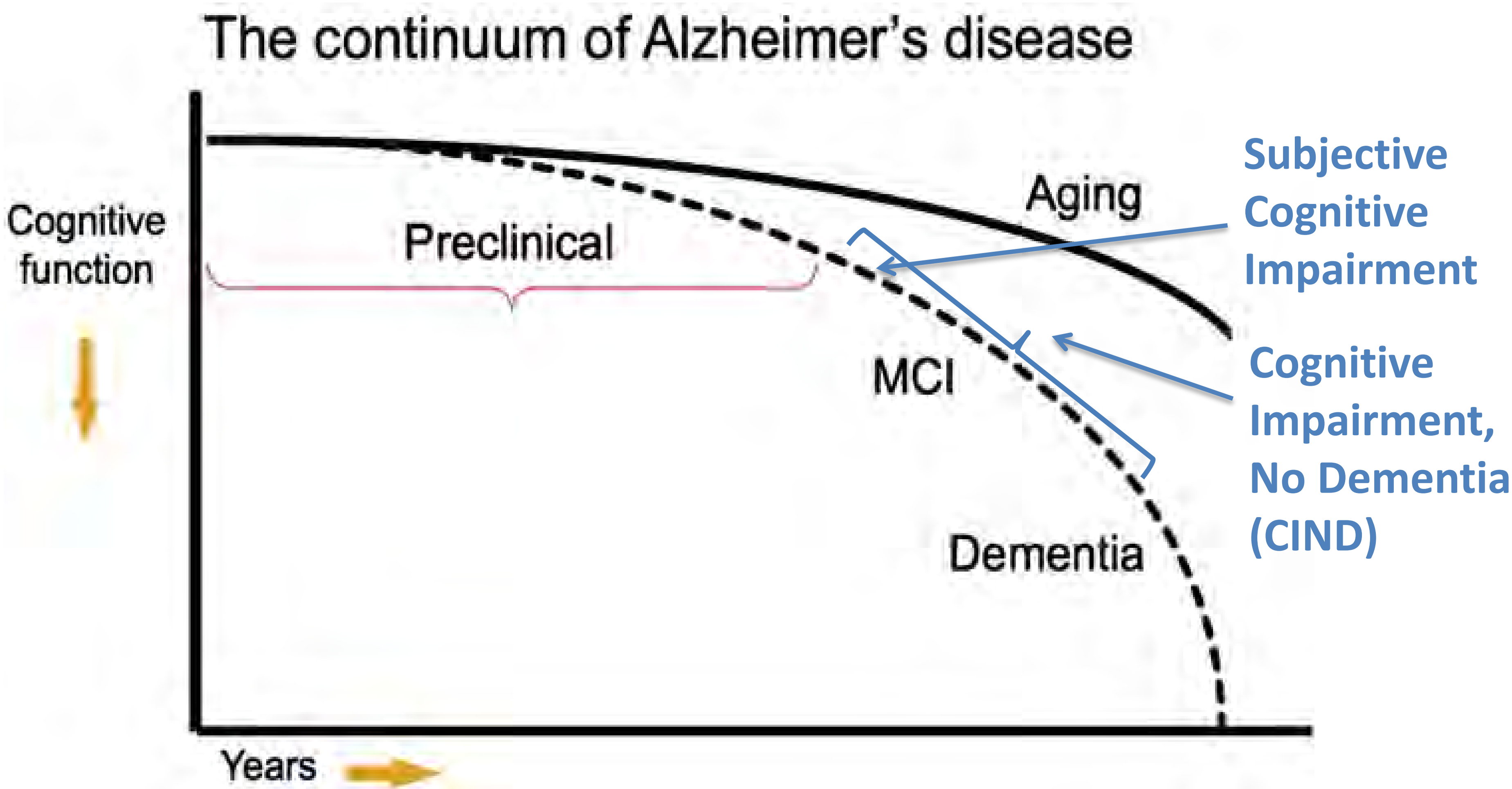
- In Canada alone: 750,000 older adults 65+ have AD and by 2031 this number will reach ~1.4 million

Estimated effect of prevention programs:

Even a modest 1-year delay in disease onset → 11.8 million FEWER cases of AD worldwide

Alzheimer's Association Facts & Figures Report (2014); Brookmeyer et al. (2007)

Cognitive Continuum



Adapted from Sperling et al., Alz Dem, 2011

Prevention – Exercise?

- Some of the most promising strategies for the prevention of dementia include:
  - Vascular risk factor control
  - Physical activity/exercise
  - Cognitive activity
  - Social engagement

- Some evidence for beneficial effects of aerobic exercise, resistance training, dual-task training/simultaneous cognitive-physical ("mind-motor") exercise, and combined programs on brain health…BUT more high-quality studies needed!

Middleton & Yaffe (2009); Daviglus et al. (2011); Gregory, Gill & Petrella (2013)

Top 5 Research Articles: Exercise and Brain Health

Journals of Gerontology: MEDICAL SCIENCES
Cite journal as: J Gerontol A Biol Sci Med Sci 2014 April;69(4):455–462
doi:10.1093/gerona/glt144

Published by Oxford University Press on behalf of the Gerontological Society of America 2013.
Advance Access publication November 5, 2013

Cardiorespiratory Fitness and Accelerated Cognitive Decline With Aging

Carrington R. Wendell,[1,2] John Gunstad,[3] Shari R. Waldstein,[4–6] Jeanette G. Wright,[1] Luigi Ferrucci,[1] and Alan B. Zonderman[1]

Examining the influence of cardiorespiratory fitness on the trajectory of cognitive decline in aging

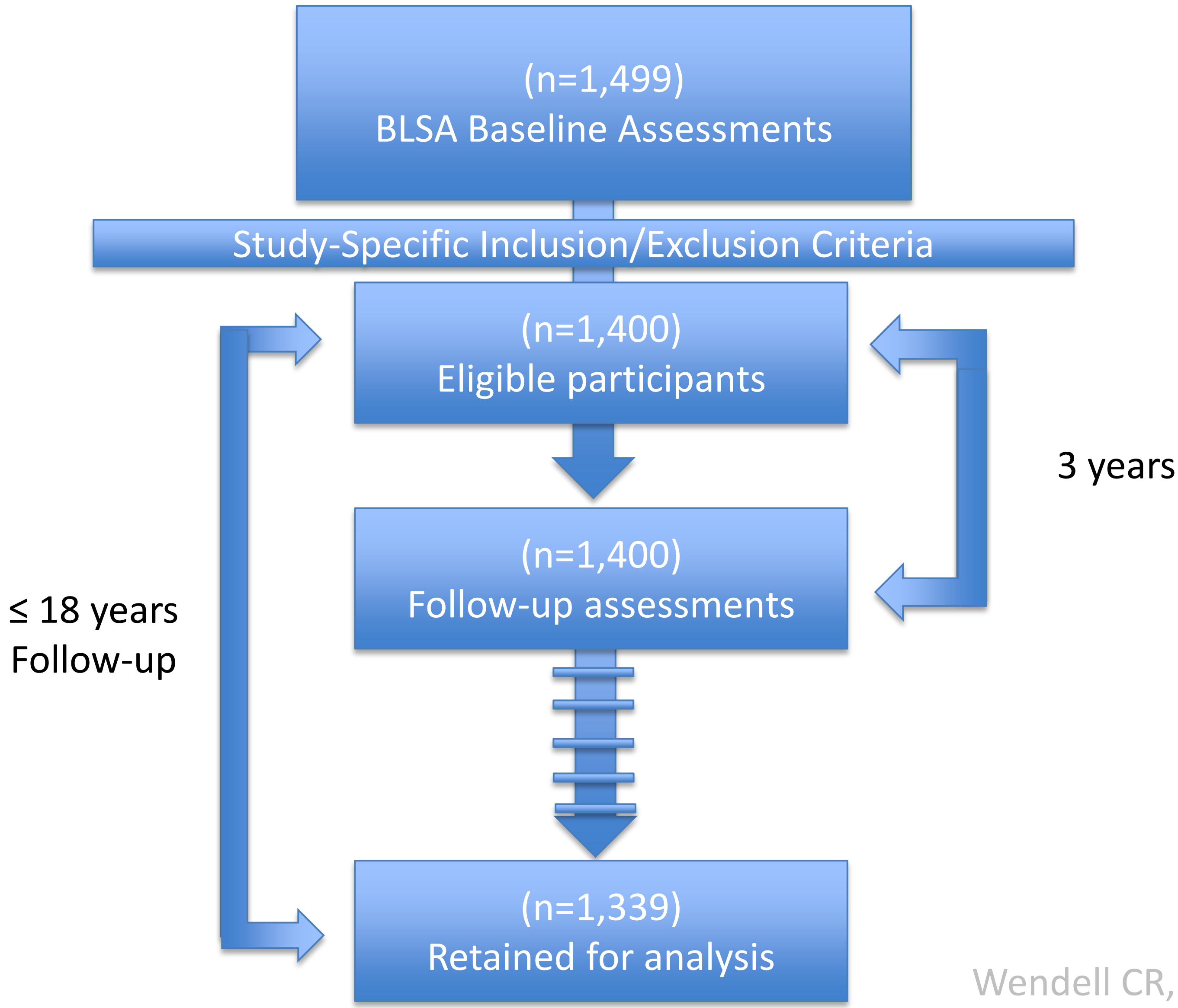
Prospective cohort study
1,400 community-dwelling participants from Baltimore Longitudinal Study on Aging (BLSA)

19-94 years old

Wendell CR, *et al.* (2014)

18 year longitudinal prospective cohort study

1,400 community-dwelling participants from the BLSA, 19-94 years old



Wendell CR, *et al.* (2014)

18 year longitudinal prospective cohort study

1,400 community-dwelling participants from the BLSA, 19-94 years old

Predictor of Interest:

- **Cardiorespiratory fitness:**
  - peak VO2 or $VO2_{max}$ (Modified Balke protocol and gas collection)

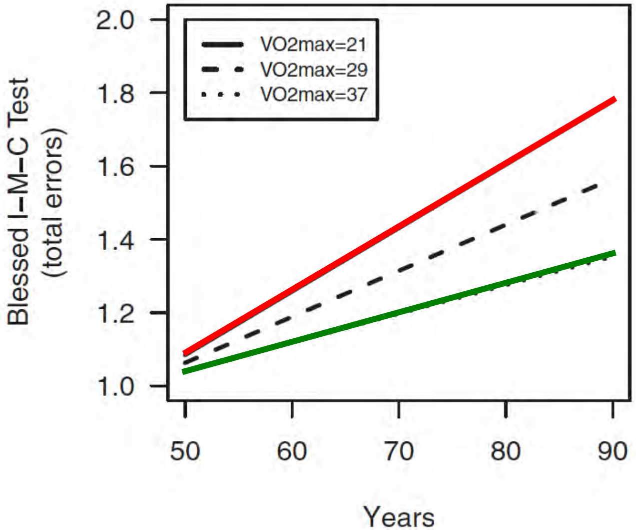
Outcomes of Interest:

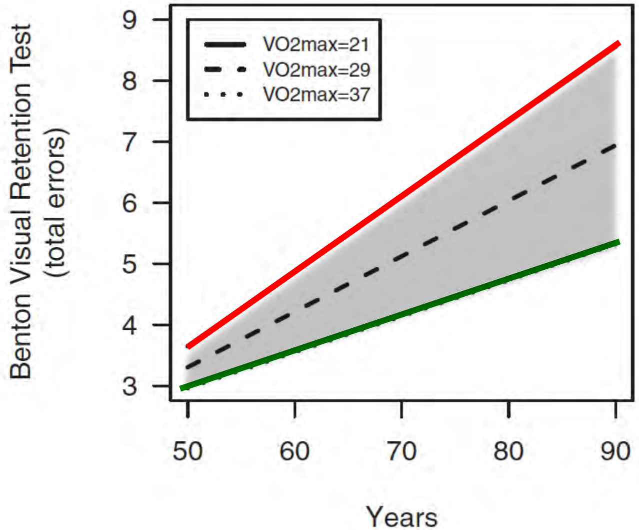
- **Neuropsychological performance:**
  - Global cognitive function (Blessed Information-Memory-Concentration test; MMSE)
  - Attention and concentration (Digit Span forwards and backwards)
  - Verbal learning and memory (California Verbal Learning Test)
  - Visual memory (Benton Visual Retention Test)
  - Executive function (Trail Making Tests part A and B)
  - Verbal fluency and language (Semantic & Phonemic fluency; Boston Naming Test)
  - Visuospatial function (Card Rotations Test)

Wendell CR, *et al.* (2014)

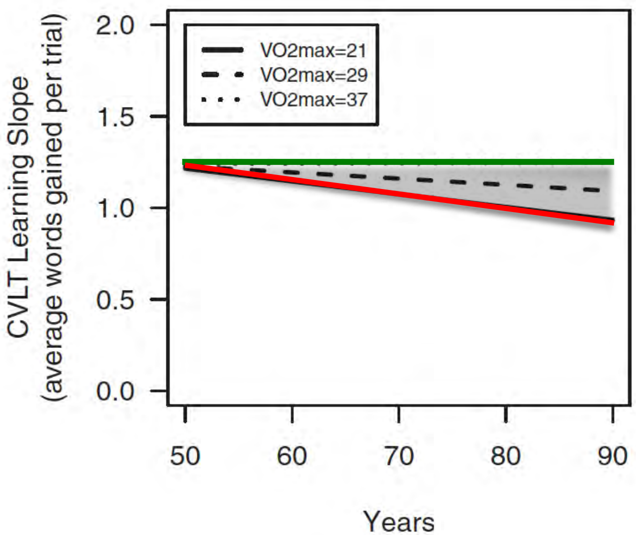
18 year longitudinal prospective cohort study

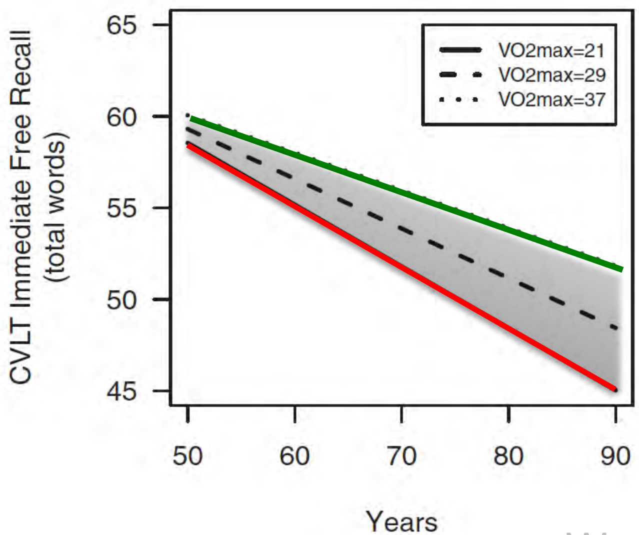
1,400 community-dwelling participants from the BLSA, 19-94 years old





Worse performance reflected with ***increasing*** scores over time





Worse performance reflected with ***decreasing*** scores over time

Wendell CR, *et al.* (2014)

18 year longitudinal prospective cohort study

1,400 community-dwelling participants from the BLSA, 19-94 years old

Conclusions:

- Greater cardiorespiratory fitness is associated with less prospective memory decline across the life span
  - Poorer baseline cardiorespiratory fitness is associated with accelerated memory decline
- Highlights the importance of early intervention to improve cardiorespiratory fitness for the preservation of cognitive function in aging

Wendell CR, *et al.* (2014)

frontiers in
AGING NEUROSCIENCE

ORIGINAL RESEARCH ARTICLE
published: 12 November 2013
doi: 10.3389/fnagi.2013.00075

Shorter term aerobic exercise improves brain, cognition, and cardiovascular fitness in aging

Sandra B. Chapman[1]*†, Sina Aslan[2]†, Jeffrey S. Spence[1], Laura F. DeFina[3], Molly W. Keebler[1], Nyaz Didehbani[1] and Hanzhang Lu[4]

[1] Center for BrainHealth®, The University of Texas at Dallas, Dallas, TX, USA
[2] Advance MRI, LLC, Frisco, TX, USA
[3] The Cooper Institute, Dallas, TX, USA
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Examining the impact of short-term aerobic exercise on brain health, cognition and cardiovascular fitness in older adults

37 previously inactive community-dwelling older adults

64.4 ± 4 years old; 73% female; preserved cognition (28 ± 1.5; MoCA; 30.2 ± 2 TICS-M)

Chapman SB, *et al.* (2013)

12 week aerobic exercise RCT

37 previously inactive community-dwelling older adults

64.4 ± 4 years old; 73% female; preserved cognition (28 ± 1.8 MoCA; 30.2 ± 2 TICS-M)

Intervention

- **Aerobic Exercise: 60 min/d, 3 d/wk**
  - Exercise bike:
    - 5 min warm-up (43 watts)
    - 50 min at 50-75% HR_{max}
    - 5 min cool-down (43 watts)
  - Treadmill:
    - 5 min warm-up (2 mph)
    - 50 min at 50-75% % HR_{max}
    - 5 min cool-down (2 mph)
- **Non-exercising Wait-list Control**

Chapman SB, *et al.* (2013)

12 week aerobic exercise RCT

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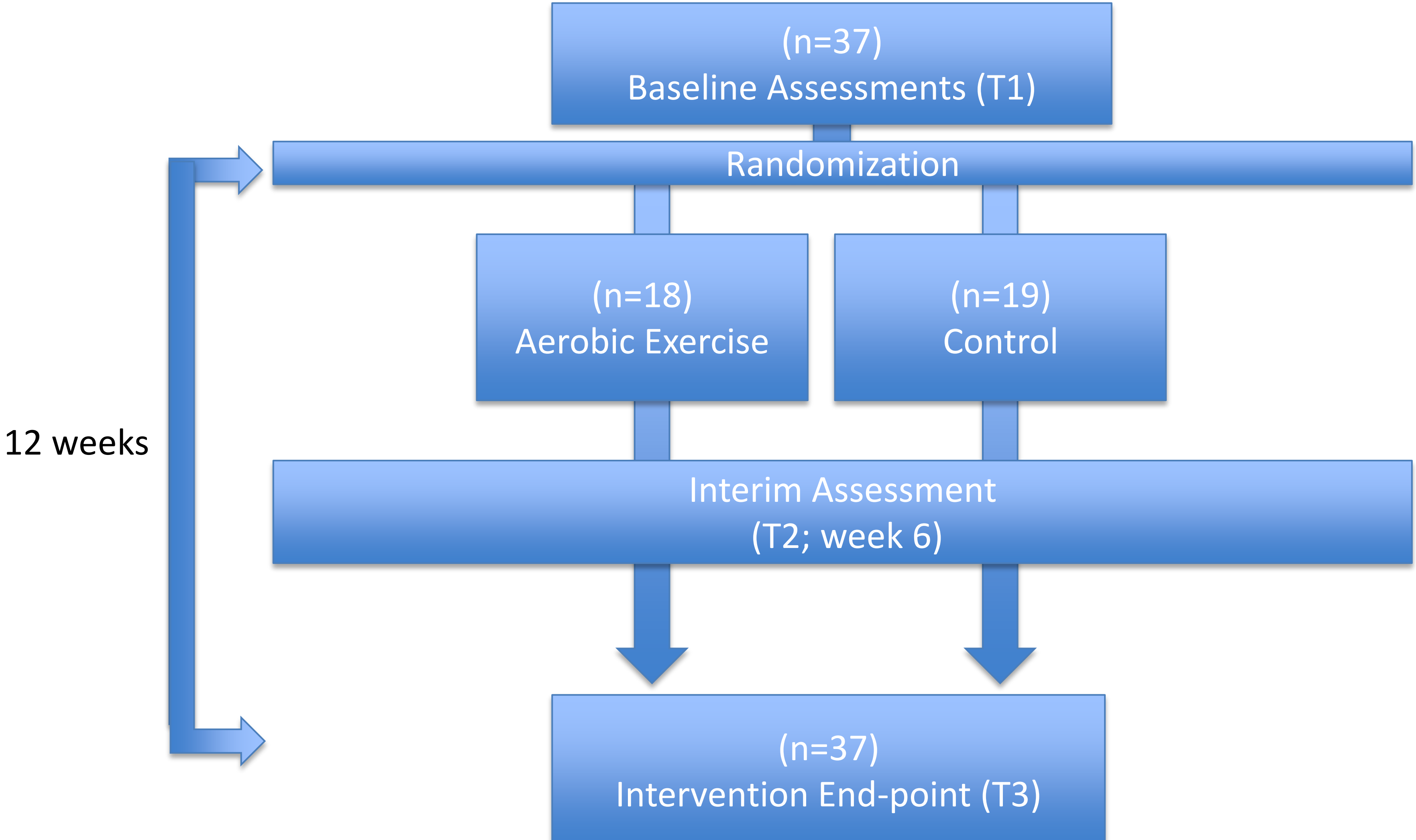
64.4 ± 4 years old; 73% female; preserved cognition (28 ± 1.8 MoCA; 30.2 ± 2 TICS-M)



Chapman SB, *et al.* (2013)

12 week aerobic exercise RCT

37 previously inactive community-dwelling older adults

64.4 ± 4 years old; 73% female; preserved cognition (28 ± 1.8 MoCA; 30.2 ± 2 TICS-M)

Outcomes of Interest

- **Cognition**
  - Executive function; TMT B-A
  - **Memory; CVLT; WMS-IV**
  - Attention; DKEFS-colour word; Backwards Digit Span

- **Cerebrovascular health and function (fMRI & rs-MRI)**
  - **Global and regional cerebral blood flow (CBF)**

Chapman SB, *et al.* (2013)

12 week aerobic exercise RCT

37 previously inactive community-dwelling older adults

64.4 ± 4 years old; 73% female; preserved cognition (28 ± 1.8 MoCA; 30.2 ± 2 TICS-M)

Results:

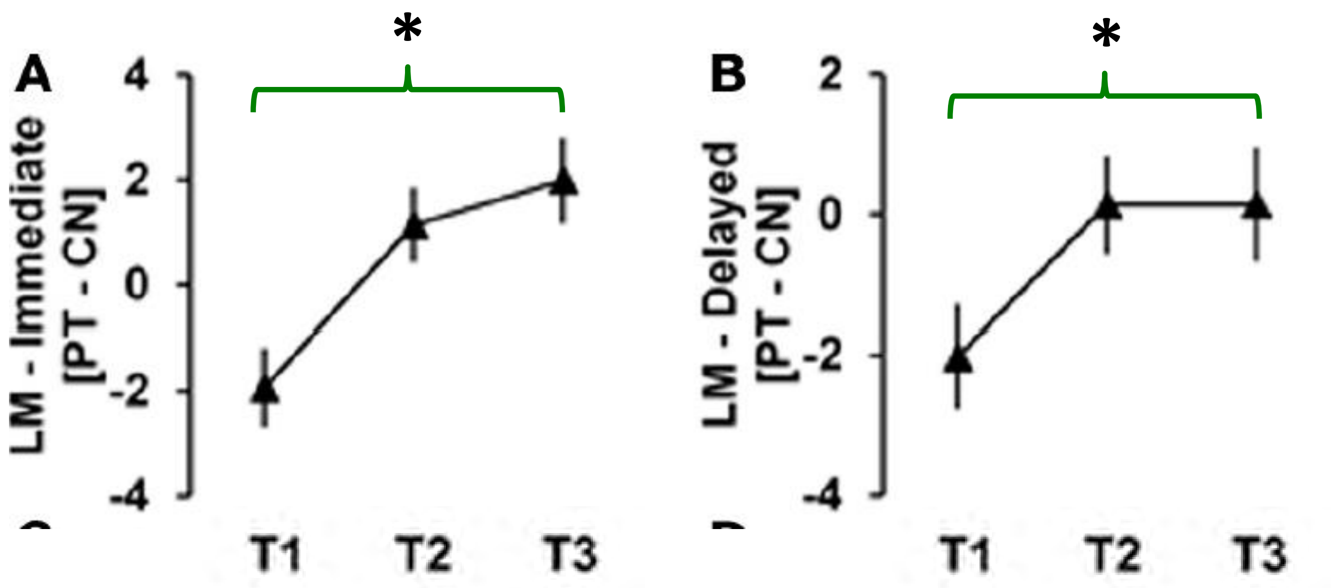


FIGURE 1 | The mean difference between Physical Training (PT) and Control (CN) groups over training sessions are shown for (A) immediate logical memory (B) delayed logical memory (C) VO_2 Max and (D) rating of perceived exertion (RPE). Significant changes from T1 to T3 are evident in **(A, B, D)** ($p = 0.003$, 0.03, and 0.01, respectively). Maximal change at T2 is evident for panel **(C)** ($p = 0.02$).

Chapman SB, *et al.* (2013)

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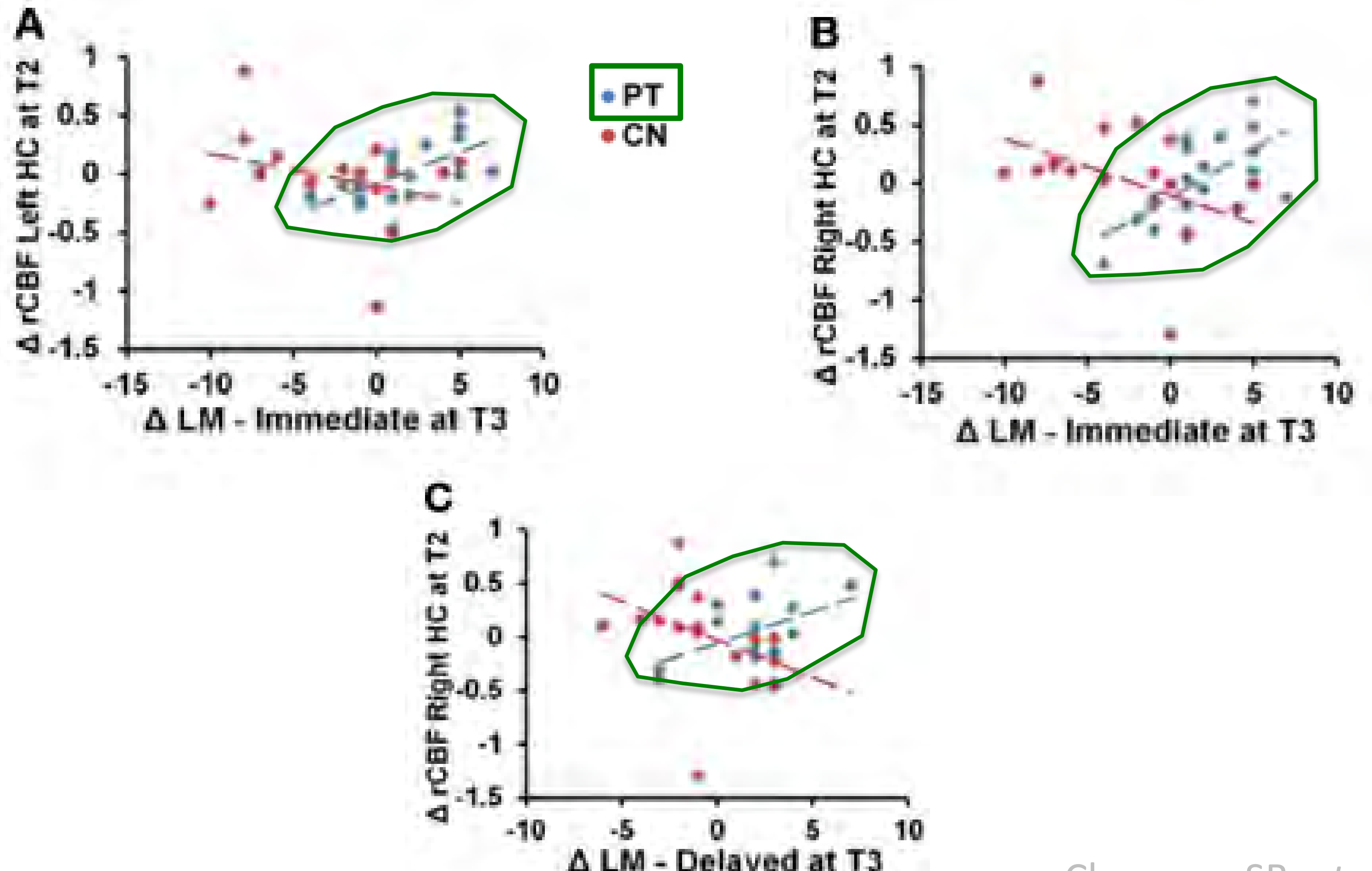


Chapman SB, *et al.* (2013)

12 week aerobic exercise RCT

37 previously inactive community-dwelling older adults

64.4 $\pm$ 4 years old; 73% female; preserved cognition (28 $\pm$ 1.8 MoCA; 30.2 $\pm$ 2 TICS-M)

Conclusions:

– Even short-term aerobic exercise can facilitate neuroplasticity

– Aerobic exercise can serve to reduce the biological and cognitive consequences of aging to benefit brain health in previously sedentary older adults

Chapman SB, *et al.* (2013)

ORIGINAL INVESTIGATION

The Mental Activity and eXercise (MAX) Trial

A Randomized Controlled Trial to Enhance Cognitive Function in Older Adults

Deborah E. Barnes, PhD, MPH; Wendy Santos-Modesitt, MA; Gina Poelke, PhD; Arthur F. Kramer, PhD; Cynthia Castro, PhD; Laura E. Middleton, PhD; Kristine Yaffe, MD

Examining the effects of combined cognitive and aerobic exercise on cognition in older adults

126 previously inactive community-dwelling older adults with subjective cognitive complaints (SCC)

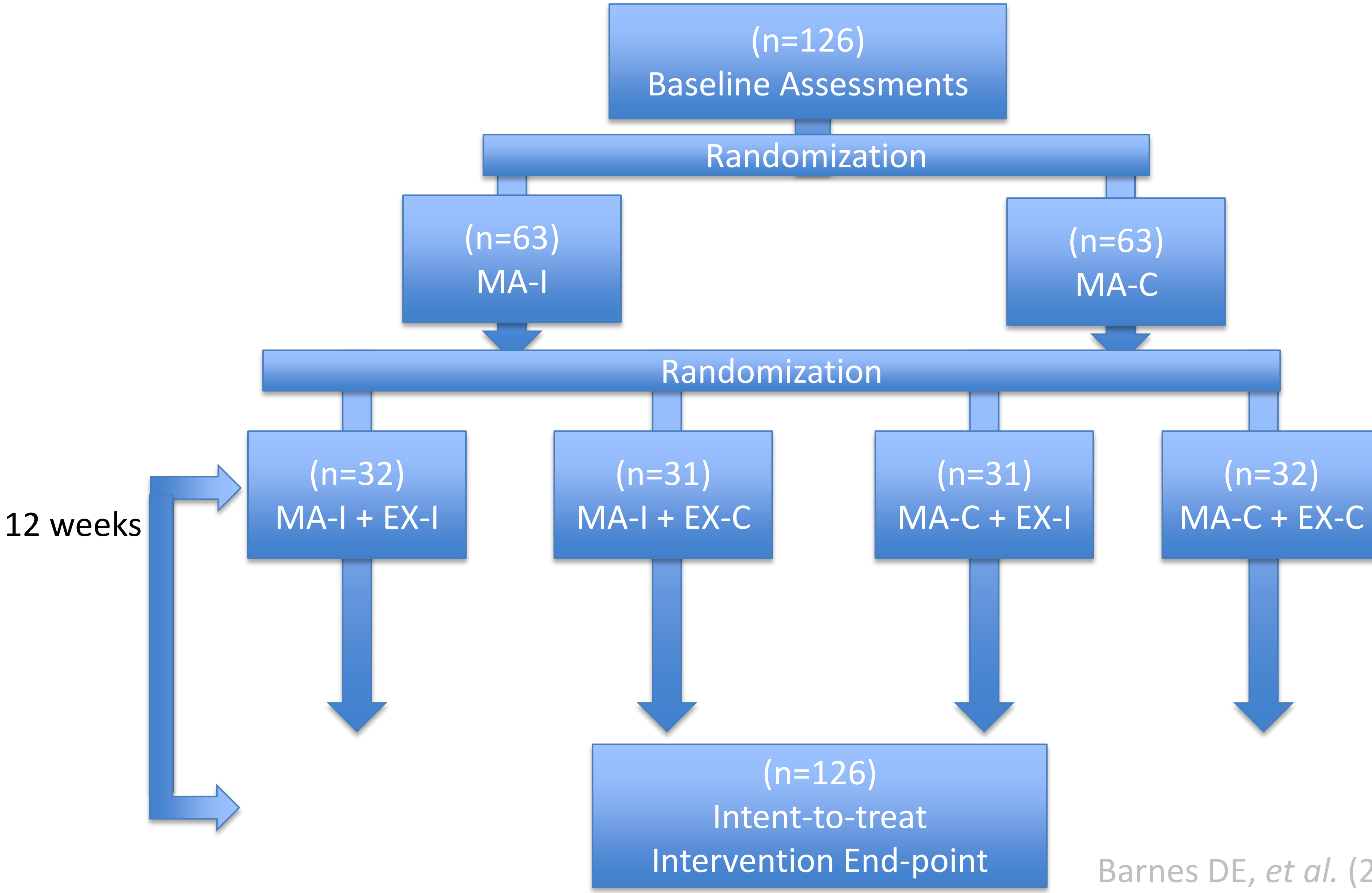
73.4 ± 5.9 years old; 62.7% female; preserved cognition (95.4 ± 4.9; 3MS) but subjective complaints

Barnes DE, *et al.* (2013)

12 week cognitive plus physical exercise RCT

126 previously inactive community-dwelling older adults with SCC

73.4 ± 5.9 years old; 62.7% female; preserved cognition (95.4 ± 4.9; 3MS)



Barnes DE, *et al.* (2013)

12 week cognitive plus physical exercise RCT

126 previously inactive community-dwelling older adults with SCC

73.4 ± 5.9 years old; 62.7% female; preserved cognition (95.4 ± 4.9; 3MS)

Interventions:

- **Cognitive Intervention: 60 min/d, 3 d/wk**
  - Intensive computer-based at-home training
- **Cognitive Control:**
  - Educational DVDs (arts, history, science)

- **Exercise Intervention: 60 min/d, 3 d/wk**
  - 10 min warm-up; 30 min dance-based aerobics; 5 min cool-down
  - 10 min strength training
  - 5 min stretching, relaxation
- **Exercise Control:**
  - Replaced aerobics with stretching and toning

Barnes DE, *et al.* (2013)

12 week cognitive plus physical exercise RCT

126 previously inactive community-dwelling older adults with SCC

73.4 ± 5.9 years old; 62.7% female; preserved cognition (95.4 ± 4.9; 3MS)

Outcomes of Interest:

- **Global cognitive function composite score**
  - Verbal learning (Rey's Auditory Verbal Learning Test)
  - Verbal fluency (Semantic and Phonemic fluency)
  - Processing speed (Digit Symbol Substitution Test)
  - Executive function/mental flexibility (TMT A & B)
  - Executive function/inhibition (Eriksen Flanker Task)
  - Visuospatial function (Useful field of view)

Barnes DE, *et al.* (2013)

12 week cognitive plus physical exercise RCT

126 previously inactive community-dwelling older adults with SCC

73.4 ± 5.9 years old; 62.7% female; preserved cognition (95.4 ± 4.9; 3MS)

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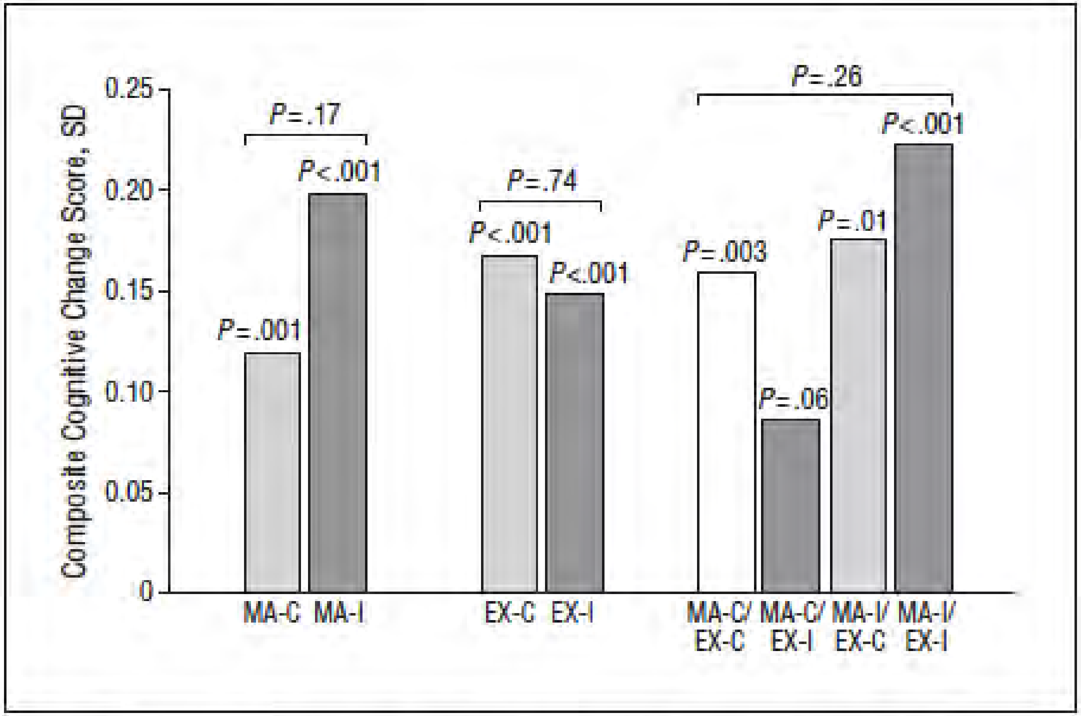


Figure 2. Effects of interventions on composite cognitive score. For the primary outcome of change in the composite cognitive score, scores improved significantly over time but did not differ between the mental activity intervention (MA-I) and mental activity control (MA-C) groups, the exercise intervention (EX-I) and exercise control groups (EX-C) groups, or all 4 randomization groups.

Barnes DE, *et al.* (2013)

12 week cognitive plus physical exercise RCT

126 previously inactive community-dwelling older adults with SCC

73.4 ± 5.9 years old; 62.7% female; preserved cognition (95.4 ± 4.9; 3MS)

Conclusions:

- 12 weeks of physical plus mental activity was associated with improvements in global cognitive function in previously sedentary older adults with subjective cognitive complaints
    - No difference between intervention and active controls

- Suggests that the amount of physical and/or mental activity is more important than the type when attempting to enhance cognition in this population

Barnes DE, *et al.* (2013)

Resistance training and functional plasticity of the aging brain: a 12-month randomized controlled trial

Teresa Liu-Ambrose[a,b,c,*], Lindsay S. Nagamatsu[a,c,d], Michelle W. Voss[e], Karim M. Khan[c,f], Todd C. Handy[a,c,d]

[a] *The Brain Research Centre, University of British Columbia, Vancouver, BC, Canada*
[b] *Department of Physical Therapy, University of British Columbia, Vancouver, BC, Canada*
[c] *The Centre for Hip Health and Mobility, Vancouver Coastal Health Research Institute, Vancouver, BC, Canada*
[d] *Department of Psychology, University of British Columbia, Vancouver, BC, Canada*
[e] *The Beckman Institute and Department of Psychology, University of Illinois at Urbana-Champaign, Urbana, IL, USA*
[f] *Department of Family Practice, University of British Columbia, Vancouver, BC, Canada*

Received 6 July 2010; received in revised form 11 May 2011; accepted 15 May 2011

Examining the effects of resistance training on executive functional plasticity in older women

52 resistance-training naïve, community-dwelling older women

69.3 ± 3 years old; preserved cognition (29.8 ± 1.1 MMSE)

Liu-Ambrose T, *et al.* (2013)

52 week resistance or balance training RCT

52 resistance-training naïve, community-dwelling older women

69.3 ± 3 years old; preserved cognition (29.8 ± 1.1 MMSE)

Interventions:

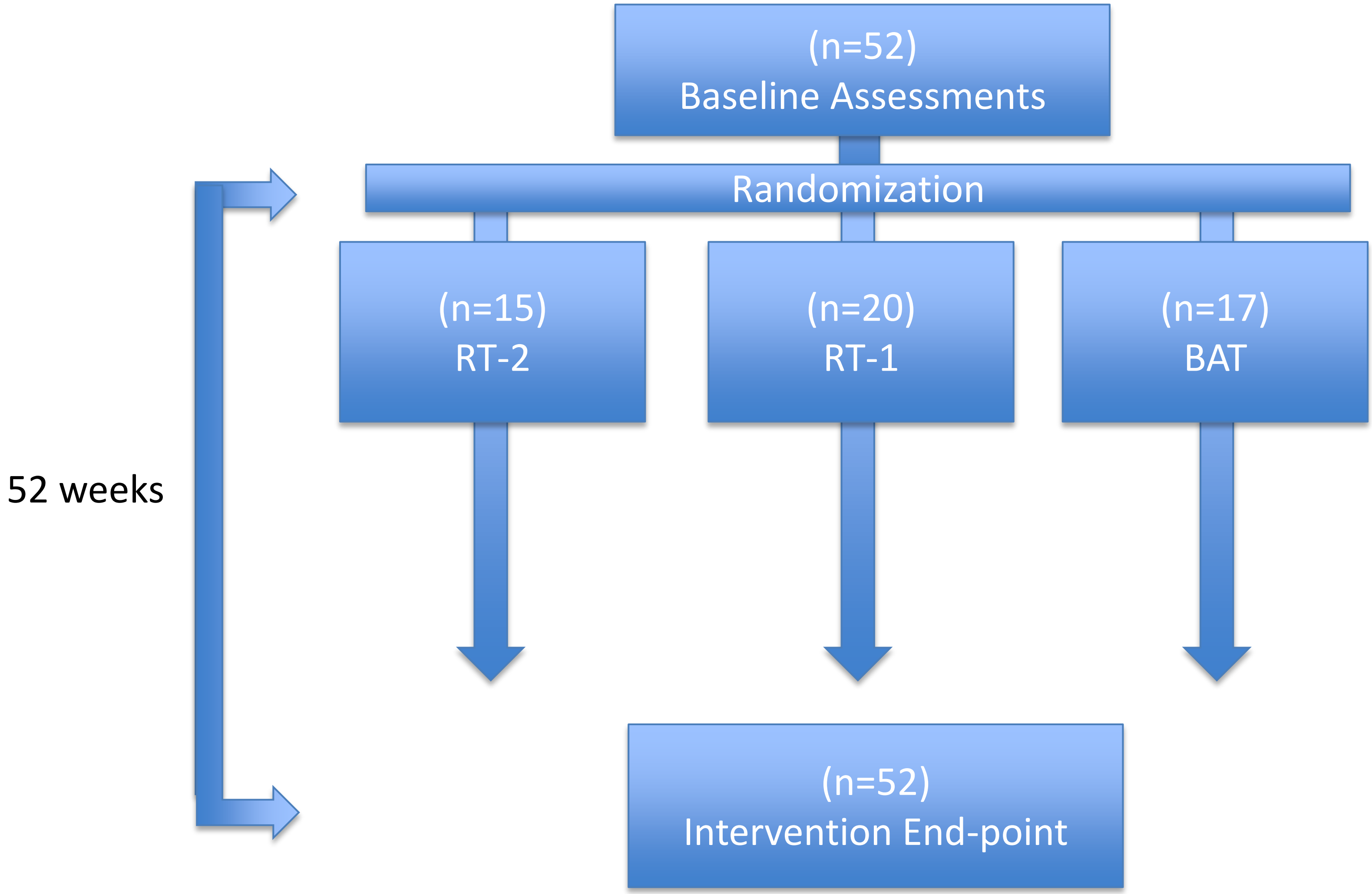
- **Resistance Training Intervention: 60 min/d, 1 *or* 2 d/wk (RT-1 or RT-2)**
  - 8 machine & free weight exercises; 2 sets, 6-8 reps
    - Progressive in loading (increased via 7RM method)
  - Also included mini-squats, mini-lunges, and lunge walks
- **Balance and Toning (BAT) Control: 60 min/d, 1 d/wk**
  - Stretching
  - Range-of-motion
  - Basic core strengthening
  - Balance
  - Relaxation

Liu-Ambrose T, *et al.* (2013)

52 week resistance or balance training RCT

52 resistance-training naïve, community-dwelling older women

69.3 ± 3 years old; preserved cognition (29.8 ± 1.1 MMSE)



Liu-Ambrose T, *et al.* (2013)

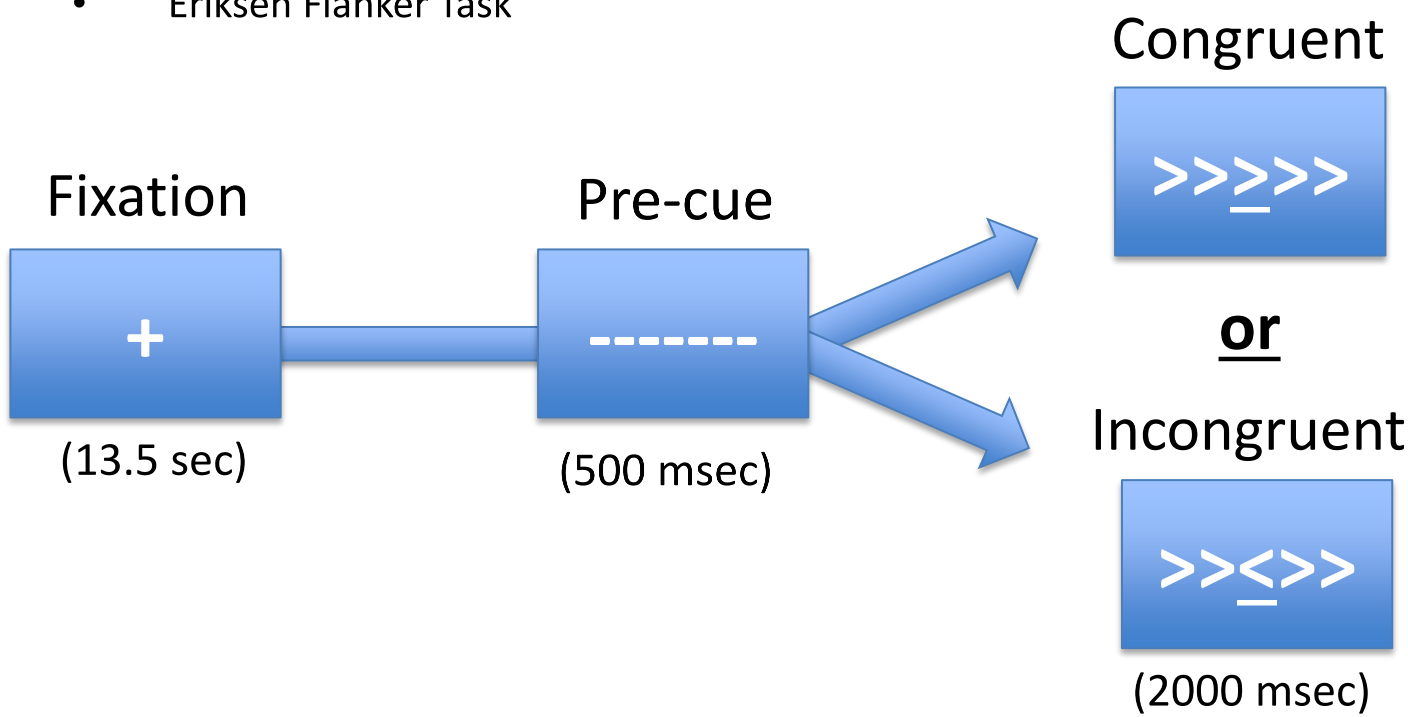
52 week resistance or balance training RCT

52 resistance-training naïve, community-dwelling older women

69.3 ± 3 years old; preserved cognition (29.8 ± 1.1 MMSE)

Outcomes of Interest:

- **Executive Functional Plasticity:**
    - **Inhibitory Control/Selective Attention Interference Score**
        - Eriksen Flanker Task



Liu-Ambrose T, *et al.* (2013)

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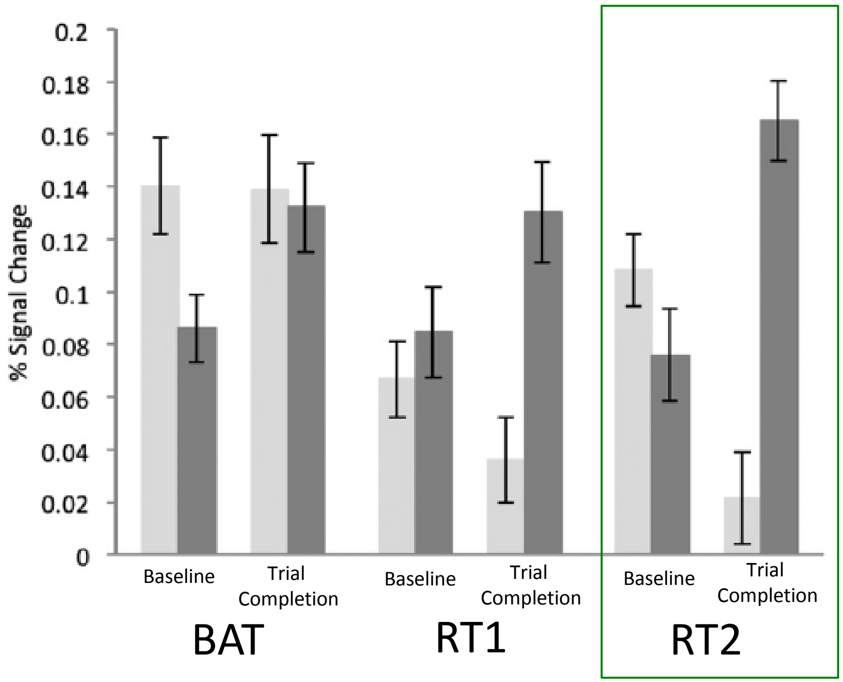
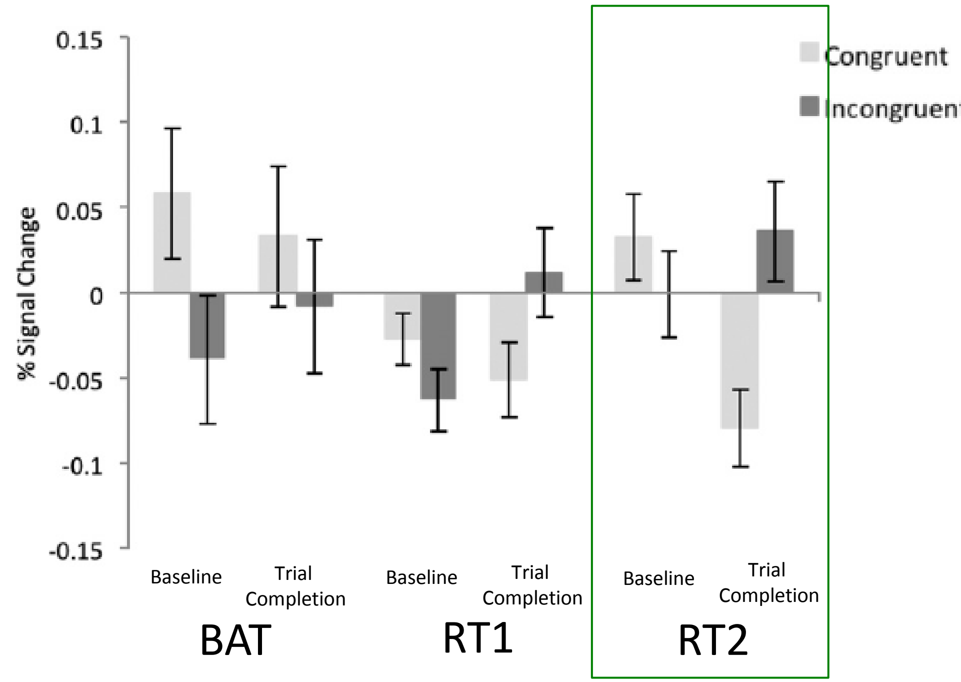
Results:



Left Anterior Insula extending into Lateral Orbito Frontal Cortex



Left Anterior Middle Temporal Gyrus

Improved response inhibition processing and inhibitory control for RT2 vs. BAT

Liu-Ambrose T, *et al.* (2013)

52 week resistance or balance training RCT

52 resistance-training naïve, community-dwelling older women

69.3 ± 3 years old; preserved cognition (29.8 ± 1.1 MMSE)

Conclusions:

- RT appears to affect regions associated with response inhibition processes and improve the ability to avoid making automatic, unwanted responses

- Complements previous work, suggesting AE increases the ability to selectively attend and perceptually filter out task-irrelevant info (Colcombe, 2004)

May be possible to use different modalities of exercise to target and improve different subsets of basic cognitive functions in older adults…

Liu-Ambrose T, *et al.* (2013)

RESEARCH ARTICLE Open Access

Effects of simultaneously performed cognitive and physical training in older adults

Nathan Theill[1,2*], Vera Schumacher[1,2,3], Rolf Adelsberger[4], Mike Martin[1,2] and Lutz Jäncke[2,5,6]

Examining the effects of simultaneously performed cognitive and aerobic exercise on cognition in older adults

51 community-dwelling older adults

72.2 ± 5 years old; 73% female; preserved cognition (MMSE > 29.1 ± 0.9)

Theill N, *et al.* (2014)

10 week simultaneous cognitive and physical exercise

51 community-dwelling older adults

72.2 ± 5 years old; 73% female; preserved cognition (29.1 ± 0.9 MMSE)

Interventions:

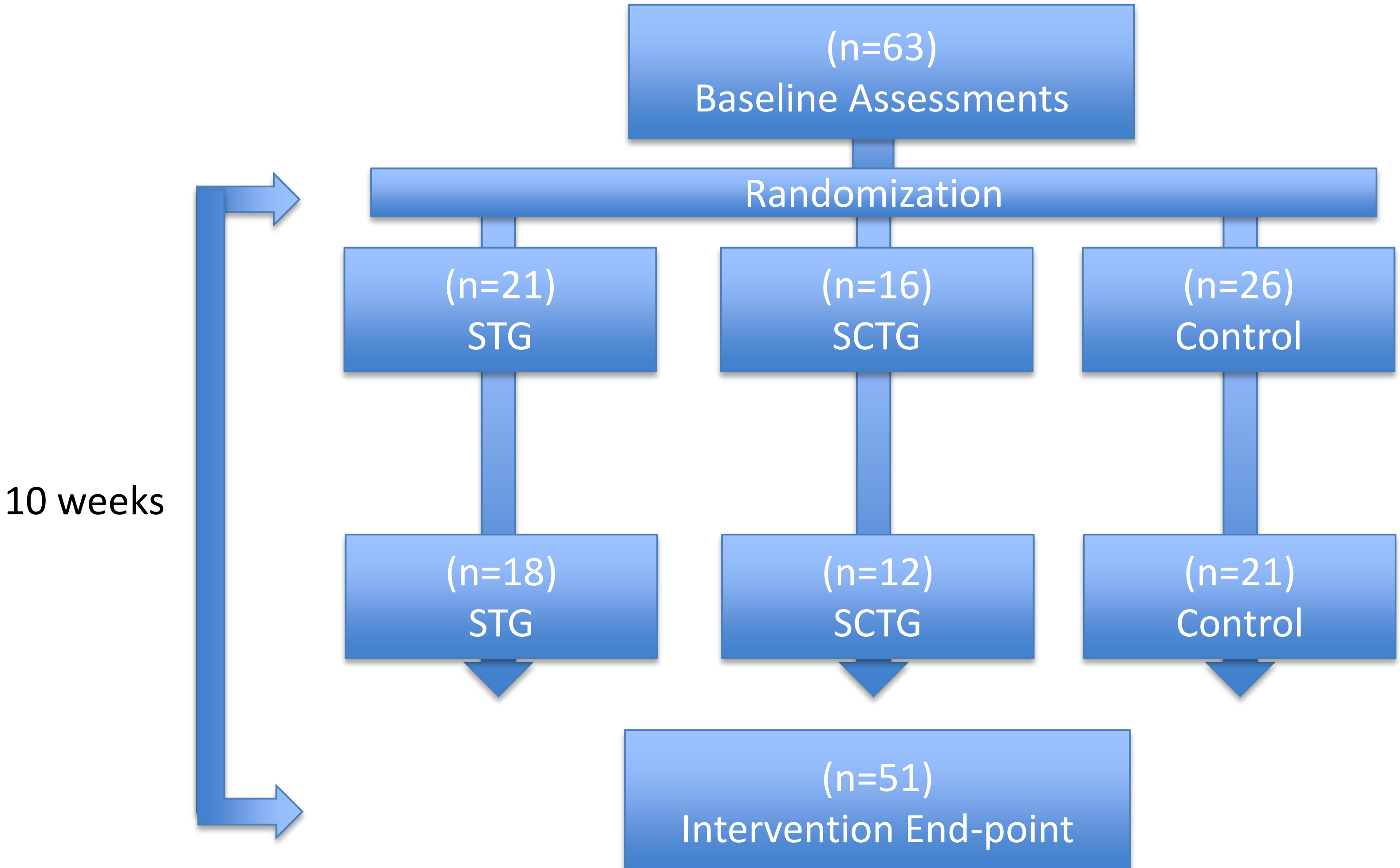
- **Cognitive & Physical Training: 2 d/wk, 20 sessions**
  - 40 min treadmill walking (60-80% HR_{max})
  - Simultaneously performing cognitive tasks
- **Cognitive Training: 2 d/wk, 20 sessions**
  - Performed cognitive tasks in isolation
- **Non-exercising control**

Theill N, *et al.* (2014)

10 week simultaneous cognitive and physical exercise

51 community-dwelling older adults

72.2 ± 5 years old; 73% female; preserved cognition (29.1 ± 0.9 MMSE)



Theill N, *et al.* (2014)

10 week simultaneous cognitive and physical exercise

51 community-dwelling older adults

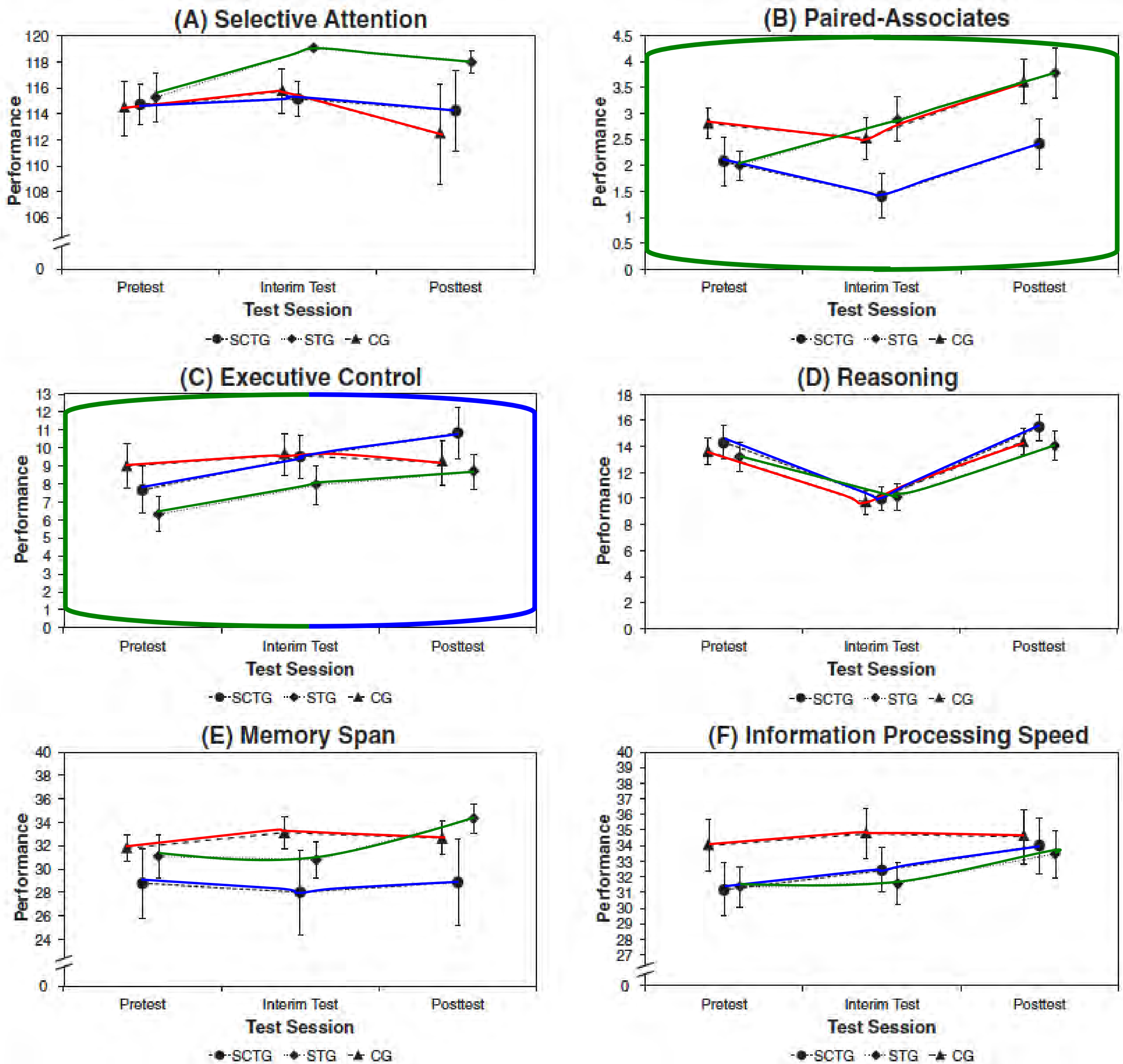
72.2 ± 5 years old; 73% female; preserved cognition (29.1 ± 0.9 MMSE)

Outcomes of Interest

- **Multiple domains of cognition:**
  - Selective attention
  - Paired-associates learning
  - Executive control
  - Reasoning
  - Memory span
  - Information processing speed

- Computerized neuropsychological battery employed

Theill N, *et al.* (2014)



Simultaneous training

Single cognitive training

Control

Figure 2 Performance in the cognitive transfer tasks (A-F). The participants of the simultaneous training group (STG) and single cognitive training group (SCTG) showed a larger improvement in the executive control task when compared to the control group (CG) ($p = .037$), with no differences between the two training conditions. In addition, the combined training group showed larger training gains in the paired-associates task compared to the single cognitive training group ($p = .018$). Bars represent ± standard error of the mean.

Theill N, *et al.* (2014)

10 week simultaneous cognitive and physical exercise

51 community-dwelling older adults

72.2 ± 5 years old; 73% female; preserved cognition (29.1 ± 0.9 MMSE)

Conclusions:

- Simultaneously performed cognitive and physical exercise training can significantly improve multiple aspects of cognition in cognitively healthy community-dwelling older adults

- These exercises more readily allow for heightened transferability of training effects than more narrowly-focused, single-domain interventions

Theill N, *et al.* (2014)

Multiple-Modality, Mind-Motor Research Program

Multiple-Modality, Mind-Motor Exercise Research Program

- Laboratory and community-based approaches
- Community-dwelling older adults
- London and Woodstock communities

Program Goal:

To determine whether combining multiple-modality exercise (or aerobic exercise) with mind-motor exercise can improve cognitive, mobility, and vascular outcomes in community-dwelling older adults who may be at increased risk for future cognitive impairment and dementia

Parkwood Case Series

Parkwood Study (June 2012 ➔)

Population - Community-dwelling older adults (60+):

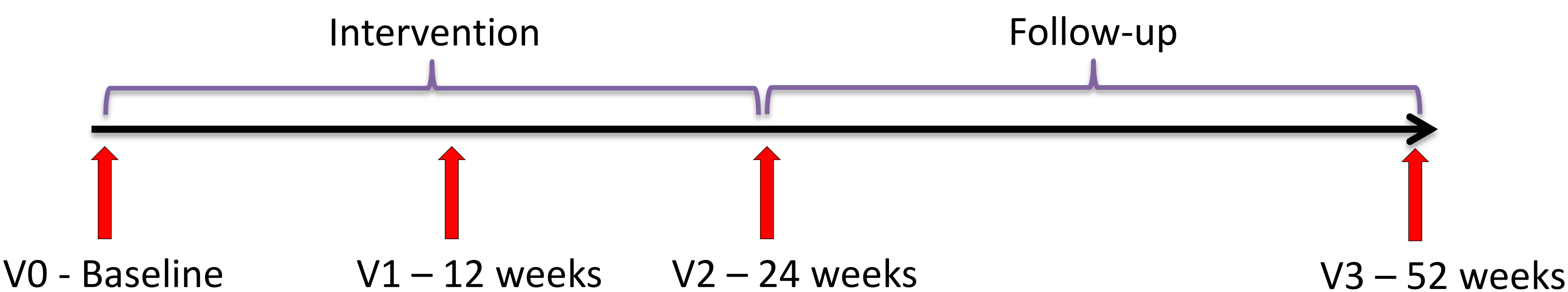
- COHORT 1: Cognitive Impairment – Not Dementia
- COHORT 2: "Cognitively Normal"

Design:

- Experimental case series (both cohorts)
- One-on-one training @ ARGC – Parkwood

Outcomes:

- Executive function (1°)
- Other cognitive, mobility and vascular measures (2°)



Parkwood – Intervention

Exercise Sessions
(*3x/week for 6-months*)

1. 5 minute warm-up
2. 15 minutes of walking at a target pace and step length, while receiving real-time visual feedback + answering cognitively challenging questions
3. 15 minutes of moderate to vigorous intensity aerobic exercise
4. 5 minute cool down

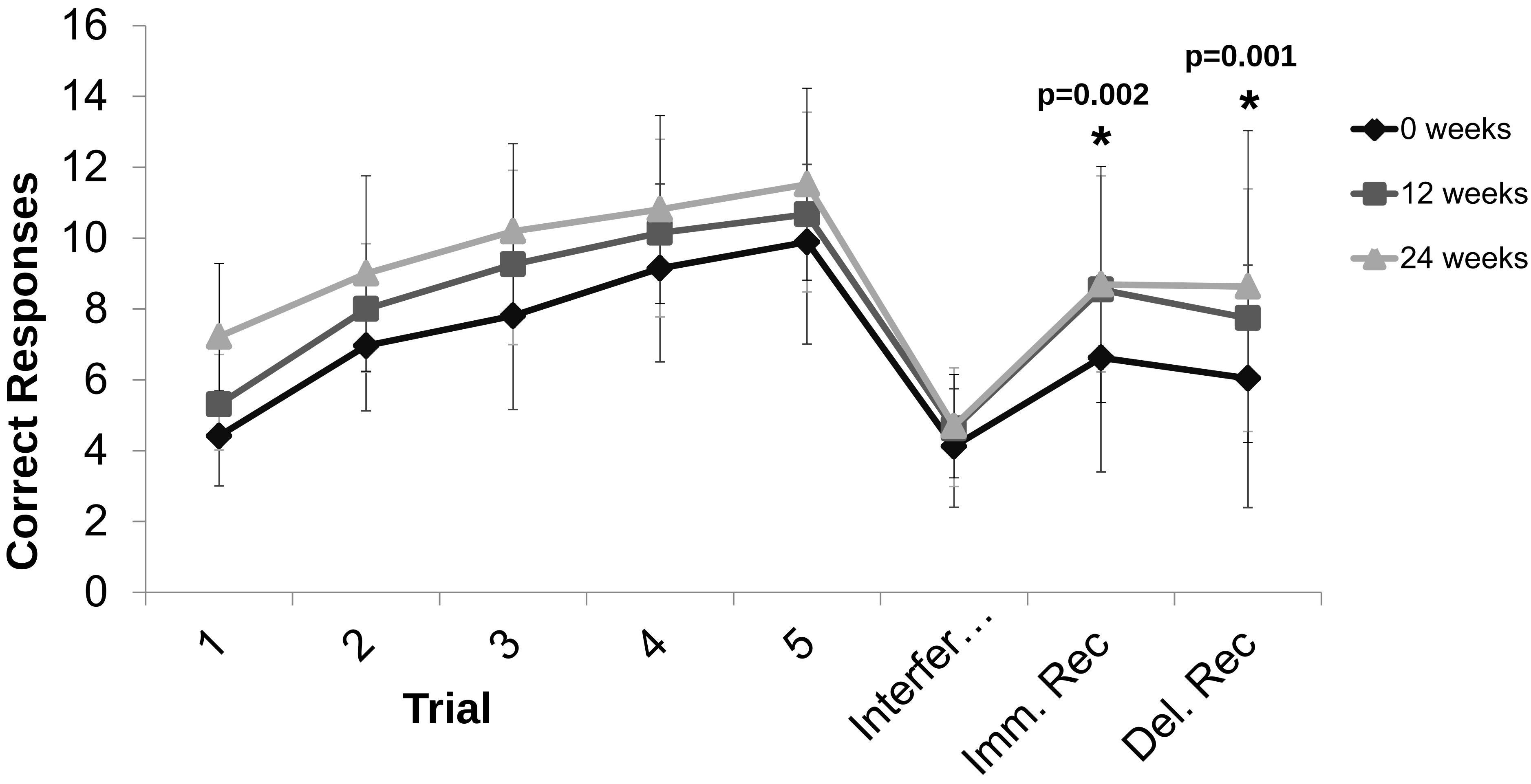
Parkwood Study – Interim Results

27 participants with CIND have completed the intervention (Feb. ‘14)

Characteristics (n=27)	
Age (years), mean ± SD	72 ± 7.1
Females, n (%)	13 (48%)
Education (years), mean ± SD	15 ± 3.8
MoCA Score (max 30), mean ± SD	24 ± 1.9
MMSE Score (max 30), mean ± SD	28 ± 1.5
Subjective Cognitive Complaint, n (%)	18 (67%)
VO2max (mL O_2/kg•min)	28.9 ± 8.8
Medical History	
Hypertension, n (%)	21 (78%)
Hypercholesterolemia, n (%)	14 (52%)
Diabetes, n (%)	7 (26%)
Previous cerebrovascular event, n (%)	5 (19%)

Parkwood Study – Interim Results

Significant improvements in memory were observed following 24-weeks of DAE training



Parkwood Study – Interim Results

Significant improvements in single- and dual-task gait performance were observed following 24-weeks of DAE training

	Baseline	12-weeks	24-weeks	95% CI	*p*
Gait Characteristics					
Single-task					
gait speed (m/sec)	1.02 ± .17	1.1 ± .18	1.1 ± .15	[-.14, -.04]	.036
step length (cm)	59.4 ± 7	62.7 ± 7	62.1 ± 6	[-4.6, -.7]	.006
step length variability (CoV)	3.9 ± 2.3	3.5. ± 1.7	3.8 ± 2	[-.9, 1.1]	1.0
Dual-task (serial 7's)					
gait speed (m/sec)	0.82 ± .24	0.85 ± .26	0.90 ± .24	[-.13, -.02]	.005
step length (cm)	53.5 ± 8	55.8 ± 9	57.1 ± 8	[-5.7, -1.5]	.001
step length variability (CoV)	5.2 ± 2.5	5.3 ± 2.4	5.4. ± 2.9	[-1.8, 1.4]	1.0

**All data is presented as mean ± SD*

CCAA Pilot RCT

CCAA Study (July 2012 – May 2014)

Population:

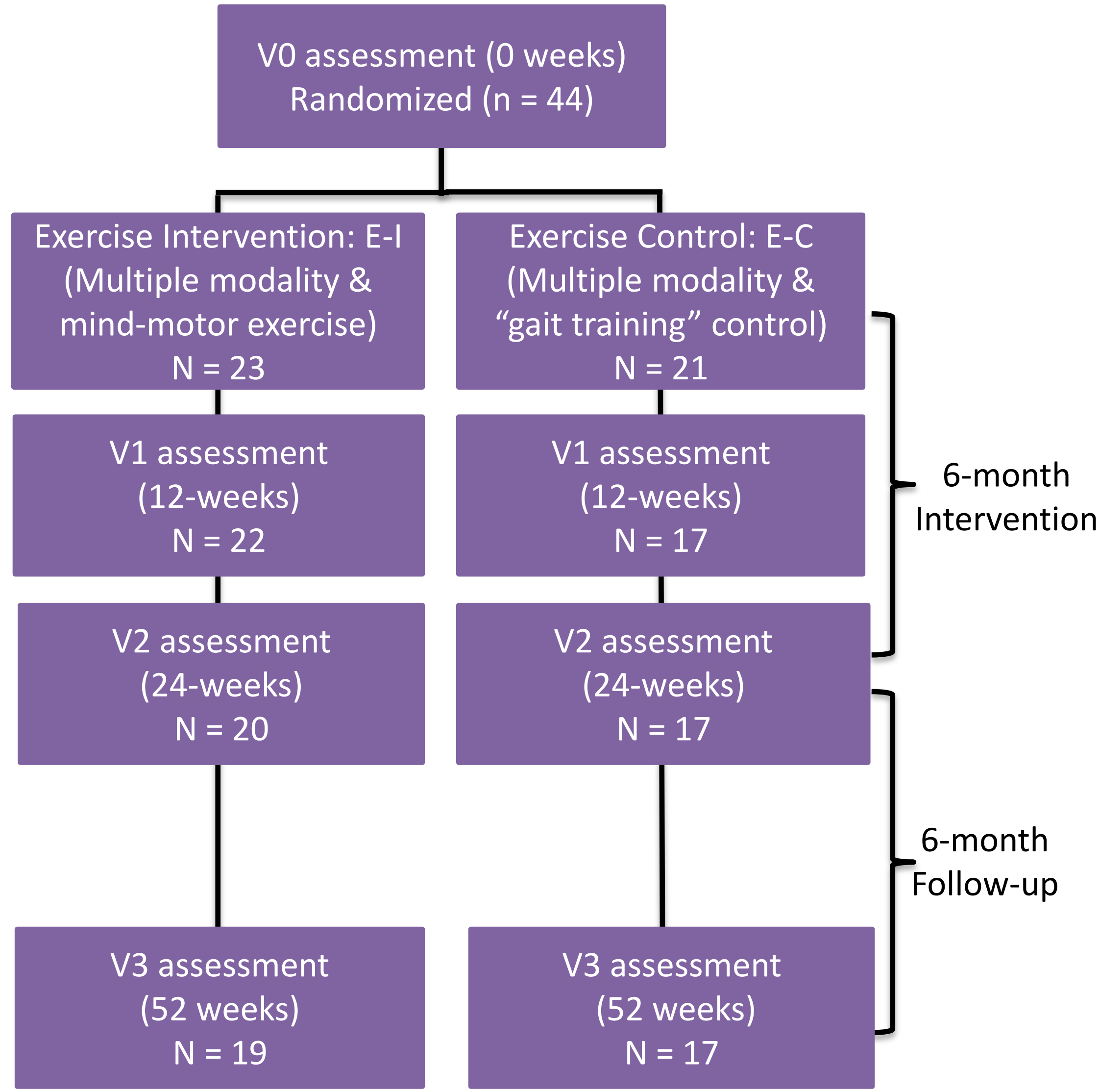
- Community-dwelling older adults (55+) without dementia

Design:

- Single-blind RCT (pilot)
- Group-based
- N= 44 randomized

Outcomes:

- Executive function (1°)
- Other cognitive, mobility and vascular measures (2°)



CCAA Study – Intervention

Both Groups:

- Accumulate a minimum of 150 minutes of structured exercise/week, of which at least 120 minutes is from the CCAA combined classes.
- Take part in 45 minutes of Square Stepping Exercise (SSE) each week (beginner protocols only).

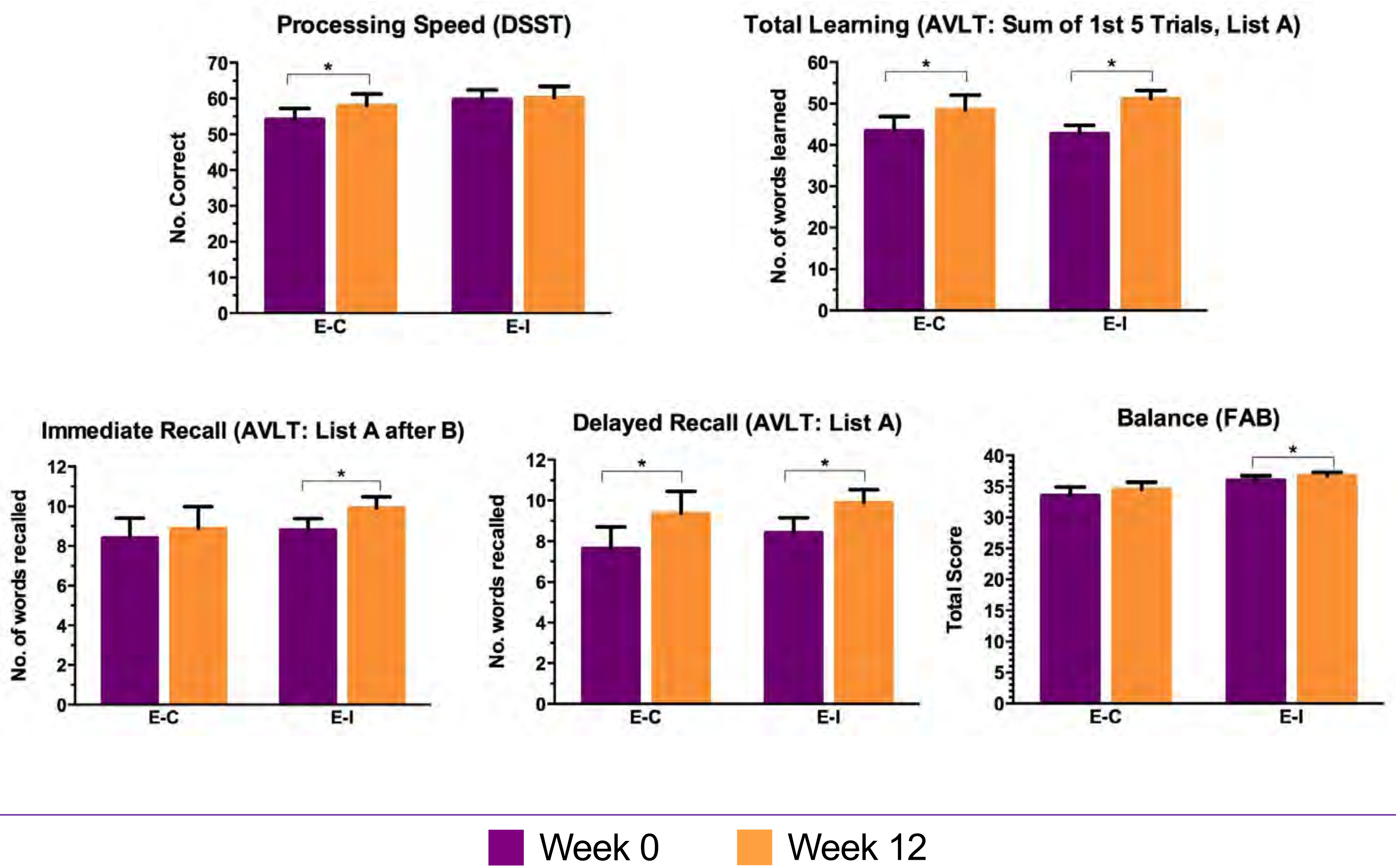
Exercise Intervention Group:

- Also answer cognitively challenging questions while doing SSE (e.g., naming objects from categories; arithmetic)

CCAA Study - Participant Characteristics

	E-C (n = 21)	**E-I (n = 23)**
Age, mean (SD), y	74.5 (7.0)	72.6 (7.4)
Female sex, No. (%)	15 (71.4)	15 (65.2)
Education, mean (SD), y	15.8 (2.3)	17.1 (2.6)
Memory worse, No (%)	11 (52.4)	13 (56.5)
MMSE score, mean (SD)	28.9 (1.3)	28.7 (1.0)
MoCA score, mean (SD)	24.7 (1.7)	25.1 (2.1)
Fitness ($_p$VO2max), mean (SD)	27.6 (10.3)	27.8 (8.6)
Body mass index, mean (SD)	27.2 (3.9)	27.7 (4.4)
Former smoker, No. (%)	10 (47.6)	13 (56.5)

CCAA Study: 3-Month Results



Woodstock RCT

Woodstock Study (Feb 2014 →)

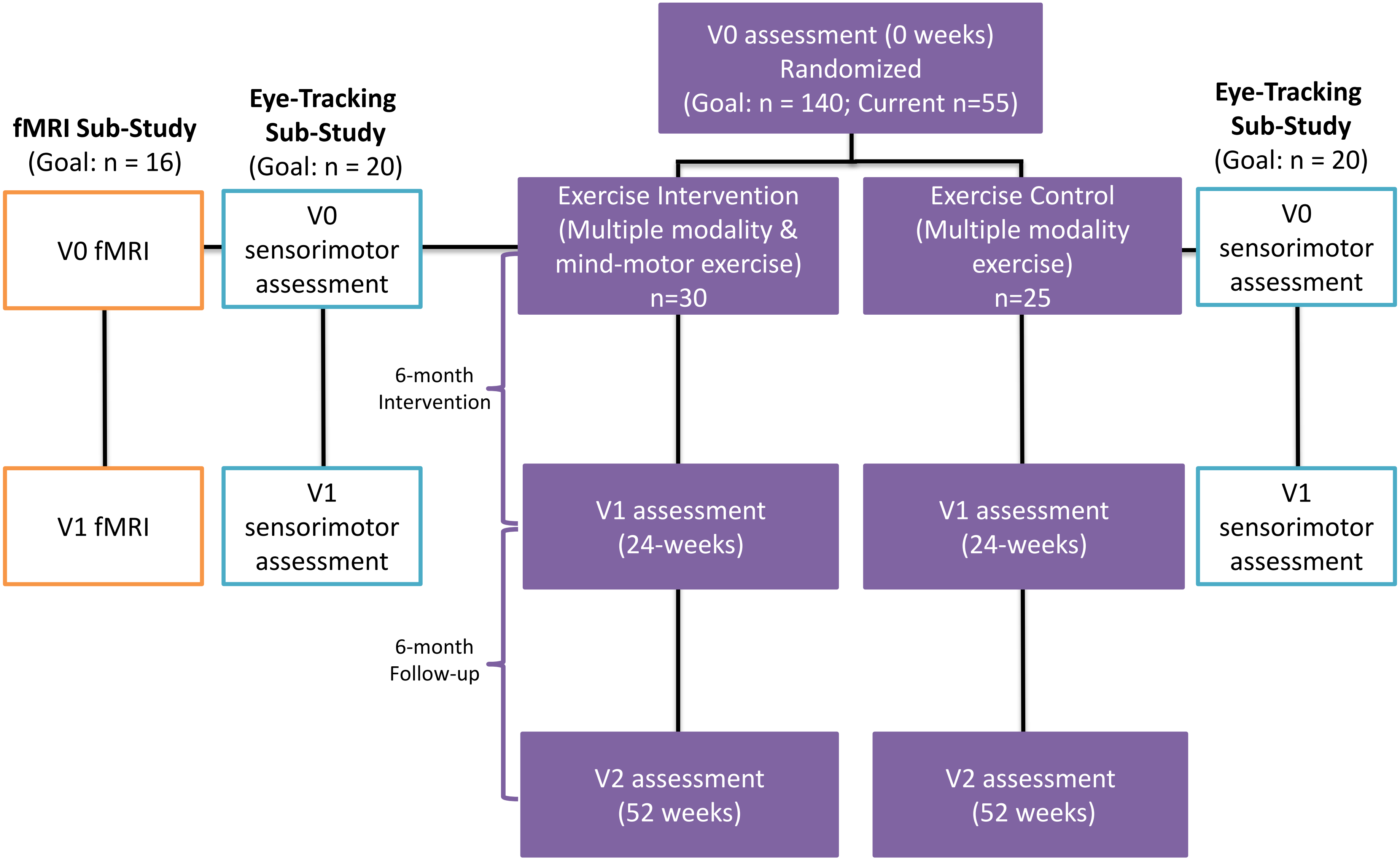
Population:
- Community-dwelling older adults (55+), with self-reported cognitive complaints but no dementia

Design:
- Single-blind RCT; Group-based
- Exercise Control (multiple-modality) vs. Exercise Intervention (multiple-modality + mind-motor)

Outcomes:
- Global cognitive functioning (1°)
- Specific cognitive domains, mobility and vascular (2°)

Intervention:

Woodstock Study



Take Home Message

- With the global population aging, there is a growing urgency to identify the MOST effective strategies to prevent cognitive decline.

- Evidence is continuing to build – some evidence for AE, RT, combined AE + cognitive training, simultaneous cognitive-physical training...but more high-quality studies needed!
  - In 2011, an expert panel concluded that there was insufficient evidence that a specific program of exercise and/or cognitive training can prevent cognitive decline (Daviglus et al., 2011)

- Similar to conclusions drawn by the MAX trial (Barnes et al., JAMA Intern Med 2013), it may be the **amount of activity** rather than the type that is most important for brain health.

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