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Research Article

Yoga Training Impacts Physical Function 12 Months Post Intervention for Care Partners of those with Mild Cognitive Impairment

Melanie J. Chandler [1, †, *], Michelle Graff Radford [1, †], Pauline Lucas [2, †], Dona E.C. Locke [2, †], Julia Crook [1, †], Colleen Ball [1, †], Maria Caselli [2, †], Angela Lunde [3, †], Vaishali Phatak [4, †], Glenn E. Smith [5, †]

1. Mayo Clinic Florida, 4500 San Pablo Rd, Jacksonville, FL, USA; E-Mails: chandler.melanie@mayo.edu; graffradford.michelle@mayo.edu; crook.julia@mayo.edu; ball.colleen@mayo.edu
2. Mayo Clinic Arizona, 13400 E. Shea Blvd., Scottsdale, AZ, USA; E-Mails: lucas.pauline@mayo.edu; locke.dona@mayo.edu; caselli.maria@mayo.edu
3. Mayo Clinic Minnesota, 200 1st St. SW, Rochester, MN, USA; E-Mail: lunde.angela@mayo.edu
4. University of Nebraska Medical Center, 988425 Nebraska Medical Center, Omaha, Nebraska, USA; E-Mail: vaishali.phatak@unmc.edu
5. University of Florida, 1225 Center Dr. Rm 3154, Gainesville, FL, USA; E-Mail: glennsmith@phhp.ufl.edu

† These authors contributed equally to this work.

* **Correspondence:** Melanie Chandler; E-Mail: chandler.melanie@mayo.edu

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Abstract

Physical exercise has been demonstrated to help maintain cognition in people with Mild Cognitive Impairment (pwMCI). We previously demonstrated yoga's benefit in maintenance of memory related activities of daily living in pwMCI. Our research also has shown yoga helps sustain positive psychological well-being of care partners at 12 months. In this analysis, we

sought to examine the impact of yoga training on physical performance in pwMCI and their care partners. In this multisite, randomized clinical trial, we enrolled 272 patients meeting National Institute on Aging–Alzheimer's Association criteria for MCI and a care partner. The intervention program was modeled on the Mayo Clinic HABIT Healthy Action to Benefit Independence and Thinking® program. Of 5 possible interventions (memory compensation training, computerized cognitive training, yoga, support group, and wellness education), 1 of 5 interventions was randomly selected to be withheld for each intervention group. This randomization allowed for the examination of the impact of receiving yoga or no yoga on physical functioning [as measured by the Short Physical Performance Battery (SPPB)] up to 1 year post intervention, as well as the comparative effectiveness on physical functioning of the various interventions. There was a general pattern of physical decline on the SPPB over the year in pwMCI, regardless of yoga training (yoga vs. no yoga d=0.06, p=0.79). Among care partners, those who received yoga had better physical function at 12 months compared to those who did not (d=0.39 points, p=0.041). While not reaching statistical significance, yoga training tended to have a greater effect on SPPB than computerized cognitive training (d = 0.46 points, p = .063) or wellness education (d = 0.42 points, p =.088). Participation in yoga had a positive impact on physical performance outcomes at 12 month follow-up for care partners, but did not counteract general physical decline in pwMCI.

Keywords
Behavioral interventions; caregiver; cognitive intervention; MCI; nonpharmacologic interventions; patient preferences

1. Introduction

There is a well-established literature supporting the benefits of physical exercise for cognitive health in aging [1]. Physical exercise has been shown to reduce the risk of dementia [2], and improve cognitive function in older adults with Mild Cognitive Impairment (MCI) or dementia [3]. Much of this research has focused on the benefit of cardiovascular activity.

There is growing evidence of the many health benefits of yoga. Yoga is a mind-body practice that combines asanas (poses) with breathing and mindfulness/meditation practices. As examples, yoga has been shown to reduce depression [4] and anxiety/stress [5] in all age groups, as well as improve quality of life and sense of well-being in older individuals [6]. Improvements in psychological outcomes such as optimism, quality of life, stress, resilience, and mood have been reported in randomized controlled trials of yoga in persons with MCI (pwMCI) [7] or multicomponent mindfulness-meditation interventions that included yoga. [8, 9]

In terms of cognitive function in normal aging, yoga was found to improve executive function and processing speed in those over age 60 in a meta-analysis of 41 studies of mind-body exercises (including yoga, Tai Chi, or Qigong) [10]. In MCI, meta-analysis of existing data suggests mind-body exercises (including tai chi, yoga, and qigong) may benefit in overall cognition, and specifically in attention, short-term memory, executive function, and visuospatial function [11]. A further review

suggests yoga may be particularly helpful in benefitting attention, processing speed, and verbal memory [12].

In our own previous comparative outcomes research, yoga, more than cognitive rehabilitation, computerized cognitive training, support groups, or wellness education, lead to better activities of daily living (ADL) function at 12 months [13] and 18 months for pwMCI [14]. Caregiver partners who participated in yoga also experienced better mood and less anxiety and caregiver burden at 12 months [15]. Mindfulness-based stress reduction techniques, including yoga, may be helpful with stress-related problems such as anxiety and depression in caregivers, but the number of quality of studies has been low to date [16].

In terms of physical function, multiple studies have shown that yoga practice improves physical mobility and balance in those over age 60 [17]. Improvements in physical function, including strength, muscle endurance, balance, and flexibility have been reported in small, non-comparison group trials of dementia patients in care facilities [18, 19], However, not all studies have shown physical benefit from yoga in dementia patients [20]. One study reported reduced fall risk in patients with MCI after a yoga intervention [21]. Otherwise, there have been no studies looking at the physical function outcomes of yoga for pwMCI or their caregivers that we know of to date. Thus, in this report, we examined the impact of participation in a 10 day yoga training program and subsequent booster sessions on physical function of pwMCI and their care partners up to 12 months post training. We hypothesized that those trained in yoga would do better on tasks of motility, balance, and speed than those who experienced other behavioral interventions, but not yoga training.

2. Materials

This study was part of a larger comparative effectiveness of behavioral interventions in MCI trial that also examined the impact of the other components of Mayo Clinic's HABIT Healthy Action to Benefit Independence & Thinking® Program, including: compensatory cognitive rehabilitation with the Memory Support System (MSS) [22], computerized cognitive training (CCT) [23], Wellness Education, and Support Groups. Full details of the study protocol and recruitment have been reported previously [24].

Unlike previous publications from this larger project, this study did not seek the comparative effectiveness of multiple interventions on a specified outcome. In contrast to other studies where any of the interventions may have impacted an outcome, for example, quality of life [13], only yoga was anticipated to impact physical functioning. As such, in this report, we compared those who were randomized to receive yoga to those who did not.

2.1 Participants

Between September 2014 and August 2016, we recruited 272 dyads consisting of a pwMCI and partner through clinical services at Mayo Clinic in campuses in Rochester, Minnesota; Scottsdale, Arizona; and Jacksonville, Florida; as well as at the University of Washington in Seattle, Washington. Eligible study participants were diagnosed with amnestic MCI, which could be either"single-domain" where the cognitive impairment was solely memory loss or "multi-domain" where memory was affected plus at least one other cognitive domain (language, visuospatial, or executive function) [25]. Inclusion criteria comprised a Clinical Dementia Rating [26] of 0.5 or lower, not taking or stable on

nootropic medication for > 3 months, fluent in English, and attendance with a cognitively unimpaired (Mini-Mental Status Examination [27] score >24) care partner with at least twice-weekly contact with the pwMCI. Exclusion criteria included current participation in another treatment-related clinical trial or major auditory, visual, or motor impairment impacting ability to participate in the program. PwMCI completed the Dementia Rating Scale-2 [28] as a measure of general cognitive function at baseline. All participants provided written informed consent.

2.2 Intervention, Randomization, and Outcomes

Subjects with MCI were randomly assigned to receive yoga or not as part of a multicomponent behavioral intervention program. They also randomly received 3 of the other possible 4 interventions (MSS, CCT, Support Groups, or Wellness Education). If not randomized to yoga, they received all 4 of the other interventions. Each of these components was originally chosen on a theoretical basis because each had support individually in the literature for effectiveness compared to no-treatment controls across a variety of outcomes (eg, cognitive functioning, QOL, mood, partner burden) [29, 30].

The intervention occurred for 10 business days in a row over 2 weeks; one hour was allotted for each intervention each day, for a 4 hour day. A 1-day booster session was provided at 6 months and 12 months post initial training delivery, and included a refresher for each of the 4 interventions originally provided (described further in our previous publication) [24] Each group session consisted of up to 20 dyads. The randomization assignment was per group session so that all members of the group were receiving the same 4 out of 5 possible interventions (Yoga, MSS, CCT, Support Groups, or Wellness Education) to help account for treatment diffusion. Group assignment was concealed from participants until they arrived for their first day of the program. Those collecting the physical outcome data were blind to group randomization.

The intervention utilized Hatha yoga. Classes included poses (asanas), breathing exercises (pranayama), meditation and relaxation exercises, and closed with affirmation or gratitude sharing. The sessions used an armless, sturdy chair placed on top of a yoga mat. We were able to adapt the yoga practice as needed so that deconditioned participants or those with imbalance could sit on chairs for some asanas (poses) and use the chair for support for balance during other standing poses and for other parts of the sequence. Our instructors had at least 200 hours of training and were Yoga Alliance certified. The appropriately sequenced yoga practice met the American College of Sports Medicine recommendation for older adults for muscle strengthening and flexibility.

Most clinical trials of yoga include group classes during the delivery phase supported by home practice in the maintenance phase. As such we provided a customized yoga DVD to participants who randomized to yoga training and encouraged its continued use and practice after the program. The DVD included sections on the following: poses, modifications, benefits, breathing, and meditation practices. Participants and partners were encouraged to strive for 150 minutes per week of physical activity (not limited to just yoga). We collected follow-up adherence questionnaires about time spent in physical activity at 6 and 12 months post intervention. Participants and partners whom engaged in at least 150 minutes of physical activity per week were assigned to the post-intervention 'adherent' category, <60 min per week were assigned to the 'non-adherent' category, and those who fell between the required standards for adherent and non-adherent were assigned to the 'indeterminate' category [31].

All participants (pwMCI and the care partners) completed the Short Physical Performance Battery [32] (SPPB) at baseline, treatment end, and 12 months post-intervention. The SPPB includes a timed 400-meter walk (speed), standing with feet positioned side by side, semi-tandem and full tandem stance (balance), and a timed arms-folded rise from seated-to-standing x 4 (strength). Each section (speed, balance, strength) was worth 4 possible points for a maximum total score of 12. Higher scores indicate better physical performance. All outcome data was collected prior to the commencement of the 12 month booster session.

2.3 Statistical Analysis

Longitudinal mixed-effects regression models, separately for pwMCI and care partners, were used to evaluate the impact of yoga on SPPB scores at 12 months using data baseline, end of treatment, and 12-month follow-up. Baseline SPPB score was modelled with fixed effects for age, sex, and site. The mean change in SPPB score was modelled with fixed effects for study arm (no CCT, no MSS, no support groups, no wellness, and no yoga), age, and sex. Person-specific random effects were included to account for multiple measurements over time. For our primary aim of evaluating the impact of yoga versus no yoga on SPPB score at 12 months, we focused on estimation of the difference (d) between the average of the means in the four arms that included yoga ($\mu1 + \mu2 + \mu3 + \mu4)/4$ and the mean in the no yoga arm ($\mu5$) by expressing it as a linear contrast: $d = 0.25\mu1 + 0.25\mu2 + 0.25\mu3 + 0.25\mu4 - 1\mu5$. We constructed 95% confidence intervals (CI) using the profile likelihood method and corresponding likelihood ratio tests. We adjusted for multiple testing with Westfall stepwise adjustment. Effect sizes (ES) were expressed as multiples of the baseline standard deviation of the SPPB score. Analyses were performed using R statistical software, version 3.2.3 (R Foundation for Statistical Computing).

The conduct of the study was reviewed and approved by the Institutional Review Boards at Mayo Clinic (14-000885) and the University of Washington (49235). CONSORT reporting guidelines were followed. Trial is registered at ClinicalTrials.gov, identifier: NCT02265757.

3. Results

We enrolled 272 participants in this study. Recruitment information has been described in detail elsewhere [13]. All but 44 participants completed the study through 12 month follow up (83.8% retention). There was no significant difference in attrition between those randomized to yoga (82.4% retention) or no-yoga (89.3% retention). There were no meaningful differences in demographics or general cognitive status across sites or groups at baseline (Table 1). No adverse effects were detected as a result of this study.

Table 1 Demographic overview for pwMCI and their care partners.

	No Yoga	**No CCT**	**No Wellness Education**	**No Support Groups**	**No MSS**
pwMCI	**(n=56)**	**(n=54)**	**(n=52)**	**(n=53)**	**(n=57)**

Age, Mean (SD)	74.3 (7.3)	75.8 (8.0)	76.7 (7.3)	75.1 (7.3)	74.1 (7.9)
Education, Median (range)	17 (9-20)	16 (12-20) [1]	16 (12-20)	16 (10-20)	16 (6-20)
Male, No. %	34 (61%)	33 (61%)	30 (58%)	32 (60%)	31 (54%)
Race non-white, No. (%)*	3 (5%)	1 (2%)	1 (2%)	2 (4%)	5 (9%)
DRS-2 total, Mean (SD)	130.1 (8.7) [7]	127.5 (9.3)	128.0 (8.0) [1]	130.9 (7.6)	129.9 (8.8) [2]
Care Partner	**(n=56)**	**(n=54)**	**(n=52)**	**(n=53)**	**(n=57)**
Age, mean (SD)	70.9 (9.5)	70.9 (9.5)	70.3 (10.4)	71.6 (8.8)	67.6 (12.2)
Male, No. (%)	18 (32%)	15 (28%)	18 (35%)	18 (34%)	16 (29%)[1]
Partner relationship, No. (%)					
Spouse or partner	52 (93%)	44 (81%)	42/50 (84%)	48 (91%)	43/55 (78%)
Son or daughter	2 (4%)	6 (11%)	4/50 (8%)	3 (6%)	8/55 (15%)

Note: Number in superscript reflects missing case numbers in that data cell compared to the overall group sample. Abbreviations: CCT = computerized cognitive training; MSS =Memory Support System; pwMCI = persons with MCI; N = number of persons with available data; SD = standard deviation. Higher scores translate to better physical performance.

Table 2 shows a summary of the baseline patient and care partner SPPB total score according to study arm. There were no meaningful differences in baseline SPPB total scores between study arms for pwMCI (likelihood ratio p = 0.46) or care partners (likelihood ratio p = .63). A summary of the raw changes in SPPB scores from baseline to 12 months is also included in Table 2.

Table 2 Short Physical Performance Battery total scores at baseline and change at 12 months.

	No Yoga	**No CCT**	**No Wellness Education**	**No Support Groups**	**No MSS**
No. of dyads	56	54	52	53	57
pwMCI					
Baseline	N=55	N=51	N=47	N=52	N=50
Mean (SD)	10.38 (1.74)	10.20 (1.94)	9.87 (1.68)	10.13 (1.78)	10.60 (1.56)
Change at EOT	N=52	N=47	N=34	N=50	N=46
Mean (SD)	0.21 (1.11)	-0.30 (1.30)	0.12 (1.55)	0.36 (1.14)	-0.24 (0.97)
Change at 12 mo	N=39	N=33	N=34	N=36	N=35

Mean (SD)	-0.74 (1.76)	-0.91 (1.70)	-0.71 (1.80)	-0.06 (1.55)	-0.86 (1.31)
Care Partner					
Baseline	N=53	N=52	N=46	N=53	N=51
Mean (SD)	10.85 (1.38)	11.00 (1.39)	10.76 (1.25)	11.04 (1.22)	11.14 (1.39)
Change at EOT	N=48	N=49	N=31	N=52	N=47
Mean (SD)	0.06 (1.16)	0.08 (0.95)	0.03 (1.66)	0.40 (0.91)	-0.02 (1.13)
Change at 12 mo	N=38	N=33	N=31	N=34	N=37
Mean (SD)	-0.39 (1.53)	-0.09 (1.01)	0.10 (1.42)	-0.21 (0.84)	-0.16 (1.34)

Abbreviations: CCT = computerized cognitive training; MSS =Memory Support System; pwMCI = persons with MCI; N = number of persons with available data; SD = standard deviation; EOT = end of treatment. Higher scores translate to better physical performance. The number of pwMCI or care partners for whom the data was available did not always equal the total number of dyads in an intervention due to missing data.

In comparing SPPB total score between those randomized to the no yoga arm and those randomized to one of the other four arms that included yoga (Figure 1), there were no significant differences at end of treatment for yoga versus no yoga in pwMCI (Effect Size -0.17, 95% CI -0.40 to 0.07, P=0.16) or care partners (Effect Size -0.04, 95% CI -0.29 to 0.21, P=0.76). By 12-months post intervention, yoga did not impact SPPB total score in MCI patients (Effect Size 0.04, 95% CI -0.23 to 0.30, P=.79), but yoga training maintained SPPB total scores in their care partners at 12 months compared to a decline in the no yoga group (Effect Size 0.29, 95% CI 0.01 to 0.57, P=0.04).

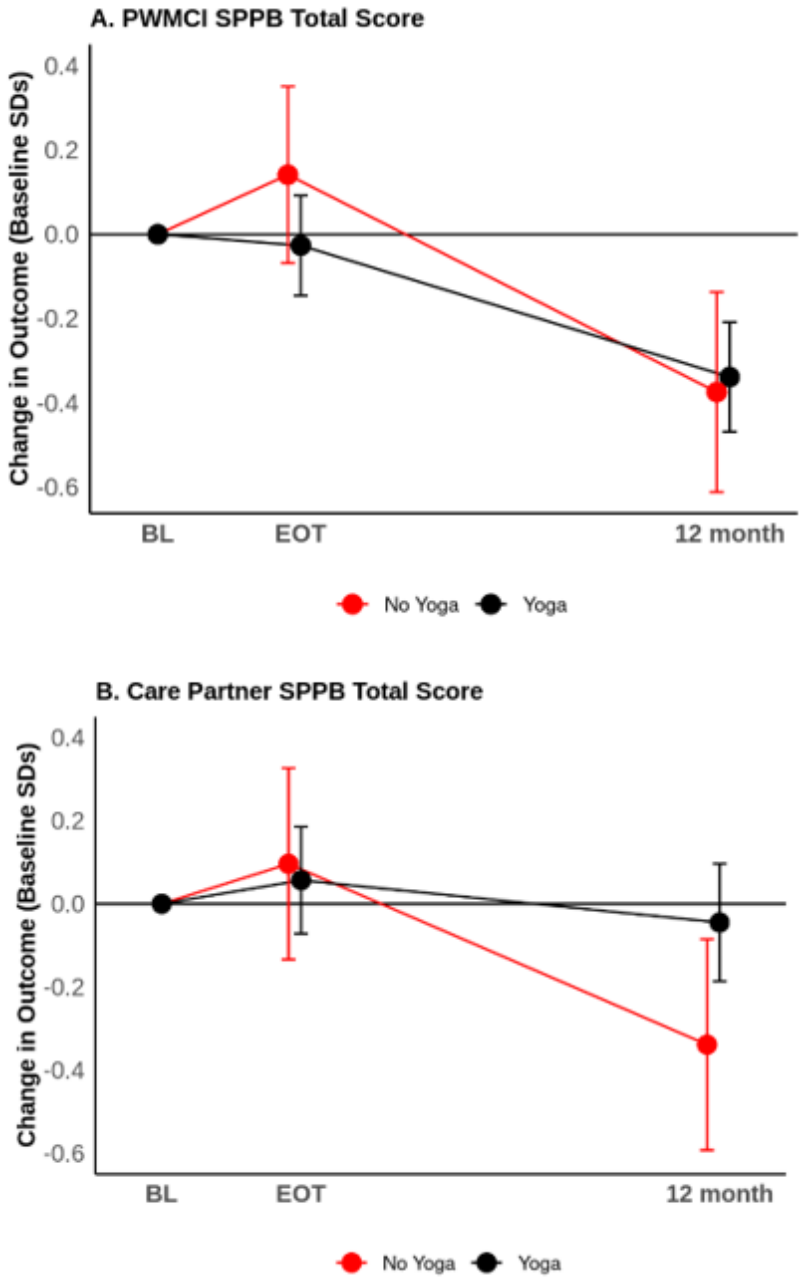

Figure 1 Effect sizes for change in Short Physical Performance Battery score for yoga vs. no yoga groups. Abbreviations: BL = Baseline; EOT = End of Treatment. Effect sizes were estimated from longitudinal mixed-effects regression models, in which a 1-unit increase in the effect size corresponded to a 1-SD improvement in outcome. Baseline SDs were 1.749 for pwMCI SPPB total score and 1.325 for care partner SPPB total score. Error bars represent 95% confidence intervals for the effect sizes.

Comparisons of the SPPB total score between the 5 study arms are shown in Figure 2 as well as Tables 3 (patients) and 4 (care partners). We found that CCT and wellness education had more of a positive effect on SPPB total score compared to support groups for our MCI patients, however these associations were not statistically significant after adjustment for multiple testing (Table 3). Among the care partners enrolled in our study, there were not any statistically significant differences in

SPPB total score between the five components, however it is worth noting that yoga had the largest effect size in comparison to all other interventions (Table 4).

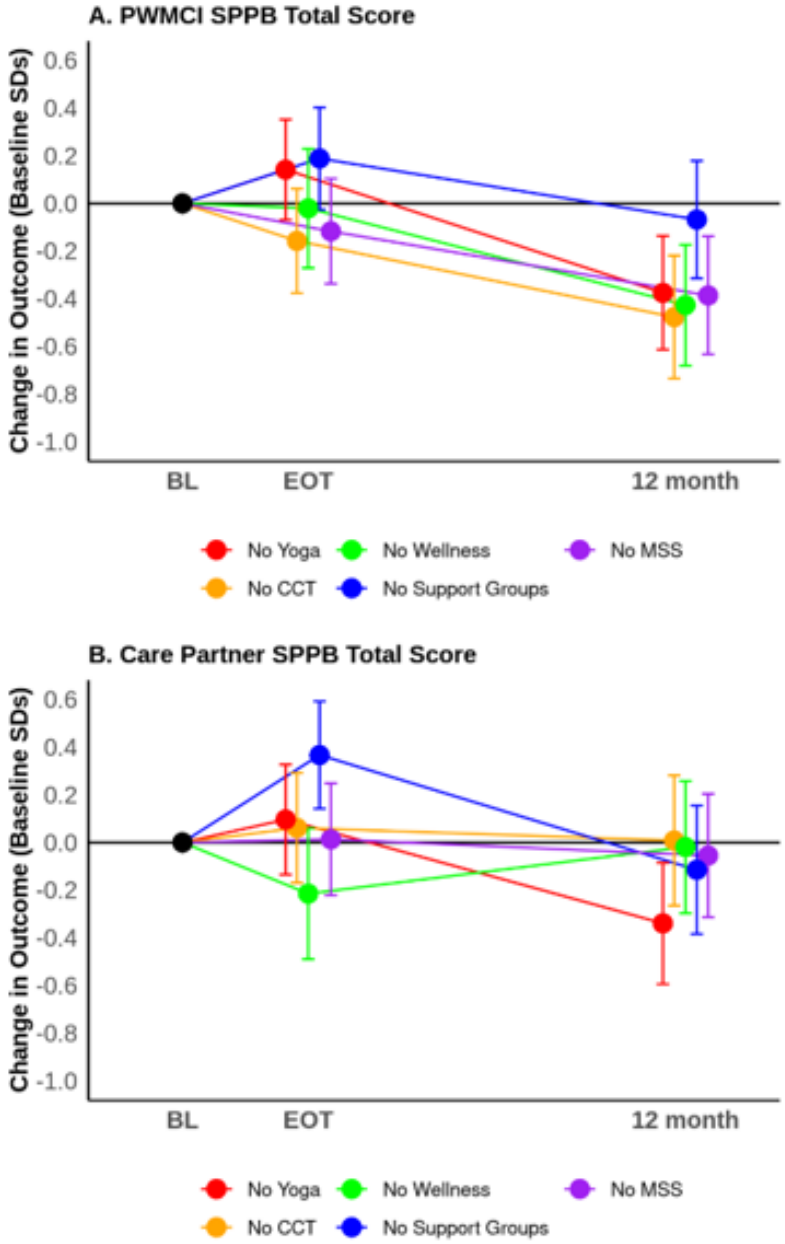

Figure 2 Comparative effectiveness of interventions on Short Physical Performance Battery score. Abbreviations: BL = Baseline; CCT= computerized cognitive training; EOT = End of Treatment; MSS= memory support system. Error bars represent 95% confidence intervals for the effect sizes.

Table 3 Comparative Incremental Effect on Patient SPPB Total Score at 12 Months for Pairs of HABIT Components.

Component	Compared to	Difference in SPPB at 12 mo (95% CI), points	Effect Size (95% CI)	Original *P* value	Adjusted *P* value
CCT	Support	0.71 (0.10 to 1.33)	0.41 (0.06 to 0.76)	0.022	0.15
Wellness	Support	0.63 (0.02 to 1.23)	0.36 (0.01 to 0.71)	0.043	0.24
MSS	Support	0.56 (-0.04 to 1.16)	0.32 (-0.03 to 0.66)	0.070	0.33
Yoga	Support	0.54 (-0.05 to 1.12)	0.31 (-0.03 to 0.64)	0.074	0.33
CCT	Yoga	0.18 (-0.42 to 0.78)	0.10 (-0.24 to 0.45)	0.56	0.94
CCT	MSS	0.16 (-0.46 to 0.78)	0.09 (-0.26 to 0.44)	0.61	0.95
Wellness	Yoga	0.09 (-0.51 to 0.69)	0.05 (-0.29 to 0.39)	0.77	0.99
CCT	Wellness	0.09 (-0.53 to 0.71)	0.05 (-0.31 to 0.41)	0.78	0.99
Wellness	MSS	0.07 (-0.54 to 0.68)	0.04 (-0.31 to 0.39)	0.82	0.99
MSS	Yoga	0.02 (-0.57 to 0.61)	0.01 (-0.33 to 0.35)	0.95	0.99

Abbreviations: CI = confidence interval CCT = Computerized Cognitive Training, MSS = Memory Support System. To ease interpretation, the two components compared are ordered such that the first component listed has a better estimated mean outcome at 12 months than the second component. Effect size is the difference in mean SPPB score at 12 months expressed as multiples of the baseline standard deviation of the SPPB score. Both original and multiple-test adjusted *P* values are shown.

Table 4 Comparative Incremental Effect on Informant SPPB Total Score at 12 Months for Pairs of HABIT Components.

Component	Compared to	Difference in SPPB at 12 mo (95% CI), points	Effect Size (95% CI)	Original *P* value	Adjusted *P* value
Yoga	CCT	0.46 (-0.02 to 0.94)	0.35 (-0.02 to 0.71)	0.063	0.34
Yoga	Wellness	0.42 (-0.06 to 0.91)	0.32 (-0.05 to 0.69)	0.088	0.41
Yoga	MSS	0.38 (-0.09 to 0.85)	0.28 (-0.07 to 0.64)	0.12	0.48
Yoga	Support	0.30 (-0.18 to 0.78)	0.22 (-0.14 to 0.59)	0.23	0.68
Support	CCT	0.16 (-0.33 to 0.66)	0.12 (-0.25 to 0.50)	0.52	0.92
Support	Wellness	0.13 (-0.37 to 0.63)	0.10 (-0.28 to 0.47)	0.62	0.95
MSS	CCT	0.08 (-0.40 to 0.57)	0.06 (-0.30 to 0.43)	0.74	0.98

Support	MSS	0.08 (-0.40 to 0.56)	0.06 (-0.31 to 0.43)	0.75	0.98
MSS	Wellness	0.05 (-0.44 to 0.54)	0.04 (-0.33 to 0.41)	0.85	0.98
Wellness	CCT	0.04 (-0.47 to 0.54)	0.03 (-0.35 to 0.41)	0.89	0.98

Abbreviations: CI = confidence interval, CCT = Computerized Cognitive Training, MSS = Memory Support System. To ease interpretation, the two components compared are ordered such that the first component listed has a better estimated mean outcome at 12 months than the second component. Effect size is the difference in mean SPPB score at 12 months expressed as multiples of the baseline standard deviation of the SPPB score. Both original and multiple-test adjusted *P* values are shown.

4. Discussion

MCI is a syndrome that impacts not just those diagnosed with the disorder, but also their loved ones. Here, we examined the impact of Hatha yoga training on the physical functioning of both pwMCI and their care partners out to 12 months after the intervention. Our previous work suggested that yoga training was the most effective of five potential interventions offered (including compensatory calendar training, computerized cognitive training, wellness education, support groups, and yoga) in maintenance of memory related activities of daily living out to 12 and 18 months [13, 14]. In this study, there was no significant improvement in physical functioning for pwMCI 12 months after yoga training (or any of the other interventions). Rather, pwMCI experienced a gradual decline in physical functioning over the 12 month follow-up, regardless of intervention group. This is consistent with prior reporting that a physical decline often co-occurs with the cognitive decline experienced in many with MCI [33, 34]. Hatha yoga training does not appear to overcome this natural decline.

Yoga training did maintain care partner physical functioning up to the 12 month follow up period of this study when compared to other groups not receiving yoga who experienced physical decline. This is the first report of the positive impact of yoga training on physical function performance in care partners of which we are aware. There have been prior reports of emotional well-being benefits to caregivers from yoga training [35]. In this same study cohort, we previously reported that yoga benefited mood, lowered anxiety, and lowered caregiver burden in care partners up to 12 month [15]. Unique to the current study, yoga training appears to not just benefit the psychological wellbeing of care partners, but also their physical well-being.

4.1 Limitations

Our Hatha yoga sessions were comprised of a combination of poses (asanas), breathing exercises (pranayama), meditation/relaxation exercises, and gratitude practice. We cannot determine from this current study which aspects of the Hatha yoga training were particularly beneficial to our care partners. However, it is reasonable to speculate that the asana practices that encouraged balance, flexibility, and core strength likely contributed to the physical function benefit.

While we encouraged yoga maintenance post training, we also emphasized engagement in physical activity in general. Our adherence measures tracked overall physical activity and not specifically adherence to yoga. We did not collect SPPB data at the 6 month follow-up session, and thus cannot speak to the impact of yoga training on physical function at that time point. At 12

month follow-up, 40.0% of pwMCI and 45.9% for partners were fully "adherent" to physical activity (> 150 minutes a week), and 82.4% of pwMCI and 87.7% of partners were exercising at least 60 minutes a week. However, individuals may have engaged in yoga, a different physical activity, or a combination of the two in the post intervention maintenance period. This limits our ability to speak to how much maintenance of yoga alone after the initial training period impacted physical function. Paper and pencil adherence questionnaires further are subject to reporting bias of recent physical activity. This potential bias is compounded in our study of pwMCI with memory impairments, and, at times, care partners reported on both the pwMCI and themselves. It is important to note that participants and care partners were only trained in yoga during the intervention regardless of the weakness of our adherence measure to capture their yoga-specific adherence. Further, yoga may have been more physically beneficial to pwMCI if more support of its continued practice was provided in the maintenance year following training delivery.

5. Conclusions

Yoga does not appear to improve physical function of patients with MCI, but yoga may maintain physical function of their care partners.

Author Contributions

Drs. Chandler, Smith, and Locke were involved in the development of the research protocol, served as Mayo Clinic site PIs, and led patient recruitment during this study. Dr. Phatak served as site PI and recruiter at the University of Washington. Dr. Crook and Ms. Ball served as statistical support and led writing of the statistical methods, results, and tables/figures. Dr. Lucas, Ms. Graff-Radford, Ms. Lunde, and Ms. Caselli were yoga instructors who helped inform the yoga programming and implementation. While Dr. Chandler took the lead role in writing the manuscript, all authors contributed to its final editing and approved the final draft.

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Competing Interests

The authors have declared that no competing interests exist.

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