



Original Research Article (Clinical)

Efficacy of Integrated Yoga and Ayurveda *Rasayana* on cognitive functions in elderly with mild cognitive impairment: Non-randomized three-arm clinical trial

Shivaji Chobe ^a, Sanjib Kumar Patra ^b, Meenakshi Chobe ^b, Kashinath Metri ^{b,*}

^a Division of Yoga and Life Sciences, Swami Vivekananda Yoga Anusandhan Samsthan (SVYASA University), #19, Eknath Bhavan, Gavipuram Circle, KG Nagar, Bengaluru, 560019, India

^b Department of Yoga, Central University of Rajasthan, Bandar Sindri, NH-8, Kishangarh Ajmer, 305817, India

ARTICLE INFO

Article history:

Received 9 March 2020

Received in revised form

21 October 2020

Accepted 17 November 2020

Available online 19 December 2020

Keywords:

Memory

Attention

Cognition

Brahmi

Meditation

Pranayama

ABSTRACT

Background: Yoga and Ayurveda are ancient sciences which emphasize on the cure of disease and the proportion of health. Both sciences are also known to reduce the aging process and are helpful in aging-related disorders.

Objective: This study investigates the effects of Yoga and Ayurveda *Rasayana* combined intervention on cognition among the elderly with mild cognitive impairment.

Materials and Methods: Seventy-two elderly persons (average age 63.3 ± 6.44 years) received Ayurveda *Rasayana* (AR) ($n = 23$) or Integrated Yoga (IY) ($n = 25$) or combined (IY plus AR) intervention ($n = 24$) for eight weeks. AR treatment consisted of *Brahmi ghrita*, and IY consisted of *asana*, *pranayama*, meditation, and relaxation techniques. Executive function, verbal fluency, attention, processing speed, short-term and working memory, and learning and verbal memory were assessed at the baseline and after eight weeks.

Results: Within-group analysis shows that there was a significant time main effect ($p < 0.05$) in all cognitive measures in the three groups (IY, AR, and IY plus AR) except Digit backward test. Bonferroni post hoc test shows a significant difference in pre to post in all variables. In the between-group analysis, there was a substantial group difference for Rey's Auditory Verbal Learning Test- hits, $F(2,69) = 4.376$ ($P < 0.016$), Rey's Auditory Verbal Learning Test-Average, $F(2,69) = 4.727$ (0.012), Digit backward test, $F(2,69) = 5.766$ (0.005) after eight weeks of intervention.

Conclusion: Both Ayurveda *Rasayana* and Integrated Yoga intervention were found effective in improving cognitive abilities among the elderly with MCI. Combined Ayurveda *Rasayana* and Yoga intervention significantly improved learning, attention, processing speed, and working memory compared to individual response among elderly persons with MCI.

© 2020 The Authors. Published by Elsevier B.V. on behalf of Institute of Transdisciplinary Health Sciences and Technology and World Ayurveda Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

In the last three decades, there is an exponential rise in the elderly population across the globe. In India, the elderly population contributes to 10% of the total population [1]. Aging often comes with multiple physical and mental health challenges. Cognitive decline is one of the common neuro-cognitive conditions among

the elderly. Recent Mexican health and aging study reported that 34% of the elderly population suffers from mild cognitive impairment (MCI) [2]. Cognitive impairment among the elderly varies from mild cognitive decline to a severe form of dementia and Alzheimer's disease [3,4]. The prevalence of cognitive decline among the elderly is reported to vary from 6.7% to 25.2% [5]. Among the elderly, the annual conversion rate of mild cognitive impairment to dementia is 7% [6]. Cognitive impairment in the elderly significantly affects the quality of life and makes them dependent on others for their routine activities. It also contributes to poor mental health and increases the risk of affective disorders such as depression and anxiety disorder [7,8]. Evidence shows that

* Corresponding author.

E-mail: kgmhetre@gmail.com

Peer review under responsibility of Transdisciplinary University, Bangalore.

interventions such as exercise, swimming, active social engagement, and sports activities are associated with decreased risk of cognitive impairment [9].

Yoga is an ancient spiritual science that originated in India. Sage Patanjali codified the yoga practices in the eight limbs or steps. They are self-discipline (*Yama*) and social discipline (*Niyam*), yogic postures (*Asana*), breathing techniques (*Pranayama*), *Pranayama* (sense-withdrawal), *Dharana* (concentration), *Dhyana* (meditation), and *Samadhi* (merging individual consciousness with universal consciousness) [10,11]. Yoga is a popular alternative and complementary medicine. Yoga enhances physical and mental health, and well-being. Scientific studies on Yoga have demonstrated its health-benefiting effects in various neuro-cognitive problems [12]. Yoga has a positive impact on mental health measures. It reduces depression, anxiety, and stress and improves mental well-being [13,14]. Yoga practices also enhance cognitive abilities in diverse populations ranging from children to the elderly [15,16]. Studies on the elderly revealed positive effects of Yoga on age-associated disorders, including neurodegenerative disorders [17,18].

Randomized control trials (RCT) on Yoga have shown significant improvement in memory, attention, and executive function among the elderly population [19,20]. A meta-analysis study of chronic and acute effects of Yoga on cognition suggests that yoga practices are moderately effective in improving cognition among populations of different age groups [21]. Another systematic review on the elderly reported that Yoga-based interventions are effective for improving memory, attention, and executive functions in the elderly [22].

Ayurveda is an Indian system of medicine. Ayurveda prescribes a lifestyle that helps in the promotion of health and prevention of disease [23]. Studies have shown various health benefiting effects of *Ayurveda* medicines in various chronic disease conditions [24,25]. Ayurveda has eight branches and "*Rasayana*" is one among these eight branches. *Rasayana* therapy promotes health and prevents the disease by nourishing and rejuvenating the tissues (*dhatu*). The classical Ayurveda *Rasayana* therapy includes cleansing and rejuvenation protocol which includes procedures called *panchakarma* followed by administration of herbo-mineral or herbal preparation depending on the condition of the individual. According to Ayurveda, *Rasayana* therapy promotes longevity, strength, complexion, memory, intellect and prevents disease. Recent studies on *Rasayana* therapy have revealed that *Rasayana* drugs have anti-inflammatory, anti-cancer, anti-oxidant, and immunomodulation effects. These drugs also promote memory, improve digestion, reduce the aging speed and proper strength, vigor, and vitality [26]. *Rasayana* therapy promotes mental well-being and quality of life [27,28]. Hence, the addition of *Rasayana* therapy may help to make the present health care system more holistic. There are various domains of *Rasayana*, including *Medhya Rasayana* (neuronutrient). *Medhya Rasayana* enhances neuro-cognitive ability through herbal and/or herbo-mineral preparations by retarding brain aging [29–31]. Evidence showed that some of the *Medhya Rasayana* such as *Ashwagandha*, *Brahmi*, *mandukaparni*, *Sankhapushpi*, etc., improve various neurocognitive abilities among elderly persons [32]. Several herbo-mineral and/or herbal preparations are mentioned in *Medhya Rasayana*; *Brahmi* (*Baccopa monnieri*) is one of those [33,34]. Scientific studies on *Brahmi* have demonstrated the various cognitive benefits of *Brahmi*. A meta-analysis on *Brahmi* concluded that it could improve cognitive functions, particularly attention [35]. Administration of *Brahmi* significantly improved memory and learning in the healthy elderly [36]. Another double-blind, randomized control trial on *Brahmi* extract showed age-associated memory improvement in older adults compared to placebo [37].

Cognitive decline is the most common and disabling condition among the elderly that affects the quality of life and general well-being of the elderly. Both Yoga and Ayurveda as an independent intervention are effective in improving cognitive functions among the elderly. However, no previous study has assessed the effect of integrated Yoga and Ayurveda *Rasayana* as a combined intervention on cognitive functions in the elderly with mild cognitive impairment. Hence, the present study intended to investigate the efficacy of Ayurveda *Rasayana* (AR), Integrated Yoga (IY), and combined (IY plus AR) on cognitive measures among elderly persons with mild cognitive impairment.

2. Materials and methods

2.1. Participants

Participants in this study were community-dwelling elderly persons aged >55 to 80 years having mild cognitive impairment.

2.2. Eligibility criteria

Consented elderly individuals (both male and female) with MCI, able to write, read and understand the Hindi / English language were considered for the study. The elderly with a history of chronic neurologic disease, psychiatric diagnosis, previous exposure to Yoga practice, taking any Ayurveda medicine, cholinesterase inhibitors, glutamatergic, and having difficulty in Yoga practice were excluded from the study.

2.3. Settings and design

It was an age, gender, and education matched non-randomized three-armed interventional study. The sample size was calculated based on the previous study "Effect of *kundalini* yoga on MCI- a randomized control trial" using variable immediate recall [38]. The effect size was ' ϵ ' = 0.57, α = 0.05 and Power = 0.95. The calculated sample was thirty-five for each group.

2.4. Ethical considerations

The present study was reviewed and approved by the institutional ethics committee of Swami Vivekananda Yoga Anusandhan Samsthan (SVYASA University). The study was also registered for the clinical trial registry of India with the registration number: REF/2018/07/020945 (B). We obtained informed written consent from all participants before group allocation.

2.5. Recruitment

An announcement was made about the study through an advertisement in the local newspaper. Interested participants were requested to contact through phone/email. A total of 247 elderly were screened for MCI using The Montreal Cognitive Assessment (MoCA) [39]. Thirty-five elderly had exclusion criteria, and 112 had no MCI. One hundred participants fulfilled the study criteria. Of these, three participants declined to participate due to the inconvenient yoga class timings, while nine expressed a dislike towards the ghee-based Ayurveda *Rasayana*. Eighty-eight participants agreed to participate in the study, and they were assigned to one of the three intervention groups (IY = 30, IY plus AR = 28, and AR = 30) after baseline assessment. Group assignment was done on a first-come, first-served basis in IY, IY plus AR, and AR groups. The study was conducted from August 2018 to March 2019 (Fig. 1).

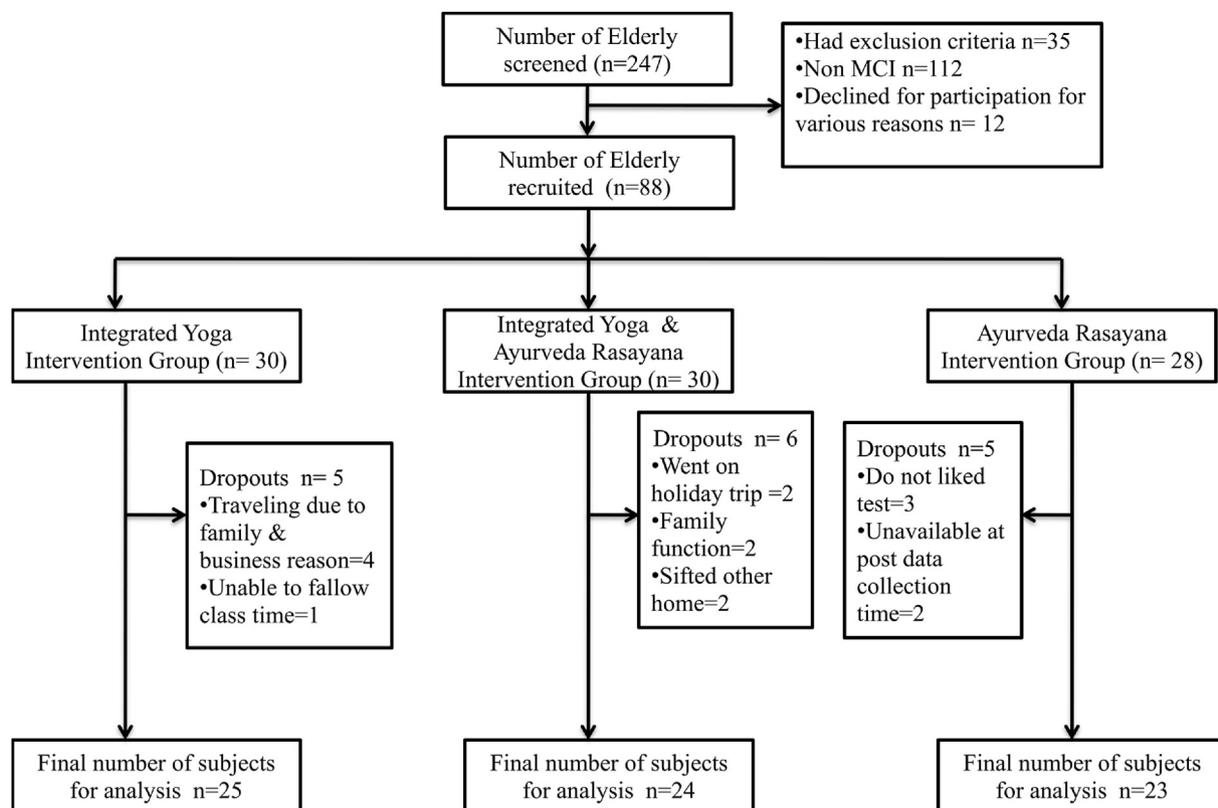


Fig. 1. Recruitment.

2.6. Assessments

All the assessments were performed at baseline and at 8-weeks. A team of a psychologist and two assistants assessed the cognitive measures. The procedures of all the tests were explained clearly to each participant. Participants were asked to come for assessments without having coffee/tea/smoking etc.

Primary outcome measures

Executive function, attention, processing speed, and memory (working and short-term memory) were the primary outcome measures.

Secondary outcome measures

The secondary outcome measures were learning and verbal memory, and verbal fluency.

2.6.1. Screening for mild cognitive decline

All the participants were screened for mild cognitive decline using the MoCA scale which was designed as a rapid screening instrument for mild cognitive dysfunction [39]. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuo-constructional skills, conceptual thinking, calculations, and orientation. It has high test-retest reliability; the interclass correlation coefficient is 0.87. The time to administer the MoCA is approximately 10 minutes. The total possible score is 30 points; a score of 26 or above is considered normal.

2.6.2. Neuropsychological battery

Assessments were conducted by an expert psychologist and his team, who were blind for groups. The average time taken for the completion of the Neuropsychological battery was 50–60 minutes. Data from participants were collected in a quiet room. We offered a

break to the participant if they wished during the assessment. Stroop color-word Task [40] for executive function, Controlled Oral Word Association Test (COWA) [41] for verbal fluency, Trail-Making Tests A and B (TMT A and TMT B) [42] for attention and processing speed, Wechsler Memory Scale (WMS) digit span forward and backward test (Digit F and Digit B) [43] for short-term and working memory, and Rey's Auditory Verbal Learning Test (RAVLT) [44] for short-term and working memory, and Rey's Auditory Verbal Learning Test (RAVLT).

2.6.3. Assessment tools

Stroop Color-Word Test [40]: It is a measurement of the time taken in seconds to read words. The words were printed in black ink (word), naming the printed colors (color) as printed XXX form, and naming the ink color while the printed name is a different color than the ink color (interference). Temporal reliability is $r > 0.80$.

Controlled Oral Word Association Test (COWA) [41]: It is a widely used test to assess phonemic fluency. In this test, participants were asked to generate as many words as possible, which begin with three specified letters *Ka, Pa, Ma*, within one-minute time limits. In category fluency, participants were asked to speak out animal names as a semantic category within one-minute time limits.

Trail Making Test (TMT A and B) [42]: TMT_A measures the time taken in seconds to connect digits in ascending order, and these digits are in a circle arranged randomly on the paper. TMT_B measures the time taken in seconds to connect circles of digits and alphabets in alternating order as fast as possible. Test-retest reliability is moderate to high for Part A ($r = .36$ to $.79$) and Part B ($r = .44$ to $.89$).

Digit Span Test [43]: It included verbal repetition of digits in forward and backward (Digit F and Digit B) order immediately after

listening verbally. The Digit Forward and Digit Backward tests measure the span of attention, concentration, and mental control. Internal reliability is high for digit span test ($r = 0.74$ to 0.93).

Key Auditory Verbal Learning Test (RAVLT) [44]: It has five learning trials with 15 words in List-A, followed by one trial of 15 words containing different words than List-A called List-B. After this trial, immediate recall and 20 min delayed recall of words from the list- A was assessed for memory. During this interval time, other assessments were carried out. The reliability for the RAVLT was 0.70 for recall of List A and 0.38 for recall of List B.

All the three groups IY, IY plus AR and AR received intervention separately after pre-assessment. After eight weeks, all the assessments were repeated. We offered yoga intervention to the AR group for a week after post-assessment.

3. Intervention

3.1. Yoga intervention

An Integrated Yoga therapy module was designed and validated by yoga experts (Table 1). Weekly six yoga sessions were administered to the IY group and IY plus AR group for eight consecutive weeks. An attendance book was maintained to record attendance. Each yoga session lasted for 60 minutes under the supervision of a yoga expert. Yoga sessions were held at 7–8 am in the morning and 5:30 to 6:30 in the evening. All the Yoga group participants were asked to come for a yoga session by wearing loose and comfortable clothes. They were asked to come on an empty stomach in the morning, and the participants in the evening session were advised to have lunch a minimum of 2 hours prior to the yoga session. The yoga intervention was conducted in a community hall.

3.2. Ayurveda Rasayana (Rejuvenation) intervention

Brahmi ghrita [45,46]: *Brahmi ghrita* is a ghee-based polyherbal Ayurvedic formulation. The classical reference of *Brahmi ghrita* is found in *Charak Samhita* of Charak, Chikitsasthana, 10/25, and *Astanga Hridayam* of Vagbhata, uttarasthana, 6/30 and [47,48]. In this study the used formulation of *Brahmi ghrita* was as per *Astanga Hridayam*. This preparation has the following herbs; *Brahmi* leaves juice, *Trikatu* (*Zingiber officinale*, *Piper longum*, and *Piper nigrum*), *Trivrut* (*Operculina terpenanthum*), *Shankhapushpi* (*Convolvulus*

pluricaulis), *Sapthala* (*Ophiorrhiza mungos*), *Vidanga* (*Embelia ribes*). We placed a special order for our study to a GMP-certified authentic and renowned pharmaceutical company to prepare *Brahmi ghrita* as per the methodology mentioned in *Astanga Hridayam* of Vagbhata, uttarasthana.

3.2.1. Dosage of Brahmi ghrita

Participants were advised to take 5 ml of *Brahmi ghrita* orally with 50 ml of warm milk/warm water on an empty stomach for eight consecutive weeks. This dose was decided based on the recommendation of three Ayurveda consultants. Hence this 5ml dose of *Brahmi ghrita* was decided. An Ayurveda physician contacted participants every two weeks to monitor and review the medication. The log was provided to participants to keep the attendance of the daily intake of ghee.

Participants who attended a minimum of 70% Yoga sessions and/or intake of *Brahmi ghrita* were considered for analysis.

4. Statistical analysis

All statistical analysis was performed in the SPSS 20. Baseline match for age, sex, education, illnesses, and cognitive impairment were assessed by using one-way ANOVA for groups. 3 X 2 ANOVA was used to evaluate all the cognitive variables using time as within factor and interventions (i.e., IY, IY plus AR and AR) as a between-subject factor. Those variable's scores were not matched at baseline for them; ANCOVA was performed by taking pre-scores of the variable as a covariate. Bonferroni post hoc test was used to assess the difference between groups.

5. Results

Demographic characteristics of all the participants were assessed, and it showed no differences between groups in the number of participants, age, gender, total years of education, and the number of illnesses. In IY, IY plus AR and AR group 60, 75, and 96 percent of participants were not doing any physical activity, respectively. Table 2 depicts the sociodemographic details of the participants. The mean attendance in IY and IY plus AR group for Yoga classes was 40.68 ± 3.31 and 39.79 ± 2.99 sessions, respectively. The mean attendance in AR and IY plus AR group for Rasayana intake was 41.60 ± 4.45 and 41.37 ± 3.20 doses,

Table 1
Integrated Yoga therapy module.

| Practice Group | Name of the practices | Duration |
|---|---|----------|
| Starting Prayer | <i>Om sahanavavatu</i> | |
| SukshmaVyayama (Loosening Practices) | 1. Ankle rotation, 2. Knee bending, 3.Knee rotation, 4. Hip rotation, 5. Hand clenching, 6. Wrist bending, 7. Wrist joint rotation, 8. Elbow bending, 9. Shoulder rotation, 10. Neck movements, 11. Waist rotation, 12. Half butterfly. Loosening of body joints with awareness. | 15 min |
| Breathing Exercises | 1. Hands in and out breathing, 2. Hand stretch breathing, 3. Ankle stretch breathing. | 05 min |
| Asanas (Yogic Postures) | 1. Standing: <i>Tadasana, Ardhaçakrasana, Aardhakaçicakrasana, Trikoçasana, Padahastāsana.</i> 2. Sitting: <i>Pāçimottāçāsana, Purvottāçāsana, Vakraçasana, Bhunamanāsana.</i> 3. Supine: <i>Nāvasana, Setubandhāsana, Savāsana,</i> 4. Prone: <i>Bhujāṅgāsana, Salabhāsana, Makarāsana</i> (On alternate days, set of sitting -standing or supine - prone asanas were practiced) | 20 min |
| Relaxation techniques | Deep relaxation Technique | 05 min |
| Pranayama (Yogic breathing) | <i>NaadiShodhana, Bhramari</i> | 10 min |
| Chanting | <i>Nadanusandhana/OM Chanting</i> | 05 min |
| Closing prayer and Sankalp (Resolve) | <i>Asotomasadgamaya, SarveBhavanthu.</i> | |

Table 2
Demographic details of the participants and comparisons between groups.

| Group | IY | IY plus AR | AR | F value | P value |
|---|---------------|---------------|---------------|---------|---------|
| No. of Subjects | 25 | 24 | 23 | – | – |
| Age in years | 62.40 ± 6.06 | 63.21 ± 6.24 | 64.39 ± 7.15 | 0.569 | 0.569 |
| Gender | Male | 12 | 13 | 0.262 | 0.77 |
| | Female | 13 | 10 | | |
| Education in Years | 10.24 ± 3.811 | 11.12 ± 3.791 | 9.26 ± 4.213 | 1.317 | 0.275 |
| BMI | 27.09 ± 4.29 | 26.46 ± 3.37 | 26.36 ± 5.08 | 0.205 | 0.815 |
| Number of chronic diseases suffering from | 1.56 ± 1.12 | 1.67 ± 1.24 | 1.09 ± 1.04 | 1.722 | 0.186 |
| Montreal Cognitive Assessment | 18.96 ± 3.867 | 18.71 ± 4.016 | 17.96 ± 4.062 | 0.407 | 0.667 |

Statistically significant with P value < 0.05. Values expressed as Mean ± Standard deviation. IY: Integrated Yoga, AR: Ayurveda rasayana.

respectively. There were no side-effects observed in any treatment group during the intervention.

Twenty-five (13 females), 24 (11 females), and 23 (13 females) participants in IY group, AR plus IY, and AR group, respectively, completed the intervention and post-assessment.

5.1. Within-group changes

Table 3 displayed a significant difference ($p < 0.05$) in time for all the variables except the digit backward test. Based on estimated marginal means by adjustment at multiple comparisons Bonferroni post hoc test showed a significant difference in pre to post in the Stroop color-word test, Rey Auditory Verbal Learning Test (RAVLT), Controlled Oral Word Association Test (COWA), Trail Making Test (TMT-A & TMT-B), and digit Span Test (Digit F) in IY, IY plus AR, and AR groups except for AVLT List B, Digit Backward in AR group; Digit B in IY and IY Plus AR group. This is suggestive of improvement in different cognitive abilities such as executive functions, verbal fluency, attention, processing speed, working memory, learning, and verbal memory following Integrated Yoga, Ayurveda Rasayana, and combined interventions after eight weeks.

5.2. Between-group comparison

Table 3 displays a significant difference ($P < 0.05$) in groups for Stroop Color, RAVLT Hits, and borderline significant for COWA category and Stroop word; group* time interaction was significant ($P < 0.05$) for Stroop color and COWA consonant.

3×2 ANOVA shows that all the variables were matched at baseline between groups except Stroop Color, RAVLT average, Digit forward and backward. The variables that were not comparable at baseline ANCOVA was performed by taking pre-scores of the variable as a covariate. Bonferroni post hoc test for Post vs. Post comparison between AR vs. IY groups was significant for RAVLT hits.

ANCOVA results show that after controlling the covariate pre score of RAVLT average, Digit backward, there was a significant difference between the groups, and after controlling the covariate pre score of Stroop Color, Digit Forward, there was no significant between groups. Bonferroni post hoc test for RAVLT average showed IY plus AR vs. AR was significant, and Digit backward IY vs. AR and IY plus AR vs. AR was significant.

6. Discussion

This study intended to investigate the efficacy of 8 weeks intervention of Integrated Yoga, Ayurveda Rasayana, and combined cognitive abilities among the elderly with mild cognitive impairment. We found significant improvement in all the cognitive measures except Digit Backward (working memory) in all three groups after eight weeks compared pre-score to post scores. It suggests that all IY, AR, and IY plus AR intervention have equal cognitive benefits among the elderly with mild cognitive

impairment. Between-group comparisons revealed that Ayurveda Rasayana was significantly better on RAVLT-hits, suggestive of recognition in learning performance compared to Yoga intervention and combined. Combined (IY plus AR) intervention was markedly better on RAVLT average indicative of acquisition and verbal learning than AR and IY. Digit backward suggestive of attention, working memory, and mental control were significant in IY vs. AR and IY plus AR vs. AR. This shows that IY plus AR, or only IY intervention, is better than AR for working memory. We did not find statistically significant differences between the groups for remaining cognitive measures.

Cognitive impairment is a common progressive degeneration problem among the elderly contributing to significant disability. It affects the individual's quality of life and makes them dependent on others for their routine activities. Conventional medicine has little role in improving cognitive impairment and preventing disability.

Our study found that Ayurveda Rasayana (*Bhrami ghrita*) has cognitive benefits on various cognitive measures such as executive functions, auditory-verbal learning, attention, processing speed, concentration, cognitive flexibility, verbal fluency, processing speed, and memory. To the best of knowledge present study is the only study of its kind assessing Ayurveda Rasayana efficacy on cognition among the elderly with MCI. Morgan A et al., in 2010, did on the extract of *Bacopa monnieri* of dose 300mg/day shown similar benefits on verbal learning, attention, and short term or working memory after three months in healthy older adults [49]. Whereas in our study, similar significant results were found in IY plus AR group compared to individual treatment after eight weeks of intervention in cognitively impaired elderly persons. However, a study by Sarkote A et al., 2013 reported significant improvement in short-term memory among school children of 10-16 years following oral intake of *Medhya Rasayana* powder for three months [50]. Though this study is not comparable with the present study, however, the improvement in cognitive function is evident in both studies following Ayurveda Rasayana.

Previous studies on Yoga intervention have shown positive effects on cognitive functions among the elderly. A study by Eyre HA et al., 2017, noticed a significant improvement in memory, executive function, and resilience following 12 weeks of *Kundalini* Yoga intervention among the 81 elderly with MCI [51]. In the present study, we also found significant improvement in executive function and memory. Our study is shorter (8 weeks) than the previous study (Eyre HA et al., 2017) and has a different type of intervention. Gothe et al., 2014 assessed the effect of eight-week yoga intervention (thrice-weekly) on executive function [52]. The results of this study showed significant improvement in working memory, cognitive flexibility among healthy elderly. In the present study, we also found significant improvement in cognitive flexibility and memory. We did not find a statistically significant difference between the groups, which could be due to active intervention in all three groups. Similar results were observed in previous studies also (Eyre HA et al., 2017).

Table 3
Within and between group comparisons of neuropsychological tests.

| Outcome Measures | Group | Pre mean ± SD | Post mean ± SD | Percentage Change | Time F (1,69) Value | Group F (2,69) value, (P values) |
|------------------------------------|------------|----------------|---------------------------|-------------------|----------------------|----------------------------------|
| Stroop-Words (Read in 45 s) | IY | 82.88 ± 14.49 | 85.6 ± 13.63** | 3.28 | 251.465 (p < 0.001) | 3.001 (0.056) |
| | IY plus AR | 81.58 ± 18.56 | 86.33 ± 15.12** | 5.82 | | |
| | AR | 72.52 ± 16.63 | 76.78 ± 16.54** | 5.88 | | |
| Stroop-Color (Read in 45 s) | IY | 53.88 ± 11.98 | 57.6 ± 11.79** | 6.90 | 280.157 (p < 0.001) | 0.749 (0.477) |
| | IY plus AR | 50.46 ± 13.96 | 53.88 ± 13.41** | 6.77 | | |
| | AR | 46.43 ± 14.04 | 49.26 ± 12.27** | 6.09 | | |
| Stroop- Color_Words (Read in 45 s) | IY | 30.76 ± 9.99 | 32.2 ± 9.45** | 4.68 | 80.173 (p < 0.001) | 0.541 (0.584) |
| | IY plus AR | 26.96 ± 9.91 | 31.33 ± 11.30** | 16.23 | | |
| | AR | 20.78 ± 8.86 | 26.57 ± 8.80** | 27.82 | | |
| RAVLT- Average | IY | 7.16 ± 1.39 | 9.236 ± 2.14** | 28.99 | 391.833 (p < 0.001) | 4.727 (0.012) |
| | IY plus AR | 7.85 ± 1.20 | 10.83 ± 1.83** | 38.00 | | |
| | AR | 7.71 ± 1.63 | 9.11 ± 2.13** | 18.15 | | |
| RAVLT-list B (Distraction list) | IY | 3.72 ± 1.97 | 4.64 ± 2.36** | 24.73 | 14.755 (p < 0.001) | 0.086 (0.918) |
| | IY plus AR | 4.83 ± 2.22 | 5.04 ± 2.73 [§] | 4.31 | | |
| | AR | 3.57 ± 2.09 | 4.17 ± 2.08 | 17.07 | | |
| RAVLT-Immediate Recall | IY | 7.08 ± 2.02 | 10.36 ± 2.64 [§] | 46.33 | 44.178 (p < 0.001) | 0.653 (0.524) |
| | IY plus AR | 6.92 ± 2.34 | 11.71 ± 2.44** | 69.28 | | |
| | AR | 7.39 ± 2.78 | 9.83 ± 2.57** | 32.94 | | |
| RAVLT-Delayed Recall | IY | 6.76 ± 2.93 | 10.6 ± 2.92** | 56.80 | 209.468 (p < 0.001) | 0.179 (0.836) |
| | IY plus AR | 6.54 ± 2.62 | 11.38 ± 2.63** | 73.89 | | |
| | AR | 6.30 ± 3.01 | 10.17 ± 2.89** | 61.38 | | |
| RAVLT- Hits | IY | 12.84 ± 2.10 | 14.28 ± 1.28** | 11.21 | 257.626 (p < 0.001) | 4.376 (0.016) |
| | IY plus AR | 13.17 ± 1.90 | 14.63 ± 0.58** | 11.08 | | |
| | AR | 13.13 ± 1.39 | 15.91 ± 7.68** | 21.19 | | |
| RAVLT-Omissions | IY | 2.16 ± 2.10 | 0.68 ± 1.25** | 68.52 | 302.797 (p < 0.001) | 2.079 (0.336) |
| | IY plus AR | 1.83 ± 1.90 | 0.79 ± 2.25** | 56.82 | | |
| | AR | 1.83 ± 1.37 | 0.65 ± 0.71** | 64.29 | | |
| RAVLT-Commission | IY | 0.84 ± 0.75 | 0.32 ± 0.48** | 61.90 | 146.770 (p < 0.001) | 2.559 (0.085) |
| | IY plus AR | 1.04 ± 0.69 | 0.08 ± 0.28** | 92.00 | | |
| | AR | 1.30 ± 1.15 | 0.39 ± 0.72** | 70.00 | | |
| COWA-Consonant | IY | 7.9996 ± 3.09 | 9.004 ± 3.25** | 12.56 | 1633.348 (p < 0.001) | 2.479 (0.091) |
| | IY plus AR | 7.89 ± 2.43 | 9.48 ± 2.59** | 20.22 | | |
| | AR | 6.89 ± 2.23 | 8.07 ± 3.45** | 17.22 | | |
| COWA- Category | IY | 9.44 ± 1.96 | 11.36 ± 2.20** | 20.34 | 358.269 (p < 0.001) | 3.028 (0.055) |
| | IY plus AR | 10.46 ± 2.59 | 12.33 ± 2.58** | 17.93 | | |
| | AR | 10.25 ± 2.37 | 11.70 ± 2.96** | 14.14 | | |
| Digit- Forward | IY | 6.64 ± 1.70 | 6.8 ± 1.63** | 2.41 | 378.247 (p < 0.001) | 2.921 (0.061) |
| | IY plus AR | 6.71 ± 1.65 | 7.46 ± 2.04** | 11.18 | | |
| | AR | 6.78 ± 2.09 | 6.52 ± 1.97** | 3.85 | | |
| Digit - Backward | IY | 3.52 ± 1.26 | 4.56 ± 1.36 | 29.55 | 0.162 (p = 0.689) | 5.766 (0.005) |
| | IY plus AR | 3.92 ± 1.69 | 4.88 ± 1.51 | 24.47 | | |
| | AR | 3.65 ± 1.23 | 3.74 ± 1.48 | 2.38 | | |
| TMT-A (in Seconds) | IY | 75.56 ± 36.20 | 54.48 ± 19.65** | 27.90 | 597.596 (p < 0.001) | 0.837 (0.437) |
| | IY plus AR | 71.79 ± 47.67 | 59.71 ± 35.46** | 16.83 | | |
| | AR | 110.57 ± 62.19 | 87.26 ± 52.55** | 21.08 | | |
| TMT-B (in Seconds) | IY | 164 ± 68.64 | 120.08 ± 48.57** | 27.90 | 502.822 (p < 0.001) | 0.677 (0.512) |
| | IY plus AR | 149.29 ± 67.77 | 113.79 ± 60.96** | 16.83 | | |
| | AR | 206.35 ± 86.04 | 171.83 ± 72.94** | 21.08 | | |

§P < 0.05, *P < 0.01, **P < 0.001 pre to post Comparison. RAVLT: Rey Auditory Verbal Learning Test, COWA:Controlled Oral Word Association Test, TMT-A & TMT-B: TrailMaking Test A and B.

Graph No. 1: Percentage Change after 8 weeks intervention in IY, IY plus AR and AR group.

Literature showed no study in the elderly with MCI with Ayurveda and only one study on Yoga intervention. The present study is unique, assessing Ayurveda *Rasayana* and yoga intervention effects among the elderly with MCI. In this study, diverse cognitive domains were assessed using robust assessment tools. Yoga protocol was found to be feasible and Well-accepted by the participants. Adherence to the yoga intervention and Ayurveda *Rasayana* was found to be satisfactory. No adverse effects of Ayurveda *Rasayana* and Yoga were found in the treatment groups.

The exact mechanism of Yoga and Ayurveda *Rasayana* in improving cognitive functions is not well established. However, there are several possible mechanisms we can speculate. First, both Ayurveda *Rasayana* and Yoga are well-known interventions that have anti-oxidant activity. Ayurveda herb *Brahmi* and the clarified butter are potent antioxidants [53,54]. Secondly, yoga intervention helps to reduce sympathetic activity and stress via down-

regulation of HPA axis. Reduced stress levels are associated with an enhancement in cognitive functions [55]. Further, yoga postures demand a lot of attention, concentration, and balance; such practices are known to enhance mindfulness and body awareness, which are positively associated with cognition [56]. Another study by Dodich A et al., in 2019, after four weeks of meditation of sixteen hours of practice in healthy adults, showed spontaneous activity in the executive control network of the brain, which is responsible for performing all cognitive actions effectively [57].

The present study has some limitations, such as; larger sample size and long-term follow-up would have yielded better results in the between-group comparison, the attrition rate was 20%, and it was a Non-RCT study. We were unable to get the number of participants as derived from the sample size calculation. We recommend further studies with a larger sample size using robust research designs. Objective cognitive variables, along with

biochemical markers, would help to draw a more appropriate conclusion.

7. Conclusion

Both Ayurveda *Rasayana* and Integrated Yoga intervention were found effective in improving cognitive abilities among the elderly with MCI. Combined Ayurveda *Rasayana* and Yoga intervention significantly improved learning, attention, processing speed, and working memory compared to individual response among elderly persons with MCI.

Sources of funding

None.

Conflict of interest

None.

Author contributions

SC contributed to Intervention monitoring, Study design, and manuscript preparation. SP was responsible for the Inception of the study, study planning, and design. MNC were Monitored Intervention and participant recruitment. KGM and SP contributed to study design, data analysis, and manuscript preparation.

Acknowledgement

We are thankful to Dr. Balaram P. for statistical analysis, and we thankful to the local organizer and participants for their valuable support during the study.

References

- [1] Rajan SI, Sarma PS, Mishra US. Demography of Indian aging, 2001-2051. *J Aging Soc Pol* 2003;15:11–30.
- [2] Renteria MA, Manly JJ, Vonk JM, Arango SM, Obregon AM, Samper-Ternent R, et al. Prevalence of mild cognitive impairment in Mexican older adults: data from the Mexican health and aging study (MHAS). *medRxiv*; 2020 Jan 1.
- [3] Ward A, Arrighi HM, Michels S, Cedarbaum JM. Mild cognitive impairment: disparity of incidence and prevalence estimates. *Alzheimer's Dementia* 2012;8:14–21.
- [4] Eshkoo SA, Hamid TA, Mun CY, Ng CK. Mild cognitive impairment and its management in older people. *Clin Interv Aging* 2015;10:687.
- [5] Petersen RC, Lopez O, Armstrong MJ, Getchius TS, Ganguli M, Gloss D, et al. Practice guideline update summary: mild cognitive impairment: report of the guideline development, dissemination, and implementation subcommittee of the American academy of neurology. *Neurology* 2018;90:126–35.
- [6] Mitchell AJ, Shiri-Feshki M. Rate of progression of mild cognitive impairment to dementia—meta-analysis of 41 robust inception cohort studies. *Acta Psychiatr Scand* 2009;119:252–65.
- [7] Artero S, Touchon J, Ritchie K. Disability and mild cognitive impairment: a longitudinal population-based study. *Int J Geriatr Psychiatry* 2001;16:1092–7.
- [8] Saraçlı Ö, Akca AS, Atasoy N, Önder Ö, Şenormancı Ö, Kaygısızlı, et al. The relationship between quality of life and cognitive functions, anxiety and depression among hospitalized elderly patients. *Clin Psychopharmacol Neurosci* 2015;13:194–200.
- [9] Brasure M, Desai P, Davila H, Nelson VA, Calvert C, Jutkowitz E, et al. Physical activity interventions in preventing cognitive decline and Alzheimer-type dementia: a systematic review. *Ann Intern Med* 2018;168:30–8.
- [10] Malhotra AK. An introduction to yoga philosophy: an annotated translation of the yoga sutras. 1st ed. London: Routledge; 2017.
- [11] Swami SS. Four chapters of freedom: commentary on the yoga sutras of sage patanjali. 2nd ed. Munger: Yoga publication trust; 2013.
- [12] Field T. Yoga research review. *Compl Ther Clin Pract* 2016;24:145–61.
- [13] Büsling A, Michalsen A, Khalsa SB, Telles S, Sherman KJ. Effects of Yoga on mental and physical health: a short summary of reviews. *Evid base Compl Alternative Med* 2012;2012.
- [14] Varambally S, Gangadhar BN. Current status of Yoga in mental health services. *Int Rev Psychiatr* 2016;28:233–5.
- [15] Luu K, Hall PA. Hatha yoga and executive function: a systematic review. *J Alternative Compl Med* 2016;22:125–33.
- [16] Gothe NP, McAuley E. Yoga and cognition: a meta-analysis of chronic and acute effects. *Psychosom Med* 2015;77:784–97.
- [17] Mooventhan A, Nivethitha L. Evidence based effects of yoga practice on various health related problems of elderly people: a review. *J Bodyw Mov Ther* 2017;21:1028–32.
- [18] Balasubramaniam M, Telles S, Doraiswamy PM. Yoga on our minds: a systematic review of Yoga for neuropsychiatric disorders. *Front Psychiatr* 2013;3:117.
- [19] Hariprasad VR, Koparde V, Sivakumar PT, Varambally S, Thirhalli J, Varghese M, et al. Randomized clinical trial of yoga-based intervention in residents from elderly homes: effects on cognitive function. *Indian J Psychiatr* 2013;55(Suppl 3):S357.
- [20] Gothe NP, Kramer AF, McAuley E. The effects of an 8-week Hatha yoga intervention on executive function in older adults. *J Gerontol Ser A: Biomed Sci Med Sci* 2014;69:1109–16.
- [21] Gothe NP, McAuley E. Yoga and cognition: a meta-analysis of chronic and acute effects. *Psychosom Med* 2015;77:784–97.
- [22] Chobe S, Chobe M, Metri K, Patra SK, Nagaratna R. Impact of Yoga on cognition and mental health among elderly: a systematic review. *Compl Ther Med* 2020;102421.
- [23] Gadgil VD. Understanding ayurveda. *J Ayurveda Integr Med* 2010 Jan;1(1):77–80.
- [24] Pole S, Sebastian J. Ayurvedic medicine. Livingstone: Elsevier Health Sciences; 2006. p. 137.
- [25] Braun L, Cohen M. Herbs and natural supplements. An Evidence-Based Guide. 2nd ed., vol. 2. Elsevier Health Sciences; 2015.
- [26] Peterson CT, Lucas J, John-Williams LS, Thompson JW, Moseley MA, Patel S, et al. Identification of altered metabolomic profiles following a Panchakarma-based Ayurvedic intervention in healthy subjects: the Self-Directed Biological Transformation Initiative (SBTI). *Sci Rep* 2016 Sep 9;6:32609.
- [27] Conboy LA, Edshteyn I, Garivaltis H. Ayurveda and Panchakarma: measuring the effects of a holistic health intervention. *Sci World J* 2009 Apr 27:9.
- [28] Rege NN, Thatte UM, Dahanukar SA. Adaptogenic properties of six rasayana herbs used in Ayurvedic medicine. *Phytother Res: Int J Devoted to Pharmacol Toxicol Eval Nat Product Derivatives* 1999 Jun;13(4):275–91.
- [29] Tripathi B, editor. Commentary Caraka Chandrika (Hindi) on Carak samhita of Agnivesa elaborated by Caraka and Dradhhabala, Chikitsastana; Rasayna adhyaya: Chapter 01, Verse 07. 1st ed. Varanasi: Subharati Prakashan; 2009. p. 5.
- [30] Kulkarni R, Girish KJ, Kumar A. Nootropic herbs (MedhyaRasayana) in ayurveda: an update. *Phcog Rev* 2012;6:147–53.
- [31] Tripathi B, editor. Commentary Caraka Chandrika (Hindi) on Carak samhita of Agnivesa elaborated by Caraka and Dradhhabala, Chikitsastana; Apasmara chikitsa adhyaya: Chapter 10, Verse 25. 1st ed. Varanasi: Subharati Prakashan; 2009. p. 411.
- [32] Singh RH, Narsimhamurthy K, Singh G. Neuronutrient impact of Ayurvedic Rasayana therapy in brain aging. *Biogerontology* 2008 Dec 1;9(6):369–74.
- [33] Singh HK, Dhawan BN. Neuro-psychopharmacological effects of the ayurvedic nootropic Bacopa monniera Linn.(brahmi). *Indian J Pharmacol* 1997;29:359–65.
- [34] Raghav S, Singh H, Dalal PK, Srivastava JS, Asthana OP. Randomized controlled trial of standardized Bacopa monniera extract in age-associated memory impairment. *Indian J Psychiatr* 2006;48:238–42.
- [35] Kongkeaw C, Dilokthornsakul P, Thanarangsarit P, Limpeanchob N, Scholfield CN. Meta-analysis of randomized controlled trials on cognitive effects of Bacopa monnieri extract. *J Ethnopharmacol* 2014;151:528–35.
- [36] Morgan A, Stevens J. Does Bacopamonnieri improve memory performance in older persons? Results of a randomized, placebo-controlled, double-blind trial. *J Alternative Compl Med* 2010;16:753–9.
- [37] Raghav S, Singh H, Dalal PK, Srivastava JS, Asthana OP. Randomized controlled trial of standardized Bacopamonniera extract in age-associated memory impairment. *Indian J Psychiatr* 2006;48:238.
- [38] Eyre HA, Siddarth P, Acevedo B, Van Dyk K, Pahalpak P, Ercoli L, et al. A randomized controlled trial of Kundalini yoga in mild cognitive impairment. *Int Psychogeriatr* 2017;29:557–67.
- [39] Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 2005;53:695–9.
- [40] Scarpina F, Tagini S. The stroop color and word test. *Front Psychol* 2017;8.
- [41] Rao SL, Subbakrishna DK, Gopukumar K. NIMHANS neuropsychology battery. Bangalore, India: NIMHANS Publications; 2004.
- [42] Tombaugh TN. Trail Making Test A and B: normative data stratified by age and education. *Arch Clin Neuropsychol* 2004;19:203–14.
- [43] Wechsler D. Wechsler memory scale. 3rd ed. San Antonio, TX: The Psychological Corporation; 1987.
- [44] Schmidt M. Rey auditory verbal learning test: a handbook. Los Angeles: Western Psychological Services; 1996.
- [45] Manu Prabhakar, Kumar Shetty Suhas, Savitha HP. Critical review on effect of brahmi ghrita in psychiatric disorders. *Int J Res Ayurveda Pharm* 2017;8:16–8.
- [46] Gubbannavar JS, Chandola H, Harisha CR, Kalyani R, Shukla VJ. Analytical profile of brahmi ghrita: a polyherbal ayurvedic formulation. *Ayu* 2012;33:289.

- [47] Tripathi B, editor. Commentary Caraka Chandrika (Hindi) on Carak samhita of Agnivesa elaborated by Caraka and Dradhabala, Chikitsastana; Apasmara chikitsa adhyaya: Chapter 10, Verse 25. 1st ed. Varanasi: Subharati Prakashan; 2009. p. 411.
- [48] Srikantha Murthy KR, editor. Astanga Hrdayam of Vagbhata, Uttarasthana; Unmada pratisedha (treatment of insanity): Chapter 6, Verse 23-25. 1st ed. Varanasi: Chowkhambha Krishna das Academy; 2004. p. 43.
- [49] Morgan A, Stevens J. Does Bacopa monnieri improve memory performance in older persons? Results of a randomized, placebo-controlled, double-blind trial. *J Alternative Compl Med* 2010;16:753-9.
- [50] Sarokte AS, Rao MV. Effects of MedhyaRasayana and Yogic practices in improvement of short-term memory among school-going children. *Ayu* 2013;34:383.
- [51] Eyre HA, Siddarth P, Acevedo B, Van Dyk K, Paholpak P, Ercoli L, et al. A randomized controlled trial of Kundalini yoga in mild cognitive impairment. *Int Psychogeriatr* 2017;29:557-67.
- [52] Gothe NP, Kramer AF, McAuley E. The effects of an 8-week Hatha yoga intervention on executive function in older adults. *J Gerontol Ser A: Biomed Sci Med Sci* 2014;69:1109-16.
- [53] Simpson T, Pase M, Stough C. Bacopamonnieri as an anti-oxidant therapy to reduce oxidative stress in the aging brain. *Evidence-based complementary and alternative medicine*. 2015. p. 2015.
- [54] Hazra T, Parmar P. Natural anti-oxidant use in ghee-A mini review. *J Food Res Technol* 2014;2:101-5.
- [55] Gard T, Noggle JJ, Park CL, Vago DR, Wilson A. Potential self-regulatory mechanisms of Yoga for psychological health. *Front Hum Neurosci* 2014;8:770.
- [56] Tops M, Boksem MA, Quirin M, Ijzerman H, Koole SL. Internally directed cognition and mindfulness: an integrative perspective derived from predictive and reactive control systems theory. *Front Psychol* 2014;5:429.
- [57] Dodich A, Zollo M, Crespi C, Cappa SF, Laureiro, et al. Short-term Sahaja Yoga meditation training modulates brain structure and spontaneous activity in the executive control network. *Brain Behav* 2019;9:e01159.