Assessing mindfulness-based training for neuropsychological outcomes in mild cognitive impairment

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Impact statement

We certify that this work is novel. In contrast with previous positive findings, this clinical trial reports some positive effects a mindfulness-based intervention on cognitive function, but no effect compared with treatment-as-usual, possibly as mood was unchanged with this mindfulness program. These are important data considering the current scarcity of high-quality trials in this area, and mixed findings in the literature.

Key Points

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- A mindfulness-based intervention (MBI) was superior to cognitive rehabilitation in improving delayed memory, but not superior to treatment as usual.
- Mood did not improve after MBI, possibly accounting for the null result.

Why does this matter?

The effects of mindfulness on cognitively impaired persons may depend on mood improvements.

Abstract

Background: Current pharmacological and behavioural treatment options for mild cognitive impairment and dementia are limited, motivating a search for alternative therapies that might slow the progression of cognitive decline in these disorders. In this study, we aimed to investigate the effectiveness of a cognition-focused mindfulness-based intervention in achieving this aim.

Design: Open-label, three-arm randomized controlled trial,

Setting: Public tertiary medical centre

Participants: Older persons (ages 45-75; N = 76) diagnosed with mild cognitive impairment (MCI)

Intervention: Mindfulness-based training (MBT), cognitive rehabilitation therapy (CRT), and treatment as usual (TAU). Participants in the intervention arms received 8 weekly 2-hour sessions delivered in a group setting and were encouraged to engage in home practice.

Measurements: Primary outcomes measures of this trial were change in index scores for attention, immediate memory, and delayed memory measured using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Depression was a secondary outcome.

Results: Using intent-to-treat analysis, we found that participants receiving MBT showed significant improvements in global cognition ($d = 0.26$; [95% CI 0.03 - 0.56]) and delayed memory ($d = 0.36$; [95% CI 0.17 - 0.57]), with significantly greater improvements in delayed memory than CRT ($\eta_p^2 = 0.10$). However, there was no benefit of MBT over TAU. No change in depression was observed in the MBT group. Reductions in depression were associated with improvements in cognitive functioning in the MBT group only.

Conclusion: Our results suggest that a cognition-focused MBT did not improve cognitive functioning in MCI patients substantially more than spontaneous reversion rates, possibly as mood symptoms were not significantly alleviated in this group.

Trial Registration: ClinicalTrials.gov Identifier: NCT04000984

Key words: mindfulness, mild cognitive impairment, neuropsychological outcomes, depression

Introduction

The burden from common age-related brain disorders (e.g. Alzheimer's Disease) has doubled from 1990 to 2016, and is expected to rise with increased longevity.¹ Current treatment options are limited: drugs such as cholinesterase inhibitors have only a slight and short-term effect in mitigating cognitive decline^{2,3} as do behavioural treatments such as cognitive rehabilitation therapy.⁴ Against this backdrop, calls have been made to focus on modifiable risk factors for dementia, with an estimate that this might prevent up to 40% of cases,⁵ and towards this end, meditation and the practice of mindfulness have been proposed as useful tools to mitigate cognitive decline. Aside from evidence that mindfulness training can improve cognition among healthy individuals,⁶ practicing mindfulness also has known associations with improvements in mood,⁷ sleep,⁸ and well-being,⁹ all of which are protective factors against developing dementia.

Mindfulness, which is cultivated through several formal meditative practices, is a mental state achieved by focusing one's attention and awareness on the present moment, while calmly acknowledging and accepting one's feelings, thoughts, and bodily sensations.¹⁰ Mindfulness-based interventions (MBIs) consist of a series of exercises designed to improve these skills, and can be implemented in a group setting at low cost and with a low risk of negative consequences. While standard programs emphasize the effects of mindfulness on stress and negative emotions, training protocols can also be modified to highlight the relationship between the mindfulness exercises and the individual's cognition, specifically attention and memory.

There is currently some evidence that MBIs can slow or reverse cognitive decline in persons with neurodegenerative disorders,¹¹⁻¹⁴ with a recent systematic review suggesting that effect sizes are in the small-to-medium range.¹⁵ In particular, it has been suggested that early intervention, such as at the stage of mild cognitive impairment (MCI), is more effective than when patients progress to more severe disease. MCI is a transitional state between normal aging and very early dementia marked by progressive cognitive decline.¹⁶ While 50% of those with MCI will develop dementia within 5 years, approximately 14-40% of these individuals will return to normal cognitive functioning over time.¹⁷ Although this reversibility indicates that this group is a prime target for early intervention, it also suggests the need for studies that use both active and passive control conditions in order to account for diagnostic instability.

Based on this logic, our aim was to test the potential of a shorter 8-week MBI for clinical use in patients with cognitive impairment using both an active and passive control

arm. To achieve this, we used an MBI program modified to focus on how the skills of mindfulness might specifically benefit cognition, and examined the effects of the intervention on individual cognitive domains. Patients with MCI were randomized to receive either an MBI, cognitive rehabilitation therapy or standard care. Our primary outcome variables were scale scores of attention, immediate memory, and delayed memory on a standardized neuropsychological battery, the Repeatable Battery for the Assessment of Neurological Status (RBANS). We hypothesized that patients in the MBI group would experience significantly improved scores on the RBANS following the intervention in comparison with the active and passive control groups, with corresponding increases in mood (i.e. lower depression scores).

Methods

This study was an open-label, assessor-blinded, parallel, randomized clinical trial. Ethical approval was obtained from both the SingHealth Centralised Institutional Review Board (cIRB 2015/3049) as well as the National University of Singapore Institutional Review Board (NUS-IRB: H-19-048) and was conducted in accordance to the 1964 Helsinki declaration and its later amendments. All participants provided written informed consent and were reimbursed up to SG\$180 for their time, based on their attendance.

Participants

Study participants were recruited through five main channels: i) through the outpatient memory clinic at a tertiary hospital; ii) from members of the community who attended public events on healthy aging and cognition, iii) using posters within the tertiary hospital, iv) through online forum pages targeted at older people, and v) through email groups related to dementia. Members of the community who expressed interest in participating in the study were assessed with a diagnostic neuropsychological test battery (Appendix A) administered by a clinical psychologist.

Inclusion criteria

To be eligible for this study, participants needed to be a) between the ages of 45 to 75, b) fulfil the Diagnostic and Statistical Manual of Mental Disorders version five (DSM-V) diagnostic criteria for Minor Neurocognitive Disorder or Mild Cognitive Impairment, and c) have a Clinical Dementia Rating Score (CDR) = 0.5 and d) have an MMSE score of > 19.

Exclusion criteria

Participants were excluded from the study if they had a) any presence of a major neurological conditions such as epilepsy, stroke, Parkinson's Disease and/or traumatic brain injury b) presence of any major psychiatric conditions such as major depression or schizophrenia, c) contraindications for fMRI scanning (e.g. pacemakers, metallic implants, claustrophobia) d) moderate to severe levels of depression measured by the Geriatric Depression Scale (GDS)¹⁸ or e) were unable to give independent consent.

Power analysis

The current study was powered to detect differences at post-intervention testing between MBT and each control condition, with a large effect size ($d = 0.7$) at $\beta = 0.80$. Based on these parameters, we decided that a minimum sample size of 25 participants per group was required.

Data acquisition

Eligible participants were scheduled for two visits to collect pre- and post-intervention data, which included neuropsychological assessments and questionnaires, and a 1-hour MRI scan (not reported in this paper). All pre-intervention data collection occurred no earlier than 3 months from the first intervention session and all post-intervention data collection session occurred no later than 3 months after the last intervention session.

Randomization and blinding

Participants were randomly assigned to each treatment arm 1 week prior to the start of the intervention, which was conducted when a sufficient number of participants had been recruited to form 3 treatment groups. The initial 24 participants were randomized to groups in a 1:1:1 ratio. Due to difficulties in subject recruitment, a pragmatic decision was made to change this ratio to 2:2:1 (with fewer individuals randomized to TAU) for the remainder of the trial. Pretesting was double blinded while post testing session was conducted by a blinded team member.

Interventions

Mindfulness Based Training (MBT) Program

The Mindfulness-based intervention program consisted of a Mindfulness-based training (MBT) program eight weekly sessions (Supplementary Table 1); each session was approximately an hour and a half in duration. Weekly group sessions included an introduction and practice of mindfulness exercises, a discussion of participants' experiences

and how mindfulness relates to their cognitive abilities, and an assignment of the activities to do on their own between sessions. To help incorporate mindfulness into their daily lives, participants were asked to spend a minimum of 15 minutes a day practicing these exercises and to record them in a journal that was given to them at the start of the program.

Participants were also given audio tracks of the various exercises taught during the session to aid their practice at home; these guided practices were no longer than 30 minutes. Unlike programs such as Mindfulness-Based Stress Reduction,¹⁰ the intervention in this study did not include a retreat.

Cognitive Rehabilitation Training (CRT) Program

The cognitive rehabilitation training program also consisted of eight weekly sessions, each lasting up to an hour and a half (Supplementary Table 1). Each session had the following components: (i) identifying and working on at least one personal rehabilitation goal related to everyday life that is associated with cognitive difficulties; (ii) reviewing and building on the use of practical memory strategies, and/or introducing and teaching the use of a new strategy or memory aid; (iii) introducing techniques for learning new information and associations, identifying the preferred strategy, and encouraging the application of this strategy in daily life; (iv) providing practice in maintaining attention and concentration; and (v) exploring current ways of coping with stress and anxiety as well as providing relaxation techniques to aid with coping.¹⁹

To facilitate their understanding and practice of the strategies taught and discussed during the session, participants were provided with a training book. The training book also contained logs to help them record, monitor, and evaluate their progress.

Treatment as Usual (TAU)

The third group received treatment as usual, which was the standard care offered by the memory clinic. Participants received no intervention and were prospectively monitored on a yearly basis by their attending neurologist.

Outcome Measures

Neuropsychological tests

The Singapore validated versions of the Mini Mental State Examination (MMSE)²⁰ and the Montreal Cognitive Assessment (MoCA)²¹ were both used as global cognitive screening tests.

The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)²² was used to assess multiple areas of cognitive functions and includes different test forms for

use before and after the interventions. Test forms A and B were alternately used as either the pre- or post-intervention measure to reduce test order effect on the results. The pre-registered primary outcome measures for this study were the subscale scores for attention, immediate memory, and delayed memory. For completeness, we also analyzed the language and visuospatial subscales of the RBANS in secondary analysis. Details of the subtests comprising each subscale score are reported in Appendix A.

Mood assessment

We measured mood using the 20-item Modified Geriatric Depression Scale (GDS-M)²³. GDS-M has good internal consistency ($\alpha=.85$)²⁴.

Trait mindfulness

Trait mindfulness was assessed using the Mindful Attention and Awareness Scale (MAAS)²⁵ which is a 15-item questionnaire that measures an individual's level of awareness and attention to present events and experiences. The MAAS has shown good internal consistency ($\alpha \sim .90$) across several studies.^{26,27}

Statistical analysis

Participants were included in the final analysis if they contributed data at pre-intervention and were randomized to an intervention arm. Missing data for participants who dropped out after randomization were filled using intent-to-treat analysis, using the pooled average of five imputed values derived from an iterative Markov Chain Monte Carlo method with predictive mean matching. Demographic and pre-intervention clinical measures were used as predictor variables.

As the MBT was our treatment of interest, data were analyzed using 2x2 repeated-measures ANOVA with time (pre/post-intervention) as a within-subjects factor and group as a between-subjects factor. Two sets of analyses were conducted: MBT against active control (CRT), and the second compared MBT against TAU. We considered comparisons to be statistically significant at Cronbach $\alpha=.05$.

Finally, to explore the correlations between cognition and mood, we conducted Pearson's correlations on the change in GDS scores and the change in MMSE scores within each intervention arm.

Results

Participant flow

Figure 1 depicts the CONSORT flowchart for this trial, and Table 1 reports baseline demographic and clinical characteristics. 605 participants were assessed for initial eligibility, 191 were consented to be screened, 81 were enrolled into the study and 5 participants withdrew from the study prior to randomisation. Data from 76 participants were included in the analysis. Participants ranged between 53 and 75 years old ($M=67$; $SD=5.3$), spoke either English ($N = 45$) or Mandarin ($N = 31$) and were predominantly female (56.3%).

Thirty-two participants were randomised into the MBT group (male = 16; mean^{age}(SD) = 67.6 (5.3); mean attendance = 6.3 sessions), 27 participants were randomised into the CRT group (male = 10; mean^{age}(SD) = 67.1 (3.4); mean attendance = 6.1 sessions), and 17 participants were randomised to receive TAU (male = 8; mean^{age}(SD) = 66.3 (6.6)). One participant who completed the CRT intervention was lost to follow-up and 2 participants in the TAU group were lost to follow-up.

Data were collected between April 2016 and September 2019. Recruitment stopped when we reached our predetermined sample size.

Missing data

Three participants did not contribute GDS data at baseline. Data were also not available for 2 participants for the RBANS-visuospatial scale score as they lacked the manual dexterity to complete the tasks.

Baseline characteristics

Using one-way ANOVA on the intent-to-treat sample (ITT), we found no significant differences among the three groups in any demographic or clinical variables ($P > .05$).

We compared dropouts and completers on demographic characteristics (age, gender) and scores on primary clinical outcomes (MMSE, MoCA, RBANS subscale scores) using independent-samples t-tests to assess for risk of bias. Dropouts from the study tended to be younger than completers (64.3 vs. 67.7; $t = 2.15$; $P = .04$). No other significant differences were found in these tests ($P > .05$).

Means and standard deviations of all measures pre- and post-intervention are presented in Table 2.

Neuropsychological outcomes

MBT vs CRT

Among the primary outcome variables (Table 3), repeated-measures ANOVA of the two active treatment groups showed that participants improved from pre-to post-intervention on the MMSE ($P = .03$), MoCA ($P = .009$), and the RBANS delayed memory subscale ($P = .009$). We further found a significant time by group interaction on the RBANS delayed memory subscale ($P = .01$), driven by a larger improvement in the MBT group. Post-hoc analyses demonstrated that the MBT group alone showed significant improvements on all of these outcomes except the MOCA (MMSE: $t_{31} = 2.09$, $d = 0.26$, [95% CI, 0.03 - 0.56], $P = .044$; MOCA: $t_{31} = 1.94$, $d = 0.25$, [95% CI, -0.06 to 0.49], $P = .06$; RBANS-delayed memory: $t_{31} = 3.96$, $d = 0.36$, [95% CI, 0.17 - 0.57], $P < .001$).

In the two secondary outcome variables, we found a significant improvement over time in the RBANS-visuospatial subscale ($P = .03$), with no time by group interaction. Post-hoc analysis showed that MBT participants improved significantly on this subscale (RBANS-visuospatial: $t_{30} = 2.20$; $d = 0.33$; [95% CI, 0.01 - 0.65]; $P = .04$).

MBT vs TAU

Among the primary outcome variables (Table 4), repeated-measures ANOVA of the MBT and passive control group showed that participants improved from pre-to post-intervention on the MoCA ($P = .01$), the RBANS attention subscale ($P = .001$), and the RBANS delayed memory subscale ($P = .001$). We further found a significant time by group interaction on the RBANS attention subscale ($P = .04$), driven by a larger improvement in the TAU group.

In the two secondary outcome variables, we found a significant improvement over time in the RBANS-visuospatial subscale ($P = .007$), with no time by group interaction.

Self-report outcomes

No changes in trait mindfulness were observed in comparisons of MBT with either of the two control groups (Tables 3-4).

With regard to depression, we observed significant decreases in GDS scores over time in the comparison of MBT and CRT ($P = .03$), and a significant time by group interaction driven by a greater decrease in the CRT group ($P = .03$) (Table 3).

Associations between mood and cognition

To explore the relationship between mood and cognition, we correlated change in GDS scores from pre- to post-intervention with change in MMSE scores (Supplementary Figure 1). In this analysis, we found a significant relationship in the MBT group ($r = -.38$; P

= .04) but not CRT ($r = -.14$; $P = .49$) or TAU ($r = -.12$, $P = .65$). However, correlation coefficients did not differ significantly between MBT and CRT ($z = -0.91$; $P = .18$) and between MBT and TAU ($z = -0.85$; $P = .20$).

Discussion

In this randomized controlled trial, we studied the effects of a mindfulness-based intervention against both active and passive control conditions on a comprehensive, repeatable neuropsychological battery. Compared with CRT, MBT participants showed greater improvements in delayed memory, significant but non-superior improvements in global cognitive functioning (measured by the MMSE) and visuospatial processing. Surprisingly, these outcomes were not superior to TAU, as participants in this group showed substantial amounts of spontaneous improvement in cognitive functioning. Overall, these results are equivocal, and suggest that the lack of diagnostic stability in MCI may have played a large role in the cognitive improvements observed in this trial. Notwithstanding this possibility, our data also suggest that MBT is a marginally more effective intervention than CRT for patients comparing these two options.

Several previous RCTs have been conducted comparing MBIs with an active control condition, and with neuropsychological testing among their outcomes. Smaller pilot studies have generally not found positive effects ^{28,29}. In a two-year trial, Quintana-Hernández, Miró-Barrachina, Ibáñez-Fernández, Pino, Quintana-Montesdeoca, Rodríguez-de Vera, Morales-Casanova, Pérez-Vieitez Mdel, Rodríguez-García, Bravo-Caraduje ¹² randomized N = 120 Alzheimer's Disease patients to receive mindfulness training (Mindfulness-Based Alzheimer's Stimulation), cognitive stimulation therapy, progressive muscle relaxation, or treatment with Donepezil. Mindfulness-Based Alzheimer's Stimulation and cognitive stimulation therapy were superior to progressive muscle relaxation in maintaining cognitive functioning as early as six months, and were superior to the other two control conditions at the study endpoint. Yu, Rawtaer, Feng, Fam, Kumar, Kee-Mun Cheah, Honer, Su, Lee, Tan, Kua, Mahendran ¹⁴ randomized MCI patients to receive either an MBI or a health education program. No significant changes in cognition were observed at three-month follow-up. At nine-month follow-up, a time by group interaction was observed on a forward digit span task, and on interference effects on the Color Trails Test.

Overall, the literature of using MBIs to combat cognitive decline in the early stages of dementia is highly mixed, comprising small effects that are heterogeneous across cognitive domains ¹⁵. Consistent with this pattern, we did not observe a clear benefit of MBI over TAU, even though the treatment was effective in improving global cognition (MMSE scores) and superior to CRT in improving delayed memory.

We posit two reasons for the modest effect of MBI in our study compared with previous work. First, our protocol was focused more sharply on the cognitive aspects of mindfulness, which paradoxically may have detracted from the effectiveness of the program by de-emphasizing its other important components. For example, mindfulness training is an effective means in reducing depression³⁰, which is a risk factor for the development of MCI³¹. In fact, a meta-analysis of MBIs for patients with dementia showed that depression (but not anxiety or stress) is effectively targeted by this treatment³². Contrary to this finding, we did not observe changes in depression in the MBI group in our study, while significant decreases were in fact seen in both CRT and TAU. However, we did observe that decreases in depression were correlated with improvements in global cognition in the mindfulness group only (albeit this relationship did not differ significantly from the slopes in CRT and TAU). This pattern of results suggests that the MBI administered in this protocol was not as effective as previous interventions in improving mood, possibly because of its strong emphasis on the relationship between mindfulness and cognition, and that paradoxically, programs that more effective in targeting negative mood may also have greater effects on cognition through the mediating effect of lowered depression.

Second, participants in the TAU group showed a strong effect of spontaneous reversion in our sample. Prior studies have shown that a substantial percentage of patients revert to normal cognitive functioning with time without any pharmacological or non-pharmacological intervention. This is true even in the relatively short-term; for example, Diniz, Nunes, Yassuda, Forlenza³³ reported that 23% of patients diagnosed with MCI reverted to normal cognitive functioning over a 12-month period, and Han, Kim, Lee, Park, Lee, Huh, Park, Jhoo, Lee, Kim³⁴ reported a reversion rate of 28.5%. This effect may be enhanced through participation in research studies (such as ours) that promoted engagement in activities that are cognitively stimulating, even among those assigned to the “treatment-as-usual” arm who are required to contribute data and interact with research staff.

The reported trial has a number of limitations. First, we were unable to conduct longer-term follow-up, and thus cannot ascertain whether the benefits to cognition were retained over time. It is conceivable that the benefits of MBI over CRT and TAU may only be seen on the order of months following the interventions. Second, the trial had relatively high dropout rates, particularly before participants were randomized to condition, increasing the likelihood of attrition bias. Finally, as the trial was open-label, participants were not blind to condition, or to the interventions being administered in the other study arms, which may have led to expectancy effects.

To conclude, in the context of prior positive results, the current study suggests that a more careful assessment is needed to identify the circumstances under which mindfulness training benefits persons with MCI. These may include population or intervention

characteristics, or disease severity/subtype. Such trials may permit more confident recommendations for if and when MBIs should be recommended as an aid to improve cognition in this patient group.

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Author contributions: KD and JL conceptualized the study, KW SH and QF collected the data, all authors contributed to data analysis, interpretation, and manuscript preparation.

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Figures and tables

Fig 1. Consort Flow Diagram of the study. MBT = mindfulness-based treatment, CRT = cognitive rehabilitation therapy, TAU = treatment as usual, ITT = intent-to-treat.

Table 1. Demographic variables of intent-to-treat sample

	<i>N</i>	Gender (Male, %)	Age <i>M</i> (<i>SD</i>)	Language (Eng, %)	No. of sessions attended (<i>SD</i>)
TAU	17	8 (47%)	66.3 (6.7)	11 (65%)	---
MBT	32	16 (50%)	67.6 (5.3)	18 (56%)	6.28 (2.43)
CRT	27	10 (37%)	67.1 (3.4)	16 (59%)	6.11 (2.9)

Table 2. Means and standard deviations of outcome variables pre- and post-intervention

	MBT		CRT		TAU	
Measure	Pre-int.	Post-int.	Pre-int.	Post-int.	Pre-int.	Post-int.
<i>Neuropsychological outcomes</i>						
MMSE (0-30)	26.19 (2.73)	26.73 (2.53)	26.27 (2.45)	26.84 (2.52)	26.37 (3.30)	26.94 (2.21)
MoCA (0-30)	22.41 (4.00)	23.47 (3.85)	23.86 (3.33)	24.53 (3.75)	23.00 (3.83)	24.41 (3.63)
RBANS - attention (40 to 160)	95.81 (21.16)	98.09 (22.82)	93.41 (19.78)	97.71 (17.53)	90.75 (15.08)	101.49 (15.11)
RBANS – immediate memory (40 to 160)	84.67 (18.31)	88.75 (21.84)	90.82 (15.48)	90.14 (23.48)	92.13 (22.66)	94.76 (20.55)
RBANS – delayed memory (40 to 160)	79.56 (23.06)	87.32 (23.27)	91.27 (22.03)	90.65 (24.05)	91.56 (20.27)	95.96 (23.21)
RBANS language - (40 to 160)	86.59 (11.42)	86.67 (9.69)	91.86 (12.12)	88.88 (8.99)	88.50 (17.37)	92.81 (14.07)
RBANS – visuospatial (40 to 160)	87.07 (15.77)	92.21 (17.89)	88.41 (18.60)	89.44 (17.82)	89.56 (18.37)	96.30 (22.14)
<i>Self-reported variables</i>						

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GDS (0-15)	4.97 (4.08)	4.92 (4.55)	5.20 (4.03)	3.56 (2.59)	5.41 (4.03)	4.88 (3.91)
MAAS (15-90)	60.22 (14.62)	61.38 (13.73)	66.32 (9.51)	64.36 (10.49)	58.38 (13.04)	65.14 (10.62)

MBT = mindfulness-based treatment; CRT = cognitive rehabilitation therapy; TAU = treatment as usual; MMSE = mini-mental state examination; MoCA = Montreal Cognitive Assessment; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; GDS = Geriatric Depression Scale, MAAS = Mindful Attention and Awareness Scale

Table 3. Repeated Measures ANOVA F values for ITT analysis (MBT vs. CRT)

Measure	Time ($F_{1,57}$)	p	η_p^2	Time*Group ($F_{1,57}$)	p	η_p^2
<i>Neuropsychological outcomes</i>						
MMSE	4.78	.03	.08	0.27	.60	.005
MoCA	7.39	.009	.12	0.019	.89	.0003
RBANS - attention	3.69	.06	.06	0.019	.89	.0003
RBANS – immediate memory	2.28	.14	.04	0.38	.53	.007
RBANS – delayed memory	7.24	.009	.11	6.56	.01	.10
RBANS - language	0.64	.43	.01	0.11	.75	.002
RBANS - visuospatial	4.97	.03	.08	0.09	.77	.002
<i>Self-reported variables</i>						
GDS	5.34	.03	.09	4.78	.03	.08
MAAS	0.01	.92	.0001	0.02	.89	.0003

ITT = intent-to-treat; MBT = mindfulness-based treatment; CRT = cognitive rehabilitation therapy; MMSE = mini-mental state examination; MoCA = Montreal Cognitive Assessment; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; GDS = Geriatric Depression Scale, MAAS = Mindful Attention and Awareness Scale

Table 4. Repeated Measures ANOVA F values for ITT analysis (MBT vs. TAU)

Measure	Time (F _{1,57})	p	η_p^2	Time*Group (F _{1,57})	p	η_p^2
<i>Neuropsychological outcomes</i>						
MMSE	3.86	.06	.08	0.28	.60	.006
MoCA	7.16	.01	.13	0	.66	.004
RBANS - attention	12.71	.001	.21	4.45	.04	.09
RBANS – immediate memory	3.04	.09	.06	0.10	.76	.002
RBANS – delayed memory	12.62	.001	.21	1.68	.20	.03
RBANS - language	1.47	.23	.03	2.62	.11	.05
RBANS - visuospatial	8.13	.007	.15	0.08	.78	.002
<i>Self-reported variables</i>						
GDS	0.69	.41	.02	0.49	.49	.01
MAAS	1.58	.21	.03	2.11	.15	.04

ITT = intent-to-treat; MBT = mindfulness-based treatment; TAU = treatment as usual; MMSE = mini-mental state examination; MoCA = Montreal Cognitive Assessment; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; GDS = Geriatric Depression Scale, MAAS = Mindful Attention and Awareness Scale

Supplementary Table 1: Intervention contents. Details of individual activities and practices are available on reasonable request from the corresponding author

Session	Topic	Content
Mindfulness-based intervention		
1	Introduction to Mindfulness	<ul style="list-style-type: none"> a) Introduction to mindfulness and its principals b) Mindfulness of the Breath c) Setting your daily practice
2	Getting to Know Your Body	<ul style="list-style-type: none"> a) Body Scan b) What to do when you encounter pain
3	Becoming Aware of Your Environment	<ul style="list-style-type: none"> a) Mindfulness of the Senses b) Mindful Walking
4	Bringing Mindfulness into the Everyday	<ul style="list-style-type: none"> a) Mindful Eating b) Setting a Daily Informal Practice
5	Gratitude and Compassion	<ul style="list-style-type: none"> a) Introduction to empathy and compassion b) Loving Kindness Practice
6	Observing the Nature of Your Mind	<ul style="list-style-type: none"> a) Leaves on a Stream (letting go) Practice b) Review of progress
7	Listening to Self and One Another	<ul style="list-style-type: none"> a) Listening to self b) S.T.O.P. Practice c) Listening to others
8	Putting it Altogether: Creating Your Practice	<ul style="list-style-type: none"> a) Setting up your daily practice b) Commitment pledge to practice c) Closing
Cognitiive Rehabilitation Therapy		
Session	Topic	Content
1	Cognition: Areas of Thinking	<ul style="list-style-type: none"> a) Introduction to cognition and areas of thinking b) Getting to know your difficulties c) Goal setting and SMART goals

2	Attention	a) Understanding attention b) Strategy 1: Notice Observe Describe (the NOD) c) Strategy 2: Verbal mediation
3	Learning and Memory: Encoding I	a) Understanding memory and encoding b) Strategy 1: Space Retrieval Method c) Strategy 2: Subtracting cues/ Backward chaining
4	Learning and Memory: Encoding II	a) Mental strategies: Mnemonics b) Setting memory goals
5	Learning and Memory: Retrieval	a) External memory aids b) Strategy 1: Memory aids c) Strategy 2: The 1 husband and 5 wives approach
6	Executive Function I: Planning and Organizing	a) Understanding executive functioning b) Strategy 1: Goal management training c) Activity: Sandwich Chef
7	Executive Function II: Problem Solving	a) Activity: Mystery activity b) Post activity reflection
8	Review and Reflect	a) Review and reflect b) The road ahead

Fig S1. Scatter plots of the change in GDS and MMSE for each group. This relationship was MBI group ($r = -.38$, $p = .04$) but not CRT ($r = -.14$, $p = .49$) or TAU ($r = -.12$, $p = .65$).

Appendix A. Details of neuropsychological assessments

Screening assessments

Interested study participants who had not previously received a diagnosis of mild cognitive impairment (MCI) prior to contact with the researchers were administered a short test battery scored on the following cognitive domains: global dementia screening, executive function, attention, language, verbal memory, visuo-spatial construction, and visuo-motor speed. Participants were also evaluated on the ability to perform activities of daily living and behavioural and psychiatric symptoms. All screening results were evaluated by the study PI, a clinical psychologist. Participants who were determined to meet criteria for MCI (per DSM-V criteria) were invited to enroll in the study.

The global dementia screening domain consisted of the Singapore version of the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MOCA). Participants with the equivalent of primary education or less needed to score 23 and above for the MMSE to be in the normal range and participants with secondary education or higher needed to score 26 or above to be in the normal range.

The Executive function screening domain consisted of the Frontal Assessment Battery and the Colour Trails 1 and 2. Participants with primary education or less needed to score 13 and above for the FAB to be in the normal range and participants with secondary education or higher needed to score 14 or above to be in the normal range. Colour Trails performance was scored based on norms.

The attention screening domain consisted of the RBANS forwards and backwards Digit Span. Individuals with primary education or less needed to score 5 or more to be considered normal for the forwards span and 3 or more to be considered normal for the backwards span. Individuals with secondary education or higher required scores of 6 and 4 respectively to be considered normal.

The language screening domain consisted of the 1-minute free recall from the MOCA. All participants needed to score at least 9 or more to be considered normal.

The verbal memory screening domain consisted of the immediate, delayed and recognition of the RBANS word list recall. A 10-item word list was read to the participant at 1 word per second. The participant then had to repeat the list back and was scored on the number of correct words recalled. This was repeated for 3 times for a maximum total score of 30. A delayed memory and recognition test was performed 15 minutes following the

immediate recall. The delayed test consisted of a free recall of the 10 words for a maximum score of 10. The recognition test consisted of 20 items (10 old and 10 new items).

Participants were scored based on the number of correct responses minus the number of false alarms, for a maximum of 10 points. Participants with primary education or less required at least 11, 3 and 5 points to be considered normal while participants with secondary education and higher required 12, 4 and 6 points respectively.

The visuo-spatial construction screening domain consisted of the first 3 items on the MOCA: simplified color trails, cube copy and clock drawing test. Participants needed to score 4 or higher to be considered normal, out of the maximum score of 5. Participants were instructed to draw a continuous line on ascending numbers in alternating shapes for 1 point, copy a 3D line drawing of a cube without reference for 1 point, and to draw a clock, set the time to 10 past eleven and fill in all the numbers for 3 points: 1 point for the contour of the clock, 1 point for correct numbers and 1 point for the correct clock hands.

The visuo-motor speed screening domain consisted of the digit cancellation task and maze navigation test from the RBANS. Participants with primary education or less needed to score at least 14 out of 40 for the digit cancellation task and 54 or above out of 240 for the maze task. Participants with secondary education or higher required a score of 20 or 46 respectively.

The activities of daily living screening domain consisted of the Katz index of independence in activities of daily living (Katz et al., 1963) and Lawton-Brody instrumental activities of daily living scale (Lawton & Brody, 1969). Participants were required to be independent to be eligible for the study.

Behavioural and psychiatric symptoms was evaluated using the geriatric depression scale (GDS), a 20-item self-report questionnaire. Participants need to score less than or equals to 10 points to be eligible to participant in the study.

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