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Investigating a Mindfulness-Based Intervention as an Attentional Network Training to Improve Cognition in Older Adults with Amnestic Mild Cognitive Impairment: A Randomized-controlled Trial

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Episodic memory deficits, often combined with impaired attention, are typical in older adults with amnestic mild cognitive impairment (aMCI). A Mindfulness-Based Intervention (MBI) could promote cognitive decline prevention or remediation through attentional network training. This randomized-controlled trial examined MBI's effects on objective (tests) and subjective (self-reported) measures of memory and attention, compared to a Psychoeducation-Based Intervention (PBI), in 41 older adults with aMCI. No distinctive benefits of the MBI were observed on objective tests, with both interventions improving attentional control. Moreover, the appreciation of one's cognitive functioning through questionnaires similarly improved for both interventions. Only in semi-structured interviews did a greater proportion of participants report benefits following the MBI compared to the PBI. This study does not provide sufficient support for the implementation of a MBI to enhance objective cognition by means of attentional network training in aMCI. However, it suggests a positive impact of non-pharmacological interventions on perceived cognition.

Keywords: cognitive dysfunction, memory, attention, mindfulness, amnestic mild cognitive impairment

Les déficits de mémoire épisodique, souvent combinés à des problèmes attentionnels, sont des atteintes centrales observées dans le trouble cognitif léger amnésique (TCLa) chez les personnes âgées. Une intervention basée sur la pleine conscience (IBPC) pourrait promouvoir la prévention ou la remédiation de ce déclin cognitif en entraînant les capacités attentionnelles. Cet essai randomisé-contrôle s'est intéressé aux effets d'une IBPC sur des mesures objectives (tâches) et subjectives (auto-rapportées) de l'attention et de la mémoire chez 41 personnes âgées ayant un TCLa, comparativement à une intervention basée sur la psychoéducation (IBP). Aucun bénéfice distinctif de l'IBPC n'a été observé sur les tâches cognitives, les deux interventions améliorant le contrôle attentionnel. De plus, les deux interventions ont permis d'améliorer la perception du fonctionnement cognitif des participants à la fin du questionnaire. Seules les entrevues structurées ont permis d'observer une plus grande proportion d'amélioration de l'attention après une IBPC plutôt qu'après une IBP. Cette étude ne permet pas de soutenir qu'une IBPC permet d'améliorer la cognition objective par l'entraînement du contrôle attentionnel chez des adultes âgés ayant un TCLa. Toutefois, les résultats suggèrent un impact positif d'interventions non-pharmacologiques sur la cognition perçue.

Mots clés : dysfonction cognitive, mémoire, attention, pleine conscience, trouble cognitif léger amnésique

Alzheimer's disease (AD) is a neurodegenerative condition with multiple etiologies that leads to brain structure and function deterioration, ultimately impairing cognition and autonomy. About one third of AD cases could be explained by modifiable risk factors, including depression and cognitive inactivity. The modifiable risk factors constitute promising clinical targets considering that their reduction by 10 to 20% could prevent from 8.8 to 16.2 million AD cases worldwide (Norton, Matthews, Barnes, Yaffe, & Brayne, 2014). As prevention efforts are deployed, there is increasing interest in holistic approaches fostering both cognitive and psychological health in older adults with amnestic mild cognitive impairment (aMCI), who are known to be at high risk for AD.

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According to longitudinal models of AD development, individuals first experience subjective cognitive decline that is not captured by objective tests (Molinuevo et al., 2017; Reisberg & Gauthier, 2008). As a matter of fact, perception and worries about below average cognitive capabilities compared to peers of the same age are associated with an increased risk for aMCI (Mitchell, Beaumont, Ferguson, Yadegarfar, & Stubbs, 2014) or AD (Jessen et al., 2010; Mitchell et al., 2014). As time passes, individuals for whom cognitive complaints suggest early AD pathology see their memory deteriorate to the point of impaired performance in objective tests, resulting in aMCI. aMCI diagnosis requires episodic memory impairment, with or without deficits in other cognitive domains, and no significant alteration of autonomy (Albert et al., 2011; Petersen et al., 2014).

Among other cognitive domains, attentional control was found to be impaired in aMCI (Belleville, Chertkow, & Gauthier, 2007; Van Dam et al., 2013), as part of the AD-related pathology (Balota & Faust, 2001; Belleville et al., 2007; Faust & Balota, 2007; Fernandez-Duque & Black, 2006), and was suggested to contribute to memory impairment (Castel, Balota, & McCabe, 2009). Indeed, the incapacity to properly encode and retrieve information in memory was associated with impaired attention processes in AD (Balota & Faust, 2001; Castel et al., 2009). Effective encoding requires the activation of brain networks related to attentional control, while effective retrieval happens with deactivation of the same networks (Huijbers et al., 2013). This process is called the encoding/retrieval flip, which happens through flexible engagement and disengagement of attentional control and default-mode networks, the latter being associated with mind-wandering and distraction. The link between attentional control and memory, notably at this advanced stage of neurodegeneration, brings into question whether interventions training attentional control might benefit memory performance at the aMCI stage.

The use of a Mindfulness-Based Intervention (MBI) appears doubly promising in the context of aMCI because it is expected to target attention and memory symptoms of this condition as well as the worries and distress associated with losses. Typically, a MBI consists in eight weekly sessions that aim at developing the participants' capacity to live in greater awareness and acceptance of the present moment through mindfulness meditation and attitudes (Chiesa & Serretti, 2011; Kabat-Zinn, 1990; Lindsay & Creswell, 2017). In mindfulness meditation, participants bring a stable, open, and non-judgmental attention to inner (e.g., breath, body sensations) or outer (e.g., sounds, feeling the floor underneath the feet) experiences, with the instructions to avoid as much as possible mind-wandering, dulling, and mental elaboration (Carlson & Speca, 2010; Kabat-Zinn, 1990). Indeed, this kind of intervention successfully boosted both the psychological (Goyal et al., 2014) and the cognitive functioning in a wide range of clinical population despite normal cognition at baseline (Gard, Holzel, & Lazar, 2014; Newberg et al., 2013). Along with potential cognitive benefits, the use of a MBI is justified by its potential to alleviate biological markers (e.g., stress hormones, inflammation, telomerase) associated with AD degeneration (Larouche, Hudon, & Goulet, 2015) and anxio-depressive symptoms which signal poor prognosis (Modrego & Ferrandez, 2004).

Available research with populations at risk for AD, although methodologically limited, is encouraging. The only randomized-controlled trial conducted in patients with aMCI showed no MBI group profit on verbal memory compared to a usual care control group (Wells et al., 2013). The same study found maintained cognitive flexibility after a MBI, while controls declined over time. Although indicative of a MBI's potential to improve cognition, the small sample (n = 14) of this previous study limits the conclusions that can be drawn in aMCI patients. A recent pre-post design study in aMCI patients, also with a small sample (n = 12), found gains on the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) after an eight-week MBI (Wong, Coles, Chambers, Wu, & Hassed, 2017). Benefits on the MoCA persisted over twelve months and were larger, with higher compliance to at-home meditation requirements as quantified by total minutes of practice. No other study investigated the effects of mindfulness in aMCI, but some addressed its impact in older adults with subjective cognitive decline (Hyer, Scott, Lyles, Dhabliwala, & McKenzie, 2014; Lenze et al., 2014; Wetherell et al., 2017) or AD (Innes, Selfe, Brown, Rose, & Thompson-Heisterman, 2012). Studies conducted in older adults with subjective cognitive decline found benefits post-MBI on at least one objective memory measure (Hyer et al., 2014; Lenze et al., 2014; Wetherell et al., 2017) and on an attentional control measure (Lenze et al., 2014; Wetherell et al., 2017). Although these effects seem promising for aMCI clinical studies, findings in subjective cognitive decline do not necessarily translate to aMCI, where cognitive decline and neurodegeneration are more pronounced (Molinuevo et al., 2017). An eight-week MBI in five dyads of older adults with AD and their live-in caregivers only lead to self-reported retrospective memory gains (Innes et al., 2012). Considering that AD is more advanced than aMCI in terms of overall decline and functioning, such subjective results present a fair likelihood of replication in aMCI patients.

It is surprising that in the quest for clinical interventions to revert or slow down aMCI decline, no study, thus far, focused on improving specific components of attention with mindfulness meditation training. Indeed, all studies only measured one aspect of attentional control, either inhibition (Lenze et al., 2014; Wetherell et al., 2017) or cognitive flexibility (Wells et al., 2013), without dissecting processes or targeting different aspects of the same participant. Malinowski and Shalamanova (2017) suggested that a "network training" (or near transfer) could occur following repeated meditation practice as a form of neurocognitive exercise with immediate or short-term benefits. Hasenkamp, Wilson-Mendenhall, Duncan, and Barsalou (2012) proposed a model that dissects a cycle of focused attention meditation practice, the main form of meditation taught in a MBI, into four phases: "FOCUS" on the chosen object, distraction from the object through mind wandering (MW), "AWARE" of the MW, and "SHIFT" back to the chosen object. Each phase is associated with a specific neurocognitive process (cf., Hasenkamp et al., 2012) that is repeatedly called for during the course of a mindfulness meditation session (as many times as the chosen object of attention is lost to distraction). Each of the four phases proposed in Hasenkamp et al.'s model (2012) could be isolated and rendered operational using a combination of the Sustained Attention to Response Task (SART; Smallwood et al., 2004) and the Attention Network Task (ANT; Fan, McCandliss, Sommer, Raz, & Posner, 2002). No study yet investigated alterations on the SART in aMCI patients, but a greater number of errors were reported in older adults with AD compared to healthy older adults (Huntley, Hampshire, Bor, Owen, & Howard, 2017). This result suggests that weak focalised attention could be present from the aMCI stage and profit from meditation training. Patients with aMCI (Van Dam et al., 2013) and AD (Fernandez-Duque & Black, 2006) were found to suffer impairments of the ANT conflict monitoring network only, suggesting attentional control and inhibition deficits.

The scarce albeit interesting results call for a pursuit of the investigation of mindfulness meditation effects on perceived and objective cognitive decline in older adults at risk for AD. Replication of the preliminary findings requires studies with stronger designs, at least including a larger sample of older adults with confirmed aMCI and an active control group, for comparison purposes. Along with replication, there is a secondary concern with specifying how mindfulness meditation impacts attention and memory, if so, in older adults with aMCI.

The Present Study

This single-blind randomized-controlled trial aimed at investigating the effects of a MBI on cognitive complaints and on objective cognitive impairment in older adults with aMCI. Computerized tasks of attention and memory, questionnaires, and individual semi-structured interviews were selected to assess a MBI's objective and subjective effects on attention and memory, compared to an active control Psychoeducation-Based Intervention (PBI). Greater attention and memory benefits were expected from the MBI based on theory (Malinowski & Shalamanova, 2017) and considering previous observations of improved cognition through a meditation practice in healthy adults and those at risk for AD (Gard et al., 2014; Hyer et al., 2014; Innes et al., 2012; Lenze et al., 2014; Newberg et al., 2013; Wells et al., 2013; Wetherell et al., 2017; Wong et al., 2017).

Methods

Participants

Forty-eight older adults with aMCI were recruited in two blocks of 24 participants. All participants spoke French as their maternal language, and all interviews, questionnaires, and tasks were administered in French. Individuals from each block were randomly assigned to the intervention. From the initial 48, 41 participants remained engaged in the intervention protocol for the eight weeks, all attending more than five intervention sessions, and were included in the analyses, in a "as treated" protocol (Armijo-Olivo, Warren, & Magee, 2009). Therefore, data was collected in 20 and 21 participants for the MBI and PBI conditions, respectively.

Most exclusion criteria attempted to circumscribe the etiology of impaired cognition to aMCI pathophysiology. Exclusion criteria at screening were: history of neurological disease, traumatic brain injury, intracranial surgery, or stroke; current psychiatric illness according to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM–5; American Psychiatric Association, 2013) criteria; substance abuse in the last twelve months; general anesthesia or oncologic treatment in the past six months; uncorrected vision or hearing impairments; untreated or unstable metabolic condition (e.g., Type 2 diabetes, hypothyroidism); recent treatment that may impact cognition; recent or sustained meditative experience; and anticipated unavailability to attend one or more of the first four intervention sessions.

Participants with aMCI met the following diagnosis criteria: 1) complaint about cognitive changes expressed by the patient, a relative, or a clinician; 2) objective impairment in one or more cognitive domains, including at least episodic memory, with a performance under 1.5 standard deviation based on local norms (Dion et al., 2014); 3) preserved overall functional autonomy; and 4) absence of dementia (Albert et al., 2011; Petersen, 2004). The project was reviewed and approved by the Ethics Research Board of the *Institut universitaire en santé mentale de Québec* (IUSMQ #398).

Materials

Clinical and neuropsychological battery. A complete clinical and neuropsychological battery was administered to participants to verify inclusion/exclusion criteria. The presence of an objective cognitive impairment was determined based on normative data. General cognitive functioning and cognitive complaints were evaluated using the MoCA (Larouche et al., 2016; Nasreddine et al., 2005) and the *Questionnaire de Plainte Cognitive* (Thomas-Antérion, Ribas, Honoré-Masson, Million, & Laurent, 2004), respectively. Verbal episodic memory was assessed with the *Test de Rappel Libre/Rappel Indicé à 16 items* (RL/RI -16; Van der Linden, 2004) and semantic memory, with the Pyramids and Palm Trees Test (Howard & Patterson, 1995), for which Dion et al.'s (2014) and Callahan et al.'s (2010) normative data were used, respectively. The Rey-Osterrieth Complex Figure Test (Osterrieth, 1944; Rey, 1941), a task requiring participants to copy a complex figure, targeted both visuo-constructive abilities, and visual episodic memory with participants required to recall the figure after three minutes, normality/abnormality being based on Tremblay et al. (2015). Visuo-perception was measured with the Size-Match task from the Birmingham Object Recognition Battery (Riddoch & Humphreys, 1993) and processing speed, with the Coding subtest from the WAIS-III (Wechsler, 1997). Language was tested by the 15-item Boston Naming Test (Calero, Arnedo, Navarro, Ruiz-Pedrosa, & Carnero, 2002) and the Phonemic (T-N-P) and Semantic (animals) Fluency Tests (Consortium des Universités de Montréal et de McGill, 1996), the latter normalized by St-Hilaire et al. (2016). Executive functioning was inferred from the D-KEFS version of the Stroop (Delis, Kaplan, & Kramer, 2001).

Free recall in episodic memory task. To measure participants' objective memory performance, many outcomes were derived from a verbal episodic memory task adapted from Moulin, James, Freeman, and Jones (2004). Three 15 words lists, semantically equivalent, were developed to be presented in a random order to participants. The words across the three lists were equivalent in terms of subjective frequency, length, and imagery level, based on psycholinguistic norms (Desrochers, 2006). Every word was made of two syllables and had high subjective frequency and imagery level. The test was administered using E-Prime 2.0 (Psychology Software Tools) and for each immediate recall trial, the words were presented for 3 seconds on the computer screen, with a 0.5 second inter-stimuli interval. Participants were asked to read the words presented on the screen and to memorize as many words as possible. Before recalling the words during the immediate recall trials, participants proceeded to a countdown from 100 for 20 seconds to impede recall from working memory. Participants undertook three immediate recall trials, followed by an unannounced delayed recall trial 20 minutes later. After the delayed recall trial, a recognition task (yes/no) was completed by the participants. For recognition, a total of 45 words were presented to the participants, including the 15 target words from the list, 15 semantically-related distractors, and 15 non-semantically-related distractors. All the distractors were comparable to target words for subjective frequency, length, and imagery level. In addition to total number of words recalled from a list in free and delayed recall, this task evaluated encoding in more details. It did so by providing insight of inter-trial gains and losses, along with an indicator of consolidation in long-term memory. The method to measure gains and losses from one trial to the next was used for the second and third immediate recall trial. Gains were represented by the proportion of items newly recalled at the trial $n + 1$ among the items that were not remembered in the trial n. Losses access was represented by the proportion of items not recalled at the trial $n + 1$ among the items that had been recalled in trial n. Gains and losses presented in the results section were averaged from the second and third trial. Consolidation was represented by the proportion of items recalled at delayed recall that had also been recalled at the third immediate recall trial. Immediate recall scores ranged between 0 and 45 words, and delayed recall and recognition scores ranged between 0 and 15 words. Proportions of gains, losses, and consolidation ranged between 0 and 1.

Sustained Attention to Response Task. The SART (Smallwood et al., 2004) is a Go/No-go task that measures one's capacity to remain vigilant and focused on a task. The SART has been mostly used as a measure of focused attention, by opposition to moments of MW when one's attention is less sharp. The parameters of the task used in this study were the same as those in Smallwood's study (2004). The test was administered using E-Prime 2.0 on a portable computer. During the task, stimuli (digits between 1 and 9) were presented in the middle of the computer screen. Participants were asked to press on the space bar every time a non-target digit is presented, and to refrain from pressing when the target digit (3) is presented. The task comprised 220 non-target trials and 15 target trials, always presented in the same order, which was determined randomly in the first place. Participants were instructed to complete every trial as quickly as they could, while committing the fewer errors they could. With regards for Hasenkamp et al.'s (2012) model, the SART measures the capacity to remain focused on a monotonous task and successfully withhold a habitual response on target trials. It also signals the propensity to let the mind wander after an error, resulting in post-error slowing of response time (RT). The two efficacy measures used in this study were the amount of commission errors (pressing the space bar on a target trial) and the RT of the trial after an error (Jackson & Balota, 2012; Smallwood et al., 2004). A greater number of errors is associated with the presence of more thoughts not related to the task, or more MW (Smallwood et al., 2004). A greater RT after an error, or "post-error slowing", was associated to a greater propensity to ruminate on the errors, reducing the efficacy in performing the task afterwards (Jackson & Balota, 2012).

Attention Networks Task. The ANT, originally developed by Fan et al. (2002), measures the efficacy of three different networks of attention. The task measures the capacity to detect salient information (alerting network), to direct the attention deliberately (orienting network), and to resolve conflicts and inhibit unwanted automatic responses (conflict monitoring network). The task was presented on a portable computer with E-Prime 2.0. The parameters used for the task were the same as the ones used by Van Dam et al. (2013) in their study with older adults with aMCI. For every trial, a row of five arrows was presented and participants were asked to determine towards which direction the center arrow (target) pointed, either left or right. Participants received the instruction to press the *F* key with the left hand if the center arrow pointed to the left, and the *J* key with the right hand if the center arrow pointed to the right. A fixation cross was presented in the center of the screen for the whole duration of the task, and participants were asked to keep their eyes on it. The stimuli were presented either over or under the fixation cross, in boxes that were always present, but were empty between the trials. The four other arrows (two on each side of the target) were oriented in the same direction as the center arrow in congruent trials and in the opposite direction in incongruent trials. Each trial was preceded by one of the three cue conditions: 1) no cue; 2) double cue; and 3) spatial cue. Cues consisted in a flash of the relevant box 900 milliseconds before the stimulus presentation, depending on the cue condition. The no cue trials did not provide any temporal or spatial information. In the double cue trials, both boxes flashed, providing temporal information only, and in spatial cue trials, only the box where the stimuli were to be presented flashed, providing both temporal and spatial information.

When put in relation to Hasemkamp's et al.'s (2012) model of attention network training, the ANT investigated the effects of a MBI on both AWARE and SHIFT phases. It tested the capacity to detect salient information by measuring performance benefits driven by access to temporal cues (alerting network; AWARE). The ANT also informed on SHIFT. First, it measured one's capacity to resolve conflicts arising from the presentation of ambiguous stimuli and to inhibit unwanted automatic responses normally driven by the ambiguity (conflict monitoring network), thus bearing commonalities with the inhibition of MW once detected. Second, it assessed the capacity to direct the attention, deliberately based on increased performance on trials with spatial cues (orienting network).

Alerting network scores were calculated by subtracting the average RT of trials with double cues to the average RT of trials without cue. Orienting network scores were calculated by subtracting the average RT of trials with spatial cues to the average RT of trials with double cues. Both scores were calculated without consideration for the congruency of the arrows' directions. The conflict monitoring network scores were calculated by subtracting the average RT for congruent trials from the average RT for incongruent trials, without consideration for cue condition. A higher value on the alerting and orienting networks indicated a better efficacy of the network, while a lower value indicated a better efficacy on the conflict monitoring network, or reduced interference of the side arrows.

Self-reported memory and attention. The perception of memory and attention difficulties was measured using the French version of the Cognitive Difficulties Scale (McNair & Kahn, 1984). This 39-item questionnaire was developed to measure the level of self-reported cognitive difficulties in older adults. Cognitive domains covered by the tool are memory, attention, concentration, language, praxis, knowledge about others, and time orientation. In this study, eleven items related to memory (items: 1, 2, 5, 6, 8, 9, 18, 27, 32, 33, 35) and nine items related to attention and concentration (items: 3, 10, 17, 19, 23, 25, 26, 31) were used, constituting two different homemade scores.

Semi-structured interviews. Semi-structured individual interviews were conducted by research assistants with every participant to determine whether or not they perceived an impact of the intervention on different aspects. Themes covered were general appreciation of the intervention, perceived effects on mood, stress levels, and anxiety, along with perceived changes in attention and memory. For every efficacy theme, participants were encouraged to indicate whether or not they perceived a change (positive or negative) and to elaborate on what they observed by giving concrete examples.

Interventions

Participants were administered one of the two intervention programs. Both programs comprised eight sessions of two and a half hours, which were administered to groups of ten to twelve participants. Both interventions were built with similar structures, including segments on education about weekly themes, segments where participants completed concrete exercises, and segments allocated to group discussions.

Mindfulness-Based Intervention. The MBI was based on Kabat-Zinn's (1990) Mindfulness-Based Stress Reduction and Segal, Williams, and Teasdale's (2002) Mindfulness-Based Cognitive Therapy. It also incorporated tools and exercises from other sources (Bartley, 2011; Carlson & Speca, 2010; Fournier, 2013; Monestès & Villatte, 2011). On top of accommodation already reported in mindfulness studies with older adults, such as shorter meditation duration, no full-day retreat, and shorter home practices (Geiger et al., 2016), the authors proceeded to minor adaptations of the program to meet the specificities of aMCI (e.g., using concrete examples that are relevant to the daily life of the retired elderly). The essence and goals of leading mindfulness programs were respected. Every session comprised a guided meditation, group discussions on meditation and home practices, and psychoeducation about mindfulness themes, along with stress management and obstacles (cf. Table 1 for weekly themes). Details of the program are currently published in a collective manual about mindfulness (Larouche, Chouinard, Morin-Alain, Hudon, & Goulet, 2008).

Psychoeducation-Based Intervention. The PBI (Parent, Larouche, & Hudon, 2015) was based on recent literature about aging and on a lay book discussing healthy aging (Juhel, 2014). The PBI excluded all forms of memory training or mindfulness/relaxation practices. Every session comprised psychoeducation about the weekly theme (cf. Table 1 for details), reflecting about one's situation with the help of exercises, and group discussions on the theme. The PBI was co-facilitated by a licensed psychoeducator assisted by trained graduate students.

Procedure

Participants were recruited from the community through newspaper advertising, local physicians' referrals, and the laboratory's database. A research professional in charge of recruitment contacted potential participants to ensure they did not meet exclusion criteria presented in the Participants section. If no exclusion criteria were present at that stage, potential participants were invited to meet a trained evaluator at the CERVO Brain Research Centre to provide written informed consent and to undertake the complete clinical and neuropsychological assessment. Participants meeting the aMCI criteria were invited to join the project and scheduled for a pre-intervention evaluation.

The 48 participants, recruited in two separate cohorts of 24 participants, completed a baseline evaluation in which they underwent the cognitive tasks and filled-up the questionnaires. At the end of the baseline evaluation, participants were given one out of 24 numbered envelops assigned using Microsoft Excel® random function, with an invitation for one of the two interventions. Also, they participated in the semi-structured interview post-intervention about the psychological and cognitive outcomes and about their general appreciation of the intervention.

Table 1

Weekly Intervention Themes for Both Intervention Programs

Intervention	MBI	PBI
Week 1	Autopilot vs. mindfulness	Normal vs. pathological cognitive aging
Week 2	Handling obstacles and supporting meditation practice efforts	Dementia continuum and types of dementia
Week 3	The wandering mind	Memory function and other cognitive issues in aMCI
Week 4	Acknowledging stress and its impact of one's life to better manage it	AD risk factors and pharmacological treatments
Week 5	Reflecting on how one could live in increased acceptance of one's situation	Medical follow-ups and discussions with physicians about cognitive concerns
Week 6	The role thoughts play in the maintenance of distress and stress	Relationships and discussions about cognitive decline with close relatives
Week 7	How to take better care of oneself	Everyday living with cognitive decline and coping with difficulties
Week 8	Sustaining a meditation practice beyond the program	What to do next with all the new knowledge acquired in the program

Note. MBI = Mindfulness-Based Intervention; PBI = Psychoeducation-Based Intervention; aMCI = amnestic mild cognitive impairment; AD = Alzheimer's disease.

Statistical Analyses

For the two groups, demographic information and neuropsychological performance at baseline were compared using Chi-square tests for frequencies of categorical data and Student's *t*-tests for continuous data. Repeated measures analysis of variance (ANOVA) assessed the efficacy of the two intervention programs using time of measurement, condition, and condition x time interaction as fixed factors. The Toeplitz covariance structure was used (Wolfinger, 1993) to account for the covariance difference between close measurement times (T0 and T1, or T1 and T2) and more distant ones (T0 and T2).

Regarding participants' responses to the interview questions, reporting benefits after the intervention was coded *1* and not reporting benefits was coded *0.* A binary ranking of interview responses was chosen, since only two participants reported memory worsening associated with the passage of time and intervention inefficacity, and none reported attention worsening. Chi-square analyses helped to determine if there were different frequencies of perceived gains for memory or attention between conditions. For all analyses, the alpha level was set at .05.

Results

Demographic, clinical, and neuropsychological data

Table 2 presents demographic and clinical data along with *Z*-scores on neuropsychological tests. Participants were aged from 56 to 87 years, had between 5 and 22 years of education, and were predominantly men. Participants from both groups were equivalent in terms of age, education, sex distribution, as well as clinical scores, and neuropsychological *Z*-scores.

Main outcomes

Longitudinal mixed model analyses tested the effects of time, condition, and time x condition interaction on objective and subjective measures of memory and attention. Table 3 presents the model-estimated adjusted marginal means for both interventions and Table 4 presents the time, condition, and condition x time interaction effects for all variables. First, for attention, there were time effects for ANT orienting network, ANT conflict monitoring network, and self-rated attention. No condition or condition x time interaction effects were found for any of the orienting, conflict monitoring, or self-rated attention. No effects of time, condition, or interaction were found for SART errors and post-errors, nor were there effects for ANT errors and alerting network. Regarding memory outcomes, there was a significant time effect on delayed recall consolidation, with the number of words recalled again at delayed recall decreasing over time, but no effect of condition and no interaction. No significant time, condition, or interaction effects were found for immediate and delayed recall, recognition, as well as gained or lost access.

Exploratory analyses of the specificities of each intervention were carried out. Table 5 presents simple effects ANOVAs for both groups for variables showing a time effect, that is, consolidation, self-rated memory, orienting and conflict monitoring ANT networks, and self-rated attention. For consolidation and self-rated memory, the MBI group did not show a significant time simple effect, while the PBI group did. Both interventions led to a significant time simple effect for the orienting ANT network, and only the MBI did for the conflict monitoring network. Neither intervention showed significant time simple effects for self-rated attention.

During the interviews, 50% of MBI and 33.3% of PBI participants reported better memory after participating in their respective intervention. Chi-square analyses revealed no distribution difference between the two conditions (c^2 (1, N = 41) = 1.17, p = .350). Also, during the interviews, 75% of MBI and 28.6% of PBI participants mentioned higher attention skills after the intervention. Chi-square analyses showed that significantly more participants of the MBI condition acknowledged attention gains (c^2 (1, N = 41) = 8.84, p = .005).

Discussion

In this study, we investigated the efficacy of a MBI to improve subjective and objective cognitive function in older adults with aMCI, compared to a PBI. We did so by measuring attention components directly targeted by mindfulness meditation (Hasenkamp, 2017; Hasenkamp et al., 2012) and by dissecting memory processes. We expected to observe a greater impact of a MBI than that of a PBI on attention and memory, as measured by objective computerized tasks, subjective questionnaires, and individual interviews. This hypothesis was not supported, except for interview-reported changes in attention.

The MBI led to comparable outcomes to the PBI for all memory-related variables. A deterioration of consolidation and a decrease of self-reported memory impairments from baseline to post-intervention were the only significant results. The absence of benefits on objective memory after a MBI concurs with the only study in aMCI that included a control group (Wells et al., 2013). The observed subjective memory improvement post-intervention for both interventions is coherent with findings for a MBI in older adults with AD and their caregivers (Innes et al., 2012). With regards to other studies showing memory benefits after a MBI in adults at risk for AD or with AD, they either used a

Table 2

Mean (Standard Deviation) Z-scores or Values for Sociodemographic, Clinical, and Neuropsychological Variables for the Two Conditions of Intervention

	Task	MBI		PBI		*t* value	*df*	*p*
		n	Mean (*SD*)	*n*	Mean (*SD*)			
Sociodemographic characteristics								
Age (years)		20	72.6 (7.0)	21	70.7 (5.6)	-.91	39	.368
Education (years)		20	13.7 (3.0)	21	14.1 (3.4)	.40	39	.614
Sex (% male)**		20	60%	21	57%	.03	1	.853
General cognitive functioning and complaint								
Complaint (/10)	CCQ	20	5.7 (2.5)	21	4.8 (2.3)	-1.13	39	.264
General cognition (/30)	MoCA test	20	24.4 (2.9)	21	24.4 (2.5)	.04	39	.971
Episodic verbal memory								
Free recall 1	16-word free and cued recall	20	-1.15 (0.90)	21	-1.07 (1.03)	.25	39	.800
Free recall 2		20	-1.21 (1.39)	21	-0.96 (1.22)	.63	39	.533
Free recall 3		20	-1.33 (0.89)	21	-1.51 (0.91)	-.65	39	.522
Delayed recall		20	-1.73 (1.28)	21	-1.60 (1.54)	.29	39	.773
Episodic visual memory								
Visual memory	Rey figure copy task	20	0.41 (1.68)	21	-0.30 (1.72)	-1.32	39	.194
Semantic memory								
Semantic (% normal)	PPTT	11	100%	9	100%	-	-	-
Verbal fluency								
Lexical	T-N-P fluency	20	-0.45 (0.73)	21	-0.67 (1.01)	-.78	39	.442
Semantic	Animal fluency	20	-0.42 (0.80)	21	-0.26 (1.35)	.45	39	.655
Confrontation naming								
Spontaneous	15-item Boston naming test	20	0.03 (0.78)	21	-0.07 (0.85)	-.39	39	.699
Total		20	0.09 (0.79)	21	-0.05 (0.79)	-.58	39	.569
Visual functions								
Construction	Rey figure copy task	20	-0.76 (1.44)	21	-0.92 (1.22)	-.30	39	.690
Perception	BORB circles	20	-0.16 (0.88)	21	-0.11 (1.16)			.861
Executive functions								
Inhibition time	Stroop D-KEFS	20	-0.05 (1.02)	21	-0.03 (1.14)	.06	39	.955
Switching time		19	0.07 (1.15)	21	-0.17 (1.31)	-.91	39	.547
Inhibition errors		20	0.25 (0.61)	21	0.02 (0.99)	-.62	38	.368
Switching errors		19	-0.30 (1.05)	21	-0.13 (1.10)	.51	38	.614
Processing speed								
Substitution	Code WAIS-III	20	0.13 (0.61)	21	-0.14 (0.79)	-1.25	39	.218

Note. Standardized *z*-scores are presented for variables when no value is indicated at the end of the variables name. **chi-square analysis; *n* = number of observations; MBI = Mindfulness-Based Intervention; PBI = Psychoeducation-Based Intervention; *df* = degrees of freedom; *SD* = standard deviation; BORB = Birmingham Object Recognition Battery; CCQ = Cognitive Complaint Questionnaire; D-KEFS = Delis-Kaplan Executive Function System; MoCA = Montreal Cognitive Assessment; PPTT = Pyramids and Palm Trees Test; WAIS = Weschler Adult Intelligence Scale.

Table 3

Adjusted Means of Outcomes as a Function of Time of Measurement and Condition

		Time of measurement					
		Pre (T0)		Post (T1)		Follow up (T2)	
Variable	Condition	Adjusted mean	SE	Adjusted mean	SE	Adjusted mean	SE
Immediate recall (/45)	MBI	20.8	1.4	20.8	1.4	21.4	1.4
	PBI	21.3	1.4	20.9	1.4	21.4	1.4
Delayed recall (/15)	MBI	7.9	0.7	7.0	0.7	7.4	0.7
	PBI	7.8	0.6	7.3	0.6	6.9	0.7
Recognition (/15)	MBI	14.2	0.3	14.4	0.3	14.2	0.3
	PBI	13.8	0.3	14.0	0.3	13.7	0.3
Gained access	MBI	0.43	0.04	0.38	0.04	0.46	0.04
	PBI	0.41	0.04	0.40	0.04	0.41	0.04
Lost access	MBI	0.24	0.03	0.23	0.03	0.24	0.03
	PBI	0.20	0.03	0.23	0.03	0.23	0.03
Consolidation	MBI	0.79	0.05	0.70	0.05	0.68	0.05
	PBI	0.80	0.05	0.79	0.05	0.66	0.05
Self-rated memory (/44)	MBI	24.0	1.7	22.7	1.7	22.3	1.7
	PBI	23.5	1.6	19.4	1.6	20.1	1.6
SART errors	MBI	1.8	0.4	1.9	0.4	1.4	0.4
	PBI	1.8	0.4	2.2	0.4	1.7	0.4
SART post-error slowing[a]	MBI	885.1	86.5	943.7	88.1	728.2	89.2
	PBI	781.7	83.3	730.7	82.1	654.6	91.9
ANT errors	MBI	10.5	1.9	11.1	1.9	7.0	1.9
	PBI	8.0	1.8	6.5	1.8	7.8	1.9
Alerting	MBI	32.5	8.5	35.7	8.5	37.7	8.5
	PBI	34.9	8.3	28.7	8.3	37.6	8.5
Orienting	MBI	58.7	10.6	76.1	10.6	104.0	10.6
	PBI	42.2	10.3	68.4	10.3	73.4	10.5
Conflict monitoring	MBI	-154.0	11.9	-123.2	11.9	-117.2	11.9
	PBI	-132.8	11.6	-112.6	11.6	-107.8	11.8
Self-rated attention (/36)	MBI	13.2	0.8	11.8	0.8	12.0	0.8
	PBI	12.0	0.8	10.8	0.8	11.4	0.8

Note. [a]n = 37; SE = standard error; MBI = Mindfulness-Based Intervention; PBI = Psychoeducation-Based Intervention; SART = Sustained Attention to Response Task; ANT = Attention Network Task.

Table 4

Time, Condition and Interaction Effects of Repeated Measures ANOVA

	Time effect				Condition effect				Interaction effect			
Variable	*F*	*df*	*p*	η^2_p	*F*	*df*	*p*	η^2_p	*F*	*df*	*p*	η^2_p
Immediate recall (/45)	.31	2, 50.9	.733	.01	.02	1, 39.1	.903	.00	.05	2, 50.9	.954	.00
Delayed recall (/15)	2.55	2, 47.3	.089	.10	.01	1, 39.6	.935	.00	.81	2, 47.3	.452	.03
Recognition (/15)	.45	2, 60.2	.642	.01	1.18	1, 38.1	.285	.03	.02	2, 60.2	.978	.00
Gained access	2.41	2, 55.4	.100	.08	.13	1, 38.2	.717	.00	1.05	2, 55.4	.356	.04
Lost access	.11	2, 58.6	.900	.00	.36	1, 39.4	.550	.01	.24	2, 58.6	.784	.01
Consolidation	4.97	2, 57.7	**.010**	.15	.36	1, 39.1	.551	.01	.97	2, 57.7	.384	.03
Self-rated memory (/44)	8.41	2, 59.0	**.001**	.22	.84	1, 39.0	.365	.02	1.77	2, 59.0	.180	.06
SART errors	1.73	2, 60.4	.186	.05	.21	1, 38.0	.648	.01	.33	2, 60.4	.718	.01
SART post-error slowing[a]	2.65	2, 40.7	.082	.12	1.89	1, 32.3	.179	.06	.084	2, 40.7	.438	.04
ANT errors	.55	2, 63.4	.580	.02	1.55	1, 38.2	.220	.04	1.16	2, 63.4	.319	.04
Alerting	.28	2, 61.6	.759	.01	.04	1, 39.1	.852	.00	.23	2, 61.6	.794	.01
Orienting	11.00	2, 60.3	**.000**	.27	2.47	1, 38.7	.124	.06	1.05	2, 60.3	.358	.03
Conflict monitoring	7.89	2, 54.4	**.001**	.22	.96	1, 39.2	.333	.02	.73	2, 54.4	.731	.01
Self-rated attention (/36)	3.39	2, 55.7	**.041**	.11	.08	1, 39.3	.373	.02	.18	2, 55.7	.840	.01

Note. [a]$n = 37$; SE = standard error; SART = Sustained Attention to Response Task; ANT = Attention Network Task.

screening test instead of a validated memory measure (Wong et al., 2017), or recruited older adults not cognitively impaired (Hyer et al., 2014; Lenze et al., 2014; Wetherell et al., 2017). Since older adults with aMCI are considered more advanced in AD-related neurodegeneration than those with subjective cognitive decline only (Molinuevo et al., 2017; Reisberg & Gauthier, 2008), the absence of cognitive changes in aMCI could be attributed to the ongoing neurodegeneration. Although it was not possible to distinguish the effects of the interventions over time, effect sizes were more pronounced in, but not specific to, the PBI condition for consolidation performance decrease and improvement of self-reported memory function. PBI gains on self-reported memory could be attributed to a greater sense of competence towards cognitive impairments, eased by the provided information and advice, but this should be confirmed in future research. Furthermore, the lack of a passive control group did not allow to tell if the observed changes simply occurred because of participation in a study protocol or of reassuring contact with trained facilitators. Therefore, these findings may be indicative of limited impacts of mindfulness once neurodegeneration and cognitive impairments reach the aMCI-level, but more rigorous randomized-controlled trials including a passive control group must be conducted before concluding so.

Table 5

Simple Effect ANOVAs for Time Effect Within Both Interventions

Variable	Condition	*F*	*df*	*p*	η^2
Consolidation	MBI	2.09	2, 57.2	.133	.07
	PBI	3.84	2, 56.9	**.027**	.12
Self-rated memory	MBI	1.42	2, 58.7	.251	.05
	PBI	8.94	2, 58.1	**.000**	.24
Orienting	MBI	7.74	2, 59.9	**.001**	.21
	PBI	4.33	2, 59.5	**.018**	.13
Conflict monitoring	MBI	5.56	2, 53.8	**.006**	.17
	PBI	2.58	2, 53.8	.085	.09
Self-rated attention	MBI	2.00	2, 55.2	.145	.07
	PBI	1.55	2, 55.0	.221	.05

Note. MBI = Mindfulness-Based Intervention; PBI = Psychoeducation-Based Intervention.

Regarding attention, the MBI was not superior to the PBI on any cognitive computerized task or self-reported questionnaires. The only significant result distinguishing the two conditions was the ratio of interview-exposed benefits, as participating in the MBI led to more reports of positive changes. There were significant improvements after both interventions relative to baseline for the orienting and conflict monitoring networks and for subjective attention. The simple effect analyses showed larger effect sizes on the MBI for attention networks and subjective attention function than on the PBI, but these results should be interpreted with caution, as no difference between the interventions over time was found. In addition, benefits cannot be distinguished from a practice effect on the ANT in the absence of data as to how the passage of time affects ANT performance in aMCI, which should be addressed in future studies by adding a passive control group.

With regards to Hasenkamp et al.'s (2012) model of attention network training, we expected to observe an improvement post-MBI in the efficacy of the FOCUS, AWARE, and SHIFT phases and a reduction of MW. It was anticipated to observe AWARE efficacy gains, as measured by an ANT alerting network performance increase. No improvement was observed on the alerting network, which remained stable from baseline to post-intervention for the two interventions. The MBI also led to no significant changes on the FOCUS and MW phases, as measured by the SART errors and post-error slowing. The results of the present study do not allow to confirm the efficacy of a MBI to benefit these three phases of Hasenkamp et al.'s (2012) model.

The only phase that profited from MBI participation is the SHIFT phase. Indeed, both orienting and conflict monitoring networks were used to measure MBI's impact on the SHIFT phase soliciting attentional control. The orienting network benefits are in line with findings in older adults at risk for AD elsewhere (Wells et al., 2013), which showed improvement of cognitive flexibility, as measured by the Trail Making Test (TMT), part B. The Trail B of the TMT includes strong components of attentional control, as it requires participants to willingly switch and alternate between two responses (Sanchez-Cubillo et al., 2009). Improvement of the conflict monitoring network is coherent with findings in worried older adults with subjective cognitive decline using the Stroop Interference Test (Lenze et al., 2014), but not in clinically depressed or anxious older adults experiencing subjective cognitive decline (Wetherell et al., 2017). As conflict monitoring is impaired in aMCI and AD (Fernandez-Duque & Black, 2006; Van Dam et al., 2013), improvements induced by non-pharmacological interventions are encouraging. Similar to memory findings, to dismiss a practice effect interpretation and support MBI's efficacy, future research must replicate MBI-benefit findings for the two attention networks, compared to both an active and a passive control group.

Training attention in older adults with aMCI can also be challenging because of the ongoing cognitive and cerebral decline. Novel practice of mindfulness meditation requires much effort and monopolizes attentional resources (Lutz, Jha, Dunne, & Saron, 2015; Vago & Silbersweig, 2012), already compromised in aMCI (Balota & Faust, 2001; Belleville et al., 2007; Faust & Balota, 2007). It is only with long-standing and frequent practice that meditation comes to require less attentional resources, allowing for the widening of attentional scope of awareness and the reaching of a novel state of constant attentional availability (for more detailed explanations, see Lutz et al., 2015; Vago & Silbersweig, 2012). In sum, an introductory eight-week mindfulness training could be insufficient to induce attention network changes important enough to be observed behaviorally in aMCI, which would require much more meditation practice over a long period, possibly years.

Self-reports of memory or attention using questionnaires did not allow for a differentiation of the two interventions but did improve over time. Considering that there were no objectified memory benefits, it brings into question whether older adults with aMCI retain the capacity to self-evaluate their memory, and if questionnaires target experienced memory impairments or worries of impairments. While anosognosia has long been considered a clinical marker of AD progression (Agnew & Morris, 1998), its occurrence in aMCI is not systematic and is unrelated to future decline risks (Roberts, Clare, & Woods, 2009). At this point, it is not possible to draw clear conclusions about the contribution of anosognosia to the discrepancy between results, but future studies should consider external reports of cognitive impairments. Indeed, informants' or relatives' ratings of the participants' memory function were shown to be more congruent with objective memory assessments than self-ratings (Frerichs & Tuokko, 2006), and more accurate in predicting subsequent decline (Slavin et al., 2015).

Another complex issue is whether subjective cognitive defects are informative of objective memory function or of depression and anxiety. Preliminary findings indicate a significant association between subjective cognition function, and depression and worries (Larouche, Chouinard, Morin-Alain, Goulet, & Hudon, 2018), while there was no association between subjective and objective cognitive functions (Larouche, Chouinard, Morin-Alain, Hudon, & Goulet, 2017). Depressive and anxious symptoms in aMCI were associated with poorer cognition (Callahan et al., 2015; Hudon, Belleville, & Gauthier, 2008) and a greater risk to develop AD (Mourao, Mansur, Malloy-Diniz, Castro Costa, & Diniz, 2016; Rosenberg et al., 2013). Cognitive complaints are also related to the depressive or anxious status of older adults with aMCI (Hülür, Hertzog, Pearman, Ram, & Gerstorf, 2014; Hülür, Hertzog, Pearman, & Gerstorf, 2015; Montejo et al., 2014; Yates, Clare, Woods, & MRC CFAS, 2017). Both objective and subjective decline heighten the risk of AD in older adults with aMCI, but perceived symptoms also directly contribute to psychological distress. Therefore, while preventing further decline is a key research objective, alleviating current perceived symptomatology is also of great interest to foster life satisfaction in this growing population of cognitively fragile elderly.

The present study provides interesting insight on whether a MBI can benefit cognition in older adults with aMCI, pointing to a great need for more research in this field. While this study focused on cognitive functions deemed closely associated with mindfulness meditation network training, future research should also include more traditional clinical cognitive measurements, such as the Stroop Test for inhibition, the TMT for cognitive flexibility, or the California Verbal Learning Test for verbal memory. These tasks have been used in more studies and were validated for various populations, perhaps allowing for better comparisons. Ensuring concordance of these validated tasks with the ANT and the SART could also be a key issue for a better understanding MBI's impact on cognition. Future research should include measures of potential mechanisms of action of the control intervention, here the PBI, allowing a distinction of the interventions' actions on outcome variables.

Limitations

This study is the first to investigate in such details the evolution of subjective and objective memory in older adults with aMCI following a MBI or a PBI, and it presents some limitations. First, including no long-term evaluation (i.e., ≥ one year) of cognition limited the capacity to size interventions' impacts on cognitive decline. Since progression from initial cognitive impairments to AD occurs in years rather than months, future research should ideally include longitudinal assessment of participants' cognitive status, months before and years after the interventions. A second limitation of this study is the absence of a passive control group that would have provided a measure of passage of time and practice effect on cognition, allowing insights on the test-retest fidelity of memory and attention tasks and questionnaires. This would have allowed for the calculation of minimal clinically important differences from reliability indexes and the creation of a reference point to interpret cognitive changes (Beaton, Boers, & Wells, 2002).

Conclusion

This randomized-controlled trial showed that both MBI and PBI are unlikely to improve memory, as measured by cognitive tests, in older adults with aMCI. Similar subjective attention and memory benefits were seen for both interventions, along with attentional control benefits, as measured by the ANT. Only interviews favored the MBI, with a significantly greater proportion of participants reporting benefits. This study also sheds light on a limited potential of a MBI to benefit cognition through the network training pathway proposed by Malinowski and Shalamanova (2017). However, it supports the impact of non-pharmacological interventions on perceived cognition.

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