

# Enhancing latent cognitive capacity in mild cognitive impairment with gist reasoning training: a pilot study

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**Objective:** Cognitive training offers a promising way to mitigate cognitive deterioration in individuals with mild cognitive impairment (MCI). This randomized control pilot trial examined the effects of Gist Reasoning Training on cognition as compared with a training involving New Learning in a well-characterized MCI group.

**Methods:** Fifty participants with amnesic MCI were randomly assigned to the experimental Gist Training group or an active control New Learning group. Both groups received 8 h of training over a 4-week period. We compared pre-training with post-training changes in cognitive functions between the two training groups.

**Results:** The Gist Training group showed higher performance in executive function (strategic control and concept abstraction) and memory span compared with the New Learning group. Conversely, the New Learning group showed gains in memory for details.

**Conclusion:** These findings suggest that cognitive training in general yields benefits, and more specifically, training programs that target top-down cognitive functions such as gist reasoning may have a broad impact on improving cognition in MCI. © 2016 The Authors. *International Journal of Geriatric Psychiatry* Published by John Wiley & Sons Ltd.

**Key words:** MCI; cognitive training; gist reasoning; executive function; memory; RCT

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The burden of cognitive impairment caused by Alzheimer's disease (AD) has escalated over the years because of increased longevity. Recent advances in our knowledge make it possible to detect AD in the early stages when individuals experience subtle cognitive deterioration with no significant functional impairment referred to as mild cognitive impairment (MCI) (Weiner *et al.*, 2013; Cohen and Klunk, 2014). Steps taken to improve early detection of MCI will be most beneficial when interventions can mitigate cognitive deterioration (Petersen *et al.*, 2014) because annual conversion rate to dementia varies from 5–7% and is especially higher in those with the amnesic subtype (e.g., Manly *et al.*, 2008; Roberts

*et al.*, 2013). Available pharmacological treatments for AD have offered limited benefits in improving cognition or slowing progression from MCI to dementia (Thal *et al.*, 2005; Feldman and Lane, 2007). With 200 failed AD drug candidates (Becker and Greig, 2013), the need to explore additional approaches that slow cognitive decline is urgent.

Cognitive training is one avenue to harness the residual brain capacity in MCI. Several studies have examined cognitive training effects in MCI, mostly in the amnesic subtype, but the findings have been contentious. While a Cochrane review of randomized control trials (RCT) found no benefits of cognitive training in MCI relative to controls (Martin *et al.*,

2011), several other reviews (Jean *et al.*, 2010; Stott and Spector, 2011; Cotelli *et al.*, 2012; Simon *et al.*, 2012; Huckans *et al.*, 2013; Reijnders *et al.*, 2013) and a meta-analysis (Li *et al.*, 2011) have found positive outcomes. A number of factors, such as poorly defined study-populations, limited RCT, and lack of active control groups make it challenging to establish training benefits (Hampstead *et al.*, 2014). Another potential limitation is that cognitive training studies have largely targeted memory functions, known to be most vulnerable and perhaps less modifiable in MCI. The training formats (individual vs. group; computer-based vs. low technology vs. mixed), the dose, and the outcome measurements have varied widely (e.g., Greenaway *et al.*, 2008; Hampstead *et al.*, 2008; Belleville *et al.*, 2011) with inconsistent generalization beyond the trained domain and limited improvements in functional outcomes (Gates *et al.*, 2011; Hampstead *et al.*, 2012; Simon *et al.*, 2012).

Cognitive training that targets non-memory domains in MCI would allow us to harness the neuroplastic potential of brain regions and networks that are relatively unaffected in the early stages of AD. Supporting this view, one of the largest RCT to date, the advanced cognitive training for independent and vital elderly (ACTIVE) trial, reported that individuals with low memory showed gains with abstract reasoning training, which targeted the ability to solve problems involving serial patterns of letter or number sequences, in contrast to memory training (Unverzagt *et al.*, 2007). This reported benefit was revealed in a subgroup analysis of individuals whose memory scores were 1.5 standard deviations below the population mean. Although these individuals were not clinically diagnosed with MCI, the findings suggest a potential benefit of targeting reasoning skills in a lowered-memory population. Additionally, empirical findings involving various forms of reasoning training in cognitively normal adults have shown generalized cognitive gains (Willis *et al.*, 2006; Anand *et al.*, 2011; Chapman *et al.*, 2015) and lasting benefits in self-reported independent activities of daily living (Rebok *et al.*, 2014). Research from our group offers further motivation to examine reasoning training that focuses on gist abstraction abilities in MCI (Chapman and Mudar, 2014).

Gist abstraction is defined as the ability to synthesize and derive diverse interpretations from complex information (e.g., written documents and verbal information). Gist represents the preferential propensity to glean global meaning rather than details from complex information as described in van Dijk and Kintsch's (1983) discourse framework and gist representation

in Reyna and Brainerd's (1995) fuzzy trace theory. Evidence suggests that advanced reasoning engages gist processing (Reyna and Brainerd, 1995, 2011; Reyna and Lloyd, 2006), and such gist reasoning skills are integral to successful academic, occupational, and functional performance (Reyna and Brainerd, 1995, 2011; Reyna and Lloyd, 2006; Chapman *et al.*, 2012). A series of gist reasoning training (henceforth referenced to as Gist Training) trials (Chapman and Mudar, 2014), which targeted gist abstraction abilities in normally aging seniors (Anand *et al.*, 2011; Chapman *et al.*, 2015) and adults with traumatic brain injury (Vas and Chapman, 2012; Vas *et al.*, 2015) have shown cognitive and neural benefits.

Studies on Gist Training involving normal older adults, in particular, have demonstrated not only gains in abstraction but also generalized benefits in untrained measures of cognitive control including cognitive switching, fluency, and concept abstraction (Anand *et al.*, 2011; Chapman *et al.*, 2015). Furthermore, normal older adults who underwent Gist Training showed increases in global and regional cerebral blood flow in the default mode network and the central executive network compared with waitlisted controls. Increased functional connectivity in the same brain networks was noted in addition to increased structural connectivity in the left uncinate fasciculus (Chapman *et al.*, 2015). These brain gains were significantly linked to cognitive improvement. This convergent pattern suggests the brain's residual neuroplastic potential could be tapped by training top-down cognitive functions such as gist reasoning, to achieve cognitive and neural benefits.

The purpose of this randomized control pilot study was to examine the effects of Gist Training on cognition in individuals with MCI as compared with an active control training consisting of New Learning. We hypothesized significant gains in the Gist Training group compared with the New Learning group in executive functions whereas we predicted the New Learning group would show gains in memory. We expected both groups to self-report gains on real life memory performance due to engagement/stimulation offered by the training programs.

## Method

Fifty community-dwelling seniors (see Table 1 for Demographics) participated in this study after providing informed consent according to the guidelines of The University of Texas at Dallas Human Protection Program and in accordance with the Helsinki Declaration

Table 1 Demographics and performance on screening measures

	Gist Reasoning	New Learning
	( <i>n</i> = 23; females = 11)	( <i>n</i> = 27; females = 16)
Years of Education	16.22 (2.26)	17.26 (1.48)
Age at test	75.65 (8.51)	69.78 (8.01)
MMSE	27.74 (1.36)	28.11 (1.60)
GDS	1.27 (1.19)	1.91 (1.35)
BDI	7.67 (3.17)	5.75 (2.06)

GDS Gist group *n* = 11, New Learning group *n* = 23; BDI Gist group *n* = 12, New Learning group *n* = 4. BDI, Beck Depression Inventory; GDS, Geriatric Depression Scale; MMSE, mini-mental state examination.

of 1975, as revised in 1983. All participants were native English speakers, had a minimum of high school education, and 46 were right-handed. Individuals of both genders were included with no exclusions made based on racial or ethnic factors. All participants completed the mini-mental state examination (MMSE, Folstein *et al.*, 1975), the Wide Range Achievement Test 4 (WRAT4, Wilkinson and Robertson, 2006), and either the Geriatric Depression Scale (GDS, Yesavage *et al.*, 1982) or Beck Depression Inventory (BDI, Beck *et al.*, 1996). Only participants with scores of 25–30 on the MMSE, ability to read at a 12th grade reading level, a score of 4 or below on the GDS or a score below 13 on BDI were included. All participants showed adequate visual and auditory acuity by being able to read 12 point font-type and following conversation in a quiet environment, respectively.

Participants met Petersen criteria for MCI (Petersen *et al.*, 2001) and were of the amnesic subtype. They had (i) subjective memory concerns; (ii) objective memory loss (e.g., a Wechsler Memory Scale-III (WMS III, Wechsler, 1997b) logical memory subtest delayed recall score of 5–9 (8–15 year of education) and 9–12 ( $\geq 16$  years of education) for early MCI (EMCI);  $\leq 4$  (8–15 year of education) and  $\leq 8$  ( $\geq 16$  years of education) for late MCI (LMCI)) (Aisen *et al.*, 2010); (iii) a Clinical Dementia Rating (CDR, Morris, 1993) of 0.5; (iv) preserved activities of daily living determined by instrumental activities of daily living scores; and (v) an absence of dementia. Diagnosis of MCI was made by a research team of neurologists, neuropsychologist, cognitive neuroscientists, and speech-language pathologists. Four (two in each group) of the 50 patients were taking cholinesterase inhibitors when tested and were on stabilized doses

of donepezil for at least 3 months. Participants with history of other neurologic disease, medical illnesses, major psychiatric disturbance, substance abuse, or taking psychoactive medications were excluded.

In the pre-training phase, participants' baseline performance was established using cognitive measures of executive function and memory as well as a validated, self-rating memory measure; after which, they were randomized into one of the two training groups (Gist Training *n* = 23 [14 EMCI, 9 LMCI]; New Learning Training *n* = 27 [17 EMCI, 10 LMCI]). The same measures were used in the post-training phase to examine outcomes. The pre-training and post-training assessments were done by three experienced clinicians per manualized protocol. Scoring was done by two clinicians independently, one of whom was unaware of the group assignment and time of testing (pre or post), and no significant differences were observed between scores of the two raters ( $p < 0.05$ ).

## Measures

Executive function measures included similarities subtest from the Wechsler Adult Intelligence Scale III (Wechsler, 1997a), strategic attention score from a list learning task (Hanten *et al.*, 2007), and complex abstraction from an experimental text processing task (Anand *et al.*, 2011). Memory measures included the logical memory subtest from WMS III, memory span from the list learning task, and memory for details from the text processing task. Participants rated their memory on the metamemory questionnaire (MMQ, Troyer and Rich, 2002). See Table 2 for details of experimental measures.

Gist Training and New Learning Training programs were delivered in small groups of 3–5 individuals over 4 weeks with two 1-h sessions per week. The cognitive training was led by a clinician who had previously completed a 3-stage process prior to study implementation consisting of reading about the programs, observing a trained clinician deliver a 4-week program, and leading training sessions under supervision to ensure treatment fidelity. The training dose was determined based on a previous study involving normal controls (Anand *et al.*, 2011). Training equity was based on similar group size, same number of sessions, similar opportunity for interaction and social contact, and comparable home assignments (reading an article or watching a short video estimated to take about 20 min a day). While compliance was not formally tracked, the majority of participants were observed to complete their assignments during the

Table 2 Description of experimental outcome measures

Neurocognitive measure	Description	Administration and scoring
List learning	Three different lists of 16 words adapted from Hanten <i>et al.</i> (2007) were used. For each list, the words were divided into two similar sets of 8 words (one set spoken by a female voice and the other by a male voice, randomized within the list). The words within a list were designated by voice (male or female) as either high-value (10 points) or low-value (1 point).	Words were presented one at a time auditorily. Recall elicited at the end of each list. <b>Scoring</b> <i>Strategic Attention</i> : Number of high value words recalled on each trial. <i>Memory Span</i> : Total number of words recalled on each trial
Text processing	Narrative of 550 words about a man's life and the eight jobs he attempted throughout his life in an effort to make life better for others.	Participant asked to read the narrative, generate lessons, and recall details. <b>Scoring</b> Adopted from previous studies by Ulatowska <i>et al.</i> (1998) and Chapman <i>et al.</i> (2002). <i>Abstraction</i> : Scored on a pre-established scale of 0–6. Scores fall on a continuum, representing qualitative differences in the nature of response, with lower scores indicating problems in abstracting meaning and higher scores indicating greater ability to abstract meaning across the text content. <i>Detail memory</i> : Number of details recalled out of a possible 24 details.

homework discussion period at the beginning of each session.

### Cognitive training programs

*Gist reasoning training.* Gist Training is a strategy—rather than content-based program. The primary objectives are to promote utilization of three core strategies: strategic attention, integrated reasoning, and innovation summarized in Table 3 (Chapman *et al.*, 2012; Chapman and Mudar, 2014). The strategy instruction is hierarchical and dynamically interdependent, with each strategy building on previous strategies. A wide variety of information sources such as articles, short stories, and audio clips were used to provide intense practice with these strategies. Participants were encouraged to utilize the three strategies as often as possible within the context of their own life

activities and goals throughout their day (e.g., listening to a lecture, reading a newspaper/book, watching television, or engaging in conversation).

*New learning training.* This training uses an educational approach to teach and discuss interesting facts about how the brain works and what factors influence its health. This program was originally developed at the Rotman Institute, Canada (Binder *et al.*, 2008) and has been used by others in cognitive training studies (Chen *et al.*, 2011; Levine *et al.*, 2011; Novakovic-Agopian *et al.*, 2011). For this study, an adapted curriculum to approximate the general structure of Gist Training matching the number of sessions, duration, discussions, and homework assignments, was used. Topics outlined in Table 3, among others were covered. Information across a multitude of sources was presented to

Table 3 Training protocols

Training	Description
Gist Reasoning Training	Hierarchical strategies Strategic attention: Consciously blocking distractions/less relevant information (e.g., reducing multitasking; turning off TV/email notifications) and focusing on important information (e.g., highlighting text). Integrated reasoning: Binding explicit facts with world knowledge to construct generalized meanings. Innovation: Deriving multiple interpretations and generalized applications beyond the concrete content reflecting fluency and fluidity of thinking.
New Learning Training	New Learning about brain functions and influences on cognition. Example topics covered: Brain structures and functions; Neuroplasticity and neurogenesis; Memory and the brain; Social bonds and the brain



facilitate socially engaged discussion and New Learning. Individuals were encouraged to share with others what they were learning in the program as often as possible.

## Statistical analysis

Each cognitive measure was entered in a general statistical linear model that included a training effect (pre-assessment and post-assessment) and a group effect from the two cognitive training therapies (Gist Training and New Learning), and the interaction between them. The interaction term (group  $\times$  time) was of primary interest; therefore, we restricted inference to mean change over the assessment periods between the two training groups. Covariates, such as age and education, were included in the model as simple additive terms, but any effect of age and education was differenced out of the interaction contrasts. Also included in the model were three variance components from random effects due to variability within subjects, across subjects, and between stages of MCI (EMCI and LMCI). For each outcome measure the interaction contrast of means were obtained, which were transformed to student's *t*-statistics. The corresponding *p*-values are reported in Table 4.

## Results

Overall, we observed three significant two-way interactions between training effect and training types. Gist

Training showed increased post-assessment means from baseline relative to New Learning training on executive function and memory measures, specifically strategic attention (high value points) ( $p=0.011$ ) and memory span (total number of words) ( $p=0.016$ ) on trial 3 of the list learning task. In each case, the New Learning group showed no mean change from baseline (Figure 1). Conversely, Gist Training showed a smaller increase in post-assessment means from baseline relative to the New Learning training for detail memory ( $p=0.045$ ). Additionally, we observed two important trends wherein Gist Training showed improvements in concept abstraction on the similarities subtest ( $p=0.066$ ) and memory on the logical memory subtest ( $p=0.075$ ) relative to the New Learning group (Figure 2). We also observed a larger mean reduction in subjective memory mistakes with Gist Training, although not significant ( $p=0.188$ ).

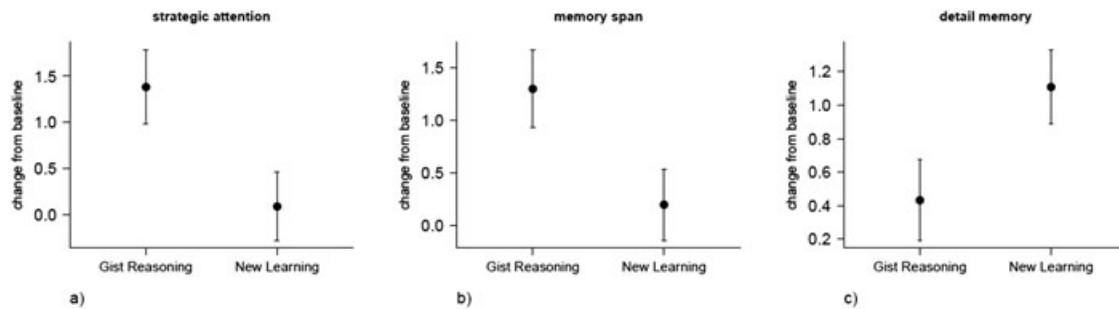
## Discussion

This study is one of the first pilot RCT to investigate the impact of Gist Training in individuals with amnesic MCI as compared with an active control training program that targeted New Learning. Individuals who received Gist Training strategically recalled more high value items compared with low value items on the trial of interest (trial 3) during list learning compared with the New Learning group. Strategic processing is achieved when individuals are able to attend to the most important/relevant information while ignoring the less relevant details (Dayan *et al.*, 2000). Such strategic

Table 4 Pre-training to post-training changes in cognitive functions in the two training programs

Neurocognitive measures	Gist Reasoning		New Learning		Interaction <i>p</i> -value
	Pre	Post	Pre	Post	
Executive function					
WAIS-III Similarities (SS)	13.32 (0.56)	14.27 (0.56)	13.89 (0.50)	13.96 (0.51)	0.066
List learning strategic attention—trial 3	2.95 (0.39)	4.34 (0.40)	4.30 (0.37)	4.39 (0.38)	0.011
Text processing complex abstraction	2.96 (0.36)	3.37 (0.38)	3.04 (0.33)	3.45 (0.35)	0.498
Memory					
WMS-III Logical	10.45 (1.31)	12.67 (1.32)	10.11 (1.30)	11.00 (1.30)	0.075
List learning memory span	3.31 (0.42)	4.62 (0.43)	4.98 (0.40)	5.18 (0.41)	0.016
Text processing detail memory	4.61 (0.26)	5.04 (0.26)	4.89 (0.24)	6.00 (0.24)	0.045
Self-evaluation memory					
MMQ Feelings	33.14 (4.58)	38.27 (4.58)	31.28 (4.08)	34.13 (3.94)	0.278
MMQ Mistakes	41.83 (3.93)	44.20 (3.93)	42.32 (3.54)	41.32 (3.39)	0.188
MMQ Strategies	32.13 (4.22)	36.38 (4.22)	40.98 (3.88)	40.22 (3.66)	0.168

WAIS-III, Weschler adult intelligence scale III; MMQ, metamemory questionnaire.



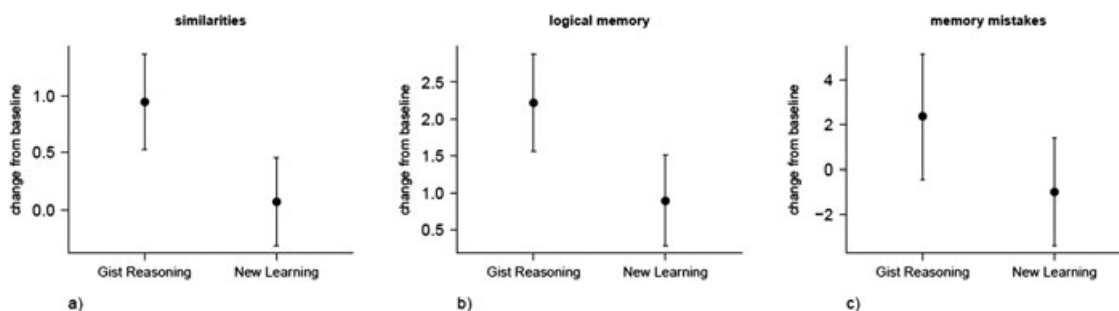
**Figure 1** Gist Training showed increased post-assessment means from baseline relative to New Learning Training for (a) third trial of strategic attention, and (b) memory span. New Learning training showed increased post-assessment means from baseline relative to Gist Training for (c) detail memory.

processing is related to cognitive efficiency (Castel *et al.*, 2007) and may serve to improve diminishing memory capacities in individuals with MCI. Gains in strategic attention with Gist Training are relevant to mitigating cognitive losses in MCI because previous research has shown that AD impairs cognitive control in early disease stages (Castel *et al.*, 2009). Our finding suggests that a residual capacity to select important information and inhibit less important information and exert better top-down control may be improved in MCI through Gist Training.

The Gist Training group also showed a trend towards gains in concept abstraction on similarities subtest similar to our previous findings involving normal aging individuals (Anand *et al.*, 2011; Chapman *et al.*, 2015). The similarities subtest captures an individual's ability to process and abstract relationships (e.g., how are a car and train alike). Our findings suggest that training focused on abstracting meaning from complex information showed transfer benefits to untrained concept abstraction. However, unlike other cognitive training trials involving Gist Training in normal aging (Anand *et al.*, 2011; Chapman *et al.*, 2015), we did not find gains in complex gist abstraction during text processing. It is possible that the MCI group

may have needed a higher training dose than 8 h to experience gains in complex abstraction.

With regard to memory benefits, both groups showed significant gains on different immediate memory measures. The Gist Training group improved significantly pre-test to post-test on memory span for items during list learning. Thus, not only did they strategically remember more high value items, but by using this strategy, they were able to improve their memory span (i.e., number of items recalled), a gain that was not observed in the New Learning group. Furthermore, the Gist Training group also showed a trend towards improvement on logical memory scores, a more complex memory measure, although not significant probably because of small subject numbers and variability contributed by EMCI and LMCI stages. Moro *et al.* (2015) reported similar improvements in memory in individuals with MCI following executive function training and attributed those gains to enhanced memory efficiency. One key gain observed in the New Learning group was a significant pre to post increase in memory for facts. The ability to remember more factual information is an important gain and was directly related to the nature of New Learning Training that mainly targeted memory for facts and is consistent with the findings of



**Figure 2** Gist Training showed (i) trends towards increased post-assessment means from baseline relative to New Learning training for (a) similarities scaled score (b) logical memory raw score, and (ii) a reduction in number of subjective memory mistakes.

other training studies that have targeted memory functions in MCI (Li *et al.*, 2011; Martin *et al.*, 2011; Simon *et al.*, 2012; Reijnders *et al.*, 2013).

Few studies have reported quantitative data related to perceived gains/benefits following cognitive training. In the present study, participants in the Gist Reasoning group more often reported reduced frequency of memory mistakes on MMQ in everyday memory situations, such as remembering appointments, names, and telephone numbers. MMQ was incorporated into the study design after we completed a few waves of training; thus, we had data on only a subset of participants. Nonetheless, a similar number of MMQ measures were collected for both groups. Implication of improved daily memory may suggest a potential generalization to real life benefits; however, a no-contact control group is needed to determine the true influence of the subjective changes on memory. Future studies are warranted to examine whether an increased training dose would achieve larger gains and whether perceived memory gains are associated with objective memory gains.

This pilot study should be interpreted within the context of its limitations. First, our sample size was relatively small to derive conclusive patterns. However, the positive cognitive gains support verification in a larger study. With the promising evidence of benefits from relatively brief Gist Training dose, future trials would be improved if different training dose effects were tested. The addition of neural markers measuring the brain's response to cognitive training would also be informative in light of prior evidence of brain and cognitive gains following Gist Training in other populations. Also, the small sample size did not allow us to examine individual factors that contribute to response to training such as stage of MCI. Because the classification of EMCI and LMCI is not universally accepted, our goal for staging was to account for variability caused by such differences during analysis. Future studies with larger samples should explore treatment response between these stages. Also, longitudinal studies are necessary to determine maintained effects and to determine whether cognitive interventions early in the disease are able to slow the rate of decline or conversion to dementia. Only a handful of studies have shown that training effects are maintained from 2 weeks to 6 months (Rapp *et al.*, 2002; Kinsella *et al.*, 2009; Greenaway *et al.*, 2012); however, few have examined conversion rates subsequent to training (Huckans *et al.*, 2013).

To summarize, rapid advances in early identification of AD necessitate development of multi-dimensional treatment options to halt or slow cognitive deterioration in this population. This study offers preliminary evidence that Gist Training

offers a promising protocol to engage and build cognitive capacity in individuals with MCI. More work is needed to establish long term benefits of such approaches in slowing cognitive deterioration and in extending years of functional competency in this population.

## Conflict of interest

None declared

### Key points

- This represents one of the first randomized pilot training trials to compare the cognitive benefits of a Gist Reasoning Training versus New Learning in Mild Cognitive Impairment (MCI).
- The reasoning trained MCI group improved in measures of executive function and memory.
- The New Learning MCI group improved on detail memory.
- Findings support the potential for Gist Reasoning Training to harness and strengthen the latent cognitive capacities in MCI.

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