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Alleviated Anxiety Boosts Memory Training Gains

Alleviated Anxiety Boosts Memory Training Gain in Older Adults with Subjective

Memory Complaints: A Randomized Controlled Trial

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Highlights

- What is the primary question addressed by this study? We investigated whether memory training combined with group counseling would induce greater memory gains than memory training or group counseling alone in older adults with subjective memory complaints.
- What is the main finding of this study? Group counseling decreased symptoms of anxiety, memory

training increased associative learning, and the combination of two intervention induced larger memory gain than memory training alone.

What is the meaning of the finding? The results suggest that it may need to include treatment for anxiety in memory intervention for older adults with subjective memory complaints.

Abstract

Objective: Older adults with subjective memory complaints (SMC) have a higher risk of dementia and commonly demonstrate symptoms of depression and anxiety. The study aimed to examine the effect of a memory training program for individuals with SMC, and whether additional group counseling aimed at alleviating depression and anxiety would boost memory training gains.

Design: A three-armed, double-blind, randomized controlled trial.

Setting and Participants: Community-dwelling older adults with SMC, age ≥ 60 .

Methods: Participants (n = 124) were randomly assigned to memory training (MT), group counseling (GC), or GC+MT intervention. The GT+MT group received 3 sessions of group counseling followed by a 4-week memory training, while the MT group attended reading and memory training, and the GC group received group counseling and health lectures. Cognitive function and symptoms of depression and anxiety were assessed at baseline, mid-, and post-intervention.

Results: After group counseling, the GC+MT and GC groups showed reduced symptoms of anxiety compared to the MT group. Memory training enhanced associative learning in both

MT and GC+MT groups compare with the GC group, but the GC+MT group demonstrated a larger memory improvement (Cohen's d = 0.57) than the MT group (Cohen's d = 0.44).

Conclusion and Implications: Group counseling decreased symptoms of anxiety, memory training increased associative learning, and the combination of two intervention induced larger memory gain than memory training alone. The results suggest that it may need to integrate treatment for anxiety into memory training for older adults with SMC to achieve better intervention effect.

Trial Registration: ChiCTR-IOR-15006165 in the Chinese Clinical Trial Registry.

Key words

subjective memory complaints, memory training, group counseling, anxiety, depression

INTRODUCTION

Individuals with subjective memory complaints (SMC) report declining memory without measurable cognitive deficits. SMC crosses the boundary between normal aging and mild cognitive impairment ¹, and is associated with higher risks of subsequent cognitive decline and dementia ², as well as poor quality of life ³. Cross-sectional and longitudinal evidence shows older adults with SMC have increased likelihood to manifest Alzheimer's Disease biomarkers such as brain amyloid deposition ⁴, glucose hypometabolism ⁴, and hippocampal volume loss ⁵. SMC is considered as a "promising" stage for non-pharmacologic interventions aimed at delaying cognitive decline and preventing cognitive impairment ⁶.

Cognitive training is one of the most used non-pharmacologic interventions. Some studies have shown older adults with SMC benefit from cognitive training ^{7,8}, while others

fail to find significant cognitive improvement training ^{9,10}. A meta-analytic study ¹¹ revealed that cognitive training could improve cognitive function in older adults with SMC, resulting in a small to moderate effect size (Hedge's g = 0.38). Memory strategy training can benefit older adults in both objective memory performance and subjective memory measures including memory efficacy and memory beliefs^{12,13}. A common criticism of cognitive training is that the training-related improvements are typically observed in domain-specific activities with little evidence of generalization to other domains or situations¹⁴. In contrast, multimodal intervention embedded in real-world situation may produce large transfer. For instance, the Experience Corps Program showed that a year of volunteering induce broad improvements in memory, executive function, brain functioning and physical health^{15,16}.

Another limitation of cognitive training is that cognitive training is usually implemented in homogenized participants, rarely targeting older adults with symptoms of depression and anxiety. Symptoms of anxiety and depression are widespread in aging population. The prevalence of anxiety symptoms ranges from 15% to 52% in community samples¹⁷. The prevalence of clinically relevant depressive symptoms varies between 7% and 49% in old age ¹⁸. Depression and anxiety can lead to greater cognitive decline ¹⁹, and an increased risk of progression to dementia ²⁰. Individuals with SMC commonly demonstrate symptoms of depression and anxiety ²¹. Depression and anxiety are found detrimental to memory performance ²², Animal studies demonstrate that exposure to psychological distress may harm older adults' memory by causing neurological deterioration to the limbic system including hippocampus ²³. As the close relationship

between depression/anxiety and memory functioning, alleviating depressive and anxious symptoms may need to be incorporated into memory training program to optimize the training efficacy ²⁴. There may be greater memory improvement if intervention for depression and anxiety is added to memory training in older adults with memory complaints.

To our knowledge, no experimental study has directly examined whether memory training combined with psychological interventions for depression and anxiety would outperform traditional memory training. A few training studies ^{25,26} integrated stress management techniques into memory training in healthy older adults and found these comprehensive memory training programs reduced symptoms of anxiety and improved cognitive performance compared to placebo or waitlist groups. However, comparison with passive control groups cannot isolate the effect of stress management from pure memory training.

The aim of this study was to determine whether interventions for depression and anxiety would facilitate training gains on memory performance in older adults with SMC. We have developed a comprehensive memory training program by combining psychological interventions with memory training. We evaluated the efficacy of combined interventions by comparing it with memory training and psychological intervention alone. Participants in the combined group and psychological intervention group were expected to have better scores on psychological measures as compared with the memory training group. Participants randomized to the combined group and memory training group were expected to show greater improvement in memory ability compared with the psychological intervention group. Moreover, we hypothesized that improved mood would boost memory training gains, that is, the memory improvements would be greater in the combined intervention group as compared with the memory training group.

METHODS

Research Design

This study was an active controlled, randomized trial conducted between June 2013 and July 2014. It was retrospectively registered in the Chinese Clinical Trial Registry (<u>www.chictr.org.cn</u>, identifier ChiCTR-IOR-15006165). The protocol was approved by the Ethics Committee of the Institute of Psychology, Chinese Academy of Sciences (CAS). All participants provided written informed consent according to institutional guidelines. The study was reported according to the Consolidated Standards of Reporting Trials ²⁷ (CONSORT) and the extension for social and psychological interventions ²⁸ (CONSORT-SPI; see Supplementary Materials for the CONSORT-SPI 2018 checklist).

Participants

Community-dwelling older adults were recruited from neighborhoods near the Institute of Psychology, CAS through advertisements and flyers posted in the community service stations. The inclusion criteria were: (1) age \geq 60; (2) level of education \geq 6 years; (3) a score >21 on the Montreal Cognitive Assessment - Beijing Version ²⁹ (MoCA-BJ); (4) with SMC; (5) right-handed; (6) free of neurological deficits or traumatic brain injury; (7) a score \leq 15 on the Activities of Daily Living scale³⁰; (8) no severe visual or auditory impairment which would hinder intervention. The cut-off score of MoCA-BJ was

recommended from our previous study ²⁹.

The following criteria were used for screening SMC: (1) Subjectively reported a decline in memory, rather than other domains of cognitive function; (2) Onset of SMC within the last 5 years; (3) Worries associated with memory decline; (4) Feeling of worse memory performance than others of the same age group; (5) Performance on the objective memory scale was within the normal range or within 1 standard deviation below the normal value.

Power analysis was calculated using G*Power 3.1 ³¹ based on the efficacy of memory training on associative learning. A minimum sample size of n=93 is necessary to detect a small to moderate effect of the within-between interaction using the repeated measures two-way analyses of variance (ANOVA) (alpha=0.05, power=0.80, f=0.15, number of groups=3). Two hundred and nineteen participants were contacted and assessed for eligibility. One hundred and twenty-four eligible participants consented to participate in the intervention. After baseline evaluation, they were randomly allocated to three groups: memory training (MT) group (n = 38), group counseling (GC) group (n = 44), and GC+MT group (n = 42). A researcher who did not involve in study design, participant enrollment, intervention implementation, and assessment used SPSS 21.0 (IBM Corporation, Somers, NY) to generate the random allocation sequence and assigned participants to three groups.

Intervention

Three groups of participants attended seven weeks of intervention, respectively. During the first three weeks, the GC and GC+MT groups attended weekly group counseling while participants in the MT group completed reading assignments at home as

control activities. From Week 4 to Week 7, the MT and GC+MT groups received memory training, and the GC group attended lectures as control activities. Group counseling, memory training and lectures were group-based, delivered at the Institute of Psychology CAS. Table 1 demonstrated details of the intervention program. Intervention and control activities were matched in frequency, duration, and format for group counseling and memory training. Participants had a break of about four weeks for Chinese New Year vacation between Week 3 and Week 4. Assessments on cognitive function, emotional indicators, and memory complaints were administrated at three time points: baseline, mid-(before Week 4), and post-intervention. The GC+MT group and GC groups had resting-state fMRI scanning at mid- and post-intervention. Results of fMRI data were not presented here. Participants were blind to study design and hypotheses. Counseling psychologists and training instructors were blind to study design and hypotheses, and all assessors were blind to group allocation and study design. Participants who completed intervention received a cash incentive of 300 RMB after post-intervention assessment, and those who attended fMRI scanning received extra 200 RMB.

Outcome Measures

The primary outcome was episodic memory assessed by the Associative Learning Test ³² (ALT) and Auditory Verbal Learning Test (AVLT) WHO/UCLA version ³³. In the ALT, A list of 12 pairs of nouns was presented aurally to participants. Half of the word pairs were semantically associated (e.g., sun-moon in ALT-easy condition), and the other six were unrelated pairs (e.g., teacher-railway in ALT-difficult condition). Immediately After listening to the list, the first noun in each word pair was given as a cue, and participants

were asked to recall the second noun. Participants scored 0.5 points for each correct answer in the easy condition (ALT-easy) and 1 point for each correct answer in the difficult condition (ALT-diff). A composite ALT score that ranged from 0 to 27 was calculated. For the AVLT, the scores of immediate recall and 30-minute delayed recall were respectively calculated (range 0-15).

The secondary outcomes included global cognition, working memory, emotional indicators, and subjective memory complaints. The MoCA-BJ was used to measure global cognition. The Digit Span Forward (DSF) and Digit Span Backward (DSB) tasks ³⁴ were used to assess working memory. The emotional indicators included the state of anxiety measured by the Self-rating Anxiety Scale ³⁵ (SAS), depressive symptoms measured by the Center of Epidemiological Survey-Depression ³⁶ (CESD) scale, subjective well-being measured by the Satisfaction with Life Scale ³⁷ (SWLS), and attitudes towards aging (ATA) assessed by the Attitude Toward Own Aging Sub-Scale from the Philadelphia Geriatric Center Morale Scale ³⁸. Subjective memory complaints were assessed by the Memory Inventory for the Chinese ³⁹.

Statistical Analysis

All statistical analyses were conducted using SPSS 21.0. Missing values ranged from 0 to 4.0% at baseline, 10.5% to 12.1% at mid-test, and 13.7% to 15.3% at post-intervention. The Little's MCAR test showed that the missing values were completely missing at random. Expectation-Maximization (EM) method was used to impute the missing values.

Statistical analyses were performed in two steps. The primary analyses were intention to treat (ITT) for all participants (n=124), and the secondary analyses were conducted for

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completers (n=97). As results were similar, detailed results of the completer analyses were presented in the supplementary materials.

Baseline characteristics of the three groups (MT vs. GC+MT vs. GC) were analyzed using the chi-squared test, one-way ANOVA, or Mann-Whitney U (nonparametric) test. To examine intervention effects on emotional indicators and cognitive function, repeated measures two-way ANOVA were conducted with Group (MT vs. GC+MT vs. GC) as the between-subject factor and Time (baseline vs. mid- vs. post-intervention) as the within-subject factor. As multiple comparisons were conducted for both emotional indicators and cognitive function, we used the Bonferroni method to control for the familywise error rate. Thus, the alpha level was set at 0.05/n (n equals to the number of tests). Thus, for emotional indicators (SAS, CESD, SWLS, and ATA), the alpha level was set at 0.05/4=0.0125. For cognitive function (AVLT immediate, AVLT delayed, ALT, MoCA, DSF, and DSB), the alpha level was set at 0.05/6=0.0083. In addition, to describe memory improvements in the MT and GC+MT groups, intervention effect on cognitive measures were calculated by the standardized mean difference (Cohen's d) of changes from baseline to post-intervention between the intervention group and controls (the GC group). To explore whether emotional changes will predict memory improvements, linear regression analyses were performed with age, gender, and education years included as covariates.

RESULTS

Figure 1 summarizes the flow of participants from screening to post-intervention. Out of 124 participants randomized, 97 participants completed intervention. At

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post-intervention, the attrition rates were 23.68%, 21.43%, and 20.45% in the MT, GC+MT, and GC groups, respectively. During intervention, no adverse event was reported by participants.

Table 2 presents the demographics and neuropsychological characteristics of three groups at baseline. Three groups did not differ significantly in gender, age, years of education, cognitive function, or emotional indicators.

Intervention effects

Emotional indicators. As shown in Table 2, the ANOVA revealed a significant Group \times Time interaction in anxiety (F_(3.76, 227.66)=3.53, p=0.009, η_p^2 =0.055). Follow-up comparisons suggested that both GC+MT and GC groups showed decreases in anxiety from baseline to post-intervention, whereas no significant difference was found in the MT group (Figure 2). No significant interaction was observed in depression, subjective well-being, or ATA.

Cognitive function and memory complaints. As shown in Table 2 and Figure 2, a significant Group × Time interaction was observed in ALT ($F_{(4, 242)}=3.53$, p=0.003, $\eta_p^2=0.063$), but not in AVLT delayed recall ($F_{(3.41, 206.32)}=0.48$, p=0.722, $\eta_p^2=0.008$). Post hoc comparisons revealed that ALT scores improved from baseline to post-intervention in all three groups. No significant difference was observed across three groups at baseline and mid-intervention, while at post-intervention the GC+MT and MT groups performed better than the GC group on ALT. Further analysis of two conditions of ALT revealed that participants improved their performance in the difficult condition ($F_{(4, 242)}=6.80$, p<0.001, $\eta_p^2=1.101$) but not the easy condition ($F_{(3.73, 225.55)}=0.15$, p=0.957, $\eta_p^2=0.002$). No

significant interaction was observed for other cognitive outcomes or subjective memory complaints. Effect size analyses suggested that the GC+MT group demonstrated a larger effect size in ALT (Cohen's d = 0.57, GC+MT group vs. GC group) compared with the MT group (Cohen's d = 0.44, MT group vs. GC group). Linear regressions were further performed to explore the relationship between changes in anxiety and improvement. Regression analyses showed no correlation between change in anxiety and memory improvement in the whole ITT sample (β =0.011, p=0.845) or in each group (the MT group, β =0.036, p=0.744; the GC+MT group, β =-0.004, p=0.976; the GC group, β =0.013, p=0.864).

DISCUSSION

This study examined whether memory training combined with group counseling aimed at alleviating depression and anxiety would produce greater training gains in older adults with memory complaints. The three-armed randomized trial compared the combined intervention (GC+MT) group with memory training and group counseling groups. Results suggest that 3 sessions of group counseling alleviated status of anxiety and 4 weeks of memory training significantly improved associative learning performance. Moreover, the combination of group counseling and memory training demonstrated a larger improvement in associative learning than memory training.

Both GC+MT and GC groups showed a decreased anxiety compared with the MT group, consistent with previous studies reporting memory training containing stress management techniques could reduce symptoms of anxiety ^{25,26}. Group counseling induced no significant alleviation in depressive symptoms. One possible explanation may be the

low level of depressive symptoms at baseline.

The GC+MT and MT groups significantly increased performance in associative learning compared with the GC group. Specifically, memory training improved performance in the difficult condition of ALT, suggesting that participants had adopted mnemonics learned from memory training to memorize semantically unrelated word pairs. This is consistent with previous studies which found memory strategy training enhance objective memory ability ^{12,40,41}. However, the beneficial effect of memory training was found only in ALT but not AVLT, showing no transfer to other cognitive domains. Memory training regimen in the current study primarily targeted on the utilization of various memory strategies. Although we included 30-minute executive function games in each session of memory training, the total training time of process-based training might be substantially insufficient to induce improvements in cognitive domains beyond episodic memory compared with typical computer-based cognitive training ⁴². Neither GC+MT nor MT group showed decreased memory complaints, suggesting that learned strategies might not be transferred to everyday situations. It is difficult for older adults to generalize learned strategies to untrained situations ⁴³. Previous studies suggest that the "learner-oriented approach" and to practice strategy use in everyday life are effective ways to induce meaningful transfer to daily life ^{12,44}.

More importantly, the GC+MT group demonstrated a larger improvement in memory (Cohen's d = 0.57) than memory training group (Cohen's d = 0.44), suggesting alleviated status of anxiety may boost the effect of memory training. The present study expands previous multicomponent memory interventions by providing direct evidence supporting

the synergistic effects of psychological intervention and memory training on objective measure of memory. The synergistic effect may involve two pathways. First, treatment of anxiety symptoms may produce an improvement in memory. A study showed that pharmacological treatment for anxiety resulted in enhanced episodic memory and executive function in a sample of older adults with Generalized Anxiety Disorder ⁴⁵. In the present study, a significant improvement in ALT was observed in the GC group from baseline to post-intervention. The improvement within the GC group may suggest cognitive benefit from group counseling, but alternatively it could be explained as a result of repeated testing. Second, older adults typically demonstrate mnemonic utilization deficit because of age-related executive function decline ⁴⁶, and executive function are inversely correlated with anxiety symptoms in older adults ^{47,48}. Thus, decreased anxiety may lead to better executive functioning that facilitates memonic application.

The lack of association between the change in anxiety and memory improvement seems contrast to the hypothesis that improved mood may boost memory training gains. One possible explanation was the measure of anxiety. Symptoms of anxiety could be categorized into somatic, affective, and cognitive symptoms. A study showed that memory performance was correlated with affective symptoms of anxiety but not somatic or cognitive symptoms ⁴⁸. Memory improvement may be related to the change in affective symptoms of anxiety, but SAS used in this study could not distinguish different components of anxiety.

There are several strengths in the present study. First, by combining psychological intervention with cognitive training, we made the pilot experimental work which found

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decreased state of anxiety would amplify efficacy of memory training, which helps to have a better understanding of the relationship between memory and anxiety in individuals with SMC. Second, we used an active-controlled design, the intervention and control activities were matched in frequency, duration and format for both group counseling and memory training. It enabled us to control several potential confounding factors such as expectation effect, social interaction during group training and general cognitive stimulation of using tablets. Our finding highlights the importance of treatment for symptoms of anxiety correlated with subjective memory decline. Integrating psychological intervention into traditional memory training may be promising to augment effectiveness on cognitive performance for older adults with SMC.

Some limitations also should be mentioned in the present study. First, the duration of group counseling and memory training was relatively short, so it might limit emotional and cognitive benefits derived from the intervention. Also, there was a 4-week gap between the end of group counseling and the start of memory training because of Chinese New Year vacation. The long break possibly diminished the intervention effects of both group counseling and memory training. It would be better to avoid long break during the intervention. Second, the control activity for group counseling was reading at home. Although reading materials shared same topics with activities and discussion in group counseling, and estimated time to complete reading was approximate to the duration of group counseling, social contacts in reading activity were not comparable to those in group counseling. Third, it would be optimal to use a four-group design (GC + MT, GC control + MT, GC + MT control, and GC control + MT control) which could isolate the effects of

group counseling, memory training, and the combination of two intervention. Fourth, no follow-up data was collected so we cannot evaluate whether the superior intervention effect in the combined group would be maintained.

Conclusions and Implications

In conclusion, the present study show that group counseling decreased symptoms of anxiety, memory training increased associative learning, and the combination of two intervention can induce larger memory gain than memory training alone in older adults with SMC. It may be important to integrate treatment for anxiety into memory training for older adults with memory complaints to achieve better intervention effect.

List of abbreviations

SMC, subjective memory complaints; MT, memory training; GC, group counseling; ALT, Associative Learning Test; ATA, attitudes towards aging.

Disclosure

Ethics approval and consent to participate

The protocol was approved by the Ethics Committee of the Institute of Psychology, Chinese Academy of Sciences (CAS). All participants provided written informed consent according to institutional guidelines.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

Study concept and design (Yin S, Zhu X, Li J), Acquisition of data (Yin S, Huo L, Ren W, Niu Y), Analysis and interpretation of data (Yin S, Li R), Drafting of the manuscript (Yin S, Zhu X), and Critical revision of the manuscript for important intellectual content (Yin S, Zhu X, Li J).

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Conflicts of Interest and Source of Funding

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References

- 1. Jessen F, Amariglio RE, van Boxtel M, et al.: A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. Alzheimers Dement 2014; 10:844–852.
- Buckley RF, Ellis KA, Ames D, et al.: Phenomenological characterization of memory complaints in preclinical and prodromal Alzheimer's disease. Neuropsychology 2015; 29:571–581.
- 3. Mol M, Carpay M, Ramakers I, et al.: The effect of perceived forgetfulness on quality of life in older adults; a qualitative review. Int J Geriatr Psychiatry 2007; 22:393–400.
- 4. Vannini P, Hanseeuw B, Munro CE, et al.: Hippocampal hypometabolism in older adults with memory complaints and increased amyloid burden. Neurology 2017; 88:1759–1767.
- 5. Stewart R, Godin O, Crivello F, et al.: Longitudinal neuroimaging correlates of subjective memory impairment: 4-year prospective community study. Br J Psychiatry 2011; 198:199–205.
- Hyer L, Scott C, Lyles J, et al.: Memory intervention: the value of a clinical holistic program for older adults with memory impairments. Aging Ment Health 2014; 18:169–178.
- 8. Kwok TCY, Bai X, Li JCY, et al.: Effectiveness of cognitive training in Chinese older people with subjective cognitive complaints: a randomized placebo-controlled trial. Int J Geriatr Psychiatry 2013; 28:208–215.
- 9. Barnes DE, Santos-Modesiti W, Poelke G, et al.: The Mental Activity and eXercise (MAX) trial: a randomized controlled trial to enhance cognitive function in older adults. JAMA Intern Med 2013; 173:797–804.
- van Hooren SAH, Valentijn SAM, Bosma H, et al.: Effect of a structured course involving goal management training in older adults: A randomised controlled trial. Patient Educ Couns 2007; 65:205–213.
- 11. Smart CM, Karr JE, Areshenkoff CN, et al.: Non-Pharmacologic Interventions for Older Adults with Subjective Cognitive Decline: Systematic Review, Meta-Analysis, and Preliminary Recommendations. Neuropsychol Rev 2017; 27:245–257.
- 12. Belleville S, Hudon C, Bier N, et al.: MEMO+: Efficacy, Durability and Effect of Cognitive Training and Psychosocial Intervention in Individuals with Mild Cognitive Impairment Journal of the American Geriatrics Society 2018; 66:655–663.
- 13. Hudes R, Rich JB, Troyer AK, et al.: The impact of memory-strategy training interventions on participant-reported outcomes in healthy older adults: A systematic review and meta-analysis Psychology and Aging 2019; 34:587–597.

- 14. Sala G, Gobet F: Cognitive Training Does Not Enhance General Cognition Trends in Cognitive Sciences 2019; 23:9–20.
- 15. Carlson MC, Erickson KI, Kramer AF, et al.: Evidence for Neurocognitive Plasticity in At-Risk Older Adults: The Experience Corps Program The Journals of Gerontology: Series A 2009; 64A:1275–1282.
- Carlson MC, Saczynski JS, Rebok GW, et al.: Exploring the Effects of an "Everyday" Activity Program on Executive Function and Memory in Older Adults: Experience Corps® The Gerontologist 2008; 48:793–801.
- 17. Bryant C, Jackson H, Ames D: The prevalence of anxiety in older adults: Methodological issues and a review of the literature Journal of Affective Disorders 2008; 109:233–250.
- 18. Djernes JK: Prevalence and predictors of depression in populations of elderly: a review Acta Psychiatrica Scandinavica 2006; 113:372–387.
- 19. Petkus AJ, Reynolds CA, Wetherell JL, et al.: Temporal dynamics of cognitive performance and anxiety across older adulthood. Psychol Aging 2017; 32:278–292.
- 20. Gulpers B, Ramakers I, Hamel R, et al.: Anxiety as a Predictor for Cognitive Decline and Dementia: A Systematic Review and Meta-Analysis. Am J Geriatr Psychiatry 2016; 24:823–842.
- 21. Balash Y, Mordechovich M, Shabtai H, et al.: Subjective memory complaints in elders: depression, anxiety, or cognitive decline? Acta Neurol Scand 2013; 127:344–350.
- 22. Gatchel JR: Late-Life Neuropsychiatric Symptoms: Windows Into Cognitive Decline? Am J Geriatr Psychiatry 2020; 28:72–74.
- 23. Phelps EA: Emotion and cognition: insights from studies of the human amygdala. Annu Rev Psychol 2006; 57:27–53.
- 24. Allen AP, Doyle C, Commins S, et al.: Autobiographical memory, the ageing brain and mechanisms of psychological interventions. Ageing Res Rev 2018; 42:100–111.
- 25. Small GW, Silverman DH, Siddarth P, et al.: Effects of a 14-day healthy longevity lifestyle program on cognition and brain function The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry 2006; 14:538–545.
- 26. Valentijn SA, van Hooren SA, Bosma H, et al.: The effect of two types of memory training on subjective and objective memory performance in healthy individuals aged 55 years and older: a randomized controlled trial Patient education and counseling 2005; 57:106–114.

- 27. Schulz KF, Altman DG, Moher D: CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ 2010; 340:c332.
- 28. Montgomery P, Grant S, Mayo-Wilson E, et al.: Reporting randomised trials of social and psychological interventions: the CONSORT-SPI 2018 Extension. Trials 2018; 19:407.
- 29. Yu J, Li J, Huang X: The Beijing version of the Montreal Cognitive Assessment as a brief screening tool for mild cognitive impairment: a community-based study. BMC Psychiatry 2012; 12:156.
- 30. Lawton MP, Brody EM: Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969; 9:179–186.
- 31. Faul F, Erdfelder E, Lang A-G, et al.: G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007; 39:175–191.
- 32. Xu S, Wu Z: The construction of "The Clinical Memory Test" Acta Psychologica Sinica 1986; 18:100–108.
- Maj M, Satz P, Janssen R, et al.: WHO Neuropsychiatric AIDS study, cross-sectional phase II. Neuropsychological and neurological findings. Arch Gen Psychiatry 1994; 51:51–61.
- 34. Gong YX: Manual of Wechsler Adult Intelligence Scale-Chinese Version Changsha, Chinese Map Press, 1992.
- Zung WW: A rating instrument for anxiety disorders. Psychosomatics 1971; 12:371– 379.
- 36. Radloff LS: The CES-D Scale: A Self-Report Depression Scale for Research in the General Population Applied Psychological Measurement 1977; 1:385–401.
- 37. Diener E. Emmons RA, Larsen RJ, et al.: The Satisfaction With Life Scale. J Pers Assess 1985; 49:71–75.
- 38. Lawton MP: The Philadelphia Geriatric Center Morale Scale: a revision. J Gerontol 1975; 30:85–89.
- Lam LCW, Lui VWC, Tam CWC, et al.: Subjective memory complaints in Chinese subjects with mild cognitive impairment and early Alzheimer's disease. Int J Geriatr Psychiatry 2005; 20:876–882.
- 40. Frankenmolen NL, Overdorp EJ, Fasotti L, et al.: Memory Strategy Training in Older Adults with Subjective Memory Complaints: A Randomized Controlled Trial Journal of the International Neuropsychological Society 2018; 24:1110–1120.

- 41. Li B, Zhu X, Hou J, et al.: Combined Cognitive Training vs. Memory Strategy Training in Healthy Older Adults Front Psychol 2016; 7.
- 42. Lampit A, Hallock H, Valenzuela M: Computerized Cognitive Training in Cognitively Healthy Older Adults: A Systematic Review and Meta-Analysis of Effect Modifiers PLOS Medicine 2014; 11:e1001756.
- 43. Cavallini E, Dunlosky J, Bottiroli S, et al.: Promoting transfer in memory training for older adults Aging Clin Exp Res 2010; 22:314–323.
- 44. Cavallini E, Bottiroli S, Capotosto E, et al.: Self-help memory training for healthy older adults in a residential care center: specific and transfer effects on performance and beliefs International Journal of Geriatric Psychiatry 2015; 30:870–880.
- 45. Butters MA, Bhalla RK, Andreescu C, et al.: Changes in neuropsychological functioning following treatment for late-life generalised anxiety disorder The British Journal of Psychiatry 2011; 199:211–218.
- Kirchhoff BA, Anderson BA, Barch DM, et al.: Cognitive and Neural Effects of Semantic Encoding Strategy Training in Older Adults Cerebral Cortex 2012; 22:788– 799.
- 47. Beaudreau SA, O'Hara R: The association of anxiety and depressive symptoms with cognitive performance in community-dwelling older adults Psychology and Aging 2009; 24:507–512.
- 48. Yochim BP, Mueller AE, Segal DL: Late life anxiety is associated with decreased memory and executive functioning in community dwelling older adults Journal of Anxiety Disorders 2013; 27:567–575.

Intervention	Frequency and Duration	Description
Week 1-3		
Group	About 6 hours for	The GC and GC+MT groups attended group counseling. Group
Counseling	group activities	counseling was led by two licensed counseling psychologist and
	and homework.	administrated in small groups (6-10 people). Activities were
	Group activities: 3	designed to provide information on aging process and cognitive
	weekly sessions,	aging, strategies of coping with stress and depression in late life,
	90 minutes/session	knowledge on lifestyle and brain health. Participants were
		encouraged to share personal experiences and make interpersonal
		communications. Homework was assigned after each session.

Table 1 Intervention details for each group

D 11							
Reading	Estimated 6 hours.	The MT group received reading assignments. Participants were					
(Control		instructed to complete reading independently at home and to					
Activity)		record their reading progress on a log sheet. The reading materials					
		were articles on healthy/positive aging, and strategies for coping					
		with late-life stress and depression.					
Week 4-7							
Memory	Group-based, 12	The MT and GC+MT groups attended memory training. Each					
Training	sessions in total; 3	session included 60-minute mnemonic training and 30-minute					
	sessions/week, 90	brain game playing. Mnemonic training was designed to promote					
	minutes/session	elaborate encoding and retrieval in older adults by teaching them a					
		series of mnemonics, including generation of mental images, item					
		association (interactive imagery and sentence generation), and the					
		method of loci. Participants were assigned homework to continue					
		practicing mnemonics at home. Brain games were designed to					
		train three components of executive function (inhibition,					
		switching, and updating) through three tablet video games (Li et					
		al., 2014). Training was guided by trained instructors according to					
		a detailed manual.					
Lectures	Group-based, 12	Each session included 60-minute lecture and 30-minute casual					
(Control	sessions in total; 3	video game playing. Lectures were about health knowledge for					
Activity)	sessions/week, 90	older adults, given by trained instructors according to a syllabus.					
	minutes/session	Casual video games were commercial tile-matching games on					
		tablets. Lectures was given by trained instructors according to a					
		detailed manual.					

Notes: GC, group counseling; MT, memory training.

Table 2 Demographics and neuropsychological characteristics of the participants at baseline

Characteristics		MT	GC+MT	GC	F(df)/X ² (df)	р
Characteristics		(n=38)	(n=42)	(n=44)	r(ui)/X (ui)	value
Age, years		71.34±6.63	72.90 ± 5.29	71.93±6.46	F(2,121)=0.67	0.516
Female/Male		26/12	25/17	26/18	$X^{2}(2)=0.93$	0.627
Education, years		13.89±3.20	15.00 ± 2.71	14.16±2.69	F(2,121)=1.66	0.195
Emotional indicators	Anxiety	30.05±5.61	28.57±5.31	29.77±7.78	F(2,121)=0.62	0.539
	Depression	6.17±5.20	5.36 ± 5.18	6.65±6.49	F(2,121)=0.56	0.570
	Subjective well-being	25.94±4.78	26.38±4.71	26.49±5.63	F(2,121)=0.13	0.875
	ATA	17.07±3.43	17.33±3.68	16.68±4.07	F(2,121)=0.33	0.722
Cognitive function	MoCA	25.97±2.14	26.19±1.95	26.14±1.88	F(2,121)=0.13	0.880
	Digit span forward	7.32±1.04	7.36±1.45	7.34±1.27	F(2,121)=0.01	0.990
	Digit span backward	4.84±1.39	4.62±1.17	4.80±1.42	F(2,121)=0.33	0.723
	AVLT immediate recall	6.32±1.93	5.95 ± 2.58	5.77±1.88	F(2,121)=0.67	0.514
	AVLT delayed recall	12.17±3.02	11.83±3.48	11.95±2.57	F(2,121)=0.12	0.886
	ALT	10.64±3.95	10.80±4.10	9.64±3.80	F(2,121)=1.09	0.338
	ALT-diff	4.40±3.09	4.38±3.08	3.55±2.75	F(2,121)=1.15	0.322
	ALT-easy	6.25±1.50	6.42±1.55	6.11±1.58	F(2,121)=0.41	0.662

Memory complaints	3.38±1.09	3.19±0.94	3.02±1.11	F(2,121)=1.21	0.302
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Notes: MT - Memory Training, GC - Group Counseling, ATA – attitudes towards aging, MoCA - the Montreal Cognitive Assessment, ALT – Associative Learning Test, ALT-diff - ALT difficult condition, ALT-easy – ALT easy commendition.

Table 3 Emotional indicators and cognitive performance in SMC prior to and after intervention

	MT (n=38)			GC+MT (n=42)	1	GC (n=44)			Fр	Effec t size		
	Pre-	Mid-	Post-	Pre-	Mid-	Post-	Pre-	Mid-	Post-	(df) voluo		
Anxiety	30.05±5. 61	31.10±7. 03	29.29±5. 99	28.57±5. 31	27.16±4. 66	24.61±3. 15	29.77±7. 78		25.74±4. 49	3.53 (3.76, 227.66)	0.009	0.055
Depressio n	6.17±5.2 0	8.60±7.5 2	7.54±6.0 2	5.36±5.1 8	5.57±5.4 6	5.45±5.6 0	6.65±6.4 9		4.47±5.0 0	2.89 (4, 242)	0.023	0.051
Subjectiv e well-bein g			26.64±5. 01	26.38±4. 71	26.83±4. 16	28.61±3.	26.49±5. 63		27.77±4. 94	1.57 (4, 242)	0.183	0.025
АТА	17.07±3. 43	17.13±4. 05	17.71±3. 83	17.33±3. 68	18.85±3. 00	18.68±3. 22	16.68±4. 07	18.55±2. 60	19.29±2. 79	2.39 (3.79, 229.20)	0.055	0.038
МоСА	25.97±2. 14	26.22±2. 05		26.19±1. 95	26.51±2. 29	27.02±2. 05	26.14±1. 88	26.87±1. 74	26.96±2. 14	0.50 (3.38, 204.53)	0.702	0.008
Digit span forward	7.32±1.0 4	7.17±1.3 9	7.48±1.4 4	7.36±1.4 5	7.35±1.3 2	7.88±1.4 0	7.34±1.2 7	7.56±1.0 2	7.57±1.0 9	1.35 (4, 242)	0.252	0.022
Digit span backwar d	4.84±1.3 9	4.90±1.2 4	5.55±1.3 5	4.62±1.1 7	4.88±1.4 1	5.25±1.3 8	4.80±1.4 2	4.87±1.5 2	5.04±1.2 8	1.03 (4, 242)	0.393	0.017
AVLT immediat e recall	6.32±1.9 3	6.78±2.2 4	8.60±2.3 3	5.95±2.5 8	7.02±2.2 4	8.03±2.8 8	5.77±1.8 8	6.98±1.5 4	7.23±1.4 0	2.49 (3.80, 229.86)	0.047	0.039
AVLT delayed recall	12.17±3. 02	12.13±1. 67	13.36±1. 71	11.83±3. 48	12.15±2. 28	13.14±1. 67			12.83±2. 60	0.48 (3.41, 206.32	0.722	0.008

)		
ALT						17.03±3. 89	9.64±3.8 0		13.95±4. 23	4.07 (4, 242)	0.003	0.063
ALT-diff	4.40±3.0 9	6.63±3.9 8	8.59±3.2 4	4.38±3.0 8	5.91±2.6 8	9.39±3.2 0	3.55±2.7 5	5.76±3.3 9	6.48±3.7 3	6.80 (4, 242)	<0.00 1	0.101
ALT-easy	6.25±1.5 0	6.96±1.5 2	7.66±1.0 9	6.42±1.5 5	6.99±1.0 7	7.66±1.0 9	6.11±1.5 8	6.87±1.4 4		0.15 (3.73, 225.55)	0.957	0.002
Memory complain ts	3.38±1.0 9	3.08±1.0 5	2.69±1.3 7	3.19±0.9 4	3.27±0.9 2	2.79±1.2 9	3.02±1.1 1	2.97±0.9	2.48±1.3 2	0.83 (4, 242)	0.508	0.014

Notes: MT - Memory Training, GC - Group Counseling, ATA – attitudes towards aging, MoCA - the Montreal Cognitive Assessment, ALT – Associative Learning Test, ALT-diff - ALT difficult condition, ALVT – Auditory Verbal Learning Test.

Figure 1.	The flowchart	of the trial.	SMC: sul	ojective memory	complaints.	MT: Memory

Training. GC: Group Counseling.

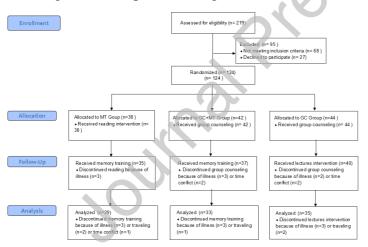
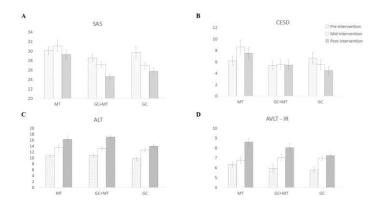


Figure 2. The effects of group counselling and cognitive training on primary outcomes of emotional indicators and cognitive performance. Bar plots show the mean scores on anxiety (SAS), depression (CESD), associative learning test (ALT) and immediate recall of auditory verbal learning test (AVLT-IR) prior to and after intervention for the Memory Training (MT), Group Counseling (GC), and GC+MT groups.



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