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執行功能對老年人客觀與主觀記憶評估之一致性影響

Level of Executive Function Influences Concurrence of Objective and Subjective Memory Evaluation in Older Adults

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摘要

過去研究發現主觀記憶抱怨與客觀記憶表現之關聯相當不一致。本研究依主、客觀記憶評估之落差分數（discrepancy score）反映主觀評估的準確程度與落差方向，以瞭解正常老年人及輕度認知功能障礙患者之執行功能對主、客觀記憶評估一致性的影響。研究發現執行功能可預測主、客觀記憶評估的落差方向，高執行功能與低估其記憶功能相關，低執行功能與高估其記憶功能相關，且正常老年人組較易出現低估傾向，輕度認知功能障礙組則較易出現高估傾向。本研究指出正常老年人及輕度認知功能障礙患者之執行功能在主觀記憶抱怨與客觀記憶表現的關聯中扮演重要角色，暗示過去研究發現的不一致結果可能和此存在於主、客觀記憶評估的落差有關。

關鍵詞：主觀記憶抱怨、執行功能、記憶功能、正常老化、輕度認知功能障礙

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Abstract

Previous literature has demonstrated inconsistent connection between subjective memory complaint (SMC) and objective memory performance. This study aimed to examine the relationship between the level of executive functioning and accuracy of SMC in cognitively intact older adults and individuals with mild cognitive impairment (MCI). Sixty-five cognitively normal (CN) and 54 MCI participants were recruited. Discrepancy scores between SMC and objective memory performances were calculated to indicate the degree and directionality of the concordance between subjective and objective measures. The results showed that executive functioning significantly predicted discrepancy scores above and beyond the non-cognitive (e.g., demographical variables) and clinical (e.g., health conditions, ApoEε4 status) factors. Lower executive functioning was associated with overestimation of objective memory functioning, while higher executive functioning was associated with underestimation. The CN and MCI groups reported similar

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degrees of SMC; however, the MCI group was more likely to overestimate their memory functioning, whereas the CN group was more likely to underestimate their memory functioning. Overall, these results indicate the level of executive functioning appears to play a unique role above and beyond the contribution of the demographic and clinical factors for the concordance between subjective and objective memory measures, which is related to the equivocal relationship between SMC and objective memory performance in both cognitively intact elderly and MCI individuals.

Keywords: subjective memory complaint, executive functioning, memory functioning, normal aging, Mild Cognitive Impairment

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Table of Contents

INTRODUCTION **1**

METHODS **8**

PARTICIPANTS 8

NEUROPSYCHOLOGICAL AND CLINICAL MEASURES 9

DISCREPANCY BETWEEN SUBJECTIVE AND OBJECTIVE MEMORY EVALUATION 13

STATISTICAL ANALYSIS 14

RESULTS **16**

DEMOGRAPHICS, CLINICAL DATA, AND NEUROPSYCHOLOGICAL PERFORMANCE 16

RELATIONSHIPS BETWEEN EXECUTIVE FUNCTION AND DISCREPANCY SCORE 19

DISCUSSION **21**

REFERENCE **28**

TABLES **47**

FIGURES **50**

APPENDIX **53**

doi:10.6342/NTU201701830

Introduction

Subjective memory complaint (SMC), a common complaint in old age, refers to the self-perception of memory decline which does not require confirmation by performance on a cognitive test. The prevalence of memory complaints in elderly people ranges from 25% to 50% dependents on the method of measuring or the characteristics of the study populations (Jonker, Geerlings, & Schmand, 2000), and Wang et al. (2000) report the prevalence of approximately 49% from a longitudinal study in a rural Taiwanese population. Current studies on SMC have revealed that such self-perception is associated with many non-cognitive factors, such as older age (Bates et al., 2009; Chen et al., 2014; Hohman, Beason-Held, Lamar, & Resnick, 2011), female gender (Jonker et al., 2000), appearance of health conditions (hypertension, diabetes mellitus, etc.; Chen et al., 2014), low education level (Chen et al., 2014), depression (Buckley et al., 2013; Chen et al., 2014; Lehrner et al., 2014; Mol, van Boxtel, Willems, & Jolles, 2006; Reid & Maclullich, 2006; Slavin et al., 2010; Zlatar, Muniz, Galasko, & Salmon, 2017) and personality traits (Reid & Maclullich, 2006; Slavin et al., 2010; Steinberg et al., 2013). In addition to a connection between the non-cognitive factors and SMC, there are evidences suggesting that SMC is associated with underlying brain changes or increasing likelihood of biomarker abnormalities which is consonant with dementia pathology

doi:10.6342/NTU201701830

(Jessen et al., 2014; Stewart, 2012). Specifically, brain structural changes in the older adults with SMC have been observed for greater gray matter atrophy in regions of medial temporal, frontal temporal, posterior cingulate and inferior parietal lobes (Peter et al., 2014; Saykin et al., 2006; Schultz et al., 2015; Toledo et al., 2015), and hyperintensities in white matter (Benedictus et al., 2015; Selnes et al., 2012; Wang et al., 2016) compared to those without SMC. Declined brain glucose metabolism (Jeong, Park, Song, Chung, & Rhie, 2017), increased amyloid-β deposition (Snitz et al., 2015; Wolfsgruber et al., 2015; Wolfsgruber et al., 2017), and alterations in brain neural synchronization and function (Erk et al., 2011; Hohman et al., 2011; Lopez-Sanz et al., 2017; Rodda, Dannhauser, Cutinha, Shergill, & Walker, 2009; Stewart et al., 2008; Yasuno et al., 2015) have also been reported for older adults with SMC. In addition, some studies have demonstrated that apolipoprotein E ε4 (ApoEε4) status correlates with increasing memory concerns (Krell-Roesch et al., 2015; Mosconi et al., 2008) and it also modulates the relationship between SMC and biomarkers such as amyloid-β burden or hippocampal volume changes (Striepens et al., 2011; Zwan et al., 2016). Furthermore, several longitudinal studies have indicated that SMC is predictive of future progression to mild cognitive impairment (MCI) or dementia (Buckley et al., 2016; Iliffe & Pealing, 2010; Jessen et al., 2011).

Some evidences have suggested connections between SMC with the changes in

doi:10.6342/NTU201701830

biomarkers and progression to MCI; however, the relationship between SMC and objective memory function has shown inconsistency. Some prior studies have found that decline in objective memory performance is associated with severity of or presence of SMC (Clement, Belleville, & Gauthier, 2008; Hohman et al., 2011; Jessen et al., 2007; Lam, Lui, Tam, & Chiu, 2005; Peter et al., 2014; Schultz et al., 2015; Seo, Kim, Choi, Lee, & Choo, 2017; van der Werf, Geurts, & de Werd, 2016). For instance, a relationship between increased SMC and poorer performance on objective memory tests has been reported by Seo et al. (2017). A study conducted by van der Werf et al. (2016) also demonstrated that subjective evaluation for memory ability predicts one-week-later objective memory function. On the other hand, other studies have not found such a relationship (Buckley et al., 2014; Edmonds et al., 2014; Lenehan, Klekociuk, & Summers, 2012; Reisberg & Gauthier, 2008; Zlatar et al., 2017).

Although subjectively reported change in memory function has been proposed as a criterion for the diagnosis of MCI (Petersen, 2004; Petersen & Morris, 2005), it has been under debate that the utility of inclusion of SMC as part of the MCI diagnosis criteria because of the inconsistent connections between SMC and objective memory performance in recent studies. There are several possible reasons that could explain these highly varying results. For example, different strategies have been

doi:10.6342/NTU201701830

applied to assess SMC, ranging from a single question with a yes/no response to more comprehensive self-report questionnaires (Snitz et al., 2015). Other variations in methodology may also contribute to heterogeneity in previous findings, such as employing a cross-sectional or longitudinal design, the heterogeneous inclusion/exclusion criteria for the study participants (i.e., inclusion or exclusion of MCI subjects; using screening tools such as the Mini-Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MoCA) as the group classification criterion), and comprehensiveness of objective memory function evaluation (i.e., using a screening test such as MMSE, or a comprehensive neuropsychological battery). Nevertheless, few of them have investigated the relationship between executive function and SMC.

Executive functioning is commonly conceptualized as higher-level cognitive process that is essential to facilitate, support, adaptation and monitor complex goal-directed behavior or high-level control over low-level functions (Royall et al., 2002; Stuss & Levine, 2002). Meta-memory, an aspect of high-level executive functioning, is self-awareness knowledge of one's own memory contents and capacities, and this monitoring function helps people judge their learning efficiency. According to literature, a consistent age-related decline in meta-memory function has been observed, in which the older adults showed less accurate memory monitoring

doi:10.6342/NTU201701830

than did the younger adults (Morson, Moulin, & Souchay, 2015; Perrotin, Isingrini, Souchay, Clarys, & Taconnat, 2006; Sacher, Isingrini, & Taconnat, 2013; Souchay, Moulin, Clarys, Taconnat, & Isingrini, 2007). Therefore, it is possible that inaccurate self-perceptual memory evaluation may occur in some cognitively normal older people with SMC which may be relate to the level of executive functioning. Similarly, inaccurate self-evaluation of memory functioning has been observed in individuals diagnosed with MCI (Chung & Man, 2009; Galeone, Pappalardo, Chieffi, Iavarone, & Carlomagno, 2011; Roberts, Clare, & Woods, 2009; Silva et al., 2016; Vogel et al., 2004). Specifically, several studies have indicated that the MCI patients tend to overestimate their memory performance on memory recognition tasks compared to the control group (Anderson & Schmitter-Edgecombe, 2010; Perrotin, Belleville, & Isingrini, 2007; Silva et al., 2016), and this overestimation tendency is related to the severity of cognitive decline (Perrotin et al., 2007; Silva et al., 2016). It is increasingly recognized that aging populations, including cognitively normal older adults and individuals with MCI, may represent a highly heterogeneous group, based in part on demonstrated variability among those individuals in executive functioning (Chang et al., 2011; Chang et al., 2010; Clark et al., 2012; Lee et al., 2012). As a result, it is reasonable to speculate that the accuracy of the memory-monitoring ability could be influenced by executive functioning in both

doi:10.6342/NTU201701830

cognitively normal elderly and MCI patients.

Some previous studies measured the discrepancy between self- and informant-rating on parallel questionnaires to indicate the accuracy of awareness (Buckley et al., 2015; Caselli et al., 2014; Slavin et al., 2010). This method assumes that the informant could accurately assess the participant's function, which, however, in fact depending upon the informant's knowledge about cognitive functioning or accuracy of the observations. On the other hand, some other studies employed a method that evaluated the discrepancy between self-rating and actual performance on objective task in individuals with MCI (Lin et al., 2010; Scherling et al., 2016). However, those studies have focused on using a specific test designed to measure "in session" awareness (e. g., Feeling-Of-Knowing test, judging in-session memory testing performance immediately following the memory testing), which may not necessarily reflect the memory concerns that participants face in their daily life. Moreover, none of those studies considered non-cognitive factors (e.g., depression) in their analyses or provide definitive diagnosis information of the subjects. Overall, these methodological concerns in previous study warrant further investigation.

Thus, the aim of the present study was to examine the relationship between the level of executive functioning and the accuracy of SMC while jointly taking into account of non-cognitive factors (e.g., demographic variables, mood, ApoEε4 status,

doi:10.6342/NTU201701830

health conditions, etc.) in cognitively intact older adults and individuals with MCI. To evaluate the accuracy of SMC, we calculated discrepancy scores between the self-report memory concerns and objective memory performances, which enabled us to evaluate the accuracy of SMC in two directions (i.e., overestimate or underestimate one's objective memory functioning). It was hypothesized that lower executive functioning would be associated with greater discrepancy between subjective report of memory function and objective measurement using standardized memory tests in both cognitive intact older adults and individuals with MCI, even after controlling non-cognitive (e.g., demographic variables) or clinical (e.g., health conditions, ApoEε4 status) factors.

doi:10.6342/NTU201701830

Methods

Participants

One-hundred and nineteen older adults were included in the present study, 65 individuals (54%) were classified as cognitively normal (CN), and 54 (46%) were classified as MCI. Participants were excluded if there were any current evidence of a major neurological disease that may affect the central nervous system functioning (e.g., epilepsy, head injury, stroke), psychiatry disorders, or history of substance abuse. Participants were recruited from the memory clinics or via community advertising. The present study was approved by the Ethics Committee and Institutional Review Board at both the National Taiwan University Hospital and the Taipei City Hospital. Written informed consent was obtained from all participants.

Participants were diagnosed with MCI based on the criteria recommended by International Working Group (Winblad et al., 2004). Specifically, the criteria for MCI were: (1) neither normal aging nor dementia; (2) defective performances on objective neuropsychological tests, or evidenced decline performances on the tasks over time; and (3) generally preserved basic daily activities or the slightest impaired on instrumental activities. The objective cognitive decline was determined based on the suggestion set forth by Jak et al. (2009) by the presence of at least two test scores within a cognitive domain that fell one standard deviation below age-appropriate

doi:10.6342/NTU201701830

norms. Different types of MCI (Petersen, 2004) could be classified accordingly. Specifically, the participant would be classified as amnestic-MCI (a-MCI) if episodic memory was one of the impaired cognitive domains, or non-amnestic-MCI (na-MCI) if episodic memory was preserved. Furthermore, participants had one versus more than one impaired cognitive domain would determine the classification as single or multiple domains involved in MCI (Petersen, 2004). The present sample consisted of 23 a-MCI-single, 29 a-MCI-multiple domains, and two na-MCI-single domain.

Neuropsychological and Clinical Measures

The neuropsychological tests used in the analyses were characterized into two groups: (1) executive function; and (2) episodic memory. In addition, the Framingham Heart Scale (FHS; D'Agostino, Wolf, Belanger, & Kannel, 1994) was used to evaluate the cerebrovascular risk factors and stroke risk probability in ten years. The Geriatric Depression Scale-Short Form (GDS-S Taiwan version; Liu et al., 1997) was used to evaluate participants' depressive state. The ApoEε4 data were also obtained and all the participants were noted as ApoEε4 carriers or non-carriers based on the appearance of at least one ε4 allele or not.

Executive function measures.

Five executive function tests, which assessed abstract reasoning, word generating, concept formation and mental shifting, were used in the present study. (1) The

doi:10.6342/NTU201701830

Matrix Reasoning subtest of the Wechsler Adult Intelligence Scale-III (WAIS-III), Taiwan version (Chen & Chen, 2002): it measured the non-verbal abstract reasoning by solving problems of sequence of pictures with describable pattern. (2) The WAIS-III Similarities subtest: it measured the verbal abstract reasoning by telling the similarity between two given words and scoring based on the quality of the answer. (3) The Verbal Fluency (VF; Benton, Hamsher, & Sivan, 1994; Hua, Chang, & Chen, 1997): it evaluated the ability to generate as many responses as possible within 60 seconds, which was presumed to use efficient retrieval strategies and monitoring of responses to avoid repetitions. Total number of the correct responses from two categories (animal, and fruit) was used for analysis in the present study. (4) The Modified Card Sorting Test (MCST; Nelson, 1976): it was used as a measure of concept formation and mental shifting that required participants to sort cards by different rules, which changed several times throughout the administration based on the examiner's feedbacks. The number of categories achieved was used as the MCST variable in this study. (5) The Color Trails Test (CTT-1 and 2; D'Elia, Satz, Uchiyama, & White, 1996): the test included two parts. The CTT color switching condition (CTT-2) evaluated the ability to quickly switch between two colors while correctly connecting numbers at the same time. The difference of the completion time between CTT-1 and CTT-2 (CTT-2 - CTT-1) was used in the analysis to

doi:10.6342/NTU201701830

minimize influences of motor speed on CTT-2 performance.

A composite z-score was computed to represent each participant's relative executive function performance. Specifically, the raw score of participants' performance on each of the executive measure was first transformed into z-scores based on the norms obtained from the whole participant pool in the present study. Because lower scores (i.e., less time required to complete the task) on the CTT reflect better performance, the z-score of CTT was inversed to ensure unidirectionality prior to averaging the z-scores of the five tests. The resulting composite z-scores represented the participant's relative performance on executive function, with positive number represented better performance.

Episodic memory measures.

Four episodic memory tests were assessed in the present study: the Wechsler Memory Scale-III, Taiwan version (WMS-III; Hua et al., 2005) the Logical Memory (LM), the Visual Reproduction (VR), the Visual Paired Associates (VP) subtests and the California Verbal Learning Test-II (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000). (1) The WMS-III, Taiwan version LM, a two stories learning task, measured the learning and retention of episodic memory by verbally presenting each story to the participant and the participant was asked to recall immediately and after a 30-minute delay interval. (2) The WMS-III, Taiwan version VR was used to measure the visual

doi:10.6342/NTU201701830

episodic memory by presenting five geometry patterns to the participant, and the participant was asked to draw each pattern immediately and after a 30-minute delay interval. (3) The WMS-R, Taiwan version VP also measured visual learning and retention episodic memory by assessing the ability to remember pairs of an abstract line drawing figure and its associated color. The participant was asked to recall the pairs immediately and after a 30-minute delay interval. (4) The CVLT-II was also used as measures of learning and retention of episodic memory by accessing the ability to remember a 16-item word list (List A) verbally presented over five trials. Participant was asked to recall items from list A in each five trials and a score of total recall for the five learning trials could be calculated (CVLT-II List A 1-5 total recall). Then a single interference trial using a different 16-item word list (List B) was given, followed by the immediate recall of the List A. Recall for List A were asked after 20 minutes (the long delayed recall condition).

In order to match the SMC subscales chosen in the present study, only the verbal episodic memory tests (i.e., the LM and the CVLT) were used to compute episodic memory composite scores. Raw scores of both immediate (LM I, and CVLT-II List A 1-5 total recall) and the delayed (LM II, and CVLT-II long delayed free recall) free recall scores were used to indicate objective episodic memory performance. Similar to executive function composite z-scores, a z-transforming memory composite score

doi:10.6342/NTU201701830

representing relative performance on episodic memory was computed for each participant with the same method as previously described. The resulting composite z-scores represented the participant's relative performance on memory function, with positive number represented better memory performance.

Discrepancy between Subjective and Objective Memory Evaluation

Subjective memory complaints (SMC) were accessed with the Green's Memory Complaints Inventory (Green, 2004; Green, Gervais, & Merten, 2005), which contained nine subscales representing different aspects of self-reported memory problems. Because verbal memory is the most commonly reported problems encountered by older adults (Amariglio, Townsend, Grodstein, Sperling, & Rentz, 2011), we extracted scores from two subscales—the "General Memory Problems" and "Verbal Memory Problems" subscales of the Green's Memory Complaints Inventory to indicate the level of SMC. Lower scores on the self-evaluated questionnaire reflected a lower endorsement of memory problems for the individual. In order to be consistent with the direction of objective memory results, the z-scores of SMC scores based on the questionnaire were inversed before creating discrepancy scores.

The present study used a modified discrepancy measure that was based on Miskowiak et al. (2016). The methodology was based on the premise that the absolute accuracy of subjective memory functioning evaluation would result in the

doi:10.6342/NTU201701830

same rank ordering of their objective performance. Therefore, the discrepancy between SMC and objective memory performance could be calculated for each participant by subtracting the standardized objective memory composite z-score from the inversed z-transforming SMC score. Thus, a positive value of the discrepancy score indicates that the participants' rank ordering for their subjective evaluation was higher (better) than their objective performance, that is, they overestimating their memory functioning. In contrast, a negative value of the discrepancy score indicates that the participants' rank ordering for their subjective evaluation was lower (worse) than their objective performance, implying an underestimation of their memory functioning. Scores toward zero indicates greater concordance between self-evaluated memory functioning and objective memory performance.

Statistical Analysis

Group differences were compared with analysis of variance/analysis of covariance (ANOVA/ANCOVA). Chi-square tests were used to examine differences among categorical variables. Statistical significance for demographical and clinical variables were set at an alpha level of .05, while significant level for neuropsychological measures was set at $p < .003$ based on Bonforroni correction to avoid inflated type I errors. The discrepancy scores were checked for normality using the Kolmogorov-Smirnov test, and the result indicated that our data were

doi:10.6342/NTU201701830

normally distributed (Kolmogorov-Smirnov test: $p > .20$, with a mean score of 0.01, standard deviation = 1.53). Hierarchical regression analyses were conducted to examine the predictive ability of the executive function (representing by the executive function composite z-score) for the discrepancy between subjective and objective memory evaluations. Specifically, demographic variables including age, gender and education were entered simultaneously in the first step. Then, clinical variables including FHS-Stroke risk probability, depressive state, ApoEε4 status and the group membership (i.e., CN versus MCI) were entered in the second step. Lastly, the composite z-score of executive functioning was entered in the third step to examine whether it increased the explained variances in the discrepancy score over and above the relation observed in the previous two steps. The variance inflation factor and Person's correlations between the discrepancy score and the predictive variables were checked to make sure that our analyses were not confounded by the collinearity. The variance inflation factors in the present hierarchical regression model ranged from 1.03 to 2.50, which was in an acceptable range. All statistical analyses were conducted in SPSS (version 22.0; IBM Corp.).

doi:10.6342/NTU201701830

Results

Demographics, Clinical Data, and Neuropsychological Performance

The demographic, clinical, and neuropsychological performances for each group are presented in Table 1. The two groups differed in age ($F(1, 117) = 10.49$, $p = .002$), education ($F(1, 117) = 9{,}32$, $p = .003$), and FHS-Stroke risk probability ($F(1, 117) = 6.02$, $p = .016$) but did not differ in gender distribution ($\chi^2(2, N = 119) = 0.44$, $p > .05$), frequency of ApoEε4 carriers ($\chi^2(2, N = 119) = 0.20$, $p > .05$), and scores on the depression measures ($F(1, 117) = 1.39$, $p > .05$).

After controlling for the effects of age, education and FHS-Stroke risk probability, the CN group performed significantly better than the MCI group on all executive function measures (see Table 1), including the WAIS-III Matrix Reasoning subtest ($F(1, 113) = 18.19$, $p < .001$), the VF ($F(1, 113) = 14.08$, $p < .001$), the MCST ($F(1, 114) = 26.40$, $p < .001$) and the executive function composite z-score ($F(1, 114) = 30.68$, $p < .001$), except for the WAIS-III Similarities subtest ($F(1, 113) = 6.60$, $p > .003$) and the CTT measure (i.e., CTT-2 - CTT-1; $F(1, 114) = 6.08$, $p > .003$). Furthermore, the CN group performed significantly better than the MCI group on all episodic memory measures, including the immediate recall ($F(1, 114) = 33.31$, $p < .001$), delayed recall ($F(1, 114) = 55.19$, $p < .001$) and delayed recognition ($F(1, 114) = 43.51$, $p < .001$) of the WMS-III VR subtests, the immediate ($F(1, 114) = 39.61$, p

doi:10.6342/NTU201701830

< .001) and delayed recall ($F(1, 114) = 26.01$, $p < .001$) of the WMS-R VP subtests, the immediate recall ($F(1, 114) = 44.21$, $p < .001$) and delayed recall ($F(1, 114) = 57.90$, $p < .001$) of the WMS-III LM subtest, the immediate List A 1-5 total recall ($F(1, 112) = 99.68$, $p < .001$) and long delayed free recall ($F(1, 112) = 106.55$, $p < .001$) of the CVLT-II, and the episodic memory composite z-score ($F(1, 114) = 105.36$, $p < .001$). There was no group difference in the SMC scores ($F(1, 114) = 1.12$, $p > .05$) after controlling for age, education, and FHS-Stroke risk probability. However, the two groups differed in the discrepancy scores ($F(1, 114) = 16.71$, $p < .001$) after controlling for age, education, and FHS-Stroke risk probability. This differential pattern of discrepancy scores remained significant even after additionally controlling for executive functioning ($F(1, 113) = 7.50$, $p = .007$, $\eta^2 = .06$), suggesting that the CN group, even with relatively better objective memory performance, tended to endorse more memory complaints compared with the MCI group, and the MCI group showed an opposite tendency.

Further, group differences between the a-MCI-single and a-MCI-multiple groups were also examined (see Appendix Table A1). These two groups showed significant difference in age ($F(1, 50) = 11.76$, $p = .001$), but did not differ in gender distribution ($\chi^2(2, N = 52) = 1.49$, $p > .05$), frequency of ApoEε4 carriers ($\chi^2(2, N = 52) = 0.78$, $p > .05$), education ($F(1, 50) = 0.26$, $p > .05$), FHS-Stroke risk ($F(1, 50) = 2.91$, $p > .05$),

doi:10.6342/NTU201701830

or depression measure ($F(1, 50) = 1.61$, $p > .05$). After controlling for the effects of age, the a-MCI-single group performed better than the a-MCI-multiple group on the MCST ($F(1, 49) = 12.49$, $p = .001$) and the executive function composite z-score ($F(1, 49) = 14.11$, $p < .001$), but did not showed difference in other executive function measures (including the WAIS-III Matrix reasoning ($F(1, 49) = 2.88$, $p > .003$) and similarities ($F(1, 49) = 6.63$, $p > .003$) subtests, VF ($F(1, 49) = 8.09$, $p > .003$), and the CTT measure ($F(1, 49) = 4.82$, $p > .003$)), all the episodic memory measures (including the WMS-III VR immediate recall ($F(1, 49) = 1.48$, $p > .003$), delayed recall ($F(1, 49) = 9.18$, $p > .003$) and delayed recognition ($F(1, 49) = 1.48$, $p > .003$), the WMS-III VP immediate ($F(1, 49) = 2.93$, $p > .003$) and delayed recall, the WMS-III LM immediate ($F(1, 49) = 6.76$, $p > .003$) and delayed ($F(1, 49) = 6.47$, $p > .003$) recall, the CVLT-II List A total recall ($F(1, 49) = 7.00$, $p > .003$) and long delayed free recall ($F(1, 49) = 6.36$, $p > .003$), and the episodic memory composite z-score ($F(1, 49) = 8.54$, $p > .003$)), and in the SMC scores ($F(1, 49) = 0.82$, $p > .05$). However, the two groups differed in discrepancy scores ($F(1, 49) = 4.34$, $p = .042$) after controlling for age with the a-MCI-multiple group showing larger discrepancy between the objective and subjective memory measures compared to the a-MCI-single group. However, such difference disappeared after additionally controlling for executive function ($F(1, 49) = 2.17$, $p > .05$).

doi:10.6342/NTU201701830

Relationships between Executive Function and Discrepancy Score

Table 2 showed results of hierarchical regression models predicting the discrepancy between SMC and objective memory performance. In the first step of the hierarchical regression model, simultaneously entering demographical variables (age, gender and education) displayed a statistically significant model ($F(3, 115) = 6.43$, $p < .001$). Additionally entering clinical variables (FHS-Stroke risk probability, depressive state, group membership, and ApoEε4 status) in the second step significantly increased the amount of variance explained in the discrepancy score ($F(4, 111) = 5.21$, $p = .001$). Entering the variable of executive function composite z-score in the third step significantly increased variance explained in the discrepancy score ($F(1, 110) = 5.01$, $p = .027$).

The final regression model showed that none of the demographic variables, FHS-Stroke risk probability, or ApoEε4 status was a significantly predictive factor for the discrepancy scores. However, the level of executive functioning ($\beta = -0.24$, $p = .027$; Figure 1) was a significantly predictive factor of the discrepancy scores, such that higher executive function was associated with negative discrepancy scores, indicating a higher self-evaluated memory functioning in relation to objective performance (i.e., an overestimation of memory functioning).

Depressive state ($\beta = -0.17$, $p = .046$) and group membership ($\beta = 0.26$, $p = .008$)

doi:10.6342/NTU201701830

were also significant predictors in this model (see Table 2). Specifically, increased endorsement of depressive symptoms was associated with negative discrepancy scores, which suggests that those individuals' subjective evaluation for their memory functioning were at a lower rank (worse) than that in their objective performances (i.e., an underestimation of memory functioning). Moreover, carrying a diagnosis of MCI was associated with positive discrepancy scores, which indicates that those individuals' subjective evaluation for their memory functioning were at a higher rank (better) than that in their objective performances (i.e., an overestimation of memory functioning). We further examined the frequency of overestimation versus underestimation of memory functioning for the two groups by dichotomizing the discrepancy scores into two categories (i.e., ≥ 0 or < 0). The results showed that there were 33.8% (n = 22) participants overestimated and 66.2% (n = 43) participants underestimated their memory functioning in the CN group. In the MCI group, there were 74.1% (n = 40) participants overestimated and 25.9% (n = 14) participants underestimated their memory functioning (Figure 2). The two groups showed significant difference in the frequency distribution of the two discrepancy categories ($\chi^2(2, N = 119) = 19.13, p < .001$).

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Discussion

The main goal of the present study was to investigate how the level of executive functioning affected the consistency between subjective memory complaints and performances on objective memory function measures while taking into account of demographic (e.g., age, education, gender) and clinical (e.g., symptoms of depression, ApoEε4 status, health conditions related to cardiovascular risk factors) variables in a sample composed of cognitively normal older adults and MCI participants. By analyzing the discrepancy scores between the subjective and objective measures, we found that although symptoms of depression, the group membership, and the level of executive functioning together predicted the discrepancy between the subjective and objective measures for memory functioning, executive functioning remained its predictive ability even after controlling for the symptoms of depression, group membership, or other factors.

In the current study, we used five executive functioning measures that were thought to tap on the prefrontal function (Stuss & Levine, 2002) and were essential for successful self-monitoring (Galeone et al., 2011), such as reasoning (WAIS-III Matrix Reasoning, Similarities subtests), ability to use external feedback to modify one's thinking or behaviors (MCST), and shifting and updating information (CTT, VF), to assess the relationship between executive function and the consistency

doi:10.6342/NTU201701830

between subjective and objective measures of memory functioning. As predicted, we found that lower level of the executive functioning was associated with greater discrepancy between subjective and objective measures of memory function in our elderly sample. This result was in line with emerging literatures that have demonstrated a relationship between reduced awareness of memory declines and frontal lobe dysfunctioning in patients with Alzheimer's disease (Kaszniak & Edmonds, 2010; Rosen, 2011; Zamboni et al., 2013) and MCI (Ries et al., 2007; Spalletta et al., 2014; Vannini et al., 2017). Moreover, structural (Saykin et al., 2006; Toledo et al., 2015) and functional brain changes (Erk et al., 2011; Lopez-Sanz et al., 2017; Rodda et al., 2009; Yasuno et al., 2015), as well as increased amyloid-β deposition (Snitz et al., 2015) in the frontal regions have been demonstrated in individual with SMC; although there were also evidences showing that the SMC was associated with gray matter atrophy (Schultz et al., 2015; Stewart et al., 2008) and brain functional alteration (Hohman et al., 2011; Jeong et al., 2017) in regions of the temporal or parietal lobes as opposite to the frontal lobes. Despite these evidences indicated that change in frontal lobe/executive functioning may occur early in the course of cognitively normal with SMC-MCI-dementia continuum, variations in the level of executive function or frontal involvement among individuals may exist. Indeed, we found that in both cognitive normal older adults and individuals with MCI,

doi:10.6342/NTU201701830

there were a portion of participants who demonstrated an underestimate of their objective memory functioning (see Figure 1 & Figure 3). Similarly, we also found that despite comparable memory functioning between the a-MCI-single and the a-MCI-multiple groups, the a-MCI-multiple group demonstrated larger disconcordance between the subjective and objective memory evaluations, which could be attributed by the poorer executive functioning observed in the a-MCI-multiple groups compared to the a-MCI-single groups.

An unexpected result was found in the present study with higher executive function predicting an underestimation of objective memory functioning even after controlling for the effect of depression symptoms. Previous studies have predominately focused on examining the overestimation phenomena and have failed to address such an underestimated tendency of self-evaluation memory functioning and its relationship with the level of executive functioning. It was possible that those participants with high executive functioning were keen to memory changes occurred in their daily life. Another possible explanation was that although an effort has been made to include multiple memory measures in the present study, these memory measurements might not be sensitive enough to detect the subtle within-person memory declines, as the calculations of the objective memory function was based on a comparison of the group norms.

doi:10.6342/NTU201701830

Another critical observation in this study was that the group membership not only predicted the discrepancy scores, but the two groups also demonstrated different profiles of the discrepancy scores which were beyond the contribution of the executive functioning. The CN group was more likely to underestimate their objective memory functioning, while the MCI group was more likely to overestimate their objective memory functioning. Such findings appear to be consistent with a recent study by Fragkiadaki et al. (2016) which used an in-session cognitive efficiency measure and found that cognitively normal elderly under-evaluated their performances while MCI patients over-evaluated their performances. This underestimation inclination has also been reported by Vannini et al. (2017) in cognitively healthy older people with amyloid deposition, and the authors introduced the term "hypernosognosia*"* to refer to the heightened memory self-awareness as the first stage during a hypothetical memory awareness model across the progression of Alzheimer's disease. It was possible that those cognitively intact older adults with "hypernosognosia" may represent a group of people who are at risk of developing dementia in the future, particularly when factors such as symptoms of depression, healthy conditions, which could potentially confound the interpretations of their "worries" were taking into account, as those individuals who may have higher baseline cognitive functioning compared to their counterparts and at the same time,

doi:10.6342/NTU201701830

they were also sensitive to their subtle within-person memory changes. It would be interesting to follow those cognitively normal older adults with "hypernosognosia" longitudinally to further investigate such a hypothesis. Nevertheless, the present study extended previous studies by utilizing a more ecologically relevant self-report measure to survey the concurrence between individuals' subjective memory concerns and objective memory performance, and revealed the differential patterns of the consistency between subjective memory concerns and objective memory functioning in cognitively normal older adults versus individuals with MCI.

Consistent with accumulating studies which have regarded depression as an important factor accounting for SMC (Rabin, Smart, & Amariglio, 2017), in the present study we also found that increased symptoms of depression was predictive of an increasing self-report of memory concerns and an underestimation of their memory functioning. Previous studies have indicated that more SMC was associated with more depressive symptoms regardless of the objective cognitive performance (Lehrner et al., 2014; Zlatar et al., 2017). Moreover, late-life depression has found to be at a risk factor of progression to dementia (Rabin et al., 2017). These results indicated that there may be a more complicated relationship between depression, SMC, and objective cognitive functioning than previous thought. Although the exact relationship among the above mentioned factors warrants further investigation,

doi:10.6342/NTU201701830

the present study extended previous findings by demonstrating that the contribution of executive function is important as it provides unique contribution for the concurrence between subjective and objective measures above the beyond of the symptoms of depression *per se*.

Despite the potential clinical value of our findings, there are limitations that should be noted. Frist, the executive function measures used in the present study did not specifically target at the meta-memory functioning. Although studies have illustrated that executive function was highly associated with meta-memory ability (Lin et al., 2010; Perrotin et al., 2008; Piras, Piras, Orfei, Caltagirone, & Spalleta, 2016), a more specific assessment for meta-memory may be helpful to further study the nature of the accuracy of SMC. Further, the present study only included the depressive symptoms in the analyses, and did not consider other affective factors (e.g., anxiety), which might also affect the concurrence between the objective and subjective memory measures as shown based on previous studies (Balash et al., 2013; Buckley et al., 2013; Rabin et al., 2017). Moreover, the cross-sectional design of the present study precluded us from investigating the relationship among the executive function, discrepancy scores, and future functioning declines. Lastly, the sample size of the current study was relatively small, particularly when considering the number of predictive variables used for the regression model. The small sample size

doi:10.6342/NTU201701830

also prevented us from elucidating the heterogeneity among the older adults, particularly in the MCI populations. Despite that, the present study was the first to consider the various factors in investigating the consistency and directionality of such consistency between the subjective and objective measures of memory functioning, and the effect of the executive function found was relatively robust.

In conclusion, the present study reveals that while several factors may be important to be considered when evaluating the concordance between the subjective evaluation for one's memory functioning for daily life and his/her objective memory performance, the level of executive functioning appears to play a unique role above and beyond the contribution of the demographic and clinical factors. The directionality of the discordance between the subjective and objective evaluation in cognitive normal older adults versus individuals with MCI was distinguishable. Collectively, our findings reveal the complexity of the subjective memory complaints, and it also highlights the importance for clinicians to be in consideration of multiple factors, particularly the individual's level of executive functioning, when judging the meanings of the individuals' subjective memory complaints or monitoring an on-going dementing process. Inclusion of biomarkers and longitudinal follow-up data will provide further information on the mechanism of the discordance and its clinical utility on predicting future functional declines among older adults.

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Tables

Table 1

Demographics, Clinical Characteristics & Neuropsychological Performances

Variables	CN (*n* = 65)	MCI (*n* = 54)	*p-vlaue.*[#]	η^2
Demographics and clinical characteristics				
Age	68.69 (6.8)	73.46 (9.3)	.002[*]	.08
Gender (% F)	61.6	54.6	.509	-
Education (year)	13.89 (2.8)	12.07 (3.7)	.003[*]	.07
FHS-Stroke risk (%)	10.15 (8.0)	14.50 (11.2)	.016[*]	.05
GDS-S	2.37 (2.2)	2.89 (2.6)	.362	-
ApoEε4 (% carrier)	35.4	31.5	.654	-
Executive function (raw score)[a]				
Matrix Reasoning	15.42 (5.2)	9.83 (4.6)	< .001[**]	.14
Similarities	21.33 (5.9)	16.43 (6.0)	.011	-
Verbal Fluency	32.42 (7.2)	25.17 (6.4)	< .001[**]	.11
MCST category	5.52 (1.5)	3.50 (1.9)	< .001[**]	.19
Color Trails Test (2-1)[b]	53.78 (21.9)	65.69 (42.8)	.015	-
EF z-score	0.37 (0.5)	-0.44 (0.7)	< .001[**]	.21
Episodic memory (raw score)[a]				
VR immediate recall	77.46 (12.4)	58.13 (15.7)	< .001[**]	.23
VR delayed recall	57.69 (18.7)	25.28 (20.7)	< .001[**]	.33
VR delayed recognition	43.40 (2.7)	37.04 (5.9)	< .001[**]	.28
VP immediate recall	11.80 (3.8)	6.49 (3.7)	< .001[**]	.26
VP delayed recall	5.14 (1.2)	3.26 (2.1)	< .001[**]	.19
LM immediate recall	38.38 (10.3)	21.74 (11.5)	< .001[**]	.28
LM delayed recall	24.08 (8.2)	9.96 (8.4)	< .001[**]	.34
CVLT-II learning	57.92 (7.6)	38.04 (10.0)	< .001[**]	.47
CVLT-II long delayed free recall	11.27 (3.0)	4.06 (3.9)	< .001[**]	.49
Memory z-score	0.60 (0.6)	-0.74 (0.7)	< .001[**]	.48
Subjective memory complaints[a]				
GMCI score	8.89 (6.3)	11.24 (8.9)	.293	-
Discrepancy Score	-0.46 (0.9)	0.58 (1.4)	< .001[*]	.13

Note. FHS-Stroke risk, Framingham Heart Study 10 years stroke risk probability; GDS-S, Geriatric Depression Scale-Short Form; MCST, Modified Card Sorting Test; EF z-score, executive function composite z-score; VR, Visual Reproduction Associate; VP, Visual Paired Associate; LM, Logical Memory; CVLT, California Verbal Learning Test; (continued)

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Table 1

Demographics, Clinical Characteristics & Neuropsychological Performances

GMCI, Green's Memory Complaints Inventory; η^2, effect size of analysis of variance/analysis of covariance.

[a] Group difference controlling for age, education, and FHS-Stroke risk. [b] Time difference was calculated by subtracting CTT-1 from CTT-2.

[#] Significant level for neuropsychological measures was set at $p < .003$ based on Bonforroni correction

[*] $p < .05$. [**] $p < .003$.

doi:10.6342/NTU201701830

Table 2

Summary of Hierarchical Regression Analyses Displaying Ability of Executive Function to Predict Discrepancy of Subjective and Objective Memory Evaluation

Predictors	β	Adjusted R^2	ΔR^2
Step I		.12**	.14**
Age	.11		
Gender	.10		
Education	.04		
Step II		.23**	.14**
FHS-Stroke risk	.10		
GDS-S	-.17*		
Group Membership	.26**		
ApoEε4	.06		
Step III		.26**	.03*
EF z-score	-.24*		

Note. FHS-Stroke risk, Framingham Heart Study 10 years stroke risk probability; GDS-S, Geriatric Depression Scale-Short Form; Group Classification, participant was classified as cognitively normal or mild cognitive impairment; ApoEε4: participants was classified as ApoEε4 carrier or non-carrier; EF z-score, executive function composite z-score; β, standardized beta-coefficient.

* $p < .05$. ** $p < .01$.

doi:10.6342/NTU201701830

Figures

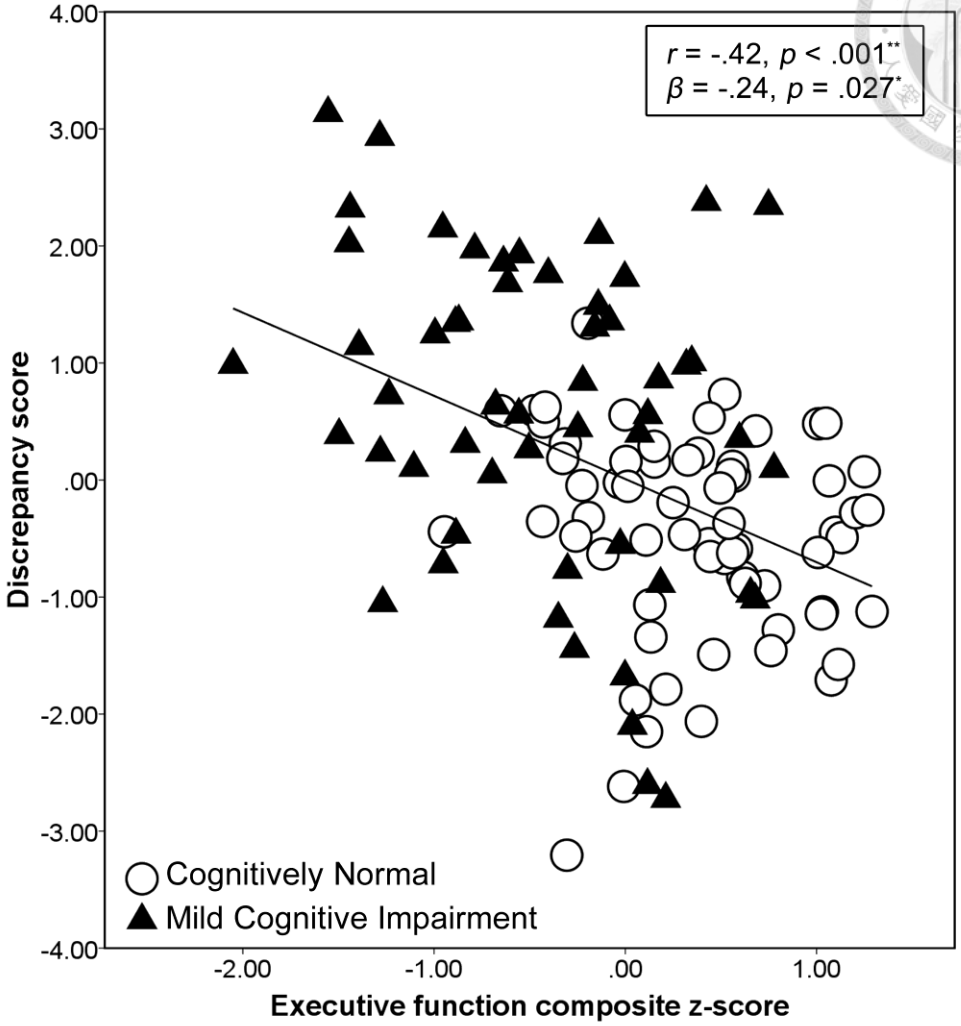

Figure 1. Relation between executive functioning and discrepancy scores between subjective memory complaints and objective memory performances. Lower executive functioning was associated with positive discrepancy scores, suggesting overestimation of memory functioning.

* $p < .05$. ** $p < .01$.

doi:10.6342/NTU201701830

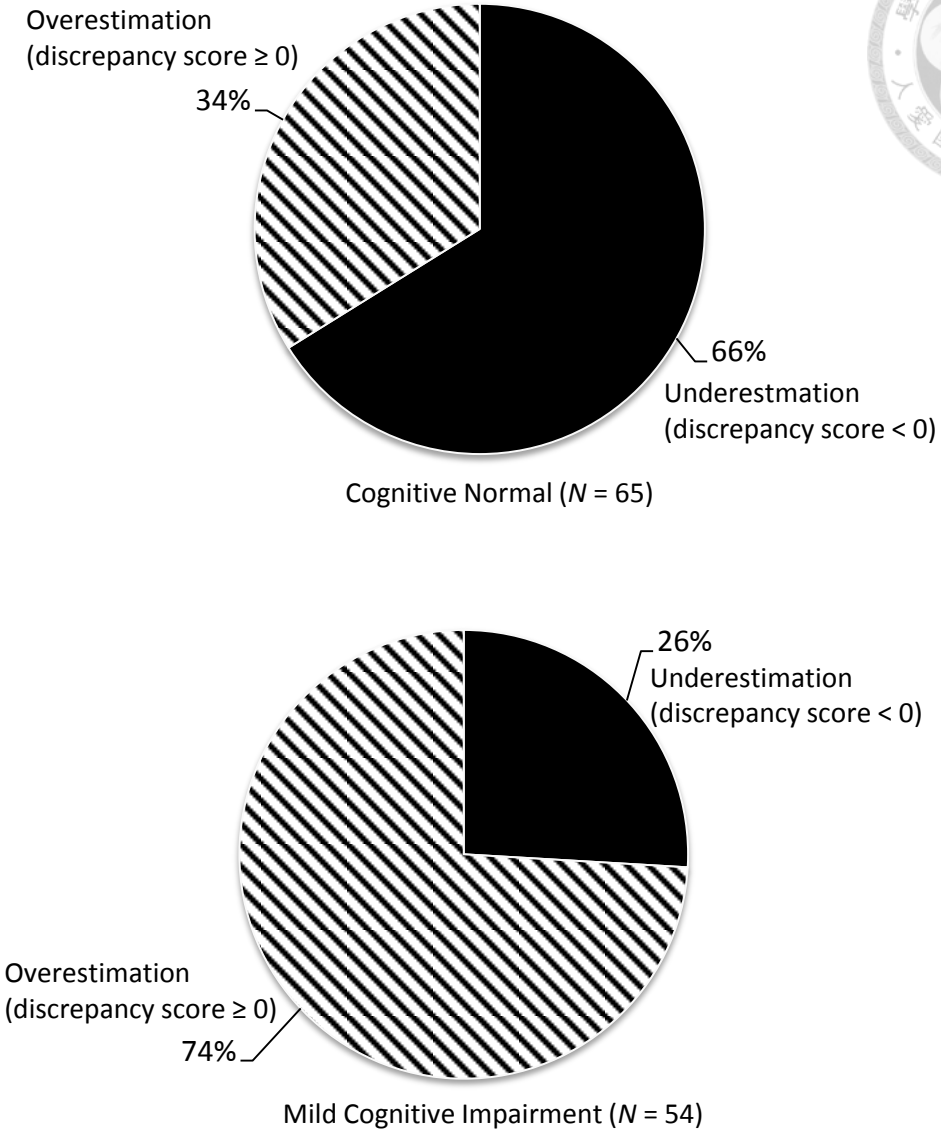

Figure 2. Pie figures showed frequency of different discrepancy categories (i.e., underestimation versus overestimation of memory functioning) in the cognitive normal and mild cognitive impairment groups. Negative discrepancy scores indicated that those individuals' self-evaluated memory functioning were at a lower (worse) rank than that in their objective performance (i.e., underestimation of memory functioning), and vice versa.

doi:10.6342/NTU201701830

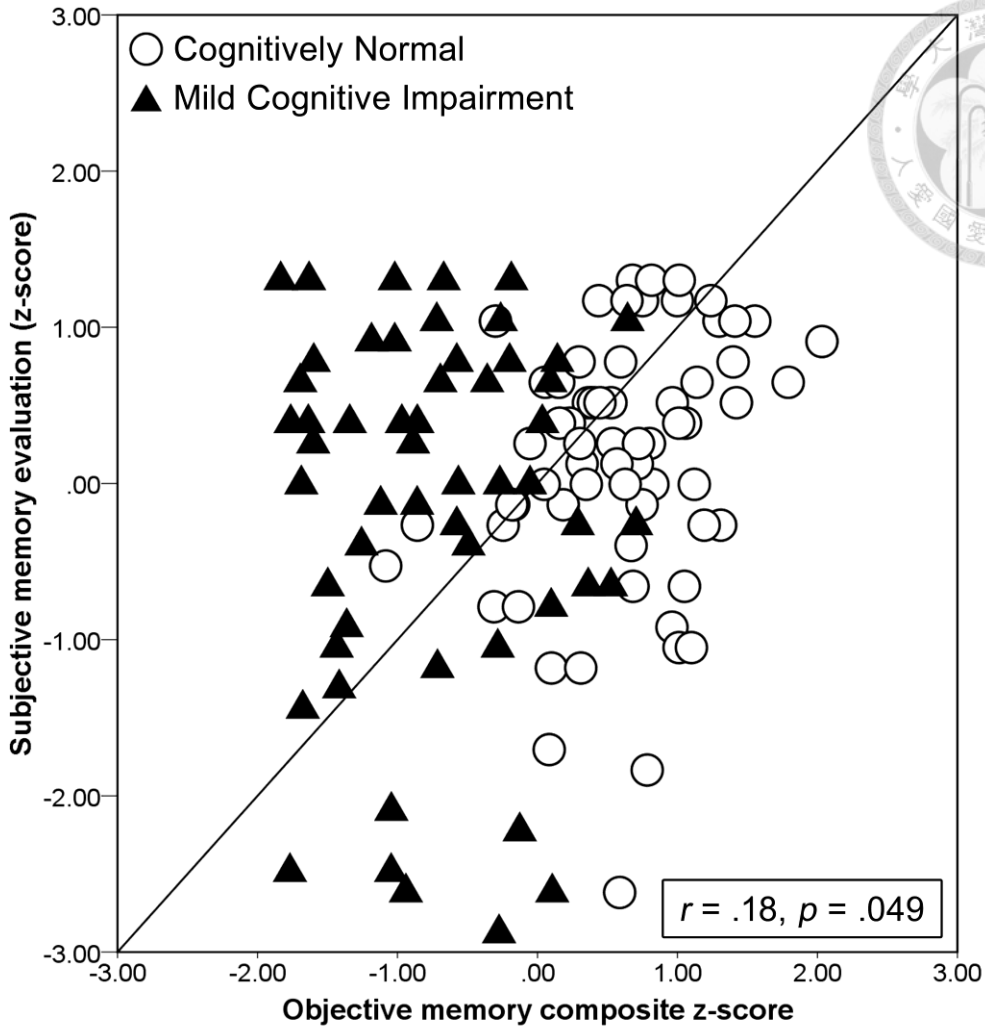

Figure 3. Relation between subjective memory evaluation (represented by inversed SMC z-score) and objective memory performance. The black line indicated the exactly accurate memory evaluation (discrepancy score = 0), and the more the subject closed to the line, the more accurate the SMC would be. Below the black line indicated that the subjective memory evaluation was higher (better) than the objective performance (discrepancy < 0), and vice versa.

doi:10.6342/NTU201701830

Appendix

Table A1

Demographics, Clinical Characteristics & Neuropsychological Performances of a-MCI-single and a-MCI-multiple domains

Variables	a-MCI-single (n = 23)	a-MCI-multiple (n = 29)	*p-vlaue.*[#]	η^2
Demographics and clinical characteristics				
Age	69.04 (6.4)	77.24 (9.3)	.001[*]	.19
Gender (% F)	65.2	48.3	.222	-
Education (year)	12.22(3.5)	11.69 (3.8)	.612	-
FHS-Stroke risk (%)	11.74 (7.7)	17.07 (13.3)	.094	-
GDS-S	2.39 (2.1)	3.31 (2.9)	.210	-
ApoEε4 (% carrier)	39.1	27.6	.378	-
Executive function (raw score)[a]				
Matrix Reasoning	12.35 (4.3)	7.90 (4.1)	.013	-
Similarities	18.30 (5.9)	14.59 (5.8)	.096	-
Verbal Fluency	28.55 (3.8)	22.21 (6.7)	.007	-
MCST category	4.70 (1.7)	2.69 (1.6)	.001[**]	.20
Color Trails Test (2-1)[b]	54.65 (27.1)	74.33 (52.0)	.033	-
EF z-score	-0.02 (0.5)	-0.78 (0.7)	< .001[**]	.22
Episodic memory (raw score)[a]				
VR immediate recall	62.48 (12.8)	53.07 (16.0)	.229	-
VR delayed recall	36.39 (19.1)	14.62	.004	-
VR delayed recognition	38.39 (5.8)	35.48 (5.7)	.230	-
VP immediate recall	7.87 (3.5)	5.10 (3.2)	.093	-
VP delayed recall	4.30 (1.9)	2.34 (1.8)	.012	-
LM immediate recall	26.87 (10.2)	17.24 (10.2)	.054	-
LM delayed recall	14.09 (8.6)	6.34 (6.3)	.014	-
CVLT-II learning	35.83 (7.5)	24.89 (10.4)	.011	-
CVLT-II long delayed free recall	5.87 (3.5)	2.21 (3.4)	.015	-
Memory z-score	-0.35 (0.6)	-1.10 (0.6)	.005	-
Subjective memory complaints[a]				
GMCI score	12.65 (9.3)	10.31 (8.7)	.370	-
Discrepancy Score	0.00 (1.3)	1.05 (1.2)	.042[*]	.08

Note. FHS-Stroke risk, Framingham Heart Study 10 years stroke risk probability; GDS-S, Geriatric Depression Scale-Short Form; MCST, Modified Card Sorting Test; EF z-score, executive function composite z-score; VR, Visual Reproduction Associate; (continued)

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Table A1

Demographics, Clinical Characteristics & Neuropsychological Performances of a-MCI-single and a-MCI-multiple domains

VP, Visual Paired Associate; LM, Logical Memory; CVLT, California Verbal Learning Test; GMCI, Green's Memory Complaints Inventory; η^2, effect size of the analysis of variance/analysis of covariance results

[a] Group difference controlling for age. [b] Time difference was calculated by subtracting CTT-1 from CTT-2. [#] Significant level for neuropsychological measures was set at $p < .003$ based on Bonforroni correction.

[*] $p < .05$. [**] $p < .003$.

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