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Components of Late-Life Exercise and Cognitive Function: an 8-Year Longitudinal Study

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Abstract The preventive effect of late-life physical exercise on cognitive deterioration has been reported in many cohort studies. However, the effect of exercise, independent of other cognitively demanding and social activities, is equivocal and little is known about the relative contributions of frequency, intensity, and duration of exercise. This study aimed to examine the relationships of exercise and its underlying components with cognitive function and rate of cognitive change over an 8-year period in a nationally representative sample of older Taiwanese. Data from the 1999, 2003, and 2007 phases of the nationwide longitudinal survey were used. Data from a fixed cohort of 1,268 participants aged 70 years or older in 1999 with 8 years of follow-up were analyzed. Cognitive function was assessed using the Short Portable Mental Status Questionnaire. Self-reported frequency, intensity, and duration of exercise were collected. A generalized estimating equation with multivariate adjustment for sociodemographic variables, cognitive and social leisure activities, lifestyle behaviors, and health status was calculated. Participants who were physically active during leisure time had better subsequent cognitive function (incident rate ratios [IRR]=0.63; 95 % CI, 0.54–0.75) and a slower rate of cognitive decline (p=0.01). Among the components of exercise, only duration emerged as a predictor of cognitive function (p=0.01). Older adults engaging in exercise for at least 30 min or more per session are likely to reduce the risk of subsequent cognitive decline. This research supports the case for physical exercise programs for older adults in order to help prevent loss of cognitive function.

Keywords Cognitive impairment · Dementia · Older adults · Physical exercise

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Introduction

As a consequence of global population aging, the prevalence of cognitive impairment and dementia is rapidly increasing and has become a substantial burden for medical and social care systems, individuals, and families (World Health Organization 2011). There were 35.6 million cases of dementia worldwide in 2010, with the numbers projected to almost double every 20 years, to 65.7 million in 2030 and 115.4 million in 2050. The largest proportion of these cases will be observed in South and East Asia, with an increase from 12.5 million people in 2010 to 51.79 million in 2050 (Prince et al. 2013). Developing feasible strategies to prevent or delay the onset of age-related cognitive decline is now an urgent issue in this region.

Physical exercise has been increasingly recognized for its beneficial effects on physical and mental health, including maintenance or improvement in cognitive functioning and reduced risk of dementia and Alzheimer's disease in older adults (Hamer and Chida 2009; UK Department of Health 2011; US Department of Health and Human Services 2008). Several prospective observational studies have revealed that physical exercise is associated with maintenance of cognitive function or reduced risk of overall cognitive decline, among older adults who stay physically active (Bherer et al. 2013). In contrast, although a body of cohort studies have demonstrated results favoring the beneficial effects of exercise, few have controlled for the potential effect of cognitively based or intellectual leisure activities, such as TV watching, reading, and solving puzzles, and social activities. Studies where there has been adjustment for frequency of cognitive and social activities among older adults have produced nonsignificant associations between exercise and risk of cognitive decline (Iwasa et al. 2012; Niti et al. 2008) and rate of cognitive change (Sturman et al. 2005). Therefore, the independent relationship of late-life exercise with cognitive function remains equivocal.

Many of the previous studies have also relied on loosely defined activity assessed by a single or few items, with frequency being the most commonly used component. Total volume of exercise is best captured through assessment of duration of sessions, and intensity, as well as frequency of exercise. Measurement of all three is needed in order to assess their independent effects. Each component may implicate different mechanisms underpinning any relationship. For example, higher intensity exercise such as running will stimulate higher demand on cardiovascular and circulatory function as opposed to lighter intensity exercise which in turn may provide a more relaxed response, as in yoga and Tai-Chi, or contribute to overall energy balance and help maintain a healthy body weight. Furthermore, a recent review indicated that studies have not been conducted to examine the optimal dose of exercise (including frequency, duration, and intensity) needed for cognitive improvement in older adults (Kirk-Sanchez and McGough 2014).

To date, few studies have examined the relationships of these exercise components with cognitive performance in older adults, especially in East Asia (Ku et al. 2012a). There is evidence indicating exercise levels among middle-aged and older adults in this region, in contrast with similar older populations in Europe and North America, do not decline with advancing age (Bauman et al. 2011; Ku et al. 2006) and so may be particularly important contributors to sustained mental health.

Our aim was to address some of these shortfalls by exploring the association between exercise and its underlying components and cognitive function over an 8-year follow-up period in a nationally representative sample of Taiwanese older adults. The specific research objectives were to (a) examine the relationships of exercise with cognitive function and its changes across time after adjusting for other types of leisure activity and (b) assess the independent associations of frequency, duration, and intensity of exercise with cognitive function.

Methods

Data and Sample

The nationally representative data were derived from the longitudinal Survey of Health and Living Status of the Elderly conducted by the Taiwan Ministry of Health and Welfare using three-stage equal probability sampling. Data were released following the approval of the study protocol by the Information Release Review Board. The six-wave household interview survey began in 1989 (n=4,049, aged 60+) and was followed up in 1993 (n=3,155, aged 64+), 1996 (n=2,669, aged 67+), 1999 (n=2,310, aged 70+), 2003 (n=1,743, aged 74+), and 2007 (n=1,268, aged 78+). The response rates of the surveys ranged between 87.2 and 91.8 % (i.e., the deceased subjects were excluded from each denominator of response rates) (Taiwan Bureau of Health Promotion 2010). This study used data from 1999 as baseline as the items concerning exercise, other leisure activities, and cognitive function were compatible from 1999 to 2007. From the original sample of 2,310 participants interviewed in 1999, a fixed cohort of 1,268 participants (50.6 % male) aged 70 years and older at baseline with 8 years (1999–2007) of follow-up were included in the subsequent analysis. The sampling strategy and research design have been described in more detail elsewhere (Ku et al. 2012b).

Measures

Independent Variable: Exercise

To assess exercise, participants were asked “Did you usually engage in any kind of exercise?” and four response categories regarding exercise frequency were provided (none, 1–2, 3–5, and 6+ sessions per week). Except for those who did not engage in any type of exercise, the participants then self-reported the duration of sessions (0, 1–14, 15–29, and 30+min per session) and perceived exertion (speed of breathing: no change, slightly fast, very fast) as an indicator of intensity of each exercise. Those who met the national exercise recommendation presented by Taiwan government (including three or more times per week for at least 30 min activity of moderate or vigorous intensity [breathing slightly or very fast] per session) were classified as being “active.” The “inactive” level denotes that participants do not engage in any forms of exercise. Participants with “less active” level are those who engage in some forms of exercise but do not reach the recommended level. (Ku et al. 2006)

The research team undertook a sub-study to further assess the reliability and validity of this measure among 75 community-dwelling older adults (male/female=22/53) in Taiwan, which is comparable to the current study regardless of age and levels of exercise. Test-retest reliability of the exercise levels with a 3-day interval was examined using Spearman's correlation (ρ=0.66, p<0.001). Concurrent validity was assessed by comparison of the self-reported exercise levels and tri-axial ActiGraph GT3X-plus accelerometer measures (ActiGraph, Pensacola, FL, USA), based on 3 days of activity monitoring (two weekdays and one weekend day). One week energy expenditure and steps were calculated as (2.5×2 weekdays)+(2×1 weekend day). This produced coefficients for energy expenditure of ρ=0.50, p<0.001, and walking steps of ρ=0.46, p<0.001 (Ku et al. 2012b; Murphy 2009). These results are comparable with other studies regarding self-reported physical activity assessment among older adults (Hagiwara et al. 2008; Harada et al. 2001).

Dependent Variable: Cognitive Function

Total range of overall performance from cognitive functioning was assessed using the 10-item Short Portable Mental Status Questionnaire (SPMSQ), which assesses global cognitive function similar to the Mini-Mental State Examination (MMSE). The eight items common to each survey were used for analyses which required participants to provide their address, age, date, day of the week, the current president, the last president, mother's maiden name, and to count backwards from 20 in steps of 3 a total of four times. A total score ranging from 0 to 8 was recorded based on the number of incorrect responses; higher scores represented poor cognitive functioning. The use of these questions as cognitive tests has been analyzed in other studies (Teng et al. 2013; Zimmer et al. 2001). The psychometric properties of this instrument were evaluated in the same sample described above. Internal consistency using Cronbach's alpha was 0.72. Test-retest reliability with a 3-day interval was r=0.69 (p<0.001). Concurrent validity was also examined by calculating the Spearman correlation between the eight-item scores and the MMSE scores (Spearman's ρ=−0.62, p<0.001).

Covariates

Covariates included sociodemographic variables previously shown to be related to both outcome and predictor variables (Coley et al. 2008), and included gender, age (70–74, 75–79, 80+), education level (no formal schooling, primary school, secondary school+), and living status (alone vs. with families/others). Also, participation in five common leisure activities among older adults, including cognitive (e.g., watching TV, listening to radio, reading newspapers/magazines/books and playing chess/cards) and social (e.g., visiting friends/relatives), was considered covariates in order to address the independent effect of exercise. The frequency of engagement in each leisure activity was coded as 0 (never), 1/4 (monthly), 2.5/4 (2 or 3 days per month), 1.5 (1 or 2 days per week), and 7 (daily) (Verghese et al. 2003). In addition, lifestyle behaviors including current alcohol consumption (yes vs. no) and current smoking (yes vs. no), and health status including body mass index (BMI), computed by measured height and weight (obesity, >26.99; overweight, 24–26.99; normal, 18.5–23.99; and underweight <18.5) (Taiwan Deportment of Health 2002), number of chronic diseases (including hypertension, heart disease, stroke, diabetes, and cancer), activities of daily living (some or great difficulties vs. no difficulties at all), and depressive symptoms (yes vs. no) assessed using the Center for Epidemiologic Studies Depression Scale (CES-D) (Ku et al. 2009) were included as covariates in the subsequent analyses.

Data Analyses

Descriptive statistics were calculated to cross-tabulate the associations between exercise levels, covariates, and cognitive function and to characterize the sample structure. Independent sample t tests and one-way ANOVAs were used to investigate cognitive performance differences in the categories of sample descriptors. Spearman's correlation was computed to assess the relationships of exercise and other leisure activities at baseline with cognition from 1999 to 2007.

Associations between exercise and cognition were analyzed using generalized estimating equations (GEE) (Liang and Zeger 1986) with negative binomial regression because the cognition variable was positively skewed and over-dispersed (Elhai et al. 2008; Norušis 2012). This approach for longitudinal data analysis utilized all three measurements (i.e., exercise, cognition, and all covariates) in 1999, 2003, and 2007. The dependency of the repeated observations within persons was defined by an exchangeable correlation structure (Dik et al. 2003), indicating better model fit (i.e., smaller QIC values) (Norušis 2012).

A fully adjusted model (model 1) was constructed first. The variables displaying significant associations with cognition in ANOVA tests were included in the adjusted GEE model simultaneously. The possible interaction effects between exercise and other leisure activities were also examined in this model, revealing that they are not significant (p values, 0.10–0.51). To examine the influence of missing data, the Little's missing completely at random (MCAR) test revealed that the missing pattern was not random (p<0.001). The missing values of the exercise variable, the cognitive function variable, and all covariates were estimated and replaced using the Expectation Maximization (EM) procedure in IBM SPSS Missing Value Analysis (SPSS 2007). After that, the preceding GEE model was repeated using the imputed data (model 2). Participants who had diminished cognitive performance before 1999 may have preclinical neurodegeneration and there is the possibility that this limits physical activity and may influence the estimates of the exercise-cognition relationships. A sensitivity analysis was therefore performed. Model 3 was rerun after excluding participants with cognitive decline from 1993 to 1999, which was defined as a difference (>0) between the eight-point scores from 1993 to 1999. Model 4 was based on model 3, which further excluded those with cognitive decline from 1999 to 2003. Finally, to clarify the temporal sequence of relationships between exposure and outcome variables, the GEE model with a time lag based on the imputed data was conducted (model 5), implying that repeated measurements of exercise and all covariates (measured in 1999 and 2003 except baseline cognitive function in 1999) were associated with cognitive performance assessed at one measurement point later (measured in 2003 and 2007) (Hoogendoorn et al. 2002). In order to determine the relative contributions of exercise components on cognition, the above analyses were repeated for each component of frequency, duration, and intensity.

Additional models were computed to test whether levels of exercise were related to differential rates of cognitive change. Cognitive function was predicted by exercise, age, and an exercise×age interaction using GEE after multivariate adjustment. These analyses were repeated after imputation and excluding those with cognitive decline from 1993 to 1999 and from 1999 to 2003.

Because of the nonlinearity of the negative binomial distribution, the regression coefficients (B) are not directly interpretable. Incident rate ratios (IRRs) (e^B) were therefore adopted. For example, if the IRR for cognitive function (i.e., number of incorrect responses) predicted by exercise (active vs. inactive [ref.]) is 0.30, the average number of incorrect responses among participants with the active level of exercise is 0.30 times lower than those with an inactive level of exercise. All analyses were conducted with IBM SPSS 20.0, and a p value <0.05 was considered significant.

Results

The cross-tabulation of cognitive performance (i.e., number of incorrect responses) at follow-up with the covariates at baseline is shown in Table 1. Except for living status, smoking, and body mass index, all variables were significantly associated with cognitive performance ($p<0.05$). Participants who had poorer cognitive performance at follow-up tended to be female, older, attain lower educational standards, had been inactive during leisure time, had no alcohol consumption, had a greater number of chronic diseases, had some or great difficulties in activities of daily living, and had depressive symptoms.

Table 1 Characteristics of participants in 1999 with cognitive function in 2007

Variables	No.	Cognitive function[a]	p value[b]
Sociodemographic			
Sex			<0.001
Male	642	2.13 (2.91)	
Female	626	3.22 (3.08)	
Age			<0.001
70–74	725	2.05 (2.78)	
75–80	399	3.15 (3.08)	
80+	144	4.44 (3.29)	
Education level			<0.001
Secondary school+	306	1.65 (2.74)	
Primary school	410	2.08 (2.91)	
No formal schooling	552	3.67 (3.04)	
Living status			0.78
Alone	125	2.58 (2.91)	
With family/others	1,059	2.66 (3.05)	
Lifestyle behaviors			
Exercise			<0.001
Active	134	2.29 (2.80)	
Less active	510	2.44 (2.93)	
Inactive	377	3.43 (3.23)	
Components of exercise			
Frequency			<0.001
6+ sessions/week	614	2.22 (2.86)	
3–5	131	2.64 (3.00)	
0–2	440	3.27 (3.17)	
Duration			<0.001
30+min	410	2.20 (2.78)	
15–29	171	2.81 (3.08)	
0–14	440	3.32 (3.21)	
Intensity			0.21
Very fast	27	2.19 (2.75)	
Slightly fast	265	2.43 (2.85)	
No change	893	2.74 (3.09)	
Smoking			0.28
Yes	228	2.46 (3.01)	
No	958	2.70 (3.04)	
Drinking			<0.001
Yes	264	1.99 (2.76)	
No	922	2.85 (3.08)	
Health status			
Body mass index			0.20
Underweight <18.5	78	3.21 (3.14)	
Normal 18.5–23.99	156	2.87 (3.19)	
Overweight 24–26.99	315	2.48 (3.01)	
Obese 27+	605	2.59 (2.99)	
Number of chronic diseases			<0.001
0	535	2.64 (3.01)	
1	404	2.26 (2.83)	

Table 1 (continued)

Variables	No.	Cognitive function[a]	p value[b]
2+	246	3.33 (3.29)	
Activities of daily living			<0.001
No difficulties at all	1,124	2.50 (2.97)	
Some or great difficulties	62	5.45 (2.83)	
Depressive symptoms			<0.001
No	900	2.29 (2.87)	
Yes	238	3.48 (3.13)	

The case number does not always add up to 1,268 because of missing values in some variables

[a] Cognitive function: number of incorrect responses; mean (standard deviation) thus higher scores indicate poorer cognitive function

[b] Independent *t* test or one-way ANOVA: *p* values represent whether the means differ significantly between groups

Spearman's correlations between exercise and other types of leisure activities at baseline and cognitive function in 1999, 2003, and 2007 are summarized in Table 2. The levels of exercise were inversely and significantly associated with the cognitive function score in all three surveys, demonstrating that physically active participants have better current and subsequent cognitive function. Except for "visiting friends/relatives," each type of leisure activity was negatively and significantly related with cognitive function across the three surveys. Among them, the associations of reading with cognitive function are stronger than the other types of leisure activities.

The fully adjusted GEE model (model 1 in Table 3) results indicate that those who engaged in higher levels of exercise had better subsequent cognitive performance ($p<0.001$). Older adults with an "active" level of exercise possessed the highest cognitive function (IRR, 0.63; 95 % CI, 0.53–0.74; reference, inactive), followed by those who were "less active" (IRR, 0.83; 95 % CI, 0.75–0.92; reference, inactive). After imputation, the fully adjusted model (model 2) also demonstrated that the associations of exercise and cognitive performance persisted. The sensitivity analysis excluding participants with cognitive decline from 1993 to 1999 (model 3: $n=$ 1,030, data not shown) yielded a similar result ($p=0.001$) (active: IRR, 0.69; 95 % CI, 0.53–0.89; less active: IRR, 0.81; 95 % CI, 0.71–0.98; reference, inactive). The associations were attenuated but remained significant in the additional sensitivity analyses ($p=0.03$), which further excluded participants with cognitive decline from 1999 to 2003 (model 4: $n=645$, data not shown) (active: IRR, 0.61; 95 % CI, 0.43–0.88; less active: IRR, 0.86; 95 % CI, 0.70–1.06; reference, inactive). Finally, the GEE with a time lag model (model 5: $n=$ 1,268, data not shown) still showed a similar trend ($p=0.03$) (active: IRR, 0.84; 95 % CI, 0.72–0.98; less active: IRR, 0.90; 95 % CI, 0.82–0.99; reference, inactive).

The relationships of the three separate components of exercise (duration, frequency, and intensity) with cognitive function are shown in Table 4. In the fully adjusted model (model 1), only the association for duration remained significant ($p=0.004$) (30+min/session: IRR=0.80; 95 % CI, 0.69–0.93; reference, 0–14 min/session). The sensitivity analysis demonstrated that the association with duration remained significant after data imputation (model 2, $p=0.01$), excluding participants with cognitive decline from 1993 to 1999 (model 3, $p=0.001$) and further excluding participants with cognitive decline from 1999 to 2003 (model 4, $p=0.03$). The association became weaker but remained significant in the GEE with a time lag model (model 5, $p=0.04$) (data of models 3–5 not shown).

Figure 1 presents the predicted cognitive function during the period of follow-up separately by levels of exercise from the age- and sex-GEE model. It shows that older adults at the inactive level had poor cognitive performance and a more rapid cognitive deterioration, followed by those with less

Table 2 Spearmen's correlation coefficients between exercise and cognitive/social leisure activities in 1999 and cognitive function in 1999, 2003, and 2007

Types of activities	Cognitive function	1999 (n=1,125)	2003 (n=1,138)	2007 (n=1,176)
Levels of exercise in 1999		−0.14***	−0.12***	−0.14***
Other types of leisure activities in 1999				
Watching television	(6.40±1.86)	−0.18***	−0.18***	−0.13***
Listening to radio	(2.13±3.07)	−0.13***	−0.08**	−0.11***
Reading	(2.37±3.25)	−0.34***	−0.37***	−0.32***
Playing chess	(0.23±0.99)	−0.15***	−0.10***	−0.12***
Visiting friends/relatives	(3.12±3.22)	0.01	−0.06	−0.09**

Cognitive function: number of incorrect responses. The case number is not 1,268 because of missing values in some variables. Figures in parentheses are mean±SD

*$p<0.05$; **$p<0.01$; *** $p<0.001$

Table 3 Generalized estimating equation (GEE) negative binomial regression for incidence rate ratios (IRRs) of levels of exercise for predicting cognitive performance

Variables	Model 1: fully adjusted (n=1,025)		Model 2: imputation (n=1,268)	
	IRR	95 % CI	IRR	95 % CI
Sociodemographic				
Sex		$p<0.001$		$p=0.02$
Male	0.74	0.66–0.84	0.87	0.77–0.98
Female (ref.)	1			
Age		$p<0.001$		$p<0.001$
70–74	0.52	0.45–0.60	0.40	0.36–0.46
75–80	0.70	0.64–0.77	0.67	0.61–0.74
80+ (ref.)	1		1	
Education level		$p<0.001$		$p<0.001$
Secondary school+	0.45	0.36–0.55	0.62	0.51–0.75
Primary school	0.52	0.45–0.59	0.62	0.55–0.71
No formal schooling (ref.)	1		1	
Lifestyle behaviors				
Exercise		$p<0.001$		$p<0.001$
Active	0.63	0.54–0.75	0.69	0.56–0.84
Less active	0.83	0.75–0.92	0.79	0.71–0.88
Inactive (ref.)	1		1	
Leisure activities		$p<0.001$		$p<0.001$
Watching television	0.94	0.93–0.97	0.96	0.95–0.97
		$p<0.001$		$p<0.001$
Listening to radio	0.97	0.95–0.98	0.9	0.94–0.97
		$p<0.001$		$p<0.001$
Reading	0.95	0.92–0.97	0.94	0.92–0.96
		$p=0.43$		$p=0.01$
Playing chess/cards	0.97	0.88–1.05	0.91	0.84–0.98
		$p=0.36$		$p=0.12$
Visiting friends/relatives	0.99	0.98–1.01	0.99	0.97–1.00
Drinking		$p=0.55$		$p=0.19$
Yes	0.96	0.83–1.11	1.11	0.95–1.29
No (ref.)	1		1	
Health status				
Number of chronic diseases		$p=0.71$		$p=0.66$
0	0.99	0.87–1.13	0.99	0.87–1.13
1	0.95	0.84–1.08	0.95	0.85–1.07
2+ (ref.)	1		1	
Activities of daily living		$p<0.001$		$p<0.001$
No difficulties at all	0.69	0.61–0.79	0.53	0.47–0.60
Some or great difficulties (ref.)	1		1	
Depressive symptoms		$p<0.001$		$p<0.001$
No	0.80	0.72–0.89	0.78	0.72–0.86
Yes (ref.)	1		1	

Cognitive function: number of incorrect responses. p values represent whether the overall effect of the variables are significant

active and active levels. With multivariate adjustment, the associations were not altered and the exercise by age interaction was significant (model 1, $p<0.001$), indicating that level of exercise was associated with the rates of cognitive changes during the follow-up. The associations remained significant after imputation (model 2, $p<0.001$) and excluding those with cognitive decline from 1993 to 1999 (model 3, $p=0.02$). It became nonsignificant when further excluding those with

Table 4 Generalized estimating equation (GEE) for incidence rate ratios (IRRs) of components of exercise for predicting cognitive function

Components	Model 1: fully adjusted (n=1,025)		Model 2: imputation (n=1,268)	
	IRR	95 % CI	IRR	95 % CI
Frequency	p=0.19		p=0.12	
6+ sessions/week	0.89	0.76–1.04	0.85	0.72–1.00
3–5	0.85	0.71–1.02	0.89	0.74–1.07
0–2 (ref.)	1		1	
Duration	p=0.004		p=0.01	
30+min	0.80	0.69–0.93	0.76	0.63–0.90
15–29	0.95	0.81–1.13	0.88	0.74–1.05
0–14 (ref.)	1		1	
Intensity	p=0.62		p=0.19	
Very fast	1.05	0.77–1.42	1.32	0.97–1.80
Slightly fast	0.95	0.83–1.08	1.07	0.93–1.23
No change (ref.)	1		1	

Cognitive function: number of incorrect responses. Model 1: variables comprised frequency, duration, intensity, sex, age, education, drinking, number of chronic diseases, activities of daily living, depressive symptoms, and five types of leisure activities. Model 2 is based on model 1 after imputation

cognitive decline from 1999 to 2003 (model 4, p=0.21) (data of models 3–4 not shown).

Discussion

This population-based longitudinal 8-year follow-up study revealed that exercise is associated with cognitive function and its changes across time. Unlike previous studies (Iwasa et al. 2012; Lee et al. 2014), these results were achieved even when adjusted for participation in cognitive and social leisure activities, health, and capacity for activities of daily living. Evidence for a dose–response effect for the exercise and cognition relationship was also identified. These results support previous findings that later life exercise can provide an independent protective effect against cognitive decline (Fratiglioni et al. 2004; Hötting and Röder 2013; Sofi et al. 2011). Among the three components of exercise, only duration, especially engagement for at least 30 min per session, was significantly associated with cognition independent of frequency and intensity. Sensitivity analyses indicated that these associations remained after excluding subjects with potential preclinical cognitive decline.

The mechanisms through which exercise may affect cognitive functioning are not fully understood. Imaging studies are finding effects of exercise training on size of the hippocampus and other changes including improved vascularization and plasticity of the brain (Kramer and Erickson 2007).

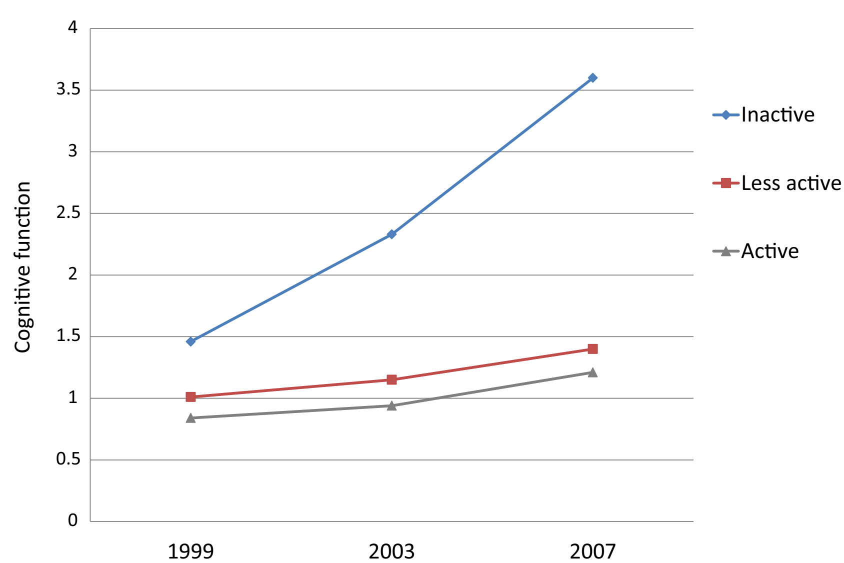

Fig. 1 Predicted cognitive function (no. of incorrect responses) during the follow-up in years by different exercise levels from the age- and sex-adjusted GEE model

Animal research has also discovered molecular and cellular changes in the brain that are attributable to increased physical exercise, such as increased neurotrophin (e.g., brain-derived neurotrophic factor, insulin-like growth factor 1 [IGF-1] and vascular endothelial growth factor) levels in some areas of the brain (Kramer et al. 2010). In addition to the neurobiological mechanisms, exercise can also provide a sense of enjoyment, fulfillment, social interaction, and belonging (Teychenne et al. 2008). These benefits may in turn maintain or improve cognitive functioning.

In this study, we found that session duration independent of frequency and intensity emerged as the strongest predictor among the three components. This has probably captured those who are engaging in sustained bouts of exercise that may be producing the most benefit for cognitive performance. It may in part reflect a high commitment to more formalized and structured activity. Few studies have examined the independent effect of duration on cognition while controlling for frequency and intensity within single intervention trials. However, one meta-analysis explored a range of moderators of the relationship between exercise training and cognition, indicating that training sessions needed to be at least 30 min long to be effective for the enhancement of cognition (Colcombe and Kramer 2003; Kramer and Erickson 2007). Furthermore, better mental health outcomes, such as anxiety symptom reduction, with exercise sessions exceeding 30 min were also observed in another meta-analysis of intervention trials among the elderly (Herring et al. 2010). Although the optimal dose of exercise needed for cognitive improvement has not been determined (Kirk-Sanchez and McGough 2014), the current study indicates that duration of exercise (30 min or more per session) may be the key component of exercise. However, more evidence, especially from randomized controlled trials, is still needed.

This study investigated long-term associations only and results may be partly explained by the presence of preclinical cognitive deterioration decreasing current and future activity engagement. However, when subjects with potential cognitive decline (1993–1999) were removed from the sensitivity analyses, the positive effects of exercise on cognitive functioning and rate of cognitive change remained. Although the association became nonsignificant when subjects with potential cognitive decline (1999–2003) were further excluded, the result is logical. It is likely that the remaining sample is healthier in cognitive function and the variations in cognitive changes are much smaller.

Both GEE (i.e., population-average model) and linear mixed models (LMM, i.e., hierarchical linear model or random effect model) are commonly used for analyzing longitudinal data. The primary distinction between them is whether the regression coefficients describe the average population or an individual's response to changes in exercise level. The LMM was further performed to model the direct effects of exercise (coefficients for active level: −0.37 [SD=0.08] and for less active level: −0.23 [SD=0.06]; reference, inactive, $p<0.001$) and age (coefficient: 0.06 [SD=0.01], $p<0.001$) as well as the interaction term of exercise and time (i.e., random effect). The results were similar to the findings derived from the GEE models so do not provide further insight

The assessment instrument of cognitive performance in the present study was short. The 10-item SPMSQ assesses memory, orientation, and calculation, which does not cover all areas of cognitive functioning. However, this study only utilized eight items to assess cognitive function ("What is your telephone number?" and "When were you born?" were not included), which may limit its precision in measuring the memory element of cognitive function. Where possible, future studies should engage more comprehensive measures of cognition so that effects on different elements may be examined. Although the measures of exercise were categorized by frequency, duration, and intensity, they are self-reported data, which may have been subject to recall bias, especially in older adults. However, physical exercise, cognition, and other covariates were assessed by multiple waves of surveys at several points during a long follow-up, which may mitigate random and nonrandom error in the assessment of exercise and cognition (Sturman et al. 2005).

This study observed the significant association between exercise and cognition after adjusting for engagement in cognitive and social leisure activities, which provides additional insight different to previous studies (Iwasa et al. 2012; Niti et al. 2008; Sturman et al. 2005). The inconsistency between these and previous findings may be due to (1) the selection of the study population—using a nationally representative sample of Chinese older adults who have seldom been studied; (2) the length of follow-up in this study is longer than other studies; and (3) level of data analyses—taking into account the more comprehensive coverage and varying nature of exposure, outcome, and covariates by using GEE models.

We have provided evidence that older Taiwanese adults who engage in more exercise, particularly in bouts lasting 30 min or more, are less likely to experience subsequent cognitive decline, regardless of their level of engagement in cognitive and social leisure activities, or their state of physical and mental health, and capacity for activities of daily living. These data suggest that the most salient element of exercise is session duration and support. These findings substantiate the importance of provision of exercise programs and opportunities for older adults. Not only will they benefit from improved physical function and disease prevention but will also improve their chances of retaining good cognitive function into their later years.

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Conflict of Interest The authors declare that they have no conflict of interest.

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