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Cognitive and physical declines and falls in older people with and without mild cognitive impairment: a 7-year longitudinal study

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ABSTRACT

Objectives: We examined longitudinal changes in cognitive and physical function and associations between change in function and falls in people with and without mild cognitive impairment (MCI).

Design: Prospective cohort study with assessments every 2 years (for up to 6 years).

Setting: Community, Sydney, Australia.

Participants: Four hundred and eighty one people were classified into three groups: those with MCI at baseline and MCI or dementia at follow-up assessments ($n = 92$); those who fluctuated between cognitively normal and MCI throughout follow-up (cognitively fluctuating) ($n = 157$), and those who were cognitively normal at baseline and all reassessments ($n = 232$).

Measurements: Cognitive and physical function measured over 2–6 years follow-up. Falls in the year following participants' final assessment.

Results: In summary, 27.4%, 38.5%, and 34.1% of participants completed 2, 4, and 6 years follow-up of cognitive and physical performance, respectively. The MCI and cognitive fluctuating groups demonstrated cognitive decline, whereas the cognitively normal group did not. The MCI group had worse physical function than the cognitively normal group at baseline but decline over time in physical performance was similar across all groups. Decline in global cognitive function and sensorimotor performance were associated with multiple falls in the cognitively normal group and decline in mobility (timed-up-and-go test) was associated with multiple falls across the whole sample.

Conclusions: Cognitive declines were not associated with falls in people with MCI and fluctuating cognition. Declines in physical function were similar between groups and decline in mobility was associated with falls in the whole sample. As exercise has multiple health benefits including maintaining physical function, it should be recommended for all older people. Programs aimed at mitigating cognitive decline should be encouraged in people with MCI.

Key words: aging, falls, cognitive disorders, longitudinal studies

Introduction

Mild cognitive impairment (MCI) is increasingly recognized as an important public health problem in older people (Petersen, 2004; Winblad *et al.*, 2004). The prevalence of MCI increases with age

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and is estimated to be between 5% and 37% in community-dwelling older people, varying according to MCI diagnostic criteria and age-group sampling differences (Lu *et al.*, 2021; Overton *et al.*, 2019; Sachdev *et al.*, 2015). MCI and fluctuating cognition (e.g. alternating between MCI and normal cognition over multiple assessments) increase the risk of developing dementia (Aerts *et al.*, 2017).

Falls represent one of the major health care issues for people with MCI. Approximately 53–63% of people with MCI fall one or more times during follow-up periods of 6–12 months (Chantanachai *et al.*, 2021). Falls can result in injuries ranging from lacerations, bruises, and abrasions, through to dislocations, sprains, fractures, and traumatic brain injury (Australian Institute of Health and Welfare, 2022), with some evidence to support people with MCI are at greater risk of fall injury (Smith *et al.*, 2021). Falls can also lead to decreased functioning in daily life, social isolation, concern about falling, loss of independent living, and reduced quality of life (Lord *et al.*, 2021).

Previous studies have shown that impaired physical function (e.g. slow gait speed, longer Timed-Up-and-Go test times, and increased postural sway) measured at a single time point is associated with prospective falls in people with MCI (Chantanachai *et al.*, 2021; Chantanachai *et al.*, 2022). Few studies, however, have examined longitudinal cognitive and physical declines and their associations with falls. Taylor *et al* found people with MCI had greater physical performance declines over 12 months, compared to cognitively normal older people and that a decline in physical function significantly increased the odds of falls across the whole sample that spanned the cognitive spectrum (Taylor *et al.*, 2019). However, the causality of the latter relationship could not be determined because both decline and falls were measured over the same timeframe (Taylor *et al.*, 2019). Another more recent study, where 12% of the sample had possible or probable dementia, reported that physical function trajectories did not provide additional discrimination in predicting time to two or more falls compared to baseline physical function alone (Kerber *et al.*, 2022).

Clearly, further research is needed to examine changes more comprehensively in both cognitive and physical function in older people with MCI allowing for contrasts to be made over longer timeframes. Understanding how these changes predispose people with different levels of cognitive impairment to falls may elucidate potential fall prevention strategies. Thus, this study had two main objectives. First, we contrasted longitudinal changes in cognitive and physical function in older people with MCI, fluctuating cognitive status (MCI converting to cognitively normal and vice versa), and normal cognition over 6 years. Second, we examined the associations between changes in cognitive and physical function over 2–6 years and prospective falls recorded after their final assessment. We hypothesized: (i) older people with MCI would have more rapid cognitive and physical function declines than cognitively normal older people and similar declines to people with fluctuating cognitive status and (ii) changes in cognitive and physical functions would be associated with falls across all groups.

Methods

Participants

The sample for this study was drawn from 1073 participants, recruited from the community in the eastern suburbs of Sydney, Australia, into the longitudinal Sydney Memory and Ageing Study (MAS). MAS followed participants up every 2 years for a total of 6 years (a total of four assessments). To be eligible for enrollment into the MAS study, participants needed to be aged 70–90 years and living in the community. The MAS study exclusion criteria were diagnosed dementia (as determined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria and a consensus diagnosis from an expert team comprised of old age psychiatrists, neuropsychiatrists, and neuropsychologists), inability to speak and understand English, current diagnosis of major psychiatric disorder and psychotic symptoms, motor neuron disease, developmental disability, multiple sclerosis, progressive malignancy (active cancer or current treatment for cancer, other than non-metastasized prostate cancer and skin cancer), and medical or psychological conditions that prevented participants from completing assessments (Sachdev *et al.*, 2010). The present study included MAS participants who agreed to additional physical assessments as part of the falls and balance substudy for at least two assessment points.

The diagnostic criteria for MCI and dementia were applied at each time point. MCI classification was determined by (a) cognitive impairment as 1.5 standard deviations (or equivalent) below published normative values (matched for age and education where available) on a neuropsychological test measure (Petersen, 2004), (b) normal or minimally impaired functional activities as determined by informant ratings on the Bayer Activity of Daily Living (ADL) scale (<3 scores) adjusted for physical impairment (Hindmarch *et al.*, 1998), (c) those with Bayer-ADL scale scores ≥ 3 underwent consensus

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diagnosis for MCI, and (d) no diagnosis of dementia (DSM-IV criteria with consensus diagnosis from an expert team comprised of old age psychiatrists, neuropsychiatrists, and neuropsychologists).

Participants were categorized into one of three groups: (1) cognitively normal; (2) MCI, and (3) cognitively fluctuating. The cognitively normal group was cognitively normal at baseline and throughout follow-up. The MCI group was classified as MCI at baseline and MCI or dementia at subsequent assessments. The cognitively fluctuating group comprised participants with fluctuating cognitive status over the follow-up as outlined in the participant characteristics section below.

The MAS study was approved by the University of New South Wales Human Research Ethics Committee (Ref number: HC17865 and HC200671), and written informed consent was provided by all participants or their informants.

Assessments

Participants who completed all assessments were assessed at baseline and then every 2 years (i.e. at 2, 4, and 6 years) by trained research staff with an additional 1 year of prospective falls follow-up after their final cognitive and physical assessments.

Demographic and health conditions

General health examinations included assessment of body mass index (BMI), history of falls, medication use, and presence of medical conditions such as stroke, heart disease, diabetes mellitus, and arthritis. Psychotropic medication use included the following medication classes: sedatives and hypnotics, anxiolytics, antipsychotics, and antidepressants.

Cognitive function

Global cognitive function was assessed with the Mini-Mental State Examination (MMSE). Processing speed and executive function were measured with the Trail Making Test (TMT) parts A and B, respectively (Bowie and Harvey, 2006). The TMT difference score (TMT-diff = TMT-B time minus TMT-A time) was calculated to reduce the influence of processing speed and provide a more precise measure of executive function (Strauss *et al.*, 2006). Memory was assessed using delayed recall of Logical Memory Story A Test (LM delayed recall) (Wechsler, 1997).

Physical function

The Timed-Up-and-Go (TUG) test was used to assess functional mobility (Podsiadlo and Richardson, 1991). The coordinated stability test, a measure of dynamic balance, assessed participants' ability to adjust their body position in a steady and coordinated way when near or at the limits of their base of support (Lord *et al.*, 1996).

Sensorimotor performance was assessed using the Physiological Profile Assessment (PPA). The PPA assesses: visual contrast sensitivity (dB), lower limb proprioception (degrees of error), isometric knee extension strength (best of three; kg force), hand reaction time (ms), and postural sway assessed while participants stood on a compliant foam rubber mat (mm) (Lord *et al.*, 2003). Weighted contributions from these five PPA assessments were used to calculate a composite sensorimotor measure, with higher scores indicating poorer physical performance (Lord *et al.*, 2003).

Ascertainments of falls

Monthly falls diaries were used to record participants' falls. When fall diaries were not returned within 2 weeks of the end of each month, participants were contacted by phone to obtain the required information. A fall was defined as "an unexpected event in which the person comes to rest on the ground, floor, or lower level" (Lamb *et al.*, 2005). Participants who reported falling two or more times in the 12-month period following their final physical and cognitive assessments were classified as multiple fallers and participants who fell 0 or 1 times in this period were classified as nonmultiple fallers.

Statistical analysis

Participants who had partial follow-up (2 and 4 years) for cognitive and physical measures were compared to those with complete follow-up (6 years) using Chi-squared tests for categorical variables and independent samples t-tests for continuous variables. Between-group (MCI, cognitively fluctuating, and cognitively normal) differences at baseline were assessed using one-way analysis of variance (ANOVAs) for continuous variables and Chi-squared tests for categorical variables. Mixed-effects regression models with random intercepts were used to determine the main effects of cognitive group (MCI, cognitively fluctuating, and cognitively normal) and time on cognitive and physical performance over 6 years follow-up. For each model, Time, Cognitive group, and Time × Cognitive group interaction terms were entered as fixed effects. The models included participants' age, sex, and years of education as covariates. Pairwise comparisons using mixed-effects models were used to examine differences in estimated marginal means between groups and over time in the cognitive and physical variables at baseline and 2, 4, and 6 years follow-up.

The average annual change in cognitive and physical performance was calculated (annual

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change = [final follow-up score − baseline score]/number years follow-up). The associations between change in cognitive and physical performance and multiple falls were assessed using binary logistic regression in Generalized Linear Models (GLM). For each logistic regression model, annual change, cognitive group (MCI, cognitively fluctuating, and cognitively normal), and Annual change × Cognitive group interaction term were entered while adjusting for age, sex, years of education, and baseline performance to determine whether there was a differential effect of performance decline on faller status by cognitive group. If the interaction term was significant, cognitive groups were examined separately. If the interaction term was not significant, the whole sample was examined while adjusting for age, sex, years of education, and baseline performance. Despite the multiple comparisons made, Bonferroni corrections were not made to p-value in this exploratory study because such adjustments may increase Type II errors (Perneger, 1998). All analyses were performed using SPSS and $p < 0.05$ was considered statistically significant.

Results

Participant characteristics

Four hundred and eighty-one participants met the inclusion criteria. These comprised 304 participants with a wave 1 baseline assessment, 149 with a wave 2 baseline assessment, and 28 participants with a wave 3 baseline assessment. One hundred thirty (27%) participants were followed up for cognitive and physical assessments for 2 years, 187 (38.9%) participants were followed up for 4 years, and 164 (34.1%) participants were followed up for 6 years with 109 (22.7%) participants completing all four assessments. Participants were then followed up for falls for an additional year following their final cognitive and physical assessments. At baseline, participants who completed 6 years of follow-up for cognitive and physical measures were significantly younger than participants who completed 2 and 4 years of follow-up (complete follow-up mean age = 77 ± 4 years; partial follow-up mean age = 79 ± 5 years; $t_{(479)} = -4.328$, $p < 0.001$) but did not significantly differ in sex or MMSE and TUG scores.

Two hundred and thirty-two were classified as cognitively normal (i.e. were cognitively normal at baseline and throughout follow-up); 92 were classified as having MCI (72 [78%] had MCI at all assessment points and 20 [22%] progressed to dementia); and 157 were cognitively fluctuating. For this latter group, 89 [57%] were cognitively normal at baseline and transitioned to MCI ($n = 86$) and/or dementia ($n = 3$) at one or more reassessments (19/86 [22%] with MCI reverted to cognitively normal), and 68 [43%] were diagnosed with MCI at baseline and reverted to cognitively normal at one or more reassessments (of which 14/68 [21%] transitioned back to MCI and 2 of these reverted back to healthy again).

Table 1 presents the baseline participant characteristics for the three groups. The cognitively normal group had significantly more women than the MCI and cognitively fluctuating groups (Table 1). There were no other statistically significant between-group differences in demographic characteristics, medical history, or medication use at baseline (Table 1).

Cognitive performance changes during follow-up

Analyses revealed a significant main effect of Cognitive group for all cognitive variables (Table 2; Figure 1), indicating cognitive performance was poorer in both the MCI and cognitively fluctuating groups, relative to cognitively normal group (Figure 1; Table 3). There was a significant main effect of Time for MMSE (global cognition), TMT-A (processing speed), and TMT-diff (executive function), indicating decline over 6 years in the total sample, but not for LM delayed recall (memory) (Figure 1; Tables 2 and S1). There were significant Time × Cognitive group interactions for MMSE, TMT-A, and TMT-diff, indicating that the differences between groups in these tests varied over time (Figure 1; Tables 2, 3 and S1). As seen in Figure 1 and Table S1, the MCI and cognitive fluctuating groups declined over time in MMSE, TMT-A, and TMT-diff while the cognitively normal group did not.

Physical performance changes during follow-up

There was a significant main effect of Cognitive group for all physical assessments (TUG, knee extension strength, coordinated stability, and sensorimotor function) (Table 2; Figure 1), indicating poorer performance for the MCI group, relative to the cognitively normal group (Table 3). There was a significant main effect for Time for TUG, knee extension strength, and sensorimotor function (Table 2; Figure 1; Table S1), indicating declines in the total sample over 6 years. There were no significant Time × Cognitive group interactions for physical function (Figure 1; Tables 2, 3 and S1), suggesting that the between-group differences did not vary with respect to time.

Change in cognitive and physical performance and falls

Baseline characteristics of faller groups are reported in Table S2. During the 12-month follow-up period, 21 participants (23%) in the MCI group, 23

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Table 1. Baseline characteristics for participants prospectively categorized as MCI, cognitively fluctuating, and cognitively normal

Characteristic, *N* (%) or mean ± SD	Total	MCI (*N* = 92)	Cognitively fluctuating (*N* = 157)	Cognitively normal (*N* = 232)	*p*-value[a]
Demographics					
Age (years)	481	78.8 ± 4.9	78.6 ± 4.4	77.7 ± 4.5	0.070
Sex (female)	481	43 (47)	71 (45)	140 (60)	**0.006**
BMI (kg/m^2)	472	27.7 ± 4.6	26.8 ± 4.3	27.5 ± 4.4	0.168
Education (years)	481	11.8 ± 3.7	11.9 ± 3.7	11.8 ± 3.3	0.988
Fall in the past year (≥ 1 falls)	477	32 (35)	49 (31)	71 (31)	0.754
Medical history					
Stroke	479	1 (1)	6 (4)	2 (1)	0.087
Heart problem	481	16 (17)	44 (28)	56 (24)	0.167
Hypertension	479	59 (64)	89 (57)	134 (58)	0.513
Diabetes	480	5 (5)	17 (11)	22 (10)	0.345
Increased cholesterol	480	49 (53)	91 (58)	135 (58)	0.682
Arthritis	479	49 (53)	86 (55)	127 (55)	0.953
Depression	465	8 (9)	18 (12)	35 (16)	0.279
Medication use					
Total number	475	5.4 ± 3.5	5.5 ± 3.5	5.2 ± 3.6	0.728
Psychotropic medication use	455	19 (21)	21 (14)	31 (14)	0.249

BMI = body mass index, kg = kilograms, m = metres, MCI = mild cognitive impairment, *N* = number of participants, SD = standard deviation. Medical history; self-reported conditions as diagnosed by a doctor. Bold *p*-values highlight statistically significant findings ($p < 0.05$). Psychotropic medication use (reported as not taking/ taking one or more) included the following medication classes: sedative/ hypnotic, antianxiety, antipsychotic, and antidepressant medications.

[a] Chi^2 for categorical variables and ANOVA for continuous variables.

participants (15%) in the cognitively fluctuating group, and 29 participants (13%) in the cognitively normal group reported ≥ 2 falls.

In GLM binary logistic regression with multiple falls as the dependent variable, the interaction terms (Annual change× Cognitive group) were not significant for TMT-A, TMT-diff, LM delayed recall, TUG, knee extension strength, and coordinated stability, indicating that the associations between performance changes per year and multiple falls did not differ significantly by group (Table 4). A greater decline in TUG performance per year was significantly associated with multiple falls in the whole sample (OR = 1.5, $p = 0.02$) while adjusting for age, sex, years of education, and baseline performance (Table 4). There were no significant associations between annual change in TMT-A, TMT-diff, LM delayed recall, knee extension strength, or coordinated stability and falls.

The interaction terms for the MMSE and PPA (MMSE Annual change × Cognitive group; PPA Annual change × Cognitive group) were significant, indicating that the associations between annual change and multiple faller status differed between the groups (Table 4). Subgroup analyses revealed greater yearly declines in MMSE and PPA test scores were significantly associated with multiple falls in the cognitively normal group but not in the MCI or cognitively fluctuating groups (Table 4).

Discussion

This study examined longitudinal changes in cognitive and physical function over 6 years in older people categorized into three groups: MCI, cognitively fluctuating, and cognitively normal. We also examined the association between average annual change in cognitive/physical performance and falls. Not unexpectedly, we found differences in cognitive performance (global cognition, processing speed, and executive function) between the MCI and cognitively normal group, and between the MCI and cognitively fluctuating group at baseline, and that the rate of decline over the follow-up period was greatest in the MCI group. We also found that the MCI group had worse physical function than the cognitively normal group at baseline; however, the rate of physical decline over time was similar across the three groups. Greater decline in mobility predicted multiple falls in the whole sample, while greater decline in global cognition and sensorimotor function only predicted falls in the cognitively normal group.

As the diagnosis of MCI is based primarily on assessments of cognitive functioning, it was expected the participants with MCI would

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Table 2. Main effects of mixed effects linear regression for time, cognitive group (MCI [$n = 92$], cognitively fluctuating [$n = 157$] and cognitively normal [$n = 232$] groups) and Time × Cognitive group interaction term for cognitive and physical performance over 6-year follow-up controlling for age, sex, and years of education

	F VALUE	*P*-VALUE
Cognitive performance		
MMSE (Global cognition)		
Time	F (3, 744) = 3.71	**0.011**
Cognitive group	F (2, 536) = 59.44	**<0.001**
Time × Cognitive group	F (6, 770) = 2.58	**0.018**
TMT-A (Processing speed)		
Time	F (3, 702) = 15.40	**<0.001**
Cognitive group	F (2, 527) = 36.47	**<0.001**
Time × Cognitive group	F (6, 726) = 2.22	**0.040**
TMT diff (Executive function)		
Time	F (3, 716) = 23.96	**<0.001**
Cognitive group	F (2, 527) = 73.45	**<0.001**
Time × Cognitive group	F (6, 739) = 5.59	**<0.001**
LM delayed recall (Memory)		
Time	F (3, 711) = 1.24	0.293
Cognitive group	F (2, 543) = 88.67	**<0.001**
Time × Cognitive group	F (6, 738) = 0.41	0.873
Physical performance		
TUG		
Time	F (3, 600) = 16.44	**<0.001**
Cognitive group	F (2, 520) = 7.83	**<0.001**
Time × Cognitive group	F (6, 621) = 0.75	0.612
Knee extension strength		
Time	F (3, 750) = 50.58	**<0.001**
Cognitive group	F (2, 533) = 4.55	**0.011**
Time × Cognitive group	F (6, 767) = 1.15	0.333
Coordinated stability		
Time	F (3, 605) = 1.28	0.280
Cognitive group	F (2, 517) = 8.89	**<0.001**
Time × Cognitive group	F (6, 624) = 0.99	0.434
PPA		
Time	F (3, 668) = 3.48	**0.016**
Cognitive group	F (2, 529) = 3.23	**0.040**
Time × Cognitive group	F (6, 693) = 1.40	0.213

LM = logical memory, MMSE = Mini-Mental State Examination, PPA = Physiological Profile Assessment, TMT-A = Trail Making Test A, TMT diff = Trail Making Test difference (TMT diff = TMT-B time minus TMT-A time), TUG = Timed Up and Go. Bold *p*-values highlight statistically significant findings ($p < 0.05$). Higher scores represent better performance for MMSE, LM delayed recall, and knee extension strength. Lower scores represent better performance for TMT-A, TMT diff, TUG, coordinated stability, and PPA score.

demonstrate poorer cognitive performance than the cognitively normal group. This is consistent with previous studies that have shown people with MCI have deficits in global cognition as well as several cognitive domains including executive function, proceeding speed, and memory (Nordlund *et al.*, 2005; Pa *et al.*, 2009). Our longitudinal findings, in the main, supported our hypothesis that older people with MCI and fluctuating cognition decline more rapidly over time across cognitive domains compared to cognitively normal older people. These findings are consistent with previous literature demonstrating the increased risk of these groups declining cognitively and developing dementia (Aerts *et al.*, 2017).

Specifically, the cognitively fluctuating and MCI groups declined in global cognition, processing speed, and executive function whereas the cognitive normal group did not, supporting our hypothesis of more rapid decline in the cognitively fluctuating and MCI groups (Table S1). These changes are reflected by larger MCI-normal and cognitively fluctuating-normal between-group differences at 4 and 6 years, compared to baseline (Table 3). Interestingly, logical memory delayed recall performance remained unchanged from baseline, for all groups. The finding of similarly preserved memory over time across all groups contrasts with a study by Johnson *et al.*, who found older people with MCI declined more rapidly in memory than cognitively normal older people over a period of 3 years (Johnson *et al.*, 2012). It is possible that a composite memory score as used by Johnson *et al*, rather than an individual assessment of memory as used here, may be more sensitive to detect subtle memory changes in older people with MCI (Johnson *et al.*, 2012).

Our hypothesis that people with MCI would decline more rapidly in physical function when compared to the cognitively normal group was not supported. We found mobility (assessed with the TUG test), knee extension strength, and sensorimotor function (assessed with the PPA) declined significantly in all groups, whereas dynamic balance (assessed with the coordinated stability test) did not significantly decline in any group. The MCI group performed significantly worse than the cognitively normal group at multiple time points in measures of mobility, knee strength, and balance, and at some but not all time-points the MCI group performed significantly worse than the cognitively fluctuating group in the knee strength and balance measures. Finally, the cognitively fluctuating group demonstrated worse sensorimotor performance as measured by the PPA than the cognitively normal group at only the final (6 years) time point. These findings do not support our hypothesis that the MCI and cognitively fluctuating groups would have more rapid declines in physical function than the cognitively normal group, and contrasts with findings from Taylor *et al.*, that older people with MCI have greater physical performance decline, including sensorimotor function, compared to cognitively normal older people, albeit over a shorter (1 year) period (Taylor *et al.*, 2019). Instead, it appears that at baseline, impairments in strength and mobility

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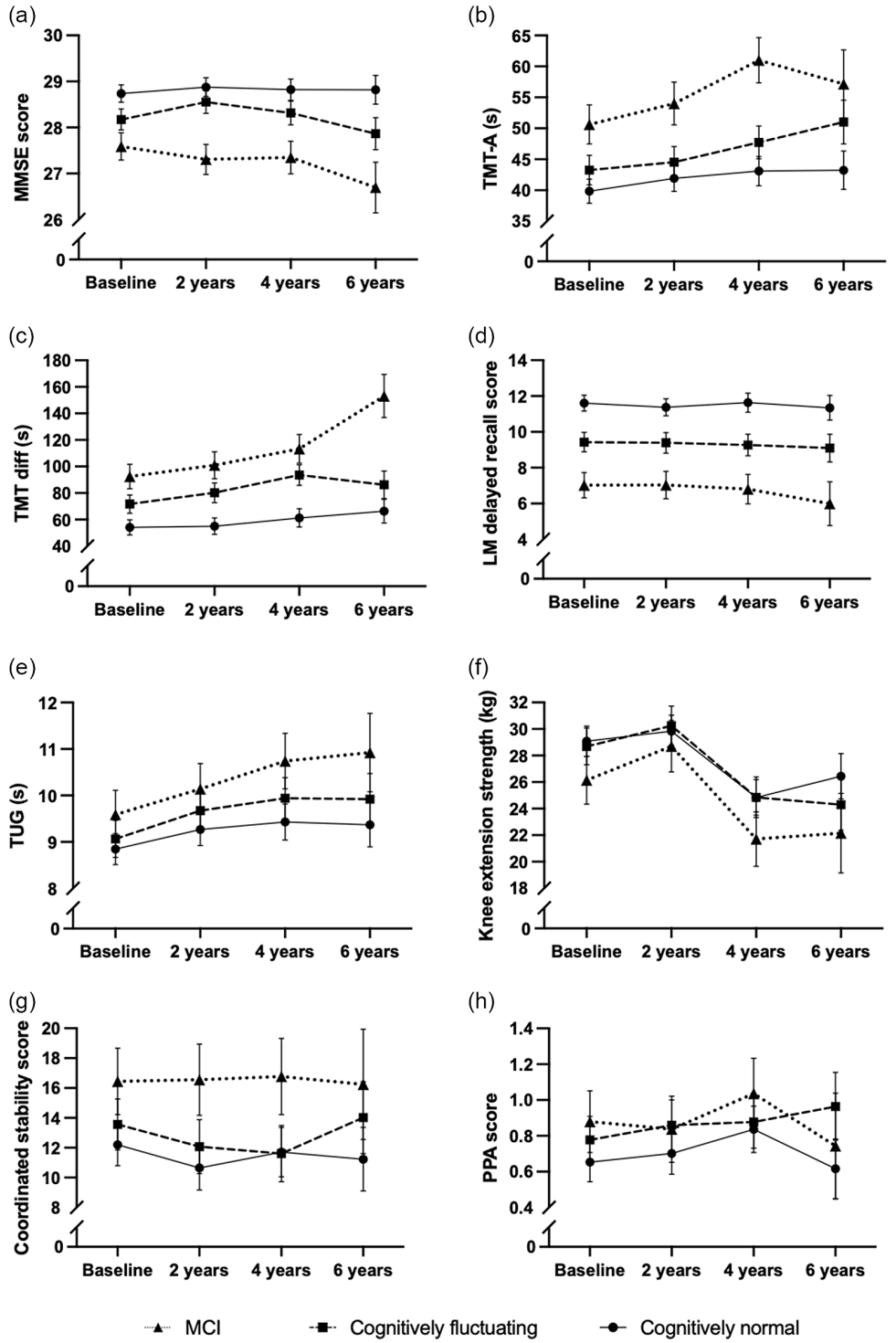

Figure 1. (a-h) Mean (95% confidence intervals) for cognitive and physical performance: (a) MMSE, (b) TMT-A, (c) TMT diff, (d) LM delayed recall, (e) TUG, (f) knee extension strength, (g) coordinated stability test, and (h) PPA at baseline, 2-, 4-, and 6-years follow-up by cognitive status (MCI, cognitively fluctuating, and cognitively normal). *Note*. kg = kilograms; LM = logical memory; MCI = mild cognitive impairment; MMSE = Mini-Mental State Examination; PPA = Physiological Profile Assessment; s = seconds; TMT = Trail Making Test; TMT-A = Trail Making Test A; TUG = Timed Up and Go; TMT diff = TMT-B time minus TMT-A time. Higher scores represent better performance for MMSE, LM delayed recall and knee extension strength. Lower scores represent better performance for TMT-A, TMT diff, TUG, coordinated stability and PPA.

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Table 3. Mean between group (MCI [$n = 92$], cognitively fluctuating [$n = 157$] and cognitively normal [$n = 232$]) differences from mixed effects pairwise comparisons for cognitive and physical performance at baseline, 2-, 4-, and 6-year follow-up

		MCI versus cognitively normal		MCI versus cognitively fluctuating		Cognitively fluctuating versus cognitively normal	
Assessment	Time	Mean difference (95% CI)	*p*-value	Mean difference (95% CI)	*p*-value	Mean difference (95% CI)	*p*-value
MMSE	B	−1.2 (−1.6, −0.7)	**<0.001**	−0.6 (−1.0, −0.1)	**0.006**	−0.6 (−0.9, −0.2)	**0.001**
	2 y	−1.6 (−2.0, −1.1)	**<0.001**	−1.2 (−1.7, −0.8)	**<0.001**	−0.3 (−0.7, 0.1)	0.134
	4 y	−1.5 (−2.0, −1.0)	**<0.001**	−1.0 (−1.5, −0.4)	**<0.001**	−0.5 (−0.9, −0.1)	**0.013**
	6 y	−2.1 (−2.9, −1.4)	**<0.001**	−1.2 (−2.0, −0.4)	**0.001**	−1.0 (−1.5, −0.4)	**<0.001**
TMT-A, s	B	10.8 (6.3, 15.3)	**<0.001**	7.4 (2.6, 12.2)	**0.001**	3.4 (−0.3, 7.2)	0.088
	2 y	12.1 (7.2, 17.0)	**<0.001**	9.5 (4.3, 14.7)	**<0.001**	2.6 (−1.4, 6.6)	0.322
	4 y	17.9 (12.6, 23.2)	**<0.001**	13.3 (7.8, 18.8)	**<0.001**	4.6 (0.3, 9.0)	**0.032**
	6 y	14.0 (6.2, 21.6)	**<0.001**	6.1 (−1.8, 14.1)	0.182	7.8 (2.0, 13.5)	**0.004**
TMT diff, s	B	38.4 (25.2, 51.6)	**<0.001**	20.8 (6.8, 34.8)	**0.001**	17.6 (6.7, 28.5)	**<0.001**
	2 y	45.9 (31.4, 60.4)	**<0.001**	20.8 (5.5, 36.0)	**0.004**	25.2 (13.4, 36.9)	**<0.001**
	4 y	52.1 (36.4, 67.7)	**<0.001**	19.8 (3.6, 35.9)	**0.011**	32.3 (19.7, 45.0)	**<0.001**
	6 y	86.8 (64.1, 109.5)	**<0.001**	66.9 (43.5, 90.4)	**<0.001**	19.9 (3.2, 36.6)	**0.014**
LM delayed recall	B	−4.6 (−5.6, −3.6)	**<0.001**	−2.4 (−3.5, −1.3)	**<0.001**	−2.2 (−3.0, −1.3)	**<0.001**
	2 y	−4.3 (−5.4, −3.2)	**<0.001**	−2.4 (−3.5, −1.2)	**<0.001**	−2.0 (−2.9, −1.1)	**<0.001**
	4 y	−4.8 (−6.0, −3.6)	**<0.001**	−2.5 (−3.7, −1.2)	**<0.001**	−2.4 (−3.3, −1.4)	**<0.001**
	6 y	−5.4 (−7.1, −3.6)	**<0.001**	−3.1 (−4.9, −1.3)	**<0.001**	−2.3 (−3.5, −1.0)	**<0.001**
TUG, s	B	0.7 (−0.0, 1.5)	0.055	0.5 (−0.3, 1.3)	0.309	0.2 (−0.4, 0.9)	0.793
	2 y	0.9 (0.1, 1.7)	**0.026**	0.5 (−0.4, 1.3)	0.455	0.4 (−0.3, 1.1)	0.378
	4 y	1.3 (0.4, 2.2)	**0.001**	0.8 (−0.1, 1.7)	0.099	0.5 (−0.2, 1.2)	0.239
	6 y	1.6 (0.4, 2.7)	**0.005**	1.0 (−0.2, 2.2)	0.146	0.5 (−0.3, 1.4)	0.372
Knee extension strength, kg	B	−2.9 (−5.5, −0.3)	**0.022**	−2.5 (−5.3, 0.2)	0.081	−0.4 (−2.6, 1.8)	0.965
	2 y	−1.1 (−3.9, 1.7)	0.705	−1.5 (−4.5, 1.4)	0.509	0.4 (−1.9, 2.8)	0.963
	4 y	−3.1 (−6.1, −0.1)	**0.037**	−3.1 (−6.3, −0.0)	**0.046**	0.0 (−2.5, 2.5)	1.000
	6 y	−4.3 (−8.5, −0.1)	**0.044**	−2.2 (−6.5, 2.2)	0.554	−2.1 (−5.3, 1.0)	0.286
Coordinated stability	B	4.2 (1.0, 7.5)	**0.005**	2.9 (−0.5, 6.3)	0.125	1.4 (−1.3, 4.1)	0.540
	2 y	5.9 (2.5, 9.3)	**<0.001**	4.5 (0.9, 8.1)	**0.010**	1.4 (−1.4, 4.3)	0.552
	4 y	5.1 (1.4, 8.8)	**0.003**	5.2 (1.3, 9.0)	**0.004**	−0.1 (−3.2, 3.0)	1.000
	6 y	5.0 (−0.2, 10.2)	0.062	2.2 (−3.1, 7.6)	0.686	2.8 (−1.1, 6.7)	0.246
PPA	B	0.2 (−0.0, 0.5)	0.087	0.1 (−0.2, 0.4)	0.731	0.1 (−0.1, 0.3)	0.399
	2 y	0.1 (−0.1, 0.4)	0.539	−0.0 (−0.3, 0.3)	0.997	0.2 (−0.1, 0.4)	0.257
	4 y	0.2 (−0.1, 0.5)	0.268	0.2 (−0.1, 0.5)	0.498	0.0 (−0.2, 0.3)	0.968
	6 y	0.1 (−0.3, 0.5)	0.843	−0.2 (−0.6, 0.2)	0.519	0.3 (0.0, 0.7)	**0.021**

B = baseline, CI = confidence intervals, kg = kilograms, LM = logical memory, MCI = mild cognitive impairment, MMSE = Mini-Mental State Examination, PPA = Physiological Profile Assessment, s = seconds, TMT-A = Trail Making Test A, TMT diff = Trail Making Test difference (TMT diff = TMT-B time minus TMT-A time), TUG = Timed Up and Go, y = years.

Bold *p*-values highlight statistically significant findings ($p < 0.05$).

Higher scores represent better performance for MMSE, LM delayed recall, and knee extension strength. Lower scores represent better performance for TMT-A, TMT diff, TUG, coordinated stability, and PPA score.

were already evident in the MCI group, and from there on, declines in the three groups occurred "in parallel" (Figure 1). As between-group differences were evident for both the cognitive and physical measures at baseline, it is not possible to elucidate whether the physical impairments preceded cognitive impairment, or vice versa.

Similar to a previous study by Kerber *et al.* (2022), we found cognitive and physical function trajectories had limited value in predicting multiple falls in people with MCI. We did find, however, that a relatively small average annual decline in mobility was associated with multiple falls in the whole sample which suggests that fall prevention programs aimed at improving and maintaining mobility should target older people in the community broadly and include people with MCI and fluctuating cognitive performance. The finding that global cognitive decline was not predictive of multiple falls in the MCI and cognitive fluctuating groups builds on recent meta-analysis and cohort studies that have reported poorer global cognition does not predict falls (typically in

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Table 4. GLM binary logistic regression with multiple falls as the dependent variable and annual change in cognitive or physical performance[a] as the independent variable adjusting for age, sex, years of education, and baseline cognitive/physical performance

Cognitive and physical performance	Annual change, mean (SD)			
	Non-multiple fallers	Multiple fallers	OR (95% CI)	*p*-value
Whole sample[b]				
TMT-A, s	1.1 (4.9)	2.4 (6.4)	1.05 (1.00, 1.39)	0.054
TMT diff, s	3.7 (12.3)	7.3 (25.5)	1.01 (1.00, 1.03)	0.091
LM delayed recall	− 0.1 (1.1)	0.1 (1.1)	1.14 (0.89, 1.45)	0.295
TUG, s	0.2 (0.7)	0.4 (0.9)	1.51 (1.07, 2.13)	**0.020**
Knee extension strength, kg	− 0.6 (2.7)	− 0.6 (2.5)	1.02 (0.91, 1.13)	0.783
Coordinated stability	− 0.1 (3.1)	0.4 (3.7)	1.05 (0.96, 1.15)	0.275
Analyses stratified by group[c]				
MMSE[c]				
Cognitively healthy	0.0 (0.4)	− 0.2 (0.5)	0.16 (0.05, 0.50)	**0.002**
Cognitively fluctuating	− 0.0 (0.5)	− 0.2 (0.6)	0.40 (0.14, 1.13)	0.082
MCI	− 0.2 (0.7)	− 0.2 (0.8)	0.96 (0.48, 1.93)	0.907
PPA score[c]				
Cognitively healthy	0.0 (0.3)	0.1 (0.3)	6.18 (1.11, 34.37)	**0.038**
Cognitively fluctuating	0.1 (0.2)	− 0.0 (0.3)	0.17 (0.02, 1.37)	0.096
MCI	− 0.0 (0.3)	0.1 (0.3)	3.06 (0.37, 25.34)	0.300

CI = confidence intervals, GLM = Generalized Linear Models, kg = kilograms, LM = logical memory, MCI = mild cognitive impairment, MMSE = Mini-Mental State Examination, OR = Odds ratio, PPA = Physiological Profile Assessment, s = second, SD = standard deviation, TMT-A = Trail Making Test A, TMT diff = Trail Making Test difference (TMT diff = TMT-B time minus TMT-A time), TUG = Timed Up and Go.

Bold *p*-values highlight statistically significant findings ($p < 0.05$).

[a] Annual change = (reassessment – baseline)/years of follow-up.

[b] The interaction term Annual change × Cognitive group was not significant and was removed from the model and the group was examined as a whole.

[c] The interaction term (Annual change × Cognitive group) was significant indicating that the association between annual change and multiple falls was different between cognitive groups, therefore analyses were stratified by cognitive group.

12-month periods) in older people with cognitive impairment or people with MCI (Chantanachai *et al.*, 2022; Chantanachai *et al.*, 2021). The findings of no significant associations between annual change in TMT-A, TMT-diff, LM delayed recall, and falls also suggest that longitudinal measurements of these specific cognitive domains do not add value to fall risk assessments that are more temporally close to falls in older people. Future research, with more frequent assessments, may elucidate whether more refined measures of decline add value over assessments that are conducted within 1 year of a fall e.g. examining gait speed using wearable devices.

The strengths of this study include the relatively large sample size, the longitudinal design with up to 6 years of follow-up, the inclusion of a cognitively fluctuating group in addition to MCI and cognitively normal groups, the assessment of multiple cognitive and physical measures and the prospective ascertainment of falls. We also acknowledge some limitations. First, our sample size was insufficient to consider MCI subtypes (i.e. amnestic vs non-amnestic, single vs multiple-domain), for which longitudinal changes in cognitive and physical performance may differ. Second, the survivor effect likely affected our findings in that participants with better prognoses may have remained in the study for longer while less healthy participants were lost to follow-up. Such a selective loss to follow-up was possibly greater in the MCI group as these participants had cognitive impairment at baseline. In consequence, these omissions may have weakened the associations found and/or lead to some of the null findings. Third, some of our cognitive and physical measures may have lacked sensitivity to detect differences between groups over time. This could be explored in future studies with a more comprehensive set of test measures and longer follow-up periods with potentially more frequent assessment e.g. yearly. Fourth, our cognitively fluctuating group comprised participants who showed multiple cognitive decline profiles over time including people who had normal cognition throughout the follow-up period except for the final assessment. Further studies, with larger samples and longer follow-up periods, could examine physical and cognitive declines in participants who continue to fluctuate cognitively vs. those who fluctuate before declining to MCI or

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dementia. Finally, we acknowledge that the multiple comparisons presented in Table 3 and Supplementary Table 1 may have increased the chance of Type I errors. However, these associations are all in the expected direction and lend support to the primary findings outlined in Table 2.

With respect to clinical implications, our findings indicate that people with MCI have lower limb strength and mobility impairments as well as poor and more rapidly declining global cognition and executive function and suggest that intervention programs should address both cognitive and physical function in this group. Moreover, decline in mobility is associated with multiple falls in the whole sample including older people with MCI. There is increasing evidence that combined physical and cognitive training is beneficial for people with MCI, as summarized in a recent systematic review and network meta-analysis of randomized controlled trials that found such combined interventions can promote both cognitive and physical health in this population (Gavelin *et al.*, 2021). Combined cognitive-motor interventions may also benefit older people with fluctuating cognition, as this "intermediate" group also demonstrated multiple cognitive and physical impairments. The demonstrated association between decline in sensorimotor function and global cognition with prospective falls in the cognitively normal group suggests that greater efforts are needed to facilitate exercise participation addressing these domains to prevent falls in this group.

Conclusion

The study findings indicate that older community-dwelling people with MCI and fluctuating cognition experience more pronounced declines in global cognition, processing speed, and executive function over 6 years compared to a cognitively normal group. However, these declines were not associated with multiple falls in the MCI and fluctuating cognition groups. While changes in physical function were also evident at baseline, these changes over time were similar between groups and mobility decline was significantly associated with multiple falls in the whole sample. Interventions should include exercise to address loss of physical function for all older people and training to mitigate accelerated declines in cognitive function in people with MCI and fluctuating cognitive performance.

Conflict of interest

The Physiological Profile Assessment (PPA, marketed as NeuRA FallScreen) is commercially available through Neuroscience Research Australia (NeuRA). Perminder Sachdev is a member of an Advisory Committee for Biogen Australia. Henry Brodaty has been a consultant or advisory board member for Biogen, Nutricia Australia, Roche, and Skin2Neuron.

Description of authors' roles

TC, DS, MT, and SL conceived the study and contributed design, analysis, and interpretation of data. JM, KD, DS, SL, MT, PS, and HB contributed to data acquisition, cleaning, and database preparation. PH contributed to statistical analysis, and interpretation. TC, DS, SL, and MT drafted the manuscript. All authors contributed to revising the manuscript and approved the final version.

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Supplementary material

To view supplementary material for this article, please visit https://doi.org/10.1017/S1041610223000315

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