Short- and long-term effects of different exercise programs on the gait performance of older adults with subjective cognitive decline: A randomized controlled trial

Kosuke Fujita\textsuperscript{a,b}, Hiroyuki Umegaki\textsuperscript{a,b}, Taeko Makino\textsuperscript{a}, Kazuki Uemura\textsuperscript{a}, Takahiro Hayashi\textsuperscript{a}, Aiko Inoue\textsuperscript{a}, Chiharu Uno\textsuperscript{a}, Tomoharu Kitada\textsuperscript{a}, Chi Hsien Huang\textsuperscript{b,c}, Hiroyuki Shimada\textsuperscript{d}, Masafumi Kuzuya\textsuperscript{a,b,*}\textsuperscript{,}\textsuperscript{**}

\textsuperscript{a} Institute of Innovation for Future Society, Nagoya University, Nagoya, Japan
\textsuperscript{b} Department of Community Healthcare and Geriatrics, Nagoya University Graduate School of Medicine, Nagoya, Japan
\textsuperscript{c} Department of Family Medicine, E-Da Hospital, Kaohsiung City, Taiwan, ROC
\textsuperscript{d} Department of Preventive Gerontology, Center for Gerontology and Social Science, National Center for Geriatrics and Gerontology, Obu, Japan

ARTICLE INFO

Section Editor: Christiaan Leeuwenburgh

Keywords:
- Cognition
- Gait-biomechanics
- Rehabilitation

ABSTRACT

Background: Older adults, especially those with cognitive decline, often have poor gait performance, which results in poor clinical outcomes due to falls or decreased daily physical activity. The effects of various exercises on gait performance have been studied, whereas the short-term and long-term effects of different exercise modalities remain unknown.

Objective: To compare the short- and long-term effects of aerobic training (AT), resistance training (RT), and combined training (CT) on the gait performance of community-dwelling older adults with subjective cognitive decline (SCD).

Design: A four-arm, randomized controlled trial.

Setting and subjects: 388 community-dwelling older adults with SCD (mean age, 72.3 years).

Methods: Participants attended an exercise or education class twice a week for 26 weeks. 10 gait performance parameters were examined at baseline, post-intervention (Week 26), and after 26 weeks of follow-up (Week 52) using an electronic walkway system.

Results: The mean adherence of exercise sessions was 82.5 to 85.9%. All exercise intervention induced an improvement in gait speed, stride time, cadence, stride length, and double-support time at Week 26 ($p < .05$), without significant intergroup differences among exercise interventions. However, only RT showed a significant effect on some spatiotemporal gait parameters at Week 52. The analyses for the gait variability parameters showed mild effects of all exercise interventions.

Conclusion: All of the exercise programs examined had a positive short-term effect on spatiotemporal gait parameters of older adults with SCD, despite no effect on gait variability parameters. RT are most recommended when long-lasting effects are the primary aim.

Introduction

A gait disorder is one of the common geriatric syndromes (Sudarsky, 1990). Gait disorder such as small stride length and increased variability confers a high risk of falls or restriction of daily physical activity on older adults ($\geq 65$ years old) (Marques et al., 2018; Rubenstein, 2006). Approximately 29% of older adults suffer a fall at least once a year, and approximately 10% of falls would be the cause of major injuries, such as hip fractures (Guirguis-Blake et al., 2018). As gait disorder itself, falls, or decreased physical activity are one of the most major causes of future loss of independence, lower quality of life (QoL), and mortality in older adults (2020 Alzheimer’s disease facts and figures, 2020; Fried et al.,...
2.1. Study design

The primary objective of this study was to compare the effect of different exercise programs with same duration (2session per week for 26 weeks), that is, AT, RT, and both (combined training, CT), on improving gait parameters in older adults with SCD. The secondary objective was to investigate the long-term (26 weeks after the end of intervention) effects of the abovementioned exercise interventions on older adults with SCD. Considering the previous systematic review (Zhang et al., 2019), we hypothesized that CT is most effective in improving both short- and long-term gait performance.

2. Methods

2.1. Study design

This four-arm, assessor-blinded, randomized controlled trial, named the TOyota Prevention Intervention for Cognitive decline and Sarcope-nia (TOPICS) trial, was conducted between October 2014 and October 2015. From this trial TOPICS, the effects of AT, RT, and CT on the frailty and intrinsic capacity are already investigated and published elsewhere (Hauer et al., 2012; Kao et al., 2018; Kemoun et al., 2010; Schwenk et al., 2014). A meta-analysis and systematic review revealed that RT with gradually increasing intensity, functional mobility training such as walking, or combination of various exercise modality are effective for improving gait speed or performance on the timed up and go test (TUG) in older adults (Kokkinos et al., 2017; Zhang et al., 2019). However, the most effective exercise modality for improving spatiotemporal gait and gait variability parameters has not been identified. Moreover, as only a few studies included follow-up investigations (Hauer et al., 2012; Kao et al., 2018), the long-term effect of exercise intervention on gait performance remains unclear. Since the effect on exercise intervention for patients with moderate to severe dementia is uncertain (Lamb et al., 2018), we have decided to target older adults with subjective cognitive decline (SCD) as subjects who are at a high risk of cognitive decline.

2.2. Study population

A mail-based, 25-item self-reported questionnaire (the Kihon Checklist) was conducted for 22,790 community-dwelling older adults (age range 65–86 years) to screening SCD. Subjects who were determined to having SCD were invited to participate in the study through a postal invitation and examined further eligibility (Araki & Satake, 2018; Maki et al., 2012). We used all three items consist of the cognitive domain of the Kihon Checklist. The questionnaires were following: “Q18: Do your family or friends point out your memory loss?” (e.g., “You ask the same question repeatedly?”); “Q19: Do you make a call by looking up phone numbers?”; and “Q20: Do you find yourself not knowing today’s date?” Residents who responded either “yes” to Q18 or Q20, or “no” to Q19, were considered to be having SCD. The exclusion criteria of the TOPICS trial were: (1) fulfilling the clinical criteria for dementia (including anti-dementia drugs use); (2) having any disability that affected the basic and instrumental activities of daily living; (3) indicated to require support or care from the Japanese public long-term care insurance system; (4) MMSE score ≤ 19; (5) having severe visual impairment; (6) diagnosed with a neurodegenerative disease (e.g., Parkinson’s disease); (7) with any medical contraindications to exercise; (8) psychiatric disease (i.e., major depressive disorder); (9) a history of serious cardiovascular, musculoskeletal, respiratory, or cerebrovascular disease with paralysis or other severe health issues; or (10) having gait disorder or need of walking aid. Participants who had a cerebrovascular disease without paralysis were excluded from the current analysis to avoid the possible confounding effects of exercise intervention on the gait performance.

2.3. Interventions

The duration, frequency and intensity of the exercise interventions were determined by the meta-analyses about exercise and cognitive function (Gates et al., 2013); participants conducted exercise 2 days a week for 26 weeks, with 52 sessions in total. Each session consisted of a 50-minute exercise program and a 5-minute medical checkup before and after the exercise. The exercise program includes a 10-minute warm-up followed by 30 min of core training, and a 10-minute cool-down at the end. Trainers took adequate intervals in each session and paid attention to the fatigue of the participants. The intensity of the program was increased gradually in conformance with the American College of Sports Medicine guidelines (Thomas et al., 2016). The detail of each exercise was presented in the supplementary file (Supplementary Table S3). Participants in the control group received information about healthy aging, healthy diet, disease prevention, and health management during the 26-week intervention period. The control subjects did not receive specific instructions about exercise, physical activity, or cognitive health.

2.3.1. Aerobic training

Subjects assigned to the AT group undertook a step-on-the-spot exercise in a chair or standing position for 10–15 min followed by a 15-min walking exercise after a 5-min rest interval. The exercise intensity was...
set according to the percent heart rate reserve (%HRR) estimated by the Karvonen method (Strath et al., 2000). The target heart rate zone was 40% HRR in weeks 1 to 2, 50% HRR in weeks 3 to 8, 60% HRR in weeks 9 to 12, and 70% HRR in the remainder of the session. Besides the supervised program in the class, the participants were recommended to practice home-based training, such as walking outdoors, by themselves.

2.3.2. Resistance training

The participants assigned to the RT group undertook resistance band exercise, including bicep curls, chest presses, side raises, seated rowing, leg presses, hip abduction, and side bends, for 10–15 min followed by a 15-minute bodyweight exercise that comprised shrugs, knee-ups, trunk curls, squats, kneeling kickbacks, toe raises, and calf raises after a 5-minute rest interval. All movements were performed with 10 repetitions for a set, and 2 sets per session. The exercise intensity was set according to the ratings of perceived exertion by using the Borg Scale. The target Borg Scale ratings were set as 10–12, 12–14, and 14–16 in weeks 1–2, 3–12, and the remainder of the session, respectively. Home-based training was recommended to all participants in the RT group.

2.3.3. Combined training

The CT group conducted RT followed by AT in the same modality and intensity, but for only half of the duration of the other two interventions. The two types of exercise included in AT (stepping exercise and walking) were each performed in turns during one week. Walking outdoors and RT were recommended as home-based training.

2.4. Measures

Trained physicians, nurses, physical therapists, and clinical psychologists were in charge of the study measurements using standardized protocols at three time points (baseline, Week 26, and Week 52). The procedure of measurements in demographic, health, physical, mental, and social assessments are detailed in supplemental file.

2.4.1. Gait performance

Six spatiotemporal gait parameters (i.e., gait speed, stride time, cadence, double support, and step width) and 4 gait variability parameters (i.e., stride-time variability, stride-length variability, double-support variability, and step-width variability) (Montero-Odasso et al., 2011) were assessed using an electronic walkway system, the MV-1000 (Anima Co. Ltd., Japan), which comprised a sheet-type pressure sensor (240 × 60 cm) with a sampling rate of 100 Hz. Spatiotemporal gait parameters were calculated using an average of 4 to 5 steps included in one trial, and gait variability parameters were defined as a coefficient of the variation (standard deviation divided by mean value) of each step. To exclude the effects of the acceleration and deceleration phase, participants started walking 1.5 m prior to reaching the electronic walkway and stopped 1.5 m beyond it. After the familiarization session, participants performed the usual gait with self-selected speed 5 times (Kressig et al., 2006), and the mean value of 5 trials was used for statistical analysis.

2.5. Statistical analysis

The results of continuous variables with normal distribution are presented as the mean and standard deviation, and variables with non-normal distribution are reported as median and interquartile range. Categorical variables are presented as number and percentage. We compared the baseline characteristics among the groups by one-way analysis of variance or Kruskal–Wallis test for continuous variables and chi-square or Fisher exact test for dichotomous variables, as appropriate. All analyses were conducted on an intention-to-treat basis. The analysis of prospective changes in the gait performance was conducted by applying generalized estimating equations (GEE) with repeated measures. The dependent variables were the spatiotemporal gait parameters and gait variability parameters, and the independent variables were the intervention group, time, and the interaction of group and time. The GEE analysis yields coefficient values that represent the associations between a factor score and the variables included in the model. The main coefficients of interest in each model presented an interaction term for the time point and the intervention group. A significant p-value for the interaction coefficient indicates a difference in the change in a factor score depending on each intervention group. No prespecified adjustment was implemented in the entire analysis.

Statistical analyses were performed by using R version 3.2.1 (R Foundation for Statistical Computing, Vienna, Austria). A two-tailed p < .05 indicated statistical significance for all analyses.

3. Results

3.1. Study population

Of the total of 415 eligible study participants, 388 (AT: n = 95; RT: n = 93; CT: n = 98, and control: n = 102) participants were used in this analysis according to the exclusion criteria. Among these 388 participants, 36 dropped out before the completion of Week 26 and 25 dropped out during the follow-up period (before the completion of Week 52) (withdrawal rate: 9.3% and 15.7%, respectively; Fig. 1). The average adherence of participation in exercise sessions was 82.5%, 85.9%, and 83.5% in the AT, RT, and CT groups, respectively. The participants in this study had a mean (SD) age of 72.3 (4.6) years, and 51.8% were men. There were no significant intergroup differences for all of the study variables at the baseline (Table 1 and Supplementary Table S1). At both week 26 and week 52, there was no statistically significant difference in the background of dropouts and continuing participants other than age in the analysis for each group.

3.2. Effects of exercise intervention on the gait performance

In the analyses of changes in the longitudinal spatiotemporal gait parameters between the baseline and Week 26, compared with the control group, all three exercises significantly improved all parameters (gait speed, stride time, cadence, stride length, and double-support time) except the step width. The longitudinal analysis between the values at
Table 1
Baseline characteristics of the four intervention groups.

| Overall (n = 388) | AT (n = 95) | RT (n = 93) | CT (n = 98) | Control (n = 102) | p-Value |
|-------------------|------------|------------|------------|------------------|---------|
| Age (years)       | 72.3 ± 4.6 | 72.2 ± 4.6 | 72.3 ± 4.8 | 72.6 ± 4.5       | 0.900   |
| Male (n, %)       | 201 (51.8) | 47 (49.5)  | 57 (50.5)  | 50 (49.0)        | 0.538   |
| BMI (kg/m²)       | 22.8 ± 2.8 | 22.6 ± 2.9 | 22.8 ± 2.8 | 23.4 ± 2.8       | 0.094   |
| Systolic blood pressure (mmHg) | 154.5 ± 19.7 | 155.1 ± 19.9 | 155.2 ± 19.1 | 156.2 ± 19.0 | 0.361 |
| Diastolic blood pressure (mmHg) | 78.9 ± 11.7 | 78.2 ± 11.8 | 78.0 ± 11.3 | 79.0 ± 11.3 | 0.286 |
| Heart rate (bpm)  | 77.7 ± 12.1 | 78.0 ± 12.2 | 77.6 ± 11.6 | 77.4 ± 12.7 | 0.985 |
| Medication (n, %) | 82 (21.2)  | 16 (17.0)  | 22 (17.3)  | 17 (16.8)        | 0.202   |
| Previous fall (n, %) | 284 (73.2) | 73 (64)    | 64 (73)    | 74 (72.5)        | 0.834   |
| 1 time             | 65 (16.8)  | 15 (18.8)  | 17 (18.3)  | 16 (17.3)        |         |
| ≥2 times           | 39 (12.9)  | 7 (8.2)    | 12 (8.8)   | 12 (11.8)        |         |
| MMSE (points)      | 26.4 ± 2.6 | 26.5 ± 2.5 | 26.1 ± 2.4 | 26.4 ± 2.3       | 0.793   |
| GDS (points)       | 3.9 ± 2.9  | 3.4 ± 2.6  | 4.1 ± 2.5  | 4.2 ± 3.0        | 0.229   |
| Comorbidity (n, %) | 56 (12.6)  | 12 (16.1)  | 18 (18.4)  | 11 (10.8)        | 0.631   |
| Diabetes mellitus  | 44 (11.3)  | 8 (11.8)   | 13 (13.3)  | 12 (11.8)        |         |
| Heart failure      | 32 (13.4)  | 13 (13.7)  | 9 (17.2)   | 14 (13.7)        | 0.535   |
| Hyperlipidemia     | 114 (35.3) | 33 (37.4)  | 30 (32.3)  | 28 (26.6)        | 0.911   |
| Hypertension       | 163 (42.0) | 40 (42.1)  | 39 (41.9)  | 45 (39.8)        | 0.382   |
| Osteoarthritis     | 39 (10.1)  | 7 (12.9)   | 12 (12.2)  | 8 (8.7)          | 0.640   |
| Osteoporosis       | 39 (10.1)  | 10 (10.5)  | 12 (10.8)  | 7 (6.9)          | 0.178   |
| Education (years)  | 11.5 ± 2.4 | 11.4 ± 2.5 | 11.6 ± 2.5 | 11.5 ± 2.2       | 0.908   |

Note: Values are expressed as means ± SD, n (%), or median [interquartile range]. Abbreviations: AT = aerobic training; BMI = body mass index; CT = combined training; DBP = diastolic blood pressure; GDS = Geriatric Depression Scale; MMSE = mini-mental state examination; RT = resistance training; SBP = systolic blood pressure; SMI = skeletal muscle index; TUG = Timed Up-and-Go test. p-Values from one-way analysis of variance for continuous variables and the chi-square test for categorical variables are presented.

The baseline and at Week 52 revealed a significant improvement in gait speed, stride length, and double-support time only in the RT group (Table 2 and Fig. 2).

In the analyses of the changes in the gait variability parameters for the three exercise programs between the baseline and Week 26, we observed an improvement of the step-width variability only with CT. There were no significant improvements in the gait variability parameters between the baseline and Week 52 in any exercise program (Table 3).

Differences in the changes in various exercise parameters between the intervention groups from the pre- and post-intervention assessments were examined; however, there was no apparent difference in any of the parameters between the different exercise groups (Supplementary Table S2). Short- and long-term changes in physical and cognitive functions other than gait performance have already been reported in elsewhere (Makino et al., 2021).

4. Discussion

The primary objective of this study was to compare the effect of AT, RT, and CT on the gait performance in older adults with SCD. The secondary objective was to investigate the long-term effects of the above-mentioned exercise interventions. We hypothesized CT is most effective in improving both short- and long-term gait performance.

Table 2
The estimated changes in spatiotemporal gait parameters that were calculated by generalized estimating equations.

| From baseline to Week 26 | From baseline to Week 52 |
|--------------------------|--------------------------|
| Gait speed (cm/s)         | Gait speed (cm/s)          |
| AT                        | Control                   |
| 11.1 (5.9 to 16.3)        | 0.001                     | 11.1 (10.1) |
| RT                        | 6.5 (1.6 to 11.4)         | 0.009       | 5.4 (0.0 to 10.7) |
| CT                        | 10.2 (5.5 to 14.9)        | <0.001      | 5.5 (<0.1 to 11.1) |
| Control                   |                           |             |                           |
| Stride time (ms)          | Stride time (ms)          |
| AT                        | 13.1 (12.4 to 21.7)       | 0.030       | 11.5 (10.7 to 24.3)      |
| RT                        | 21.7 (21.4 to 42.1)       |             | 7.8 (4.7 to 10.9)       |
| CT                        | 33.7 (22.9 to 52.9)       | 0.001       | 21.2 (< 44.3)           |
| Control                   |                           |             |                           |
| Cadence (step/ min)       | Cadence (step/ min)       |
| AT                        | 0.047                     | 1.8 (1.0 to 4.6) |
| RT                        | 0.020                     | 1.4 (1.0 to 3.7) |
| CT                        | 0.001                     | 2.1 (<0.4 to 4.6) |
| Control                   |                           |             |                           |
| Stride length (cm)        | Stride length (cm)        |
| AT                        | 1.9 (1.2 to 3.8)          | 0.003       | 1.9 (< 2.4 to 6.2) |
| RT                        | 3.3 (0.2 to 6.4)          | 0.039       | 4.1 (0.5 to 7.8) |
| CT                        | 4.7 (1.7 to 7.7)          | 0.002       | 2.3 (< 1.8 to 6.2) |
| Control                   |                           |             |                           |
| Double support time (ms)  | Double support time (ms)  |
| AT                        | 0.047                     | 3.8 (< 9.1) |
| RT                        | 0.012                     | 5.9 (< 11.4) |
| CT                        | 0.001                     | 3.9 (< 9.5) |
| Control                   |                           |             |                           |
| Step width (cm)           | Step width (cm)           |
| AT                        | 0.070                     | 0.3 (0.2 to 0.9) |
| RT                        | 0.823                     | 0.1 (< 1.1) |
| CT                        | 0.755                     | 0.2 (< 0.8 to 1.1) |
| Control                   |                           |             |                           |

Note: Reference group of intervention: control; Reference group of time: baseline. The model was adjusted for age, sex, and body mass index. Abbreviations: AT = aerobic training; CT = combined training; CI = confidence interval; RT = resistance training.
This study demonstrated that the AT, RT, and CT had a short-term effect on the spatiotemporal gait parameters, except for step width, in older adults with SCD. As consistency with a systematic review by Zhang et al. (Zhang et al., 2019), the short-term effectiveness of exercise training on the gait performance are shown. The first novelty of this research is target of intervention; the effectiveness of exercise training was found in older adults with SCD. The second novelty of this research is an insight on the long-term effect of exercise on gait performance; only RT intervention maintained a beneficial effect on spatiotemporal gait parameters until Week 52.

The beneficial effect of AT on gait parameters in this study is considered to have two separate aspects: training for cardiorespiratory fitness and functional mobility training related to walking (Bossers et al., 2014). The mechanism of the beneficial effect of training for cardiorespiratory fitness and functional mobility training on the improvements of gait performance are not elucidated sufficiently. However, some previous studies found evidence of functional and structural brain change which is generated by a repeated walking exercise in healthy individuals (Erickson et al., 2011; Mang et al., 2016; McDonnell et al., 2013). Further investigation using functional magnetic resonance imaging or functional near-infrared spectroscopy is needed to reveal the association among AT, brain structure/function, and gait performance in the future study. The relationships between gait parameters such as gait speed or stride length and the muscle strength are already known (Miyazaki et al., 2013), and previous studies have shown that RT improves the gait parameter (Schwenk et al., 2014; Uematsu et al., 2018), which is in agreement with the results of this study.

The exercise interventions in the current study had little effect on the step width and the gait variability parameters by AT intervention are expected. The mechanism of the beneficial effect of training for cardiorespiratory fitness and functional mobility training related to walking (Bossers et al., 2014) on gait abnormalities and specific cognitive functions found that executive function (e.g., cognitive flexibility and processing speed), focus, and switch attention, as well as the inhibition of distractions during walking, are responsible for controlling step width and gait variability parameters (Montero-Odasso et al., 2012; Zhang et al., 2019), which are considered to reflect gait disorders in older adults with cognitive decline, for which we found a mildly significant improvement in this study.

Because some studies have indicated that AT may have positive effects on cognitive functions, such as memory and executive function (Baker et al., 2010; Duzel et al., 2016), the improvements on the step width and gait variability parameters by AT intervention are expected. However, the result did not support our hypothesis, which may have been due to the ceiling effect. Studies have previously shown that abnormalities in gait variability parameters become apparent as the cognitive function deteriorates (Muir et al., 2012). It is possible that there was no or only a minor abnormal gait variability in the SCD participants such that an improvement effect of the exercise intervention could be confirmed. In fact, in the previous studies of older adult patients with dementia, the stride-time variability was approximately 5.2% (MMSE score = 21.0) and 4.8–6.1% (MMSE score = 14.7–20.8) (Beauchet et al., 2013; Schwenk et al., 2014). In our study, the stride-
time variability was 2.8% on average, which is much smaller than the variability reported in above studies. Further evaluation, including the measurement of actual cognitive function, of subjects with more severe cognitive impairment is needed to clarify the effect of AT on the gait variability parameters.

The short-term effects on spatiotemporal gait parameters of AT and CT did not find in 52 weeks, whereas the short-term effects on gait speed and stride length of RT persisted at 52 weeks. A systematic review showed that exercise program, including RT, could improve the short- and long-term gait speeds, although the short-term improvement of exercise interventions without RT disappeared within 3 months after the intervention (Van Abbeema et al., 2015). This suggests that incorporating RT into training is essential for long-term beneficial effects on gait speed. In contrast with our hypothesis, CT did not show a long-term effect. It may be because the CT intervention performed only half the duration of RT, which was not sufficient to improve muscle strength. On the other hands, long-term effects on other spatiotemporal gait parameters such as stride length and cadences for patients with dementia are controversial. Kao et al. reported that 8 weeks of intervention, including balance and strength training improved the stride length which was maintained for 12 months (Kao et al., 2018). In contrast, Hauer et al. found that 12 weeks of exercise, with a combination of RT and functional training had long-term improvement only in cadence (Hauer et al., 2012). Because RT in this study had a long-term effect on the stride length but not on the cadence, the result partly supports the results of Kao et al. (Kao et al., 2018). Further research investigating the mechanisms contributing to the improvement of gait performance by RT or the effect of detraining would be expected in the future.

This study had some limitations. First, because the AT in this study focused on stepping and walking, we could not conclude whether the improvement in gait performance from AT is due to the result of an increase in cardiorespiratory fitness or the result of functional mobility training. Second, not all aspects of gait function have been evaluated in this study. Examining the effects of exercise on other gait analysis parameters, such as joint angle (Ritt et al., 2017), joint power, and trunk acceleration (Doi et al., 2012) will provide deeper insights into the mechanisms of gait improvement. Third, since this study is a secondary, exploratory analysis of the TOPICS trial, the correction for multiple comparisons did not perform. Future research with a stricter design is needed. Fourth, since we have not obtained the information about the quantity and quality of the home-based training or daily physical activity during the intervention period (baseline to Week 26) and the post-intervention period (Week 26 to Week 52), the result of the short- and long-term effect may be biased. Fifth, although the intensity of RT was maintained for 12 months (Kao et al., 2018). In contrast, Hauer et al., Kao et al. (Kao et al., 2018). Further research investigating the mechanisms contributing to the improvement of gait performance by RT or the effect of detraining would be expected in the future.

In conclusion, this study demonstrated that: (1) three different exercise interventions showed effectiveness in all spatiotemporal parameters of older adults with SCD, except for step width. However, only limited effects were found on gait variability parameters. (2) Only RT intervention was able to maintain a sustained beneficial effect on spatiotemporal gait parameters until Week 52. AT, RT and CT may all have the effect of improving the spatiotemporal gait parameters of older adults with SCD. However, RT would be recommended if sustained effects are expected.

CRediT authorship contribution statement

Conceptualization, K.F., H.U., T.M., K.U. and M.K.; Methodology, K., F., T.M., K.U., C.H.H., H.S. and M.K.; Software, K.F. and C.H.H.; Validation, H.U., T.M., K.U., T.H. and T.K.; Formal analysis, K.F. and C.H.H.; Investigation, H.U., K.U. and T.K.; Resources, A.I., C.U., H.S. and M.K.; Data Curation, T.M., T.H, A.I. and C.U.; Writing - Original Draft, K.F., H.U., C.H.H. and M.K.; Writing - Review & Editing, K.F. and M.K.; Visualization, K.F. and C.H.H.; Supervision, H.U., T.M., A.I., C.U. and H.S.; Project administration, T.M., K.U., H.S. and M.K.; Funding acquisition, H.S. and M.K.

Declaration of competing interest

None.

Acknowledgments

The authors would like to acknowledge all the participants in the TOPICS trial.

Funding

This work was supported by the Center of Innovation (COI) program of Japan Science and Technology (JST) Agency for funding [grant number JPMJCE1317].

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.exger.2021.111590.

References

2020 Alzheimer’s disease facts and figures, 2020. Alzheimers Dement. 16, 391–460. Allali, G., Verghese, J., 2017. Management of gait changes and fall risk in MCI and dementia. Curr. Treat. Options Neurol. 19, 29. Arai, H., Satake, S., 2015. English translation of the Kihon checklist. Geriatr. Gerontol. Int. 15, 518–519. Bahureksa, L., Najafi, B., Saleh, A., et al., 2017. The impact of mild cognitive impairment on gait and balance: a systematic review and meta-analysis of studies using instrumented assessment. Gerontology 63, 67–83. Baker, L.D., Frank, L.L., Foster-Schubert, K., et al., 2010. Effects of aerobic exercise on mild cognitive impairment: a controlled trial. Arch. Neurol. 67, 71–79. Beauchet, O., Allali, G., Launay, C., Fantino, B., Annweiler, C., 2011. Does memantine improve the gait of individuals with Alzheimer’s disease? J. Am. Geriatr. Soc. 59, 2181–2182. Beauchet, O., Launay, C.P., Allali, G., et al., 2013. Anti-dementia drugs and changes in gait: a pre-post quasi-experimental pilot study. BMC Neurol. 13, 184. Beauchet, O., Launay, C.P., Allali, G., Hermann, F.R., Annweiler, C., 2014. Gait changes with anti-dementia drugs: a prospective, open-label study combining single and dual task assessments in patients with Alzheimer’s disease. Drugs Aging 31, 363–372. Becher, O., Launay, C.P., Montero-Odasso, M., Annweiler, C., Allali, G., 2015. Anti-dementia drugs-related changes in gait performance while single and dual tasking in patients with Alzheimer’s disease: a meta-analysis. Curr. Alzheimer Res. 12, 761–771. Bossers, W.J.R., Scherder, E.J.A., Boersma, F., Hortobagyi, T., van der Woude, L.H.V., van Heugten, M.J.G., 2014. Feasibility of a combined aerobic and strength training program and its effects on cognitive and physical function in institutionalized dementia patientsA pilot study, 9 (10), e97577. Doi, T., Makizako, H., Shimada, H., et al., 2012. Brain atrophy and trunk stability during dual-task walking among older adults. J. Gerontol. A Biol. Sci. Med. Sci. 67, 790–795. Duzel, E., van Praag, H., Sendmier, M., 2016. Can physical exercise in old age improve memory and hippocampal function? Brain 139, 662–673. Erickson, K.I., Voss, M.W., Prakash, R.S., et al., 2011. Exercise training increases size of hippocampus and improves memory. Proc. Natl. Acad. Sci. U. S. A. 108 (7), 2917–2922. Fried, L.P., Tangen, C.M., Walston, J., et al., 2001. Frailty in older adults: evidence for a phenotype. J. Gerontol. A Biol. Sci. Med. Sci. 56, M146–M156. Gates, N., Fitzarone Singh, M.A., Sachdev, P.S., Valenzuela, M., 2013. The effect of exercise training on cognitive function in older adults with mild cognitive impairment: a meta-analysis of randomized controlled trials. Am. J. Geriatr. Psychiatry 21, 1086–1097. Guirguis-Blake, J.M., Michael, Y.L., Perdue, L.A., Coppola, E.L., Beil, T.L., 2018. Interventions to prevent falls in older adults updated evidence report and systematic review for the US preventive services task force. JAMA 319, 1705–1716. Hardy, S.E., Perera, S., Roumani, Y.F., Chandler, J.M., Studenski, S.A., 2007. Improvement in usual gait speed predicts better survival in older adults. J. Am. Geriatr. Soc. 55 (11), 1727–1734.
