

Determinants of exercise adherence in sedentary middle-aged and older adults

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Abstract

Regular exercise is known to positively impact neurocognitive health, particularly in aging individuals. However, low adherence, particularly among older adults, hinders the adoption of exercise routines. While neuroplasticity mechanisms largely support the cognitive benefits of exercise, the link between physiological and behavioral factors influencing exercise adherence remains unclear. This study aimed to explore this association in sedentary middle-aged and older adults. Thirty-one participants underwent an evaluation of neuroplasticity using transcranial magnetic stimulation (TMS) to measure changes in motor-evoked potentials following intermittent theta-burst stimulation (iTBS). Health history, cardiorespiratory fitness, and exercise-related behavioral factors were also assessed. The participants engaged in a 2-month supervised aerobic exercise program, attending sessions three times a week for 60 minutes each, totaling 24 sessions at a moderate-to-vigorous intensity. They were divided into Completers (n=19), who attended all sessions, and Dropouts (n=12), who withdrew early. Completers exhibited lower smoking rates, exercise barriers, and resting heart rates compared to Dropouts. For Completers, regression models revealed that post-iTBS changes ($\beta = -7.78$, $p = .013$) and self-efficacy ($\beta = -.51$, $p = .019$) predicted exercise adherence (adjusted-R² = 0.44). Larger post-iTBS increases in motor-evoked potential amplitude indicated greater effectiveness of cortico-motor plasticity and were associated with better exercise adherence. In conclusion, this study highlights the significance of cortico-motor plasticity, self-efficacy, and cardiovascular health in exercise adherence. Given the well-established cognitive benefits of exercise, addressing sedentary behavior and enhancing self-efficacy are crucial for promoting adherence and optimizing brain health. Clinicians and researchers should prioritize assessing these variables to improve the effectiveness of exercise programs.

Title: Determinants of Exercise Adherence in Sedentary Middle-aged and Older Adults

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Abstract

Regular exercise is known to positively impact neurocognitive health, particularly in aging individuals. However, low adherence, particularly among older adults, hinders the adoption of exercise routines. While neuroplasticity mechanisms largely support the cognitive benefits of exercise, the link between physiological and behavioral factors influencing exercise adherence remains unclear. This study aimed to explore this association in sedentary middle-aged and older adults. Thirty-one participants underwent an evaluation of neuroplasticity using transcranial magnetic stimulation (TMS) to measure changes in motor-evoked potentials following intermittent theta-burst stimulation (iTBS). Health history, cardiorespiratory fitness, and exercise-related behavioral factors were also assessed. The participants engaged in a 2-month supervised aerobic exercise program, attending sessions three times a week for 60 minutes each, totaling 24 sessions at a moderate-to-vigorous intensity. They were divided into Completers (n=19), who attended all sessions, and Dropouts (n=12), who withdrew early. Completers exhibited lower smoking rates, exercise barriers, and resting heart rates compared to Dropouts. For Completers, regression models revealed that post-iTBS changes ($\beta = -7.78$, $p = .013$) and self-efficacy ($\beta = -.51$, $p = .019$) predicted exercise adherence (adjusted- $R^2 = 0.44$). Larger post-iTBS increases in motor-evoked potential amplitude indicated greater effectiveness of cortico-motor plasticity and were associated with better exercise adherence. In conclusion, this study highlights the significance of cortico-motor plasticity, self-efficacy, and cardiovascular health in exercise adherence. Given the well-established cognitive benefits of exercise, addressing sedentary behavior and enhancing self-efficacy are crucial for promoting adherence and optimizing brain health. Clinicians and researchers should prioritize assessing these variables to improve the effectiveness of exercise programs.

Keywords: Adherence, Aging Adults, Brain Health, Exercise, Neuroplasticity, Transcranial Magnetic Stimulation.

ARTWORK GRAPHICAL ABSTRACT

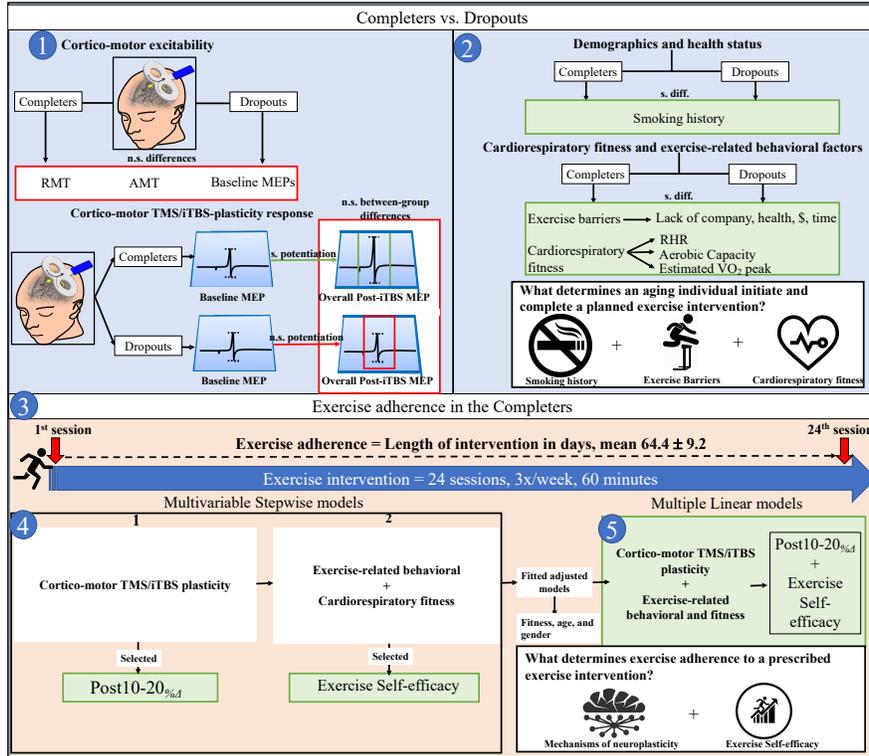


Figure 1: This is a caption

Note. Numbers 1 through 5 refer to each result labeled in the artwork’s abstract figure. Following, we present the result highlights. **1.** “Completers” and “Dropouts” differed in neither baseline cortico-motor excitability nor cortico-motor plasticity mechanisms (red color boxes). Despite no between-group differences, only “Completers” demonstrated a significant potentiation post-TMS/iTBS, but it did not hold after correction (green color arrow). Both groups demonstrated a larger effect size. **2.** We demonstrated that the Dropout participants’ exercise barriers (e.g., lack of time, health, budget, and time) were significantly greater compared to the Completers group (green filled box). We also revealed that Dropout participants had significantly lower cardiorespiratory fitness, as demonstrated by lower RHR, exercise capacity, and estimated VO₂ peak compared to “Completers.” (green filled box) **3.** In the Completers group, exercise adherence, defined as the average length of intervention in days to complete the 24 prescribed exercise sessions, was 64.4 (9.2) days. The average number of rescheduled sessions for this group was 4.3 (7.3). **4.** The interval Post10-20%_Δ was the only selected corticospinal neuroplasticity predictor of exercise adherence and explained 22% of the variance (green-filled box). By including only exercise-related behavioral and fitness variables, exercise self-efficacy was the only predictor of exercise adherence in middle-aged and older adults and explained 21% of the variance. **5.** Adjusted models were fitted and revealed that both mechanisms of neuroplasticity and exercise self-efficacy were the best predictors of exercise adherence and explained 44% of the variance (green-filled box). This result indicates that for every one-unit increase in TMS-iTBS cortico-motor plasticity mechanisms, the estimated mean length of intervention in days (exercise adherence) decreases by approximately eight days when controlling for self-efficacy. Models adjusting for age, gender, and cardiorespiratory fitness were fitted but did not improve the model.

1. Introduction

Compelling evidence indicates that regular physical activity later in life increases longevity and may prevent or delay the onset of age-related cognitive decline and functional impairment.^{1–3} Despite this potential, approximately one-quarter of men and one-third of women worldwide are physically inactive.⁴ Insufficiently active and sedentary behavior substantially increases healthcare costs and is a leading risk factor for cardiovascular events and all-cause mortality. Specifically, inactive individuals have a 20-to-30% increased risk of premature death compared to sufficiently active people.^{4–6} These findings show that sedentary individuals are not capitalizing on the potential health benefits of physical activity and highlight the urgent need to comprehend the motivating factors that can effectively engage middle-aged and older adults to adhere to an exercise program.

Despite extensive evidence highlighting the adverse impacts of sedentary behavior on health, social well-being, economic factors, and the numerous advantages of regular exercise, a substantial practical challenge remains – motivating sedentary individuals to adopt an exercise regimen. Furthermore, most sedentary older adults struggle to maintain exercise routines, and practical strategies to counter exercise attrition in this demographic are currently lacking. While most clinicians recommend that their patients increase physical activity levels and that older adults themselves recognize its health benefits, the overwhelming majority fail to participate in regular physical activity. The average adherence rates to exercise programs in clinical and research settings are also limited, and some studies report up to approximately 50% attrition.⁷ The causes of poor exercise adherence are likely multifactorial and have been suggested to include individual, social, environmental, and behavioral factors.⁸ For instance, physical fitness, cardiovascular health, self-perceived well-being, self-efficacy, and prior exercise history are commonly cited factors linked to increased exercise adherence in older adults.^{7,9–12}

While these factors offer valuable insights into the challenges of exercise adherence, an emerging frontier requires further exploration - the role of brain neurophysiology in exercise adherence. In particular, we need to investigate the efficacy of neuroplastic mechanisms, which may underlie behavioral changes and enhance decision-making, potentially aiding the initiation and maintenance of exercise programs. While evidence in this domain is still evolving, it holds promise as a significant contributor to our understanding of exercise adherence. For instance, positive changes in synaptic neuroplasticity, demonstrated by long-lasting changes in evoked postsynaptic potential or long-term potentiation (LTP) synaptic efficacy, are commonly reported as the underlying mechanisms of exercise benefits in cognitive health – e.g., learning and memory - in animal and human studies.^{13,14} Despite the abundance of data linking physical exercise and neuroplasticity, it is still not clear if, in humans, assessments of the mechanisms of neuroplasticity can predict effective and long-lasting adherence to an exercise program in middle-aged and older adults. Literature shows that sedentary behavior lacks inhibitory control and tends to reduce the attraction to a task requiring high effort and energy expenditure (e.g., physical exercise), aligning with the theory of effort minimization.^{15,16} Comprehending the mechanisms that form the basis of the connection between movement, neuroplasticity, and effort can provide a fundamental framework for developing effective strategies to support behavior change in middle-aged and older adults who are physically inactive.

Rationale Summary for the Present Study and Research Hypotheses

Compelling evidence in behavior change has widely discussed intervening exercise adherence factors and how clinicians and researchers should address these factors in older adults. However, there is still an increasing need to explore what incentivizes older adults to fully adhere to an exercise program to avoid the consequences of physical inactivity and partake in the benefits of an active lifestyle. Moreover, there is insufficient evidence of an association between physiological and behavioral mechanisms influencing adherence to an exercise program in older adults. Therefore, in this study, we compared individuals' baseline demographic characteristics, health status, mechanisms of neuroplasticity, cardiorespiratory fitness, and exercise-related behavioral measures between those who completed an 8-week aerobic exercise intervention “Completers” and those who withdrew early “Dropouts.” First, we hypothesized that the Dropouts would differ significantly in baseline health status, mechanisms of neuroplasticity, cardiorespiratory fitness (CRF), and exercise-related

behavioral parameters compared to those Completers. Thus, we predicted that when compared to the Completers, middle-aged and older adults in the Dropout group would present with 1) a greater number of cardiovascular health risk factors, 2) reduced mechanisms of neuroplasticity (as assessed by transcranial magnetic stimulation [TMS] cortico-motor response to the intermittent Theta-burst stimulation protocol), 3) lower CRF, and 4) worse performance in the behavioral parameters as demonstrated by lower self-efficacy and exercise lifetime history and a greater number of exercise barriers. Second, within the Completers, we hypothesized that baseline mechanisms of neuroplasticity would be associated with adherence to a 2-month exercise program. Consistent with the World Health Organization, we defined exercise adherence as the extent to which participants engaged in the prescribed dosing regimen.¹⁷ We predicted that greater cortico-motor plasticity would be associated with greater adherence to the prescribed exercise regimen and thus may influence long-lasting exercise engagement. Third, in the Completers, we explored predictor variables that best explain response variability in exercise adherence to a 2-month aerobic exercise intervention by combining mechanisms of neuroplasticity, CRF, and exercise-related behavioral parameters.

Method

1. *Study Design*

This study represents a secondary analysis of an interventional study in neurologically healthy but physically sedentary adults. Specifically, this study tested differences among those who completed or dropped out from the intervention and explored a hypothesis-generating analysis to search for predictor variables that best explain response variability in exercise adherence to a 2-month aerobic exercise intervention. We included pre-intervention data from 41 individuals who were recruited for an in-person option of an exercise intervention study. Nineteen participants completed the intervention, and twenty-two were lost to follow-up. Of the twenty-two participants lost to follow-up, seventeen withdrew from the study, and five were discontinued due to imposed pandemic restrictions and social distance practices. Of the seventeen that withdrew, five participants dropped out before performing any of the included assessments in this study, and thus, we did not have them in the analysis. The local institutional review board approved the study protocol and registered it in the Clinical Trials database (<https://clinicaltrials.gov>, #NCT03804528). We collected data from February 2019 to March 2020. Figure 1 shows the study design summary.

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Figure 1. Study design summary.

Participants

We recruited participants by 1) flyers throughout the University of Miami Miller School of Medicine and Coral Gables Campuses and the Miami-Dade community (e.g., public libraries), 2) online research database tools, and 3) via the University Research Informatics Data Environment Consent to Contact Initiative.

The inclusion criteria were: 1) age [?] 55 years, 2) no clinically detectable cognitive impairment (MoCA score [?] 24), 3) sedentary (defined as a ‘low’ category using the International Physical Activity Questionnaire [IPAQ] short form),¹⁸ and 4) English as a primary language. Major exclusion criteria were: 1) any unstable medical condition, 2) medical contraindication to physical exercise, and 3) contraindications to undergo TMS assessment recommended by the International Federation of Clinical Neurophysiology.^{19,20} All participants provided written informed consent, and the University of Miami institutional review board (#20180926) approved all procedures.

Data Collection

The screening process was conducted through phone interviews followed by an in-person meeting to obtain written informed consent and collect physical measures (e.g., vital signs), demographics (e.g., age, sex, education status, body mass index), and medical and family history (e.g., comorbidities). Data collection for this study included 1) mechanisms of neuroplasticity, 2) cardiorespiratory fitness, and 3) exercise-related behavioral parameters.

Outcomes Measures

1. TMS Mechanisms of Neuroplasticity

All study parameters followed the current guidelines for the safe application of TMS recommended by the International Federation of Clinical Neurophysiology,^{19,20} and all involved technicians and scientists met the recommended training criteria.²¹ The modulation of TMS-elicited motor evoked potentials (MEPs) by intermittent theta-burst stimulation (iTBS) is thought to reflect the mechanisms of an NMDA receptor-dependent form of LTP-like synaptic plasticity.^{22,23} The TMS/iTBS approach has been widely used to assess the role of LTP-like neuroplastic mechanisms in healthy individuals and those with metabolic or neuropsychiatric disorders.^{24–26}

In our study, single-pulse TMS and iTBS were delivered using a biphasic static-cooled handheld MagPro MCF-B65 figure-of-eight coil connected to a MagPro X100 stimulator (MagVenture A/S, Farum, Denmark). Cortico-motor excitability and plasticity were assessed from the hand representation of the primary motor cortex in the hemisphere representing the dominant hand, and peak-to-peak MEPs were recorded using surface electromyography (EMG) electrodes applied to the contralateral first dorsal interosseous (FDI) muscle. The infrared-based frameless stereotaxic system Localite TMS Navigator (Localite GmbH, Bonn, Germany) was used to target TMS and maintain coil position within sessions.

The TMS/iTBS assessment followed the procedures: 1) Motor cortex “hotspot” searching, 2) Resting motor threshold (RMT), 3) Cortico-motor excitability single-pulse TMS baseline response, 4) Active Motor Threshold (AMT), 5) Theta burst stimulation, and 6) Cortico-motor excitability post-iTBS spTMS stimulation response. Following IFCN guidelines,²⁷ we defined RMT as the minimum stimulus intensity that produced a small motor-evoked potential (MEP; about 50 μ V in 50% of 10 trials) during the relaxation of the FDI muscle, while AMT was defined as the minimum stimulus intensity that produces a small MEP (about 200 μ V in 50% of 10 trials) during isometric contraction of the FDI, at minimal voluntary contraction. Cortico-motor excitability was measured as the average MEP amplitude from 90 spTMS trials delivered in 3 blocks of 30 pulses (randomly jittered at 5-7 seconds) at 120% of biphasic RMT before iTBS (baseline) and regular intervals (5, 10, 20, and 30 min) post iTBS protocol. RMT, AMT, and cortico-motor excitability were measured using a 1) TMS coil handle oriented 45° relative to the participant’s mid-sagittal axis and delivering a biphasic pulse (anterior-posterior–posterior-anterior current in the brain). The iTBS protocol consisted of bursts of 3 pulses at 50 Hz repeated at intervals of 200 ms in a two-second-on, 8-second-off pattern for a total of 600 pulses delivered at 80% of AMT.²³ To reduce the influence of extreme values, we log₁₀-transformed individual MEPs, averaged across each time point, and back-transformed them into geometric means. All subsequent analyses were performed using geometric means values.

Cardiorespiratory fitness

A trained physical therapist conducted the Incremental Shuttle Walk Test (ISWT) to measure functional exercise capacity and estimate cardiorespiratory fitness.^{28,29} The ISWT is a valid, reliable, and safe cardiorespiratory fitness measure and correlates well with gold-standard measures of maximum oxygen consumption in cognitively healthy adults.^{30–32} Before the test commenced, participants were fitted with a heart rate monitor (Polar H10, Polar Electro Inc) for continuous monitoring throughout the test. We also documented blood pressure (OMRON BP7350, Omron Healthcare Inc), oxygen saturation (Diagnostix 2100 fingertip pulse oximeter, American Diagnostic Corp), and rate of perceived exertion at rest (measured with the Borg scale)³³, during, upon completion, and 5 minutes after test cessation.

Participants were asked to walk 10 m around a marking between two traffic cones, maintaining the speed indicated by the beeps on the audio recording. The walking speed increased by 0.17 meters per second (m/s), with an initial speed of 0.5 m/s. The test was terminated when: 1) the participant was not able to maintain the required speed (defined as >0.5 m from the cone when the beep sounds on a second successive 10 meters length), 2) at the request of the participant, or for any incompatible physical and neurological signs or symptoms (e.g., extreme discomfort, pain, dyspnea, dizziness, vertigo, and angina), or 3) if the researcher determined that the participant was not fit to continue (e.g., participant reaches the age-predicted maximum heart rate (220 - age). Maximum walking distance was recorded and used to estimate the VO₂ peak.³⁰ We also recorded each individual's maximal heart rate and heart rate recovery (HRR). HRR was operationally defined as the change in the heart rate from the peak of exercise to the heart rate after 1-min and 2-min cessation.³⁴

Exercise-related behavioral factors

Exercise Lifetime history. We assessed exercise lifetime history using a modified Lifetime Physical Activity Questionnaire (LPAQ), which evaluates hours spent in various physical activities across the lifespan.³⁵ We focused on moderate and vigorous activities to standardize the activities and meet the references of the minimum moderate to vigorous intensity for active individuals.⁵ LPAQ-based estimates of hours spent in each physical activity were averaged in the number of hours/week and converted into units of energy expended by multiplying the time spent in each activity by the metabolic equivalent task (MET-hours/week/year) over the lifetime. The conversion to MET values was notably extracted from the Compendium of Physical Activity.³⁶

Exercise self-efficacy. We assessed exercise self-efficacy using the Exercise Self-efficacy Questionnaire (ESEQ). The ESEQ assessed how confident participants would perform physical exercise under different conditions or constraints.³⁷ The ESEQ included nine items and generated a maximum total score of 36 (a high score means better results – meaning better exercise self-efficacy).³⁷

Exercise barriers. We assessed exercise barriers by selecting items reported in previous research that involved environmental and social influences in physical exercise practice.³⁸ The Exercise Barriers Questionnaire assessed participants' agreement with a list of statements of about 15 commonly cited barriers to the practice of physical activity and exercise. The questionnaire generated a maximum total score of 45 (a high score implies poorer results – meaning a greater number of reported exercise barriers).³⁸

Exercise Adherence (dependent variable)

Within the Completers, exercise adherence was measured to the extent to which the individual's behavior was consistent with the exercise dosage regimen prescribed in the protocol.¹⁷ Thus, based on the length of the intervention, we defined exercise adherence as *the total time in days to complete the 24 prescribed exercise sessions*. Exercise sessions were previously scheduled per protocol (3 sessions per week), and the time to complete the intervention varied on the participant's compliance, availability, and accountability. We offered participants the opportunity to make up missed sessions, and the intervention was only fulfilled when the participant completed all 24 sessions.

Intervention

The physical exercise intervention was administered at the University of Miami Miller School of Medicine Wellness Center and supervised by a study team member during all times and sessions. Each participant engaged in 60-minute (5-minute warm-up, 50 minutes of continuous exercise in the target zone, and 5 minutes of cool-down) sessions delivered three times/week for eight consecutive weeks (a total of 24 sessions). Aerobic exercise modalities were offered for participants' selection at each section and included treadmill, elliptical, stationary bike, or stationary recumbent bike. Participants were fitted with a heart rate monitor to facilitate data collection of the cardiac signals. They were instructed to maintain a moderate steady-state intensity at 55-64% of maximal heart rate (determined via the exercise test) for the first 4-weeks and a vigorous intensity of 65-90% of maximal heart rate for the second half of the exercise program. At each session, we monitored

heart rate and participant’s exertion (measured with the Borg scale) before, every 5 min of the 50-minute session, and 5 min upon completion of the exercise session. Blood pressure was assessed before and after each exercise session.

Statistical and Power Analysis

We performed all statistical analyses using JMP Pro (v15.0, The SAS Institute Inc., Cary, North Carolina, USA) and set a two-tailed 95% confidence interval ($\alpha = .05$). Data on sociodemographic characteristics and health status, TMS-iTBS neuroplasticity, and cardiorespiratory fitness were represented as means \pm *SD* and percentage (%) of the total. Data were tested for normality of distribution using the Shapiro-Wilk test, homogeneity of variances using Levene’s test, homoscedasticity by plotting residuals and predictors values, and variance inflation factor to avoid multicollinearity (mean VIF $<$ 10). We calculated effect sizes, and were reported in partial eta-squared (η^2) and interpreted as follows: small effect (.01-.05), medium effect (.06-.13), and large effect ($>$.14).³⁹ The Holm-Bonferroni method was applied to correct p-values and reduce the familywise error rate for multiple comparisons.

Sensitivity power analysis was conducted on G*Power 3.1 software.⁴⁰ Our sample of 31 participants (19 Completers and 12 Dropouts) provided a two-tailed 80% power to detect a large eta-squared between-group effect size ($\eta^2 = .22$). Within the Completers group; the sample provided 80% power to detect a correlation of $|r| = .56$ and an adjusted r -squared of 0.61 when accounting for mechanisms of neuroplasticity and self-efficacy predictors.

To test our primary hypothesis, which states significant differences in baseline health status, neuroplastic mechanisms, CRF, and exercise-related behavioral factors between Dropouts and Completers, and to analyze the determinants influencing the initiation of an exercise program, we initiated by comparing individual characteristics. This included sociodemographic, health status, cardiorespiratory fitness, and behavioral variables at baseline among participants. We employed either pooled or unpooled T-test and Chi-square test, depending on the variable category or distribution. We performed t -tests to compare differences by *Group* (Completers vs. Dropouts) in *cortico-motor excitability response* by assessing RMT, AMT, and baseline MEPs. We evaluated post-iTBS modulation of MEPs within-group by entering the MEP geometric mean as a dependent variable in random-effects linear models assessed within-group factor *Time* (Baseline, Post0-10, Post10-20, Post20-30) differences. Following a well-established approach,^{41,42} to compare iTBS-induced changes in *cortico-motor plasticity*, post-iTBS MEP geometric means were expressed as the percent change (%) from baseline and were entered into mixed-effects linear models between-*Group* factor, the within-subject factor *Time*, and the higher order interaction of *Group*Time*. Interval time response aimed to decrease variability and, thus, improve the reproducibility of the measure. This method has been reported,⁴³ and the time window within the post-iTBS time, specifically measuring the iTBS response at 10–20 minutes post-iTBS, corresponds to the peak effect of iTBS in healthy adults.⁴¹

To test our secondary hypothesis, which states that baseline neuroplastic mechanisms would be associated with exercise adherence, we fitted Pearson correlation (r) and scatterplots to represent the association visually.

To test our exploratory analysis, we fitted regression models to assess the predictors of exercise adherence in the participants who completed the exercise intervention. In these models, exercise adherence was defined as the number of days taken to complete the 24 exercise sessions prescribed, accounting for any rescheduled sessions. The independent variables were 1) *cortico-motor plasticity measures* (Post0-10%[,], Post10-20%[,], and Post20-30%[,]), 2) *exercise-related behavioral measures* (exercise lifetime history, exercise self-efficacy, and exercise barriers), and 3) *cardiorespiratory fitness* (estimated VO_2 peak). First, we performed two multivariable stepwise regression models to analyze 1) the effects of *cortico-motor plasticity measures* and 2) the effects of *exercise-related behavioral and cardiorespiratory measures on exercise adherence* using data from all participants in the Completers group (p -value threshold, put-in criteria, [?] 0.10; put-out criteria, [?] 0.10). Second, we fitted a multiple linear regression combining the variables selected in the previous stepwise regressions. Third, we adjusted the models to control for age and gender. In light of the exploratory nature

of these analyses, it is important to note that individual p-values were not adjusted for multiple comparisons and, thus, should be interpreted accordingly.

Results

Table 1 presents detailed baseline demographic and clinical characteristics of the 31 participants who started the intervention and were included in the analysis. From those, nineteen participants (61%) completed the intervention, and twelve (39%) dropped out. The smoking history was the only significant variable that differed between participants' Completers (11% smokers) and Dropouts (45% smokers, *uncorrected* $p = .03$).

Table 1. Baseline demographic characteristics and health status.

Demographics and health status <i>mean ± SD</i>	Demographics and health status <i>mean ± SD</i>	Demographics and health status <i>mean ± SD</i>	Completers (n = 19)	Dropouts (n = 12)	<i>p</i>
Demographics	Demographics				
Age, years	Age, years		61.8 ± 7.1	62.1 ± 5.3	0.91
Gender, female <i>n (%)</i>	Gender, female <i>n (%)</i>		12 (63)	4 (33)	0.10
Ethnicity, n (%)	Ethnicity, n (%)				0.12
Asian	Asian		1 (5)	1 (8)	
Black	Black		2 (11)	6 (50)	
Hispanic	Hispanic		10 (53)	2 (17)	
Hispanic/White	Hispanic/White		2 (11)	1 (8)	
White	White		4 (21)	2 (17)	
Education level, n (%)	Education level, n (%)				0.81
High School/Technical/Associate Complete	High School/Technical/Associate Complete		5 (27)	5 (42)	
College	College		9 (47)	4 (33)	
Postgraduate	Postgraduate		5 (26)	3 (25)	
Health status	Health status				
BMI, n (%)	BMI, n (%)				0.18
Normal (18,5 – 24,9)	Normal (18,5 – 24,9)		3 (16)	4 (33)	
Overweight (25 – 29,9)	Overweight (25 – 29,9)		7 (37)	3 (25)	
Obese ([?] 30)	Obese ([?] 30)		9 (48)	5 (42)	
<i>Mean ± SD, kg/m²</i>	<i>Mean ± SD, kg/m²</i>		29.5 ± 4.9	30.3 ± 7.5	0.74
Physical Activity Level	Physical Activity Level				
IPAQ total, METs, <i>mean ± SD</i>	IPAQ total, METs, <i>mean ± SD</i>		372 ± 374	330 ± 377	0.79
IPAQ weekday sitting, hours, <i>mean ± SD</i>	IPAQ weekday sitting, hours, <i>mean ± SD</i>		6.3 ± 2.8	7.3 ± 4.2	0.50

Demographics and health status <i>mean ± SD</i>	Demographics and health status <i>mean ± SD</i>	Demographics and health status <i>mean ± SD</i>	Completers (n = 19)	Dropouts (n = 12)	<i>p</i>
	Global Cognition Status	Global Cognition Status			
	MoCA <i>total, mean±SD</i>	MoCA <i>total, mean±SD</i>	25.8 ± 1.9	25.3 ± 1.6	0.56
	Diseases and Comorbidities, <i>mean±SD</i>	Diseases and Comorbidities, <i>mean±SD</i>	3.7 ± 2.8	3.6 ± 2.8	0.96
	History of smoking, yes, <i>mean±SD</i>	History of smoking, yes, <i>mean±SD</i>	2 (11)	5 (45)	0.03 ^a

Abbreviations. BMI = Body Mass Index; IPAQ = International Physical Activity Questionnaire; MET = Metabolic Equivalent; MoCA = Montreal Cognitive Assessment. a = This finding did not hold statistical significance following Holm-Bonferroni correction.

“Completers” vs. “Dropouts”

Figure and Table 2 detail results for comparing the baseline between the Completers and Dropouts groups. T-tests found no significant differences between groups for RMT ($t_{29} = 1.9$, *uncorrected* $p = .07$, $\eta^2 = .11$), AMT ($t_{29} = 1.25$, *uncorrected* $p = .22$, $\eta^2 = .05$), or baseline MEPs ($t_{28} = -1.15$, *uncorrected* $p = .26$, $\eta^2 = .05$). These results indicate that the Completers and Dropouts groups did not differ in baseline cortico-motor excitability response to TMS. A random-effects analysis indicated a significant effect of *Time* for post-iTBS MEPs in the Completers group ($F_{3,51} = 2.83$, *uncorrected* $p = .04$, $\eta^2 = .14$), see Figure 2) but not in the Dropouts, despite the larger effect size ($F_{3,21} = 1.36$, *uncorrected* $p = .28$, $\eta^2 = .16$). These results suggest a time-related effect on cortico-motor excitability within the Completers, but not within the Dropouts. Despite revealing a large effect size, this finding did not hold statistical significance following the Holm-Bonferroni correction (corrected p-values > .05). Noteworthy, the even larger effect size observed in the Dropouts highlights may simply reflect a lack of statistical power, rather than a difference in the mechanisms. To analyze a between-group comparison of post-iTBS MEPs%[?] responses, a mixed-effect linear model showed no effect of *Group* ($F_{1,23} = 2.1$, *uncorrected* $p = 0.16$, $\eta^2 = .08$) and neither with *Time* ($F_{3,67} = 1.2$, *uncorrected* $p = 0.30$, $\eta^2 = .05$) nor the *Group*Time* interaction ($F_{3,67} = 2.6$, *uncorrected* $p = 0.06$, $\eta^2 = .10$). These findings highlights non-difference in cortico-motor plasticity between Completers and Dropouts.

Figure 2. Group post-iTBS MEPs (mV) response comparison of “Completers” in blue and “Dropouts” in red.

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image3.emf available at <https://authorea.com/users/666870/articles/667490-determinants-of-exercise-adherence-in-sedentary-middle-aged-and-older-adults>

Note. Mean (Standard Error). TMS-iTBS-induced modulation of Post0-30 MEPs was significantly modulated in the “Completers” individuals but not in the “Dropouts” individuals. MEPs = motor evoked potentials; %Δ = percent change; * = this finding did not hold statistical significance following Holm-Bonferroni correction.

Cardiorespiratory Fitness and Exercise Behavior

Table 2 details the results for comparing the baseline between the Completers and Dropouts groups. T-tests found that the Dropout participants' exercise barriers were significantly greater than the Completers group ($t_{22} = 2.08$, *uncorrected* $p = .048$, $\eta^2 = .18$). Overall, the most common exercise barriers reported by the participants, respectively, were: 1) Lack of company and would be more active with a partner or in a group (53% agreed or partially agreed), 2) Getting tired easily (44%), 3) Cannot afford a membership (40%), and 4) Do not have any time for exercise (33%). We also discovered that Dropout participants had significantly lower cardiorespiratory fitness than Completers which was demonstrated by the significant differences in resting heart rate ($t_{28} = 2.24$, *uncorrected* $p = .032$, $\eta^2 = .15$), exercise capacity ($t_{24} = -2.13$, *uncorrected* $p = .043$, $\eta^2 = .15$), and estimated VO_{2peak} ($t_{23} = -2.12$, *uncorrected* $p = .045$, $\eta^2 = .16$). Despite these findings revealing a larger effect size, this finding did not hold statistical significance following Holm-Bonferroni correction. Exercise lifetime history and self-efficacy did not show a statistical difference between groups ($p > .05$; see Table 2 for detailed statistics).

Table 2. Data on length of intervention and baseline predictors outcome measures.

Variable, <i>mean</i> \pm <i>SD</i>	Completers (n = 19)	Dropouts (n = 12)	95%CI mean diff.	<i>t</i> (<i>df</i>)	<i>p</i>	$ \eta^2 $
Exercise adherence						
Length of intervention, <i>days</i>	64.4 \pm 9.2	-	-	-	-	-
Cortico-motor excitability						
RMT, %	56.0 \pm 12.7	64.9 \pm 12.7	-0.67, 18.51	1.90 (29)	.07	.11
AMT, %	46.0 \pm 11.9	51.2 \pm 9.8	-3.25, 13.58	1.25 (29)	.22	.05
Baseline MEPs, mV, <i>mean (SE)</i>	0.86 \pm .53	0.64 \pm .34	-0.56, 0.16	-1.15 (28)	.26	.05
Exercise-related behavioral parameters						
Exercise Lifetime History, <i>total METs/week/year</i>	188.3 \pm 195.2	165.8 \pm 155.0	-193.6, 148.5	-0.27 (23)	.79	.01
Exercise Self-Efficacy, <i>total score</i>	11.6 \pm 8.4	12.7 \pm 8.4	-5.2, 7.5	0.37 (28)	.71	.01
Exercise Barriers, <i>total score</i>	3.6 \pm 2.1	7.0 \pm 6.1	0.02, 6.8	2.08 (22)	.048 ^a	.18
Cardiorespiratory fitness (ISWT)						
Resting HR, <i>beats/min</i>	69.1 \pm 9.9	78.2 \pm 12.2	0.8, 17.4	2.24 (28)	.032 ^a	.15

Variable, <i>mean</i> <i>± SD</i>	Completers (n = 19)	Dropouts (n = 12)	95%CI mean diff.	<i>t</i> (<i>df</i>)	<i>p</i>	$ \eta^2 $
HR reserve, <i>beats/min</i>	62.6 ± 17.1	57.2 ± 16.8	-19.5, 8.7	-0.79 (24)	.43	.03
HRR1, <i>beats/min</i>	27.8 ± 11.4	24.1 ± 8.7	-12.8, 5.4	-0.84 (23)	.41	.03
HRR2, <i>beats/min</i>	38.1 ± 12.6	35.5 ± 6.9	-12.5, 7.2	-0.55 (23)	.58	.02
Exercise capacity, <i>ISWT</i> <i>distance, m</i>	538.7 ± 120.3	441.8 ± 105.2	-190.5, -3.2	-2.13 (24)	.043 ^a	.15
Estimated VO ₂ peak, <i>ml/kg/min</i>	23.2 ± 5.1	19.0 ± 3.8	-8.2, -1.0	-2.12 (23)	.045 ^a	.16

Notes. MET = Metabolic Equivalent; ISWT = Incremental Shuttle Walking Test; HRR = Heart Rate Recovery; HR = Heart Rate. a = This finding did not hold statistical significance following Holm-Bonferroni correction. Corrected p-values > .05.

Determinants of Exercise Adherence in the “Completers” and Exercise Modality

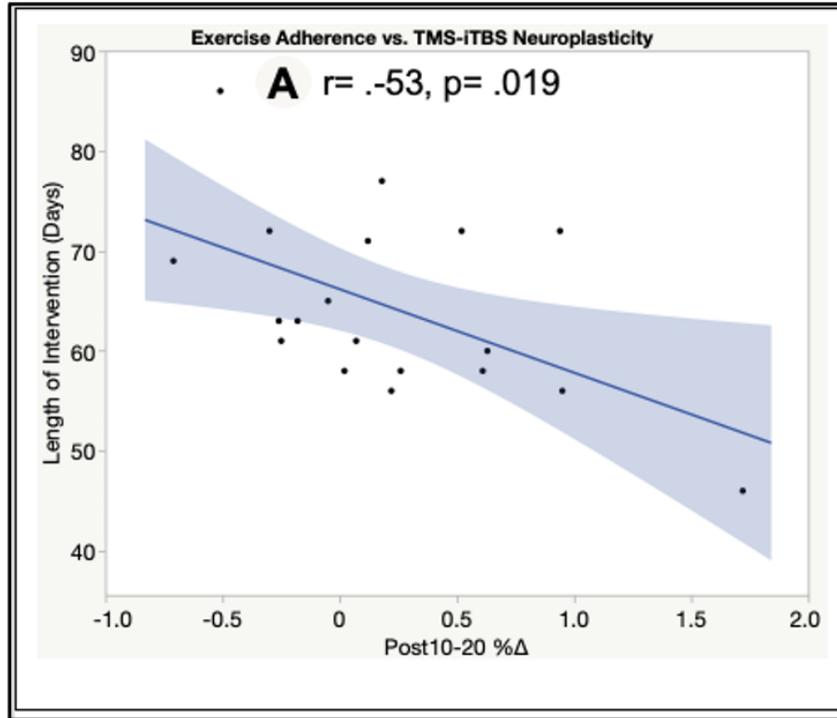
Preference

The average length of intervention in days to complete the prescribed 24 exercise sessions was 64.4 (9.2) days. The average number of rescheduled sessions for this group was 4.3 (7.3). The preferred exercise modality throughout the sessions was the stationary bike (47.4%), followed by the treadmill (43.4%) and the elliptical (8.6%).

Neuroplasticity and Exercise Adherence Correlation Analysis

For Completers, the Pearson coefficient revealed a large negative significant correlation between TMS-iTBS cortico-motor plasticity (Post10-20%[?]) and days to complete the intervention ($r = -.53$, corrected $p = 0.019$, Figure 3), indicating that individuals who had greater mechanisms of neuroplasticity also demonstrated greater adherence to the intervention.

Figure 3. Correlation between neuroplasticity and exercise adherence.



Note. Post10-20%[?] represents the percentage change (%[?]) in peak-to-peak MEP amplitude from baseline to 10-20 minutes post-iTBS. We presented the values in decimal form, where -1.0 represents a decrement in neuroplasticity of 100% and +1.0 represents an increase of 100%.

TMS-iTBS Neuroplastic Determinants of Exercise Adherence

A multivariable stepwise linear regression was fitted and selected the time interval of Post10-20%[?] (Post-iTBS MEPs percent change from baseline to 10-20 minutes) as a predictor of exercise adherence ($F_{1,18} = 6.7, uncorrected p = 0.019, adj. R^2 = .22$, Table 3). This finding aligns with prior research indicating Post10-20 as the peak effects of iTBS. It also revealed a significant association between TMS-iTBS corticomotor plasticity (Post10-20%[?]) and exercise adherence ($\beta = -8.3, uncorrected p = .024$). This suggests that for every unit increase in Post10-20%[?], the length of intervention decreases by approximately eight days, demonstrating greater exercise adherence.

Table 3. Fitted models of the association between neuroplasticity and exercise adherence.

Model 1 ^a	β $\delta\epsilon\phi\eta\zeta\iota\epsilon\nu\tau\varsigma$ (95% "I)	SE	Adj R-squared	p-value
Constant	66.2	1.95	.22	<.0001 ^b
Post10-20%[?]	-8.3 (-15.5, -1.3)	3.39		.024 ^b

Abbreviations. Post10-20%[?]= percent change in the neuroplasticity index measure from baseline to interval 10-20 minutes; SE= Standard Error; CI Confidence Interval.

Note. a = Prediction equation for model 1: Exercise adherence (days)= 66.2 +(-8.3 * Post10-20%[?])

b = significant uncorrected p-value

3.6. Exercise Behavior Determinants of Exercise Adherence

A second stepwise regression model with only behavioral and fitness variables was fitted. Exercise self-efficacy was selected as the only behavioral and fitness predictor of exercise adherence ($F_{1,18} = 5.76$, *uncorrected* $p = .028$, *adj. R*² = .21, Table 4). This result revealed a significant association between exercise self-efficacy and adherence ($\beta = -0.55$, *uncorrected* $p = .028$), indicating that individuals with higher self-efficacy tend to complete the intervention in a shorter duration, demonstrating greater exercise adherence.

Table 4. Fitted models of the association between behavioral variables and exercise adherence.

Model 2 ^a	Model 2 ^a	β $\delta\epsilon\varphi\iota\varsigma\epsilon\nu\tau\varsigma$ (95% CI)	SE	Adj R-squared	Adj R-squared	p-value
	Constant	70.8	3.2	.21	<.0001 ^b	<.0001 ^b
	Self-efficacy	-0.55 (-1.03, -.06)	.23		.028 ^b	.028 ^b

Abbreviations. SE = Standard Error; CI = Confidence Interval.

Note. a = Prediction equation for model 3: Exercise adherence (days)= 70.8 +(-0.55 * Self-efficacy)

b = significant uncorrected p-value

3.6. Neuroplasticity and Self-efficacy Predict Exercise Adherence

A multiple linear regression revealed both mechanisms of neuroplasticity ($\beta = -7.78$, $p = 0.013$) and exercise self-efficacy ($\beta = -0.51$, $p = 0.019$) as predictors of exercise adherence and explained 44% of the variance ($F_{2,18} = 7.9$, *uncorrected* $p = .0041$, *adj. R*² = 0.44, Table 5). This result indicates that for every one-unit increase in Post10-20%[?], the estimated mean length of intervention in days (exercise adherence) decreases by 7.78 when controlling for self-efficacy. Models adjusting for age, gender, and cardiorespiratory fitness were fitted but did not improve the adjusted model 1 (Table 5).

Table 5. Adjusted fitted models of the association among neuroplasticity, self-efficacy, and exercise adherence.

Adjusted Model	Adjusted Model	β $\delta\epsilon\varphi\iota\varsigma\epsilon\nu\tau\varsigma$ (95% CI)
Adjusted Model 1^a	Adjusted Model 1^a	Adjusted Model 1^a
Constant	Constant	71.9
Post10-20%[?]	Post10-20%[?]	-7.78 (-13.7, -1.9)
Self-efficacy	Self-efficacy	-0.51 (-.92, -.09)
Adjusted Model 2 ($F_{5,18} = 2.96$, $p = .053$)	Adjusted Model 2 ($F_{5,18} = 2.96$, $p = .053$)	Adjusted Model 2 ($F_{5,18} = 2.96$, $p = .053$)
Constant	Constant	71.53
Self-efficacy	Self-efficacy	-0.46 (-0.9, 0.02)
Post10-20%[?]	Post10-20%[?]	-8.30 (-14.9, -1.7)
Estimated VO2 peak	Estimated VO2 peak	0.25 (-0.5, 1.1)
Age	Age	-0.10 (-0.7, 0.5)
Gender (Male)	Gender (Male)	-0.72 (-4.8, 3.4)

Abbreviations. Post10-20%[?]= percent change in the neuroplasticity index measure from baseline to interval 10-20 minutes; Estimated VO2 peak estimated oxygen consumption at exercise peak; SE= Standard Error; CI= Confidence Interval.

Note. a = Prediction equation for adjusted model 1: Exercise adherence (days)= 71.9 +(-7.78 * T10-20%[?]) + (-0.51 * Self-efficacy)

b = significant uncorrected p-value

4. Discussion

4.1. Summary and discussion of results

The findings of this study contribute additional evidence to support the interplay between neurophysiological, cardiac-physiological, and behavioral mechanisms that can influence adherence to an exercise program in middle-aged and older adults. Importantly, participants exhibited distinct behaviors, either initiating the intervention or consistently adhering to a prescribed exercise regimen. The results provided partial support for our primary hypothesis. Specifically, the combination of risk factors, such as smoking history, low cardiorespiratory fitness, and a higher number of exercise barriers, suggested a clinical significance role in determining participants' completion or non-completion of the exercise program. The findings also supported the secondary hypothesis demonstrated by the large correlation between baseline cortico-motor plasticity and exercise adherence.

Furthermore, the results supported our exploratory analysis, suggesting the role of cortico-motor plasticity mechanisms and exercise self-efficacy as predictors of exercise adherence. These factors accounted for approximately 50% of the variation in completing the prescribed exercise regimen. The modulation of MEPs in cortico-motor plasticity response to TMS following iTBS has been interpreted as indicative of neuroplastic mechanisms resembling LTP-like response rather than directly associated with executive control areas like the dorsolateral prefrontal cortex.⁴⁴

In addition, we have identified various environmental and social barriers that hinder exercise and warrant further investigation. These include the absence of a workout partner or group, experiencing quick exhaustion, financial constraints preventing membership affordability, and a lack of available time for physical activity. These results shed new light on the importance of comprehensive screening of physiological and behavioral factors. We suggest clinicians target these measures before prescribing exercise for better adherence to exercise programs in middle-aged and older adults.

4.2. The behavioral relevance of CRF, cardiovascular and brain risk factors, and exercise barriers on exercise completion

It is well-known that sedentary behavior is influenced by multifarious biopsychosocial factors that directly and indirectly affect brain health. Similarly, our study suggests that smoking history and poorer fitness, as demonstrated by higher resting heart rate and lower exercise capacity, may not only affect brain health and increase dementia risk⁴⁵ but also compound increased sedentary behavior by acting as determinants of exercise completion. These findings are not surprising when considering the inverse relationship between smoking rate and physical fitness. Studies in young and older adults have shown lower physical endurance and decreased exercise frequency in smokers than in non-smokers.^{46–48} Over time, physical inactivity and chronic smoking often lead to all-cause mortality and comorbidities such as type-2 diabetes, cardiovascular disease, stroke, and cancer or chronic lung disease.^{49,50} Despite regular physical activity reducing up to 30% of the risk of all-cause mortality in both smokers and non-smokers, the more significant benefits are generally observed when exercising at goal levels and quitting smoking.⁵¹ In addition to tobacco use and poorer fitness, the social and health aspects linked to the significant exercise barriers reported (e.g., lack of company and easy fatigue) may have worsened the completion of the exercise. Socialization and optimal overall self-health perception are essential for exercise adherence in older adults. Social engagement during training in a group may be beneficial to increase exercise adherence, improve cognitive functions (e.g., inhibitory control), and reduce the risk of dementia.^{52–54} Thus, screening for and guiding modifiable lifestyle behavior changes, such as smoking cessation, social engagement, and regular exercise, appear essential to facilitate behavior change in this population. In summary, many exercise barriers are linked to social determinants of health, and it is crucial to identify and increase awareness of those factors that may be easily targeted through low-cost and accessible exercise programs.

4.2. Understanding the Impact of brain plasticity on behavior change and exercise adherence

Counteracting the detrimental effects of sedentariness generally relies upon one's ability to initiate and

maintain an active lifestyle. Completing an exercise program is essential, but most importantly, it is appropriately engaging by achieving the prescribed exercise dose and parameters for full benefits.⁵⁵ Along those lines, brain activity assessment-modulation, exemplified in this study by TMS/iTBS cortico-motor plasticity assessment, holds the potential to offer crucial insights into comprehending the readiness for behavioral change and understanding factors related to gaining exercise habits. One key aspect of readiness to change is the ability of an individual brain network to transition effectively between a "resting state" and a "task state." This capacity has been linked to measures of general intelligence, indicating that individuals with higher-performing cognitive abilities exhibit a greater state of readiness for engaging in behaviors than those with lower-performing cognitive skills.⁵⁶ Consistent with this concept, our study revealed a large correlation between baseline cortico-motor plasticity and exercise adherence. This finding suggests that individuals with greater efficacy of plasticity mechanisms may be more prone to initiating behavior changes, potentially explaining their ability to sustain adequate participation in the exercise program. We also demonstrated that exercise adherence (length of days to complete the intervention) is independently associated with mechanisms of neuroplasticity and self-efficacy. By combining both factors, we improved our model and revealed that greater efficacy of mechanisms of neuroplasticity and greater self-efficacy predict about half of exercise adherence in middle-aged and older adults. The length of days to complete the intervention is directly related to the participant's accountability, which was affected by the number of missed and rescheduled sessions. Therefore, it is important to acknowledge that sedentariness by itself, in combination with a lack of self-efficacy, as demonstrated in this study, can potentially alter the neuroplasticity process, posing challenges to the beneficial effects of exercise on cognitive health. Consequently, it becomes increasingly reasonable to postulate that exercise programs may encounter limitations or exhibit reduced effectiveness in sedentary aging adults due to predisposed challenges when attempting to initiate or fully engage in the prescribed exercise regimen. These challenges may include a lack of intrinsic motivation, difficulty overcoming sedentary habits ingrained over time, insufficient confidence in their physical abilities, concerns about potential discomfort or injury, unfamiliarity with exercise techniques or equipment, apprehensions related to social settings or public scrutiny, perceived time constraints, or financial limitations inhibiting access to appropriate exercise facilities or professional guidance. It is essential to proactively acknowledge and address these individual challenges to optimize the success and impact of exercise interventions among sedentary aging adults, ensuring they can reap the full cognitive and physical benefits of regular exercise.

Previously published work has offered a toolkit and summarized key points for assessing exercise adherence-related factors through brief or comprehensive assessments.⁵⁷ In essence, older adults express a need for tailored interventions that address the challenges associated with aging while incorporating planned exercise as a priority to enhance motivation, autonomy, and overall health outcomes. To develop a personalized exercise program, it is essential to consider not only measures of brain health, cardiovascular risk factors, self-efficacy, and environmental and social barriers to exercise but also other social determinants of health, physical and cognitive status, mood state (including depressive symptoms and perceived stress), stage and readiness to change, motivation and decision-making processes, self-regulation, exercise preference and tolerance, exercise perception, and knowledge, as well as health literacy. By encompassing these diverse factors in the screening and assessment process, clinicians can better understand the individual's context, desires, and values, enabling the creation of tailored exercise programs that align with their specific needs. We acknowledge that an exercise prescription should be just one component of a multimodal approach emphasizing a collaborative clinician-patient partnership. This approach empowers patients to participate in goal setting actively, enables the building of achievable objectives, and ensures care that respects the patient's unique circumstances. Moving forward, future studies should focus on examining the combination of these relevant factors mentioned above, specifically targeting long-term exercise adherence.

4.3. Targeting self-efficacy and behavioral change on exercise adherence

Our findings also suggested that self-efficacy played a critical role in exercise adherence. Self-efficacy represents a behavioral factor that is intrinsically linked to the capacity of an individual to achieve expected outcomes and inhibit undesired tasks. Older adults who demonstrate greater self-efficacy and self-control and exhibit self-regulatory strategies (e.g., goal setting) may overcome automatic low-effort tasks (e.g., seden-

tary behaviors) and favor behavior change.¹⁰ An additional element addressed in behavioral interventions is that individuals may differ in actions and time toward behavior changes. For instance, the transtheoretical model states that individuals do not change behaviors quickly and decisively, and sedentary individuals may take at least six months to incorporate the new behavior.^{58,59} It is also essential to distinguish behavioral (exercise) frequency and habit. Findings suggested that a repeated behavior, such as practicing exercise, often develops a degree of automaticity or habit that is goal-oriented and relevant not only to initiate an exercise but also to adhere to it.⁶⁰ Incorporating behavioral elements before (e.g., self-efficacy, self-goal, and motives oriented) and during an exercise intervention may help individuals create a habit, thus maintaining a behavior for long periods and reducing the likelihood of relapses.⁶⁰ In this context, self-efficacy may predict short- and long-term exercise adherence and predict maintenance 3-6 months after the protocol was terminated.³⁷ Self-efficacy also changes in response to a physical activity intervention. Multiple studies have shown self-efficacy to be a key determinant in exercise adherence in other clinical populations, including congestive heart failure,⁶¹ chronic strokes,⁶² obese-sedentary adults with knee osteoarthritis⁶³ which led to more favorable health outcomes. Therefore, we can significantly improve health outcomes by implementing strategies to improve exercise self-efficacy in rehabilitation programs across populations with various comorbidities.

4.4. Study limitations and directions for future research

Despite the promising results, it is important to acknowledge and address this study's limitations. First, an informal qualitative insight suggested that the extensive battery of assessments and exercise design (e.g., progressive exercise parameters instead of fixed high-level parameters) may have contributed to the early withdrawal of many participants. As stated in the methods, this is a secondary analysis of an interventional study that includes a comprehensive assessment battery that was not fully included in this study.⁶⁴ For future studies, we suggest adding additional characteristics to the exercise program to increase exercise adherence, including gradually increasing exercise duration, goal setting, exploring individual needs, and many others.⁶⁵ Future studies should address these elements by comparing isolated exercise interventions and an individualized multicomponent exercise intervention exploring behavioral, educational, social, personal, and physiological aspects. It is relevant to emphasize the importance of implementing supervised remote-based programs, as they can yield additional benefits in exercise engagement.⁶⁶ This approach offers several advantages, including increased accessibility, convenience, and flexibility for participants, which can enhance exercise adherence and motivation. Moreover, the use of technology, such as video conferencing or mobile applications, enables real-time feedback, personalized instruction, and progress tracking, further optimizing the effectiveness and safety of the exercise program.⁶⁷ Second, we assessed cortical excitability and plasticity from the motor cortex using EMG as the output measure. While this approach provided valuable insights into the neurophysiological effects of exercise adherence on motor-related processes, it is important to acknowledge that assessing similar measures from higher-order cognitive areas (i.e., the DLPFC) by coupling TMS and electroencephalography would also be relevant to understanding the neurophysiological mechanisms underlying exercise adherence. Additionally, a clinical implication of the current findings is called 'pragmatic neuroscience,' which implies that the use of neuromodulatory and neuro screening techniques, particularly TMS (isolated or in combination with other neuroimaging), to identify neuro markers, predict individuals' behavior, and optimize interventions by manipulating exercise program characteristics would favor the individuals' characteristics and behaviors.⁶⁸

Third, we acknowledged that our study was constrained by a relatively small sample size, which limited statistical power. The high dropout rates, exceeding 50%, also potentially introduced bias into our results. This includes participants who withdrew during the assessment phase and individuals whose participation was interrupted due to the restrictive measures imposed by the COVID-19 pandemic. Regarding the exploratory regression analysis, we acknowledge that some results may be susceptible to type II errors. In future studies with larger sample sizes, we recommend implementing p-value corrections. This will help validate our generated research hypothesis, specifically examining whether cortico-motor plasticity assessed through the TMS-iTBS approach is associated with exercise adherence in middle-aged individuals while accounting for exercise self-efficacy. Researchers should also explore additional confounding variables, such as intrinsic and

extrinsic motivation, preference and tolerance profiles, and an individual's affective response to exercise.⁶⁹ Fourth, future studies should address a follow-up assessment that would include insights into long-term adherence to the behavior, health outcomes, number of relapses, and challenges.

4.5. Conclusion

These findings offer meaningful physiological and behavioral insights and clinical applications to increase adherence to an exercise intervention. We have provided further data to support the association and behavioral relevance of cardiovascular and brain health risk factors – such as smoking and sedentariness – and the impact of cortico-motor plasticity and self-efficacy mechanisms on exercise adherence. Moreover, as existing literature highlights the critical role of neuroplasticity in facilitating post-exercise cognitive gains and promoting brain health, we have emphasized how sedentariness and low self-efficacy can potentially disrupt these mechanisms and hinder adherence to exercise programs. Therefore, considering that exercise is currently one of the most effective interventions available for mitigating cognitive decline and enhancing brain health, it is suggestive for therapists, clinicians, and scientists to prioritize the assessment of these variables. By that means, we can identify individuals who may face challenges in adhering to exercise programs and interventions, allowing for targeted strategies to improve adherence and optimize the benefits for brain health. Further understanding additional variables influencing exercise adherence will enable therapists to refine, optimize, and individualize exercise interventions for brain health.

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Data availability: The data supporting the findings described in this article will be available from the authors upon reasonable request.

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