Liu et al. BMC Public Health (2024) 24:3326
https://doi.org/10.1186/s12889-024-20741-0

BMC Public Health

RESEARCH

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Substitution of physical activity for sedentary behaviour contributes to executive function improvement among young adults: a longitudinal study

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Abstract

Background Sedentary lifestyles may affect cognitive capacities which are essential for daily tasks. There is a lack of research on the effects of replacing sedentary behaviour with physical activity on executive function, as well as the dose–response relationship between physical activity and executive function among young adults, underscoring the critical need for prompt investigation.

Methods Employing a longitudinal experimental design, the study conducted two assessments (baseline and at three months) on a cohort of participants. A total of 78 young adults with a mean age of 25 years old were recruited for the study. Physical activity and sedentary behaviour were measured using accelerometer, which provided objective data on the intensity and duration of the participants' daily activity. Executive function was measured using the Trail Making Test (TMT). An isotemporal substitution model was employed to analyze the effects of replacing sedentary time with physical activity of different intensities. Additionally, mixed-effect models were used to explore the dose–response relationships between physical activity, sedentary behaviour, and executive function.

Results The reallocation of 30 min of daily time from sedentary behaviour (SED) to light physical activity (LPA) significantly reduced Trail Making Test (TMT) completion times, suggesting improvements in cognitive processing speed. Conversely, shifting the same duration from SED to moderate-to-vigorous physical activity (MVPA) enhanced the accuracy rate on the TMT. Sedentary time was associated with longer TMT completion times but did not significantly affect the accuracy rate. Additionally, a dose–response relationship was observed, with increases in MVPA, caloric expenditure, and step count correlating with shorter TMT completion times. In contrast, increases in LPA and caloric expenditure were associated with higher TMT correct response rates.

Conclusion The substitution of sedentary behaviour with physical activity may be a beneficial strategy to enhance executive function among young adults. These results underscore the importance of reducing sedentary time

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and promoting physical activity in the daily routine of young individuals to support cognitive development. Future research should explore the underlying mechanisms.

Keywords Physical activity, Sedentary behaviour, Executive function, Isotemporal substitution model, Young adults

Introduction

Executive function is a fundamental cognitive process that enables humans to store and manipulate the input information, process various information flexibly, and control the interference of irrelevant information to the cognitive processing, leading to purposeful and orderly behaviour [1]. Young people with cognitive disorders often experience symptoms such as difficulty concentrating, impaired problem-solving abilities, and emotional dysregulation [2, 3]. The causes are complex, involving a combination of genetic predispositions, environmental influences, and psychological stress [4]. Cognitive deficits are frequently linked with mood and anxiety disorders, and neurobiological studies have demonstrated changes in brain regions responsible for emotional and cognitive regulation [5]. Despite the fact that young people are less likely to experience the cognitive disorders that are more prevalent in the elderly, executive function remains critically important during this stage of life. This is because executive function supports essential developmental milestones and facilitates effective decision-making abilities that are crucial for personal and academic success [6]. Recent studies have highlighted the importance of regular physical activity in enhancing cognitive processes, including executive function [7]. Yet, the evidence is mixed, with some research suggesting a clear positive association [8], while others find the relationship inconclusive [9, 10]. These discrepancies may stem from variables, such as the intensity of physical activity, subdomains of cognitive function, and the age of the population [11, 12]. Notably, there is a gap in the literature regarding young adults, who are often at the peak of cognition, as most research has focused on children or the elderly [13–15]. While the link between executive function and daily behaviours like physical activity, sedentary behaviour (SED), and sleep is recognized, research has often considered their health impacts in isolation. The interplay between these behaviours, and their combined impact on young adults' cognitive capacities, particularly executive function, remains underexplored.

To address these gaps, the 24-Hour Activity Cycle Model (24-HAC) offers a framework for understanding how daily activities (SED, LPA, MVPA, and sleep) impact health outcomes [16]. Given the fixed 24-h day, allocating time to one activity reduces time for others, influencing health via interconnected physiological mechanisms [17]. This is significant for young adults due to their immediate and long-term health implications. The isotemporal substitution model (ISM), introduced by Mekary et al., examines the effects of replacing one activity with another while considering the remaining activities, with recent studies enhancing this approach by addressing the compositional nature of time-use data [18–20]. These findings enhance our understanding of movement-related behaviours and their interrelationships. Recently, there has been a notable rise in research employing the ISM to explore diverse health outcomes including metabolic health, mental well-being, and mortality [21–27]. However, their application in studying the relationship between physical activity, sedentary behaviour, and executive function in adults is limited. Additionally, numerous studies have employed self-reported questionnaires to measure activity behaviours, which can be imprecise and prone to overestimation, such as the duration of physical activity [28]. Accelerometry, however, offers an objective standard, facilitating precise measurement of the duration of physical activity and sedentary behaviour [29].

Thus, the emerging perspective on activity patterns suggests a complex interaction between physical activity, sedentary behaviour, and executive function, especially among young adults. Utilizing data derived from accelerometer to assure objective measurement of activity levels, our study employs the isotemporal substitution model to examine the potential cognitive benefits of replacing sedentary behaviour with light physical activity and moderate-to-vigorous physical activity on the completion time and accuracy rate of the executive function. Additionally, we also to use the mixed effect model to investigate the dose–response relationship between activity patterns (SB, LPA, MVPA, and steps) and the completion time and accuracy rate of the executive function among young adults, with the goal of developing targeted activity protocols that improve cognitive performance during this period of adulthood.

Methods

Study design and participants

This three-month longitudinal study investigates the association between activity patterns and executive function. Data on physical activity, sedentary behaviour and executive function performance were collected at baseline (Time point 1, T1) and after three months (Time point 2, T2) through repeated measurements. A total of

78 healthy young adults (36 males and 42 females, with an average age of 25 years) participated in this study. Participants were selected based on the following inclusion criteria: young adults without chronic physical conditions, mental health disorders, or a history of substance abuse, which confirmed by questionnaires(S1) [30]. These criteria were established to ensure that data collected on physical activity and executive function, were not confounded by pre-existing health conditions. All participants provided written informed consent following a comprehensive explanation of the study's procedures. This study received approval from the Ethics Committee of the School of Medicine at Tsinghua University (IRB 20190091).

Measurement of physical activity and sedentary behaviour

This research utilized triaxial accelerometers to objectively measure and record patterns of physical activity and sedentary behaviour. Participants wore an accelerometer (wGT3x-BT, ActiGraph, Pensacola, FL, USA) on their non-dominant wrist for 7-days, and were asked not to remove the device for the duration of the 7-days except during activities that might damage the device (e.g., swimming and bathing). The accelerometer data were sampled at 10 Hz (1-min epoch) and downloaded using ActiLife software, version 6.7 (ActiGraph). For inclusion in the analysis, the data must have been recorded for more than 10 h per day, and participants must have valid data for at least 2 weekdays and 1 weekend day. Freedson (1998) cut-point thresholds were utilized due to their widespread application in physical activity research [31–33]. Counts of 0–99 counts per minute (cpm), 100–1534 cpm, and ≥ 1535 cpm distinguished sedentary behaviour, light intensity of physical activity (LPA), and moderate-to-vigorous intensity of physical activity (MVPA), respectively [31].

Assessment of the executive function

Executive function was measured using a computer-based Trail Making Test (TMT). The TMT, a widely used neuropsychological assessment, was used to assess executive functioning, and speed of cognitive processing [34]. Executive function was evaluated using two performance indicators: completion time (seconds) and accuracy rate (%). TMT required participants to draw lines as quickly as possible to connect the numbers from 1 to 25 in an ascending pattern, with the numbers distributed in random order. Participants were examined immediately after wearing an accelerometer for 7 days. Both measurements (T1 and T2) were scheduled in the morning to prevent the test results from being influenced by the test time, and were conducted in a distraction-free environment.

Covariates

To mitigate the potential confounding effects, demographic variables and covariates were controlled in the analyses. These encompassed age, sex, body mass index (BMI), place of residence (urban/rural), household income level (indicative of participants' family economic status on a graded scale from 1, denoting the lowest, to 6, indicating the highest tier), and educational levels (quantified as the total years of tertiary education completed).

Statistical analysis

Statistical analysis was performed using R software, version 3.4.1 (R Programming). Baseline characteristics associated with sedentary behaviour and physical activity were summarized through descriptive statistics, which included reporting of the means and standard deviations (SD) for continuously variables, and proportions for categorical variables. In our study, we used the isotemporal substitution model and mixed-effect model to analyze the relationship between PA and cognition. Specifically, at time point 1, we utilized isotemporal substitution model to examine the effect of replacing SED with PA, including LPA and MVPA. For the mixed-effect model, we incorporated data from both time point 1 and time point 2 to account for time effects and individual variability, to examine the association between PA and cognition. This approach allowed us to more accurately assess trends over time and the relationships between different time points.

The isotemporal substitution model was applied to evaluate the impact of reallocating 30 min of SED to equivalent time in LPA and MVPA. This 30-min interval was chosen based on its prevalent application in isotemporal substitution research [35]. The average amount of time spent in each category was calculated, and then 30 min was reallocated from SED to either LPA or MVPA. Substitution model is expressed as follows: Executive function performance = ($\beta 1$) LPA + ($\beta 2$) MVPA + ($\beta 3$) Total time + ($\beta 4$) covariates. By eliminating "SED" component from the model, the coefficient ($\beta 3$) for total time represents the omitted component (SED). The remaining coefficients represent the execution functions performance of substituting 30 min of that PA (LPA or MVPA) for SED while holding other activity types constant. Model 1 is primary variable: LPA and MVPA, Model 2 adjusted for place of residence, family income level and education levels as covariates.

To estimate the trajectory of changes in executive function across different levels of sedentary behaviour and physical activity, a mixed-effect model was employed. This approach analyzed pooled data to characterize the dose–response relationships between sedentary time, physical activity, and executive function performance. In constructing the model for longitudinal analysis, the completion time and the accuracy rate were used as dependent variables to develop the regression curves.

Results

Demographic Information

Of the 78 participants, complete data were available for all at the initial test, while at the second test, data were available for 74 participants. Table 1 presents descriptive statistics of the included participants. Participants were on average 25 years old (55% female), a high number of educational years were observed, with the majority (77%) having been born in urban areas. Mean and standard deviation descriptive statistics of the time spent in SED, LPA, MVPA are presented in Table 1.

The effects of substituting PA (LPA and MVPA) for SED

The results of the isotemporal substitution are presented in Table 2. Reallocating 30 min from SED to LPA had positive associations with completion time (B = −0.34, p = 0.03). Furthermore, reallocating 30 min from SED to MVPA had positive associations with accuracy rate (B = 0.40, p = 0.01).

The dose–response relationship of SED and executive function

Average daily SED time was significantly correlated with completion time on TMT. For every 100-min/day increase in SED time, completion time of TMT increases by 1.57s (β = 1.57, $p < 0.01$) (Table 3). A dose–response relationship was present for increased completion time of TMT with increasing of SED time. Family economic income level (β = −2.16, p = 0.03) and sex(β = 5.52, p = 0.04) were significant factor correlated

Table 1 Descriptive statistics for demographic information, physical activity and executive function

	T1	T2
N	78	74
Sex (Female, %)	53.8	55.4
Age (years)	25.23 ± 2.24	25.22 ± 2.13
Family economic income level	4.25 ± 1.24	4.03 ± 1.30
Years of education (year)	6.70 ± 1.83	6.65 ± 1.76
Place of residence (city, %)	75.6	77.0
Physical activity		
SED (min/day)	441.60 ± 109.01	444.72 ± 110.64
LPA (min/day)	440.40 ± 83.51	400.90 ± 79.49
MVPA (min/day)	102.79 ± 30.48	100.52 ± 36.37
Steps	8396.83 ± 1910.69	8249.53 ± 2396.94
Executive function (TMT)		
Completion time (s)	69.42 ± 12.95	63.23 ± 14.68
Accuracy rate	0.96 ± 0.06	0.93 ± 0.09

SED indicates sedentary behaviour; LPA, MVPA indicates light physical activity and moderate to vigorous physical activity, respectively; Continuous variables are presented as mean ± SD, Categorical variables are reported as percentages

Table 2 The effects of substituting PA for sedentary behaviour on completion time and accuracy rate

	Model	Completion time (s)		Accuracy rate (%)	
		B(95%CI)	*p*	*B*(95%CI)	*p*
LPA	1	**−0.37 (−5.21, −0.37)**	**0.02***	−0.20 (−0.06, 0.01)	0.22
	2	**−0.34 (−4.85, −0.24)**	**0.03***	−1.18 (−0.06, −0.02)	0.26
MVPA	1	−0.45 (−4.53, 3.39)	0.78	**0.36 (0.01, 0.13)**	**0.02***
	2	−0.11(−5.18, 2.44)	0.48	**0.40 (0.02, 0.14)**	**0.01****

The data of time 1 (78 participants) were used in this table. Significance levels: ** $p < 0.01$, * $p < 0.05$. Significant results are highlighted in bold. Model 1 is primary variable: LPA and MVPA, Model 2 adjusted for place of residence, family income level and education levels as covariates

Table 3 Relationships between SsED, PA and executive function for mixed-effect models

	Completion time(s)		Correct rate (%)	
	β(SE)	*p*	*β(SE)*	*p*
SED	**1.57 (0.86)**	**0.01****	0.18 (0.50)	0.72
City/Rural	5.80 (3.08)	0.06	−2.91 (1.69)	0.09
Edu	0.40 (0.68)	0.55	−0.16 (0.37)	0.67
Income	**−2.16 (1.00)**	**0.03***	−0.15 (0.54)	0.78
Sex	**5.52 (2.69)**	**0.04***	−2.16 (1.46)	0.14
BMI	0.22 (0.45)	0.63	−0.03 (0.25)	0.90
LPA	**−3.65 (2.08)**	**0.08#**	**2.48 (1.18)**	**0.04***
City/Rural	**6.92 (3.06)**	**0.03***	**−3.36 (1.70)**	**0.05***
Edu	0.50 (0.67)	0.46	−0.26 (0.37)	0.49
Income	**−2.01 (0.99)**	**0.04***	−0.21 (0.54)	0.70
Sex	**5.45 (2.66)**	**0.04***	−2.24 (1.46)	0.13
BMI	0.19 (0.44)	0.66	−0.02 (0.26)	0.94
MVPA	**−7.80 (3.64)**	**0.02****	2.39 (2.08)	0.25
City/Rural	6.96 (3.05)	0.02	**−3.09 (1.69)**	**0.07#**
Edu	0.54 (0.67)	0.55	−0.21 (0.37)	0.57
Income	**−2.12 (0.99)**	**0.03***	−0.14 (0.54)	0.79
Sex	**6.06 (2.68)**	**0.03***	−2.39 (1.47)	0.11
BMI	0.29 (0.44)	0.51	−0.05 (0.25)	0.84
Steps	**−1.18 (0.50)**	**0.02***	**0.48 (0.29)**	**0.09#**
City/Rural	**6.55 (3.05)**	**0.03***	**−3.05 (1.69)**	**0.07#**
Edu	0.66 (0.68)	0.34	−0.29 (0.38)	0.46
Income	**−2.14 (0.99)**	**0.03***	−0.13 (0.55)	0.81
Sex	**5.64 (2.67)**	**0.03***	−2.30 (1.47)	0.12
BMI	0.31 (0.45)	0.49	−0.07 (0.25)	0.78

Significance levels: ** $p < 0.01$, * $p < 0.05$, # $p < 0.1$. Significant results are also highlighted in bold with completion time on TMT. The analysis revealed no significant correlation between the duration of SED and the accuracy rate, indicating a flattened dose–response relationship (Fig. 1).

The dose–response relationship of PA and executive function

Average daily LPA time was marginally significantly correlated with completion time on TMT ($\beta=-3.56$, $p=0.08$). Completion time of TMT continued to decline with increasing LPA time, with a dose–response threshold of approximately 200 min. Demographic factors, including place of residence ($\beta=6.92$, $p=0.03$), family income level ($\beta=-2.01$, $p=0.04$), and sex($\beta=5.45$, $p=0.04$) were correlated with completion time. Average daily LPA time was significantly correlated with accuracy rate on TMT. For every 100-min/day increase in LPA time, accuracy rate increases by 2.48% ($\beta=2.48$, $p=0.04$). An increase in time allocated to LPA is associated with an enhanced accuracy rate on the TMT (Fig. 2).

Average daily MVPA time was significantly correlated with completion time on TMT. For every 100-min/day increase in MVPA time, completion time of TMT decreases by 7.80s ($\beta=-7.80$, $p=0.02$) (Table 3). Completion time of TMT continued to decline with increasing MVPA time, with a dose–response threshold of approximately 80 min. Family income level ($\beta=-2.12$, $p=0.03$) and sex ($\beta=6.06$, $p=0.03$) were significant factors correlated with completion time on TMT). No significant correlations were found between MVPA time and accuracy rate (Fig. 3).

Average daily steps were significantly correlated with completion time on TMT. For every 1000-steps/day increase in Steps, completion time of TMT decreases by 1.18s ($\beta=-1.18$, $p=0.02$) (Table 3). Completion time of

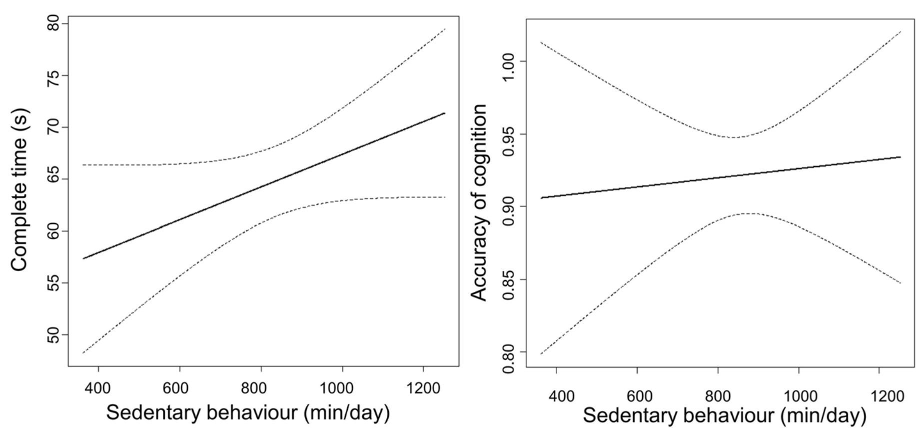

Fig. 1 The dose–response relationship of SED and executive function. *Notes:* Left: the completion time of TMT task; Right: the accuracy rate of the TMT task

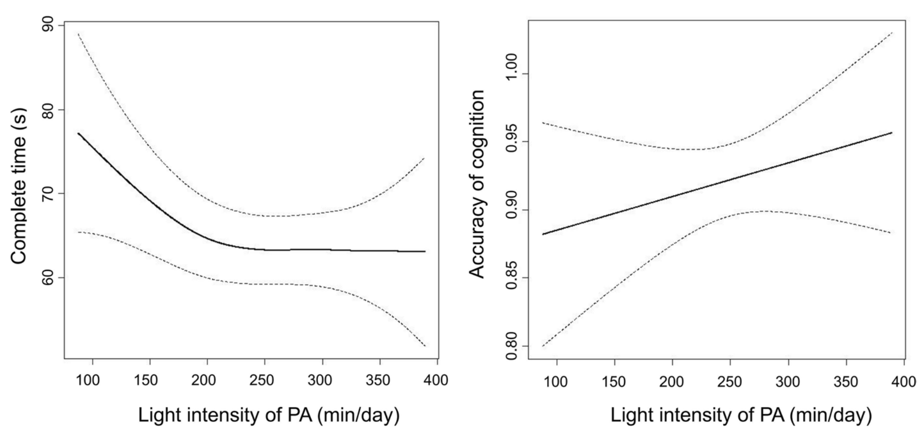

Fig. 2 The dose–response relationship of LPA and executive function. *Notes:* Left: The completion time of TMT task; Right: The accuracy rate of the TMT task

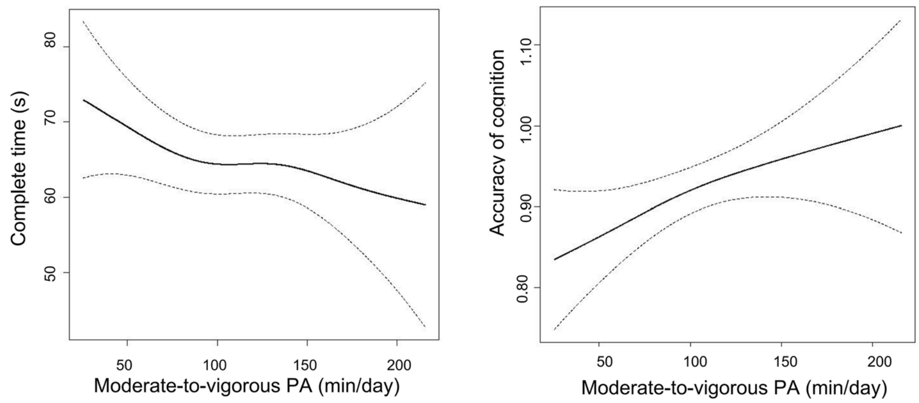

Fig. 3 The dose–response relationship of MVPA and executive function. *Notes:* Left: The completion time of TMT task; Right: the accuracy rate of the TMT task

TMT continued to decline with increasing steps, with a dose–response threshold of approximately 8000 steps. Family income level($\beta = -2.14$, $p = 0.03$) and sex($\beta = 5.64$, $p = 0.03$) were significant factor correlated with completion time on TMT. Average daily steps were marginally significant correlated with correct rate on TMT ($p = 0.08$) (Fig. 4).

Discussion

Our study utilizes a longitudinal study design with isotemporal substitution models to investigate the association between accelerometer-measured physical activity and executive function, specifically examining the impact of replacing sedentary behavior with physical activity on executive function in young adults. The main finding of our study indicates that reduced sedentary time and increased physical activity is associated with enhanced executive function performance. Substituting 30 min of sedentary time with LPA and MVPA contributes to the executive function performance. Notably, a dose–response threshold was observed, demonstrating that prolonged sedentary time inversely affects executive function performance, while greater levels of LPA, MVPA, and step count are positively associated with executive function performance. Specifically, an increase in sedentary time is associated with a longer completion time for the TMT. Conversely, higher levels of LPA correlate with an increased accuracy rate on the TMT. Greater engagement in MVPA, and increased step count are associated with reduced TMT completion times.

Our study have employed accelerometer to objectively investigate the relationship between physical activity patterns and executive function across various populations. The results suggest that substituting 30 min of SED with LPA or MVPA can enhance executive functioning among young adults. The positive impact of physical activity on executive function is supported by correlations found between increases in LPA and MVPA, reductions in sedentary behavior time, and improvements in executive function. This is consistent with previous research, which

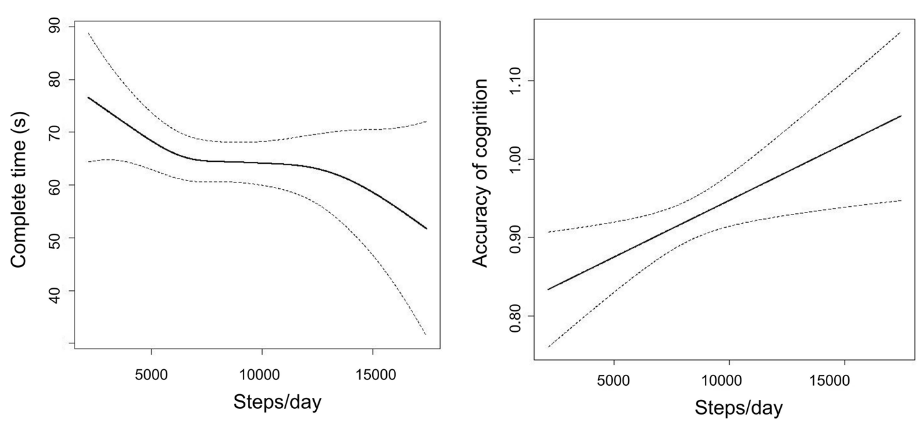

Fig. 4 The dose–response relationship of steps and executive function. *Notes:* Left: the completion time of TMT task; Right: the accuracy rate of the TMT task

also demonstrates a positive relationship between physical activity and brain health in adults [25, 31, 32]. Further, the study utilized compositional isotemporal substitution analysis to assess cognitive function in a large cohort of middle-aged Black and White adults, using accelerometer-measured SED, LPA, and MVPA. It revealed that substituting LPA with MVPA is associated with improved processing speed, working memory, and executive function in men over a 10-year follow-up period, though this association was not observed in women [36]. Moreover, it has been observed that reducing sedentary time by 30 min and simultaneously increasing LPA or MVPA by 30 min is beneficial for executive function [37, 38]. Furthermore, the findings of the current study are consistent with prior research, which investigated the long-term effects on cognition and brain function after installing treadmill workstations in offices for 13 months [39]. However, we acknowledge that even smaller changes can be significant and more manageable in real life, according to current PA guidelines, which suggest that every minute of physical activity contributes to overall health benefits [40]. Thus, while the maximal benefits are observed with higher durations, promoting smaller, incremental increases in daily MVPA remains a practical and impactful public health strategy. Further research could continue to explore the cumulative benefits of these smaller changes over longer periods. Moreover, future research should focus on exploring longitudinal changes in physical activity and their impact on executive function by implementing targeted interventions. Such studies could provide more robust evidence on the causality and mechanisms underlying the relationship between physical activity and cognitive function. Additionally, exploring different types and intensities of physical activities, as well as their long-term adherence and impact on diverse populations, would be valuable.

The current study also establishes a dose–response relationship between daily activity levels and executive function among young adults. It was found that prolonged SED is associated with slower cognitive task completion time. In contrast, increased levels of LPA, MVPA, caloric expenditure, and step count are linked to better executive function performance. Notably, the study identifies specific thresholds for these benefits. A detailed analysis revealed that every additional 100 min of daily SED time increases executive function task completion time. Conversely, an extra 100 min of daily LPA decreases task completion time, up to a 200-min daily threshold. Similarly, an increase of 100 min in daily MVPA is associated with a reduction in task completion time, with the maximum benefit observed at 80 min per day. The results obtained from model fitting indicate potential maximal benefits, but real-world applicability requires more achievable targets. Aiming for smaller, more manageable increases in daily MVPA (e.g., 30 min) can still lead to significant health benefits and improved task performance without being as daunting. An increase of 1000 steps per day is linked to a 1.18s reduction in TMT completion time, with the optimal benefit at 8000 steps per day. These findings support the notion that higher levels of physical activity are beneficial for cognitive performance in young adults, with both MVPA and LPA enhancing executive function, underscoring the cognitive advantages of an active lifestyle. This aligns with previous research indicating that MVPA and LPA are correlated with improved executive function performance in this demographic [41–43]. Future directions include a more sophisticated understanding of the dose–response relationship and finally the design of multimodal interventions that may yield broader improvements in cognitive function.

Several limitations of the present study should be noted: (1) While our study utilized three valid days to determine accelerometer use, which is a common practice as cited in several studies, we recognize that many studies use four valid days to validate accelerometer data, typically comprising three weekdays and one weekend day [44, 45]. Thus, our approach may not provide as comprehensive a picture of weekly physical activity as a longer duration. (2) While daily physical activity was assessed using an accelerometer worn on the arm, subsequent analysis suggested that this placement may lead to an overestimation of the actual physical activity levels of the participants [46]. (3) The sample size of this study was relatively small, and future research should consider increasing the sample size. However, small-sample, short-term longitudinal studies have also been employed successfully in previous research. For example, Loprinzi and Nooe (2016) conducted an 8-week longitudinal study with a sample of 18 adults, using accelerometers to perform repeated measurements of physical activity and sedentary behaviour [47]. Their study explored the relationship between executive function and sedentary time, demonstrating that such designs are feasible and effective in understanding behaviour changes and their impacts, even over shorter timeframes. (4) Our primary analysis focused on the impact of replacing 30 min of sedentary time with MVPA based on previous literature. However, we acknowledge that even smaller changes can be significant and more manageable in real life, according to current physical activity guidelines, which suggest that every minute of physical activity contributes to overall health benefits [40]. Thus, while maximal benefits are observed with longer durations, promoting smaller, incremental increases in daily MVPA remains a practical and impactful public health strategy. Further research could continue to explore the cumulative benefits of these smaller changes over longer periods.

Conclusion

In conclusion, our research demonstrates that both LPA and MVPA can enhance executive function performance among young adults when 30 min of such activities replace an equivalent duration of sedentary behaviour. The findings elucidate a dose–response relationship between physical activity and executive function, which may contribute to the development of targeted interventions. Future research should integrate sleep as a pivotal factor to further understand its role in the interplay between physical activity and executive function, and to clarify the underlying mechanisms linking daily behaviours with brain health.

Abbreviations

TMT	Trail Making Test
SED	Sedentary Dehaviour
LPA	Light Physical Activity
MVPA	Moderate-to-Vigorous Physical Activity
24-HAC	24-Hour Activity Cycle Model
SD	Standard Deviations

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-024-20741-0.

Supplementary Material 1

Acknowledgements

We thank the participants, project staff, and the supports from Tsinghua University Physical Fitness and Rehabilitation Center.

Authors' contributions

Jianxiu Liu conceived and designed the experiments, performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft. Mengxian Wei and Xingtian Li performed the experiments, analyzed the data, authored or reviewed drafts of the article and approved the final draft. Alimjan ablitip, Shiqi Zhang, and Hao Ding performed the experiments, analyzed the data, authored or reviewed drafts of the article, and approved the final draft. Kefeng Zheng analyzed the data, authored or reviewed drafts of the article, and approved the final draft. Ruidong Liu conceived and designed the experiments, authored or reviewed drafts of the article, and approved the final draft. Xindong Ma conceived and designed the experiments, authored or reviewed drafts of the article, and approved the final draft.

Funding

We appreciate the project on Ma John's physical education thought and practice of Tsinghua University, and Research Plan for Higher Education Science by the Chinese Higher Education Association (Project Number: 23TY0205). The funders did not participate in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Data availability

The data that support the findings of this study are available from the first author and corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

All participants provided written informed consent following a comprehensive explanation of the study's procedures. This study received approval from the Ethics Committee of the School of Medicine at Tsinghua University (IRB 20190091).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 25 March 2024 Accepted: 14 November 2024
Published online: 29 November 2024

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