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Effects of aerobic exercise on cognitive function in patients with type 2 diabetes mellitus: a meta-analysis

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Abstract

Type 2 diabetes mellitus(T2DM) is a chronic metabolic disease that adversely affects cognitive function. Aerobic exercise, an important non-pharmacological intervention, has controversial effects on cognitive function. The goal of this study was to systematically assess the effects of aerobic exercise on cognitive function in patients with T2DM . Seven electronic literature databases were searched: PubMed, Web of Science, Embase, Cochrane Library, Wanfang Data, CNKI, and VIP. The search was conducted from the time of construction to June 2025. The data were analyzed using RevMan5.4.1 and stata17. A total of nine studies with 841 patients were included in this study, 410 in the experimental group and 431 in the control group. The results showed that aerobic exercise had a significant effect on cognitive function in patients with T2DM [SMD=0.94, 95% CI (0.63, 1.25), P<0.00001]. Aerobic exercise significantly improves cognitive function in patients with T2DM, but more large-sample, high-quality randomized controlled trials are needed in the future.

Keywords

Exercise; aerobic exercise; t2dm; meta-analysis; cognitive function.

1. Introduction

Type 2 diabetes is a chronic metabolic disease caused by a combination of genetic, metabolic, and environmental factors[1] . Diabetes poses a significant burden on global public health and is a leading cause of premature death globally, with the International Diabetes Federation estimating that diabetes accounts for 6% of all deaths in the world's population[2] . 537 million people were living with diabetes globally in 2021, and this is projected to increase to 783.2 million in 2045. As the prevalence of diabetes continues to increase, the economic burden on society will become heavier, with total global healthcare expenditures related to diabetes estimated at $966 billion in 2021, and projected to exceed $1 trillion in 2045[3] .

People with type 2 diabetes often also suffer from costly complications such as cardiovascular disease, cognitive dysfunction, and retinopathy, which seriously affect their health and quality of life[4] . Microstructural changes occur in areas of the brain such as the frontotemporal region, cerebellum, and major WM tracts in type 2 diabetics compared to healthy individuals, which can adversely affect cognitive function[5] . Some studies have found that older adults with type 2 diabetes have poorer working memory and executive control than healthy older adults[6] . The decline in cognitive function in type 2 diabetes poses three hazards: first, an increased risk of falls[7] , which poses a serious threat to the lives of older adults with type 2 diabetes since one older adult dies every 19 minutes from a fall[8] . Second, the risk of Alzheimer's disease is higher than in the general population[9] . Thirdly, it leads to poor self-care and adherence to diabetes treatment, which reduces the overall prognosis of diabetes and increases the chances of complications[10] . Therefore, there is a need for appropriate interventions for people with

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type 2 diabetes to improve cognitive function and prevent greater harm due to deterioration of cognitive function.

Medication can improve cognitive function in people with type 2 diabetes, but there may be some risks and limitations, for example, one study found that insulin treatment was associated with a 21% increased risk of dementia[11] and another found that metformin reduced the risk of dementia significantly only in Western populations[12] . Among non-pharmacological interventions, aerobic exercise can have a beneficial effect on the brains of ordinary people, improving many aspects of cognition and performance[13,14] , but the results of existing studies on whether it improves cognitive functioning in people with type 2 diabetes are inconsistent, for example, one study found that 12 weeks of treadmill training positively impacted on cognitive outcomes[15] , while the most recent study did not detect a significant difference between the aerobic exercise group and the attention control group[16]. Ding et al. conducted a meta-analysis[17] and found that aerobic exercise significantly improved cognitive function in patients with type 2 diabetes, but the study included several trials combining aerobic exercise with medication, resulting in a meta-analysis of interventions that were not aerobic exercise alone, and the study was limited in terms of age and cognitive status of the patients.

In this study, we systematically assessed the effect of aerobic exercise on cognitive function in patients with type 2 diabetes mellitus(T2DM) through meta-analysis. The differences between this study and previous studies are as follows: (1) More accurate assessment of the effects of aerobic exercise. Previous studies have included interventions combining aerobic exercise with other interventions, which have the limitation that these other interventions might influence cognitive function, leading to results that are either overestimated or underestimated when assessing the effects of aerobic exercise on cognitive improvement. To avoid this, the study included interventions consisting solely of aerobic exercise; if aerobic exercise was combined with other interventions, it was excluded from the analysis. (2) Expanding the applicability of the results. Previous studies imposed age restrictions on study participants, limiting the applicability of the results. This study did not impose any restrictions on patients' age, gender, or other factors.The study aimed to more accurately evaluate the effect of aerobic exercise on improving cognitive function in T2DM patients, to reduce the uncertainty in the use of aerobic exercise as a non-pharmacological intervention, and hopefully to provide more effective exercise guidance for patients.

2. Materials and Methods

2.1. Literature search

The study was conducted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions and the PRISMA Statement for Systematic Evaluation[18] . Seven electronic literature databases were searched: PubMed, Web of Science, Embase, Cochrane Library, Wanfang Data, CNKI, and VIP. The search was conducted from the time of construction to June 2025. To ensure the comprehensiveness of the search, the search terms were combinations of subject and free words for interventions, outcome indicators, study subjects, and study design (Table 1). The search terms were translated into Chinese when searching the Chinese database. In addition, the reference lists of meta-analysis articles related to the topic of this study were manually searched.

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Table 1.Meta-analysis search terms

Interventions (linked by or)	Participants (linked by or)	Outcomes (linked by or)	Study (linked by or)
Exercise;Training; Physical Exercise; Exercise therapy; Physical activity; Aerobic exercise; Aerobic training; Endurance Training; Jogging; Walking; Swimming; Tai Chi; Cycling; Yoga; Climbing; Pilates; Aquatic activities; Rowing;Dancing	Diabetes Mellitus, Type 2; Diabetes Mellitus, Type II; Type 2 Diabetes Mellitus; Type 2 Diabetes; t2dm; t2d; niddm; Diabetes Mellitus; DM; diabetes; diabetic; MODY	Cognition; Cognitive Function; Cognitive Dysfunction; Cognitive Disorder; Cognitive Impairments; Mild Cognitive Impairment; Cognitive Decline; Mental Deterioration	Randomized controlled trial; RCT;random*

Interventions, Participants, Outcomes, and study are linked by 'AND'

2.2. Eligibility criteria

Inclusion criteria for selection of the study were as follows:(1) subjects were patients with type 2 diabetes of any age and gender; (2) the intervention was any form of aerobic exercise,aerobic exercise refers to activities such as running and swimming, in which large muscles are exercised rhythmically for a sustained period of time[19].; (3) the control group received usual care or maintained their previous lifestyle unchanged; (4) subjects' cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE) ; (5) the study design was a randomized controlled trial. Conference papers, dissertations, animal experiments, and articles from non-randomized controlled trials were excluded.

2.3. Literature screening and data extraction

Literature screening and data extraction were carried out independently by two researchers; if any disagreement arose during the process, the two researchers would discuss and analyze it, and if no consensus was reached, then a third researcher was consulted. Duplicates were first removed through Endnote 21 , then literature that was inconsistent with the study topic was removed by reading the title and abstract, and finally, the full text was read to determine whether to include literature based on the inclusion criteria of the selected studies. Data were extracted and cross-checked independently by two researchers, and the data extracted included basic information about the literature, information about the study participants (sample size, age, gender), intervention characteristics (form of exercise, frequency of exercise, duration of the intervention), and data on outcome indicators. For data that had been measured at different time points, only those at the end of the trial were extracted. For data where measurements were made using different instruments, only those obtained using the MoCA were extracted[20] .

2.4. Assessment of study quality and publication bias

Two researchers independently assessed the quality of the included literature using the Cochrane Collaboration's risk of bias assessment tool 2. The quality of the literature was

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systematically assessed in terms of 5 dimensions: (1) Randomization process; (2) Deviations from intended interventions; (3) Missing outcome data; (4) Measurement of the outcome; (5) Selection of the reported result. Publication bias was visually evaluated using funnel plots and further validated by Egger's test using stata17 . If disagreement arose during the process it was discussed with a third researcher to reach a consensus.

2.5. Statistical analysis

Meta-analysis of the studies was performed using RevMan 5.4.1 provided by the Cochrane Collaboration. If $P > 0.1$ and $I^2 < 50\%$ the heterogeneity was relatively small and a fixed-effects model was chosen. If $P \le 0.1$ and $I^2 \ge 50\%$ the heterogeneity was relatively large and a random effects model was chosen. Effect analysis of continuous variables used standardized mean difference (SMD) as a statistic. The reliability of the results was tested by changing the analysis model or excluding studies with lower quality and smaller sample sizes. Subgroup analyses were performed to discuss sources of heterogeneity.

3. Results

3.1. Results of Literature Screening

A total of 3,080 articles were retrieved through a search of electronic databases and a manual search of references. A total of 1,313 duplicate articles were removed by software, 1,741 articles that were inconsistent with the study topic were removed by reading the titles and abstracts, and a total of 17 articles were removed by reading the full text based on inclusion and exclusion criteria. These 17 articles were deleted for the following reasons: (1) not a randomized controlled trial; (2) the intervention was not purely aerobic exercise; (3) subjects' cognitive function was not assessed using the MoCA and the MMSE; (4) subjects were not all type 2 diabetics; (5) dissertation; (6) lack of data and failure to contact with the authors. Finally, a total of 9 articles were included in this study[21–29] , and the flow chart of literature inclusion is shown in Figure 1.

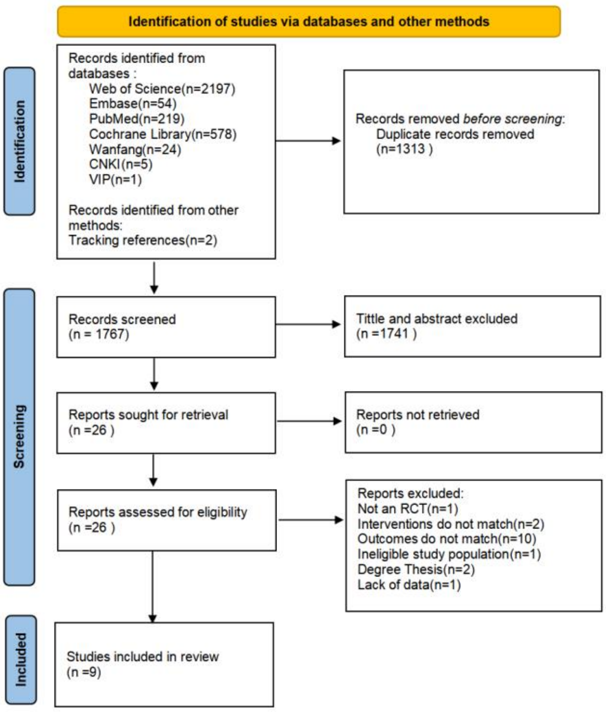

Figure 1.Flowchart of literature screening and inclusion.

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3.2. Characteristics of the included studies

A total of eight studies were included in this study with a total of 841 patients, 410 in the experimental group and 431 in the control group. All the test groups in the study received different forms of aerobic exercise. Four studies were conducted in China[21–23,26] , two in Chile[24,25] , one in Iran[27] , one in India[29] and one in Thailand[28] . Subjects in two study had normal cognitive function[23,29], and subjects in the rest of the studies had varying degrees of cognitive dysfunction[21,22,24–28] . The basic characteristics of the included literature are presented in Table 2.

Table 2.Basic characteristics of the literature

Study	Country	Sample	Age	Sex (male, %)	Interventions	Comparison	Cognitive outcomes
		Test/ Control group					
Zhang2017	China	36/38	69.53±8.02/ 69.79±6.74	47.22%/44.74%	Fitness walking, 40-50 minutes each time, ≥3 times per week for 3 months	Usual care	Moca, MMSE
Hu2019	China	49/47	65.90±3.70/65.80±3.60	51.02%/51.06%	Brisk walking or jogging, 40-60 minutes each time,4 times a week for 12 weeks	Usual care	Moca
Wang 2023	China	40/42	65.73 ± 3.99/ 68.07 ± 5.47	47.50%/52.40%	Aerobic dance, 60 minutes each time, 3 times a week for 12 months	Maintain their usual physical activity	Moca, MMSE
Molina-Sotomayor2020	Chile	55/52	72.30±3.70/ 71±3.30	0%/0%	Walking, 60 minutes each time, 3 times a week for 6 months	Maintain their usual physical activity	MMSE
Molina-Sotomayor2021	Chile	38/38	72.60±3.90/ 72.20±4.30	0%/0%	Walking, 60 minutes each time, 3 times a week for 4 months	Maintain their usual physical activity	MMSE
Chen2023	China	107/111	67.56±4.99/ 67.62±5.35	45.80%/45.90%	24-form simplified tai chi chuan, 60 minutes each time, 3 times a week for 24 weeks	Maintained their previous lifestyle	Moca
M. Ghahfarrokhi 2024	Iran	16/16	68.35±5.44/ 67.76±5.49	/	Functional training, 40-45 minutes each time, 5 times a week for 6 weeks	Maintain their usual physical activity	MMSE
PLOYDANG, T2023	Thailand	16/17	68.90±3.70/ 69.20±5.30	31.25%/41.18%	Nordic Walking in Water, 60 minutes each time, 3 times a week for 12 weeks	Maintained their previous lifestyle	Moca, MMSE
Poongothai2025	India	53/70	/	/	Yoga，35 minutes each time,once every 2 weeks for 12 weeks.	Usual care	Moca

3.3. Quality assessment of included studies

The Cochrane Collaboration's risk of bias assessment tool 2 was used to assess the quality of the included literature. The results are shown in Figure 2.Only one study showed overall “low risk” while the remaining studies showed “some concerns” due to risks in different aspects. For example, regarding the randomization process, two studies did not mention the specific random allocation method[24,25], and two studies did not provide sufficient information to indicate that the allocation sequence was concealed[21,29].

Figure 2.Evaluation of the quality of the included literature.

3.4. Meta-analysis

3.4.1. Combined effect size

Nine studies were meta-analyzed[21–29] , a total of 841 participants were included and the effect of aerobic exercise on cognitive function was assessed by using the MoCA and the results are shown by Figure 3. Due to the high heterogeneity (I^2 =76%, P<0.0001), a random effects model was chosen for the analysis, and the results showed that aerobic exercise had a significant effect on cognitive function in patients with T2DM [SMD=0.94, 95% CI (0.63, 1.25), P<0.00001], and the 95% CI was located on the right-hand side of the null line, which indicates that the result was statistically significant. Due to the high level of heterogeneity, we excluded literature one by one in an attempt to reduce the heterogeneity. After excluding the studies of Wang2023[23] and Chen2023[26] , the heterogeneity was reduced (I^2 =26%, P=0.23), and there was no significant change in the composite effect size (Figure 4), which showed that aerobic exercise had a significant effect on cognitive function in patients with T2DM [SMD=1.13, 95% CI (0.95, 1.31), P<0.00001], and the 95% CI lies to the right of the null line, indicating that this result is statistically significant. Differences in patients' cognitive status and forms of exercise may have contributed to the heterogeneity, as subjects in the Wang2023 [23] study had normal cognitive function, and both of these studies[23,26] had coaches who led the subjects through exercise and the forms of exercise were more complex than in the other studies.

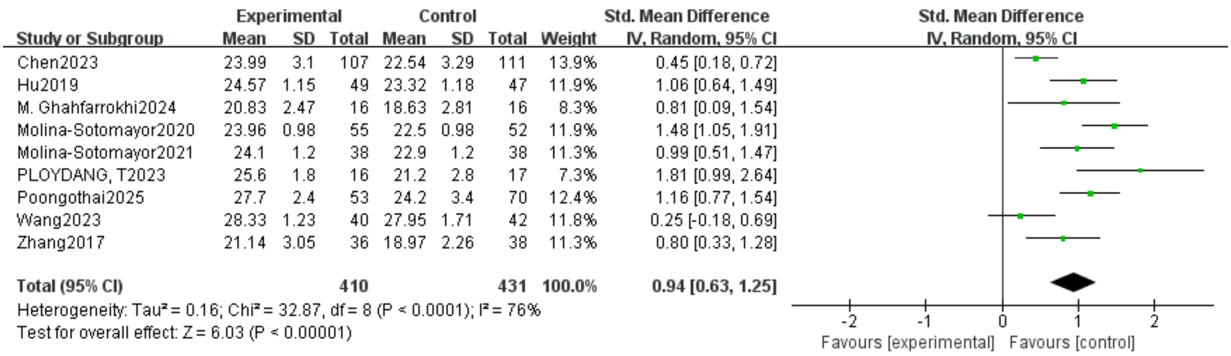

Figure 3.Effects of aerobic exercise on cognitive function in patients with T2DM.

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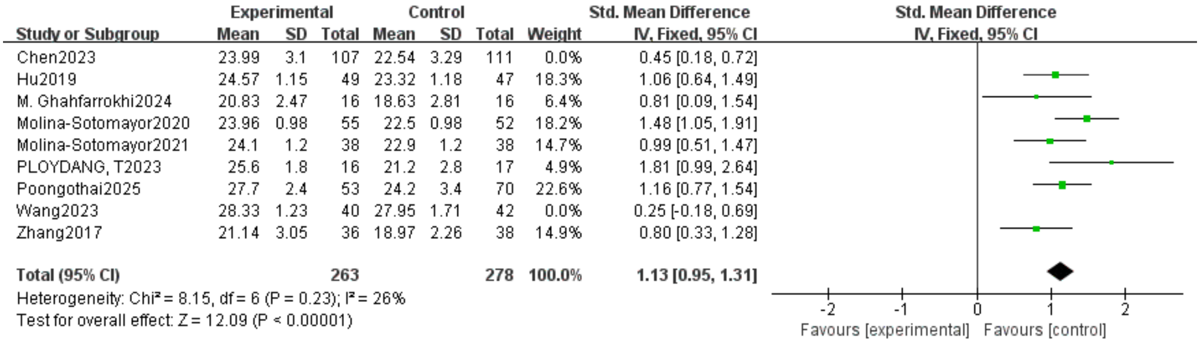

Figure 4.Effects of aerobic exercise on cognitive function in patients with T2DM after culling the literature.

3.4.2. Analysis based on subgroups of different movement forms

The included studies were divided into two subgroups according to the form of exercise, the first group with walking as the main form of exercise (5 studies included[21,22,24,25,28] , 386 subjects), and the second group was the non-walking group (4 studies included[23,26,27,29] , 455 subjects). Due to low heterogeneity, the walking based group were analyzed using a fixed-effects model, and compared with the non-walking group [SMD = 0.65, 95% CI (0.24, 1.07), P =0.002], walking based group had a more significant effect on the improvement of cognitive function [SMD = 1.15, 95% CI (0.93, 1.37), P < 0.00001]. (Table 3)

Table 3.Summary of subgroup meta-analyses

Subgroup		No. of studies	Mata analysis			I^2	P
			SMD	95% CI	P		
sports format	walking-based	5	1.15	0.93, 1.37	<0.00001	46%	0.12
	non-walking	4	0.65	0.24, 1.07	0.002	75%	0.008
frequency	≤3 times per week	6	0.97	0.53, 1.41	<0.0001	84%	<0.00001
	>3 times per week	3	0.93	0.63, 1.22	<0.00001	0%	0.69
duration	≤four months	6	1.05	0.85, 1.26	<0.00001	1%	0.41
	>four months	3	0.72	0.04, 1.40	0.04	90%	<0.0001

3.4.3. Subgroup analysis based on different exercise frequencies

The included studies were divided into two subgroups according to the frequency of exercise; the first group exercised three times per week or less (6 studies[23–26,28,29] , 639 subjects were included) and the second group exercised more than three times per week (3 studies[21,22,27] , 202 subjects were included). Heterogeneity was lower in the group exercising more than three times per week (I^2 =0%, P=0.69), and the results were not significantly affected when analyzed using a fixed-effects model [SMD=0.93, 95% CI (0.63, 1.22), P< 0.00001]. Heterogeneity was higher in the group exercising three times a week or less (I^2 =84%, P<0.00001), and the results were not significantly affected when analyzed using a random-effects model [SMD=0.97, 95% CI (0.53, 1.41), P<0.0001], differences in the areas in which the studies were conducted and large differences in the timing of the interventions(the

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shortest being 12 weeks and the longest 12 months) may have contributed to the heterogeneity. (Table 3)

3.4.4. Subgroup analysis based on different intervention times

The included studies were categorized into two subgroups according to the duration of the intervention; the first group had an intervention duration of four months or less (6 studies were included[21,22,25,27–29] , 434 subjects), and the second group had an intervention duration of more than four months (3 studies were included[23,24,26] , 407 subjects). The first group had low heterogeneity (I^2 =1%, P=0.41) and was analyzed using a fixed effects model, which showed that aerobic exercise had a significant effect on cognitive function in patients with T2DM[SMD=1.05, 95% CI (0.85, 1.26), P < 0.00001]. The second group had higher heterogeneity (I^2 =90%, P < 0.0001) and the results were analyzed using a random effects model, which was not significantly affected, and the effect produced by aerobic exercise remained significant [SMD=0.72, 95% CI (0.04, 1.4), P=0.04], and the higher heterogeneity may be because in the study of Molina-Sotomayor2020[24] subjects were all female and the form of exercise was simpler than the other two studies. (Table 3)

3.5. Sensitivity analysis and publication bias

No significant changes in the amount of combined effects were observed in the analyses conducted after using the fixed-effects model or excluding studies with lower-quality literature and smaller sample sizes, so the results of this study were relatively stable. No significant asymmetry was observed in the funnel plot (Figure 5), suggesting that there was no significant publication bias, a result that was further affirmed by Egger's test (P=0.1357) (Supplementary file 1).

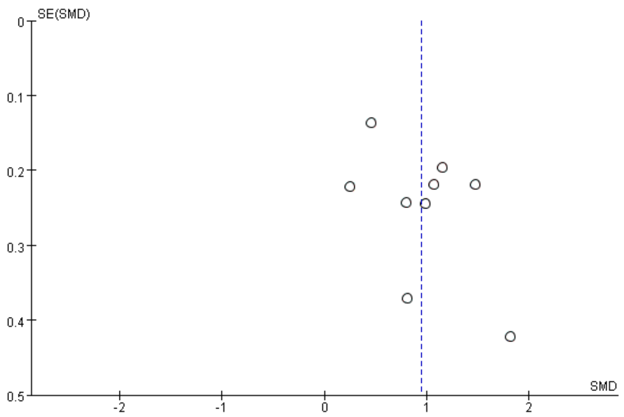

Figure 5.Funnel plot of the effects of aerobic exercise on cognitive function in patients with T2DM.

4. Discussion

T2DM adversely affects the cognitive profile, affects patients' adherence to treatment, and may lead to other complications, jeopardizing their health[10] . A total of nine studies were included in this study, aiming to analyze the effect of aerobic exercise on cognitive function in patients with T2DM, and the results showed that aerobic exercise had a significant effect on cognitive function in patients with T2DM[SMD=0.94, 95% CI (0.63, 1.25), P<0.00001]. The improvement effect of aerobic exercise with walking as the main form of exercise was better.

4.1. Effect of aerobic exercise on cognitive function in T2DM patients

Our findings show that aerobic exercise improves cognitive function in people with type 2 diabetes, consistent with previous research. A cross-sectional study conducted in Australia

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found that people who engaged in regular aerobic training had better cognitive function than those who were sedentary[30] . Recent studies have found that aerobic exercise increases hippocampal volume and protects cognitive function in people with type 2 diabetes[23] , and a meta-analysis by Ding et al. found that aerobic exercise improved cognitive function in people with type 2 diabetes[17] , which is consistent with the results of this study. Cognition tends to evolve unfavorably in diabetic patients compared to normoglycemic subjects[31] , and our results suggest that aerobic exercise could be an intervention to improve cognitive function in type 2 diabetic patients.

The mechanisms by which aerobic exercise improves cognitive function in patients with T2DM may be as follows: (1) Improvement of cognitive function in patients with T2DM through the effects on the hippocampus, in addition to increasing the volume of the hippocampus[23] , some studies have found that exercise enhances the level of presynaptic and postsynaptic proteins in the hippocampus[32] ; (2) Increase of neurotrophic factors is also a possible mechanism, aerobic exercise not only can regulate the SIRT1 pathway, decreasing the level of pro-inflammatory factors and increasing the expression of anti-inflammatory factors to reduce the inflammatory response[33] , but also reduces glutamate in the brain to increase the expression of BDNF, which has an important role in cognitive function[34] . (3) As a new mediator of the effects of exercise on cognitive function, FNDC5/irisin also stimulates BDNF expression[35] . New research has also found that increased levels of irisin have a beneficial effect on the hippocampus and neuroinflammation, which attenuates cognitive decline[36] , which is also a possible mechanism by which aerobic exercise improves cognitive function in patients with type 2 diabetes.

4.2. Effects of different forms of aerobic exercise on cognitive function in patients with T2DM

Most of the randomized controlled trials included in this study used walking as the main form of exercise, such as walking and jogging, while other forms of exercise in this study were relatively more complex, with aerobic dance, tai chi, and functional training[37] . The results of the study suggest that although different forms of exercise can improve cognitive function in patients with T2DM, walking as the main form of exercise has a better improvement effect. A study comparing tai chi with brisk walking was inconsistent with our results, finding that tai chi requires learning and memorizing new movements and has a higher cognitive demand when practiced compared to brisk walking, resulting in a greater beneficial effect on cognitive function[38] . Possible reasons for the inconsistent results are that the intervention duration was relatively longer in the non-walking group in our study, the higher cognitive demands may have led to lower compliance, making the exercise fail to achieve the desired effect, and the new study found that the longer tai chi intervention may not provide greater benefits over time[39] . Interestingly, there are also differences in the effects produced by different non-walking exercises, with one study finding that dance was effective in promoting overall cognition while tai chi was not[40] .

4.3. Effects of aerobic exercise with different exercise frequencies and intervention times on cognitive function in T2DM patients

In the literature included in this study, the exercise dosage parameter for the five randomized controlled trials was 60 minutes of exercise three times per week. The results of the subgroup analysis showed that the effect of aerobic exercise on improving cognitive function in patients with T2DM was not significantly affected by the frequency and duration of exercise. This is consistent with the results of a previous meta-analysis[41] . However, some studies have found that for older adults with cognitive impairment, implementing a short duration and frequency exercise program led to better cognitive outcomes[42] , and others have found that only the frequency of exercise affects the effectiveness of the intervention[43] . Differences in inclusion

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criteria may have contributed to the differences in the results, in our study, type 2 diabetic patients with varying degrees of cognitive impairment but without dementia were included, while the study conducted by Sanders et al.[42] included patients with dementia, in addition , the types of exercise included in the two studies were different, our study solely included aerobic exercise, while the study conducted by Sanders et al. [42] included multicomponent exercise and resistance training in addition to aerobic exercise. Due to the paucity of RCT evidence for the systematic manipulation of exercise parameters, the current data do not provide a clear picture of whether training parameters affect exercise-induced neurobiological and cognitive changes[44] , and more high-quality studies on this issue are needed for better exercise programming in the future.

4.4. Limitations

Although our results suggest that aerobic exercise can improve cognitive function in patients with T2DM, there are some limitations in this study:(1) in our study, we included only randomized controlled trials, however, the number of literature included in the study was small and of average quality; (2) most of the patients included in this study were cognitively impaired, and there was only two randomized controlled trial in which subjects had normal cognition, which would have had an impact on the results applicability; (3) most of the intervention durations in the included literature were six months or less, and only one trial had an intervention duration greater than six months, limiting our analysis of the effects of prolonged exercise interventions.

5. Summary

Our results suggest that aerobic exercise, regardless of frequency and duration, can improve cognitive function in T2DM patients, and walking as the main form of exercise may be more effective. However, due to the small number and heterogeneity of included studies, this result should be treated with caution, and more large-sample, high-quality randomized controlled trials are needed in the future to investigate the effects of aerobic exercise of different exercise forms, frequencies, and durations on cognitive function in patients with type 2 diabetes.

References

[1] Galicia-Garcia, U.; Benito-Vicente, A.; Jebari, S.; Larrea-Sebal, A.; Siddiqi, H.; Uribe, K.B.; Ostolaza, H.; Martín, C. Pathophysiology of Type 2 Diabetes Mellitus. International Journal of Molecular Sciences 2020, 21, 6275, doi:10.3390/ijms21176275.

[2] Susan van, D.; Beulens, J.W.J.; Yvonne T. van der, S.; Grobbee, D.E.; Nealb, B. The Global Burden of Diabetes and Its Complications: An Emerging Pandemic. European journal of cardiovascular prevention and rehabilitation 2010, 17, s3–s8, doi:10.1097/01.hjr.0000368191.86614.5a.

[3] Sun, H.; Saeedi, P.; Karuranga, S.; Pinkepank, M.; Ogurtsova, K.; Duncan, B.B.; Stein, C.; Basit, A.; Chan, J.C.N.; Mbanya, J.C.; et al. IDF Diabetes Atlas: Global, Regional and Country-Level Diabetes Prevalence Estimates for 2021 and Projections for 2045. Diabetes Res. Clin. Pract. 2022, 183, 109119, doi:10.1016/j.diabres.2021.109119.

[4] Zheng, Y.; Ley, S.H.; Hu, F.B. Global Aetiology and Epidemiology of Type 2 Diabetes Mellitus and Its Complications. Nat. Rev. Endocrinol. 2018, 14, 88–98, doi:10.1038/nrendo.2017.151.

[5] Sanjari Moghaddam, H.; Ghazi Sherbaf, F.; Aarabi, M.H. Brain Microstructural Abnormalities in Type 2 Diabetes Mellitus: A Systematic Review of Diffusion Tensor Imaging Studies. Frontiers in Neuroendocrinology 2019, 55, 100782, doi:10.1016/j.yfrne.2019.100782.

[6] Redondo, M.T.; Beltrán-Brotóns, J.L.; Reales, J.M.; Ballesteros, S. Executive Functions in Patients with Alzheimer's Disease, Type 2 Diabetes Mellitus Patients and Cognitively Healthy Older Adults. Experimental Gerontology 2016, 83, 47–55, doi:10.1016/j.exger.2016.07.013.

[7] Blackwood, J. Cognitive Function and Falls in Older Adults With Type 2 Diabetes Mellitus. Journal of Geriatric Physical Therapy 2019, 42, E91, doi:10.1519/JPT.0000000000000209.

[8] Bolding, D.J.; Corman, E. Falls in the Geriatric Patient. Clinics in Geriatric Medicine 2019, 35, 115–126, doi:10.1016/j.cger.2018.08.010.

[9] Zhang, J.; Chen, C.; Hua, S.; Liao, H.; Wang, M.; Xiong, Y.; Cao, F. An Updated Meta-Analysis of Cohort Studies: Diabetes and Risk of Alzheimer's Disease. Diabetes Research and Clinical Practice 2017, 124, 41–47, doi:10.1016/j.diabres.2016.10.024.

[10] Albai, O.; Frandes, M.; Timar, R.; Roman, D.; Timar, B. Risk Factors for Developing Dementia in Type 2 Diabetes Mellitus Patients with Mild Cognitive Impairment. NDT 2019, 15, 167–175, doi:10.2147/NDT.S189905.

[11] McMillan, J.M.; Mele, B.S.; Hogan, D.B.; Leung, A.A. Impact of Pharmacological Treatment of Diabetes Mellitus on Dementia Risk: Systematic Review and Meta-Analysis. BMJ Open Diab Res Care 2018, 6, doi:10.1136/bmjdrc-2018-000563.

[12] Kuate Defo, A.; Bakula, V.; Pisaturo, A.; Labos, C.; Wing, S.S.; Daskalopoulou, S.S. Diabetes, Antidiabetic Medications and Risk of Dementia: A Systematic Umbrella Review and Meta-Analysis. Diabetes, Obesity and Metabolism 2024, 26, 441–462, doi:10.1111/dom.15331.

[13] Hillman, C.H.; Erickson, K.I.; Kramer, A.F. Be Smart, Exercise Your Heart: Exercise Effects on Brain and Cognition. Nat Rev Neurosci 2008, 9, 58–65, doi:10.1038/nrn2298.

[14] Jiang, S.; Pan, X.; Li, H.; Su, Y. Global Trends and Developments in Mindfulness Interventions for Diabetes: A Bibliometric Study. Diabetology & Metabolic Syndrome 2024, 16, 43, doi:10.1186/s13098-024-01288-x.

[15] Cokar, D.; Polat, M.G.; Timurtas, E.; Sertbas, Y.; Sogut, I. Neuroprotective and Metabotropic Effect of Aerobic Exercise Training in Female Patients with Type 2 Diabetes Mellitus. Turk. J. Biochem. 2022, 47, 741–748, doi:10.1515/tjb-2022-0048.

[16] Liu, T.; Lo, W.-J.; Chen, J.; Wang, J.; Li, C. The Effects of Aerobic Exercise on Cognitive Function in Middle-Aged and Older Individuals with Type 2 Diabetes: A Pilot Randomized Controlled Trial. Geriatric Nursing 2024, 60, 677–685, doi:10.1016/j.gerinurse.2024.10.038.

[17] Ding, J.; Zeng, M.; Yu, C.; Xiao, X. The Effect of Aerobic Exercise on Cognitive Function in Patients with Type 2 Diabetes Mellitus: A Meta-Analysis. ALTERNATIVE THERAPIES 2024.

[18] Moher, D.; Liberati, A.; Tetzlaff, J.; Altman, D.G. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. Journal of Clinical Epidemiology 2009, 62, 1006–1012, doi:10.1016/j.jclinepi.2009.06.005.

[19] Bull, F.C.; Al-Ansari, S.S.; Biddle, S.; Borodulin, K.; Buman, M.P.; Cardon, G.; Carty, C.; Chaput, J.-P.; Chastin, S.; Chou, R.; et al. World Health Organization 2020 Guidelines on Physical Activity and Sedentary Behaviour. Br J Sports Med 2020, 54, 1451–1462, doi:10.1136/bjsports-2020-102955.

[20] Lu, H.-H.; Zhou, Y.; Chen, C.; Gu, Z.-J. Meta-Analysis of the Effect of Exercise Intervention on Cognitive Function in Elderly Patients with Type 2 Diabetes Mellitus. BMC Geriatrics 2024, 24, 770, doi:10.1186/s12877-024-05352-z.

[21] ZHANG Jian-Ping; WANG Jing-Ye; CHEN Jian; SHE Yi-Wen; CHEN Lang; CHENG Jie Effect of Rehabilitation Intervention on Mild Cognitive Impairment in Elderly Patients with Type 2 Diabetes Mellitus. Chin J Mult Organ Dis Elderly 2017, 16, 23–27.

[22] HU Zi-Ying; ZHANG Hui-Feng; QIN Ling-Zhi; NIU Rui-Fang The Impact of Aerobic Exercise on Cognitive Function and Its Related Risk Factors in Type 2 Diabetic Patients. Chinese Journal of Physical Medicine and Rehabilitation 2019, 41, 64–67.

[23] Wang, Y.; Wang, L.; Yan, J.; Yuan, X.; Lou, Q.Q. Aerobic Training Increases Hippocampal Volume and Protects Cognitive Function for Type 2 Diabetes Patients with Normal Cognition. Exp Clin Endocrinol Diabetes 2023, 131, 605–614, doi:10.1055/a-2105-0799.

[24] Molina-Sotomayor, E.; Onetti-Onetti, W.; Castillo-Rodríguez, A.; González-Jurado, J.A. Changes in Cognitive Function and in the Levels of Glycosylated Haemoglobin (HbA1c) in Older Women with Type 2 Diabetes Mellitus Subjected to a Cardiorespiratory Exercise Programme. Sustainability 2020, 12, 5038, doi:10.3390/su12125038.

ISSN: 2710-0170

[25] Molina-Sotomayor, E.; Gómez-Campos, R.; Ulloa-Tapia, E.; Arroyo-Jofre, P.; González-Jurado, J.; Celis-Morales, C.; Rodríguez-Rodríguez, F.; Cossio-Bolaños, M. Efectos de un programa de entrenamiento de marcha sobre las capacidad aeróbica y la función cognitiva en mujeres diabéticas de edad avanzada. Rev. méd. Chile 2021, 149, 37–44, doi:10.4067/S0034-98872021000100037.

[26] Chen, Y.; Qin, J.; Tao, L.; Liu, Z.; Huang, J.; Liu, W.; Xu, Y.; Tang, Q.; Liu, Y.; Chen, Z.; et al. Effects of Tai Chi Chuan on Cognitive Function in Adults 60 Years or Older With Type 2 Diabetes and Mild Cognitive Impairment in China: A Randomized Clinical Trial. JAMA Netw Open 2023, 6, e237004, doi:10.1001/jamanetworkopen.2023.7004.

[27] Ghahfarrokhi, M.M.; Shirvani, H.; Rahimi, M.; Bazgir, B.; Shamsadini, A.; Sobhani, V. Feasibility and Preliminary Efficacy of Different Intensities of Functional Training in Elderly Type 2 Diabetes Patients with Cognitive Impairment: A Pilot Randomised Controlled Trial. BMC Geriatrics 2024, 24, 71, doi:10.1186/s12877-024-04698-8.

[28] Ploydang, T.; Khovidhunkit, W.; Tanaka, H.; Suksom, D. Nordic Walking in Water on Cerebrovascular Reactivity and Cognitive Function in Elderly Patients with Type 2 Diabetes. Medicine & Science in Sports & Exercise 2023, 55, 1803–1811, doi:10.1249/MSS.0000000000003216.

[29] Subramani, P.; Mohan, A.R.; Satish, L.; Karthikeyan, S.; Ravi, P.; Ulagamathesan, V.; Kannikan, V.; Viswanathan, M. The Impact of Yoga Intervention on Physical and Mental Health of Adults with Type 2 Diabetes. International Journal of Yoga 2025, 18, 67–73, doi:10.4103/ijoy.ijoy_219_24.

[30] Bliss, E.S.; Biki, S.M.; Wong, R.H.X.; Howe, P.R.C.; Mills, D.E. The Benefits of Regular Aerobic Exercise Training on Cerebrovascular Function and Cognition in Older Adults. Eur J Appl Physiol 2023, 123, 1323–1342, doi:10.1007/s00421-023-05154-y.

[31] Fontbonne, A.; Berr, C.; Ducimetière, P.; Alpérovitch, A. Changes in Cognitive Abilities Over a 4-Year Period Are Unfavorably Affected in Elderly Diabetic Subjects: Results of the Epidemiology of Vascular Aging Study. Diabetes Care 2001, 24, 366–370, doi:10.2337/diacare.24.2.366.

[32] De Sousa, R.A.L.; Diniz-Magalhaes, C.O.; Cruz, P.P.; De Oliveira, G.H.B.; Prates, J.T.A.C.; De Azevedo Ferreira, C.M.; Silva, R.R.; Cassilhas, R.C. Physical Exercise Inhibits Cognitive Impairment and Memory Loss in Aged Mice, and Enhances Pre- and Post-Synaptic Proteins in the Hippocampus of Young and Aged Mice. Neuromol Med 2024, 26, 31, doi:10.1007/s12017-024-08798-x.

[33] Lang, X.; Zhao, N.; He, Q.; Li, X.; Li, X.; Sun, C.; Zhang, X. Treadmill Exercise Mitigates Neuroinflammation and Increases BDNF via Activation of SIRT1 Signaling in a Mouse Model of T2DM. Brain Research Bulletin 2020, 165, 30–39, doi:10.1016/j.brainresbull.2020.09.015.

[34] Shekarchian, M.; Peeri, M.; Azarbayjani, M.A. Physical Activity in a Swimming Pool Attenuates Memory Impairment by Reducing Glutamate and Inflammatory Cytokines and Increasing BDNF in the Brain of Mice with Type 2 Diabetes. Brain Research Bulletin 2023, 201, 110725, doi:10.1016/j.brainresbull.2023.110725.

[35] Lourenco, M.V.; Frozza, R.L.; de Freitas, G.B.; Zhang, H.; Kincheski, G.C.; Ribeiro, F.C.; Gonçalves, R.A.; Clarke, J.R.; Beckman, D.; Staniszewski, A.; et al. Exercise-Linked FNDC5/Irisin Rescues Synaptic Plasticity and Memory Defects in Alzheimer's Models. Nat Med 2019, 25, 165–175, doi:10.1038 /s41591-018-0275-4.

[36] Xu, H.; Tian, X.; Wang, Y.; Lin, J.; Zhu, B.; Zhao, C.; Wang, B.; Zhang, X.; Sun, Y.; Li, N.; et al. Exercise Promotes Hippocampal Neurogenesis in T2DM Mice via Irisin/TLR4/MyD88/NF-κB-Mediated Neuroinflammation Pathway. Biology 2024, 13, 809, doi:10.3390/biology13100809.

[37] Pollock, M.L.; Gaesser, G.A.; Butcher, J.D.; Després, J.-P.; Dishman, R.K.; Franklin, B.A.; Garber, C.E. ACSM Position Stand: The Recommended Quantity and Quality of Exercise for Developing and Maintaining Cardiorespiratory and Muscular Fitness, and Flexibility in Healthy Adults. Medicine & Science in Sports & Exercise 1998, 30, 975.

[38] Ji, Z.; Li, A.; Feng, T.; Liu, X.; You, Y.; Meng, F.; Wang, R.; Lu, J.; Zhang, C. The Benefits of Tai Chi and Brisk Walking for Cognitive Function and Fitness in Older Adults. PeerJ 2017, 5, e3943, doi:10.7717/peerj.3943.

[39] Chen, M.-L.; Wotiz, S.B.; Banks, S.M.; Connors, S.A.; Shi, Y. Dose-Response Association of Tai Chi and Cognition among Community-Dwelling Older Adults: A Systematic Review and Meta-Analysis.

International Journal of Environmental Research and Public Health 2021, 18, 3179, doi:10.3390/ ijerph18063179.

[40] Wang, S.; Yin, H.; Jia, Y.; Zhao, L.; Wang, L.; Chen, L. Effects of Mind-Body Exercise on Cognitive Function in Older Adults With Cognitive Impairment: A Systematic Review and Meta-Analysis. The Journal of Nervous and Mental Disease 2018, 206, 913, doi:10.1097/NMD.0000000000000912.

[41] Cai, Y.-H.; Wang, Z.; Feng, L.-Y.; Ni, G.-X. Effect of Exercise on the Cognitive Function of Older Patients With Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. Front. Hum. Neurosci. 2022, 16, 876935, doi:10.3389/fnhum.2022.876935.

[42] Sanders, L.M.J.; Hortobágyi, T.; Gemert, S. la B.; Zee, E.A. van der; Heuvelen, M.J.G. van Dose-Response Relationship between Exercise and Cognitive Function in Older Adults with and without Cognitive Impairment: A Systematic Review and Meta-Analysis. PLOS ONE 2019, 14, e0210036, doi:10.1371/journal.pone.0210036.

[43] Ahn, J.; Kim, M. Effects of Aerobic Exercise on Global Cognitive Function and Sleep in Older Adults with Mild Cognitive Impairment: A Systematic Review and Meta-Analysis. Geriatric Nursing 2023, 51, 9–16, doi:10.1016/j.gerinurse.2023.02.008.

[44] Silva, N.C.B.S.; Barha, C.K.; Erickson, K.I.; Kramer, A.F.; Liu-Ambrose, T. Physical Exercise, Cognition, and Brain Health in Aging. Trends in Neurosciences 2024, 47, 402–417, doi:10.1016/ j.tins. 2024.04.004.