Review

Effects of Exercise on Type 2 Diabetes Mellitus-Related Cognitive Impairment and Dementia

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Abstract. Cognitive impairment and dementia are common contributors to institutionalization and loss of quality of life in older people. Both type 2 diabetes mellitus (T2DM) and physical inactivity are prevalent and important modifiable risk factors for developing dementia. Physical activity is recommended in the management of T2DM, and there is growing evidence that exercise, a subgroup of physical activity, is also beneficial for maintaining and improving brain structure and function. This paper reviews the evidence for a benefit of exercise on T2DM related cognitive impairment and dementia. In addition, the type (e.g., aerobic, resistance), intensity, duration, and frequency of exercise are discussed. This review shows that although exercise has known benefits on the mechanisms linking T2DM to dementia, there are very few randomized controlled trials examining whether this is the case. It is concluded that the uptake of exercise for the brain has great potential to improve quality of life and provide significant cost savings, but further research is warranted to clarify the effects of exercise on T2DM and those on dementia.

Keywords: Aerobic exercise, brain health, cognitive function, eccentric exercise, physical activity, resistance exercise

INTRODUCTION

Dementia is caused by more than 200 different diseases including neurodegenerative diseases (e.g., Alzheimer’s disease) and atherosclerosis in the brain’s blood vessels [1]. Old age is the strongest risk factor for developing dementia as evidenced by only 3% of people aged 65–74 y having dementia, increasing to 47% of people over 85 y [2]. Dementia is the largest cause of disability in older people and one of the major reasons for institutionalization. Worldwide, approximately 47 million people have dementia, with numbers expected to increase to 131.5 million by 2050 [3]. Reducing the prevalence of modifiable risk factors by approximately 10% per decade could prevent 8.8 million cases by 2050 [4]. Such preventative efforts may best be addressed in people at high risk of dementia.

Risk factors for dementia include low education in early life, hypertension in midlife, smoking, obesity, physical inactivity, depression, and diabetes across the lifespan [5, 6]. Among these, physical inactivity is one of the most important modifiable risk factors [4]. Around 13% of dementia cases worldwide, and 21%
of those in the US, may be attributable to physical inactivity [6]. It is estimated from observation studies that if 25% of physically inactive people became active, 1 million cases of dementia could be prevented globally [6].

Type 2 diabetes mellitus (T2DM) is also a potentially modifiable risk factor for dementia [5], with estimates that nearly 200,000 cases of dementia could be prevented if there was a 25% reduction in T2DM [6]. Importantly, physical inactivity is one of the main causes of T2DM [7]. It has been well documented that regular exercise plays a major role in its prevention and management [8]. Thus, exercise should be effective also for prevention of dementia by reducing the risk of T2DM. In fact, there is growing evidence that exercise, as an intervention, may be beneficial for the brain [9].

In this article, we 1) review the evidence for exercise to improve brain health and describe who might benefit, 2) outline why people with T2DM may potentially be a group of people who have the most to gain from such an intervention, 3) describe the types of exercise that may be beneficial for preventing T2DM related dementia, and 4) outline any existing evidence for such a benefit.

EXERCISE FOR BRAIN HEALTH: WHO MIGHT BENEFIT

Physical activity is defined as any bodily movement produced by skeletal muscles that requires energy expenditure [10]. Exercise, is a subcategory of physical activity that is planned, structured, repetitive, and purposeful with the aim of maintaining or improving one or more components of physical fitness [10]. There is increasing evidence that the brain remains plastic throughout life and that exercise can provide an important treatment to build brain reserve to delay the onset of dementia [11]. At a cellular and molecular level, there is strong evidence from animal studies that exercise enhances neuronal health and function via the release of growth and neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and insulin-like growth factor 1 (IGF-1) that are involved in angiogenesis, synaptogenesis, and neurogenesis [11]. Exercise is particularly beneficial for the hippocampus, promoting neurogenesis and reduced decline in neural precursor numbers [12, 13]. Exercise has also been shown to reduce amyloid pathology, tau phosphorylation, and cognitive function in transgenic mouse models of Alzheimer’s disease [14].

Significant benefits of physical activity on cognition and reduced risk of dementia have been reported from human observational studies, with higher intensity physical activity showing the strongest effects [15]. However, the majority of studies utilized physical activity questionnaires, thus results may have been influenced by reporting bias. Furthermore, observational studies are unable to determine temporal relationships or cause and effect. The evidence from interventional or randomized controlled trials (RCT), that have mainly examined the effect of exercise is less certain. In brain imaging studies of people without T2DM, as little as 6–12 months of aerobic training led to measurable increases in brain volumes in prefrontal, anterior cingulate (areas serving executive function) [16], and lateral temporal cortices and the hippocampus (serving memory) [16–18]. In studies with cognition as an outcome, a 2003 meta-analysis of interventional studies of exercise (studies of aerobic and/or strength training were included) was found to benefit cognitive function (Hedges g = 0.164 for control groups and g = 0.478 for exercisers) in older people [19]. The largest effect sizes were for the domains of executive function (Hedges g = 0.68), which is the domain most strongly affected by T2DM [20, 21]. However, the numbers of participants in many of the included studies were small (<100 participants), and some studies were quasi-randomized. Importantly, a range of clinical groups were included, making it difficult to determine which clinical conditions may benefit the most from exercise. Since then there has been increasing effort to identify specific groups that may benefit from exercise for brain health.

A recent Cochrane systematic review published in 2015 found no benefit of aerobic exercise on cognition in cognitively healthy older people [22]. This review only included studies that reported measures of fitness, such as VO2 max, 6-min walk test, or 400-meter walk time. Since then, a high-quality RCT of a 24-month moderate intensity exercise program (walking, strength flexibility, and balance training) for cognition in cognitively healthy older people at risk of mobility disability (n = 1635) found no benefit of exercise on the primary cognitive outcome measures of the Digit Symbol Coding Task and the Hopkins Verbal Learning Task-R [23]. It is possible that the intensity of exercise (moderate) prescribed may not have been sufficient to induce changes in
cognition, or that the inclusion of people with physical disability may have limited their ability to reach this intensity. Alternatively, people who are cognitively healthy may not have much to gain, with exercise better targeted at people who are at high risk of cognitive decline.

In contrast, the evidence for a benefit of exercise in high-risk groups for dementia is conflicting. The majority of studies have focused on people with subjective cognitive complaints or a diagnosis of mild cognitive impairment (MCI). A 24-week program of at least 50 min, three times per week of moderate intensity exercise (mainly walking) was efficacious in improving cognitive function in older people with MCI or memory complaints [–1.3 points difference in the Alzheimer’s Disease Assessment Scale-Cog (ADAS-Cog)], with some of this benefit persisting one year after completing the intervention [24]. The Study of Mental Resistance Training (SMART) showed a 6-month progressive resistance training (pneumatic resistance machines, 3 sets of 8 repetitions for most major muscle groups × 2 per week) improved global cognitive function at 6 months (ADAS-Cog relative effect size –0.33) and executive function at 18 months (Wechsler Adult Intelligence Scale Matrices relative effect size: 0.04) [25]. However, a meta-analysis (exercise of any prescribed modality, dose, or intensity, but greater than 4 weeks duration) [26] and a RCT of aerobic exercise (one h/day, three times/week for 12 weeks) [27] published since suggested that there was very limited evidence that exercise improves cognitive function in such people, possibly due to different underlying etiological processes or heterogeneity in subtypes of MCI [26]. Interestingly, in a subanalysis of exercise type in the meta-analysis, two studies of resistance training showed positive effects for memory [26], opening up the possibility that resistance training might target different pathways to aerobic training (discussed further below). Those with T2DM, as compared with such people (e.g., MCI), may represent a distinct group who has a cluster of biological risk factors for cognitive decline that are likely to respond strongly to exercise. In support of a benefit in people with vascular disease, a recent proof of concept RCT in people with mild subcortical ischemic vascular cognitive impairment found that 6 months of three times per week aerobic training versus usual care resulted in improvements in overall cognitive function (ADAS-Cog –1.71 point difference, 95% CI –3.15 to –0.26) [28].

**T2DM MAY BE AN IMPORTANT CLINICAL GROUP TO BENEFIT FROM EXERCISE FOR BRAIN HEALTH**

There are a number of common risk factors for T2DM and dementia that can specifically be targeted by exercise. In developed nations, the highest estimated population-attributable risk is for physical inactivity (~21%), which is highly prevalent in people with T2DM [4]. In this section, we make a case for why people with T2DM may be an important group to target with exercise for brain health.

The underlying pathways in T2DM brain failure appear to be both neurodegenerative and vascular [29, 30]. T2DM is associated with lower brain volumes [30], which may be partially driven by higher levels of cerebrospinal fluid (CSF) tau [31]. Importantly, smaller hippocampal and total grey matter volumes appear to partially mediate the association between T2DM and poorer cognitive function [30]. Animal models have demonstrated that insulin resistance and diabetes impairs synaptic plasticity and neurogenesis in the hippocampus [32, 33], potentially via reductions in levels of brain-derived neurotrophic factor [34]. The association between T2DM and amyloid-β (Aβ) accumulation is less certain with some studies showing higher levels of hippocampal neuritic plaques only in those with both T2DM and the APOE4 gene [35], whereas others found no association between T2DM with Aβ levels in the CSF [31], measured on Pittsburgh compound B scans [36] or at autopsy [36]. In further contrast, a postmortem study showed lower levels of amyloid plaques in people with T2DM compared to those without T2DM [37]. Animal models have shed further light on the topic by crossing Alzheimer’s disease transgenic mice with diabetic mice, with results suggesting that diabetes increased inflammation and severe amyloid angiopathy, but not Aβ burden [38]. Interestingly, findings also suggested amyloid pathology may worsen diabetes [38]. As outlined in the previous section, exercise may benefit the above neurodegenerative pathways, particularly in the hippocampus, potentially providing an important way of slowing progression to dementia in people with T2DM.

In humans, the interaction between Alzheimer’s disease type pathology and cerebrovascular disease is likely to be additive and responsible for greater cognitive impairment [39]. T2DM is associated with cerebrovascular disease, including higher numbers
of cerebral infarcts, white matter hyperintensities, microbleeds, and reduced white matter integrity [29, 30, 40]. There are a number of vascular and metabolic mechanisms that are thought to be involved in T2DM-related dementia (further in-depth discussion can be found in other articles in this series) and are known to benefit from exercise. However, the evidence that these exercise-related improvements may also result in preserved brain function is still limited.

Dysglycemia, hypertension, central adiposity [41], chronic inflammation [42], reduced peripheral and cerebral insulin sensitivity, and defective signaling [33, 38, 43] are associated with both T2DM and dementia. Insulin can cross the blood-brain barrier and is also synthesized in the brain [33]. It has a role in synaptic health, particularly in the hippocampus [44, 45]. Insulin receptors are ubiquitously present in the brain, and neuronal insulin resistance is associated with impaired amyloid clearance [46] and increased tau phosphorylation [43, 45]. Other potential targets include advanced glycation end products [47] and abnormal central hemodynamics [48]. The likelihood of multiple interacting or additive mechanisms that are prevalent in T2DM, as well as risk factors for dementia, calls for therapeutic approaches that can address more than just individual targets to reduce the risk of T2DM-related dementia. Exercise is an extremely promising intervention in this regard (Fig. 1).

There is now compelling evidence to support the key role of regular exercise in the prevention and management of T2DM and its related risk factors [8]. Exercise, within 3–6 months, improves glycemic control, peripheral insulin sensitivity (and for at least 48–72 h after acute exercise [49]), and reduces fat mass and cardiovascular risk [8], all potential mechanistic factors associated with cognitive decline in T2DM. Animal studies add further evidence for beneficial effects with exercise improving hippocampal insulin receptor/signaling both with acute bouts and regular training [33, 50]. Interestingly, increased insulin in the brain appears to regulate peripheral insulin sensitivity, with growing evidence it may be produced in the brain [51] or by peripheral insulin crossing the blood-brain barrier, indicating the usefulness of targeting both locations [33, 52]. Further evidence from animal studies found that three months of treadmill training in leptin receptor-deficient db/db mice (obesity and diabetes) reduced neuroinflammation and reversed cognitive and synaptic plasticity impairments among hippocampal neurons to levels found in control mice [53]. Others have also demonstrated cardiovascular and metabolic benefits from exercise-induced improvements in advanced glycation end products [54], central hemodynamics [55], and inflammatory profiles [54]. In mice, exercise was able to reduce the negative effects of a high fat diet on reactive oxygen species, brain derived neurotrophic factor, as well as synaptic and neuronal plasticity [56]. In addition, a recent review paper by Bertram et al. [57] outlined possible preventative effects of regular exercise on improving endothelial function and brain capillarization, attenuating oxidative stress, reducing ceramides, improving Aβ efflux, and increasing testosterone levels—factors associated with dementia and T2DM.

**Fig. 1.** Effects of regular exercise on brain and risk factors of dementia and Alzheimer’s disease (AD) such as metabolic syndrome, type 2 diabetes mellitus, hypertension, and atherosclerosis. Exercise directly affects the brain to increase cognitive demand and brain health, prevents and treats the risk factors, and helps patients with dementia and AD by improving or maintaining their quality of life (QOL) and physical fitness and functions.

**TYPES OF EXERCISE THAT MAY BENEFIT BRAIN HEALTH IN T2DM**

Exercise can incorporate many different types of activities, and the effects of these on the brain and other organs may be different. Even for the same exercise type, how the exercise is performed in terms of intensity, duration, frequency, environment (e.g., temperature, altitude, place), and social aspects (e.g., exercise with other people), could influence outcomes. For example, when walking, velocity, duration, frequency, where it is performed (e.g., treadmill versus park or bush), and whether it is performed alone or with someone else could influence the stimulus to body systems including the brain.
Even for the same physiological intensity (e.g., heart rate level during exercise), it may be that stimuli to the brain differ between playing tennis and jogging. These intricacies of exercise on brain health have not comprehensively been considered as of yet. In this section, we focus on exercise types that have shown benefit for T2DM – namely aerobic and resistance training.

Exercise is beneficial for managing T2DM. A 2006 Cochrane review, which included 14 RCTs with a total of 377 participants, compared the independent effect of exercise training versus no training on T2DM [8]. The training interventions were 8–10 months in length and consisted of progressive aerobic training, strength training, or a combination of the two, with typically three training sessions per week. Compared to the control group, the training interventions showed a significant improvement in glycemic control in the form of a reduction in HbA1c of 0.6%. A further 2012 systematic review [58] assessed the effect of supervised exercise interventions on lipid profiles and blood pressure control in patients with T2DM. It was concluded that supervised exercise was effective in improving blood pressure control, lowering low-density lipoprotein cholesterol (LDL-C), and elevating high-density lipoprotein cholesterol (HDL-C) levels.

The above reviews did not distinguish between aerobic and resistance training. Traditionally, aerobic training has been advocated as the most suitable form of exercise for people with T2DM. However, previous work has demonstrated that high intensity progressive resistance training alone is also highly beneficial for improving glycemic control and muscle mass [59]. Both aerobic and resistance exercise are now recommended as first line treatment for T2DM [8, 60].

Aerobic exercise

Aerobic exercise is designed to improve cardiovascular fitness and includes activities such as bicycling, walking, running, and swimming. Aerobic exercise can improve fitness (VO2max) [61], HbA1c [8], obesity [62], and blood pressure [63], factors associated with both T2DM and dementia. Intensity of aerobic training may be important. A meta-analysis of aerobic type exercises found an association between higher intensity exercise and a decrease in HbA1c [61]. Human observational studies have also found a beneficial effect of exercise intensity on dementia risk [15], and animal studies have demonstrated benefits of higher intensity aerobic exercise on cortical soluble Aβ40 and Aβ42 [64]. In contrast, in mice, mild exercise but not intense exercise benefited hippocampal neurogenesis [65]. High intensity interval training involves short intervals of vigorous exercise separated by periods of rest or recovery and may improve both fitness [66] and adherence [67] to exercise compared with moderate intensity continuous exercise. In addition, interval training may improve glycemic control to a greater extent in T2DM [68]. Aerobic exercise appears to benefit attention and processing speed, executive function, and memory in both healthy individuals and those with MCI in some studies [69], as well as total brain and hippocampal volumes [16–18]. The mechanisms at play may be through improvement in cardio-metabolic profiles in addition to increased cerebral blood flow, BDNF, angiogenesis, synaptogenesis, and neurogenesis [11, 70]. A study of aerobic exercise in healthy older people found that increases in various neurochemicals (BDNF, vascular endothelial growth factor (VEGF), and IGF-1) were associated with improved temporal lobe functional connectivity [71]. Although prior studies have examined aerobic exercise at moderate to vigorous intensities, no studies to our knowledge have examined whether high intensity training is more beneficial for brain health than moderate intensity exercise in humans, particularly in those with T2DM.

Resistance exercise

Resistance exercise training aims to improve muscle mass, strength, or power (for example lifting weights). Resistance exercises consist of static (isometric), shortening (concentric), or lengthening (eccentric) muscle contractions. For example, when walking down stairs, the front thigh muscles are lengthened when supporting the body’s weight, thus this is eccentric exercise. In contrast, when walking up stairs, the front thigh muscles shorten, which is a concentric exercise. The majority of studies have not differentiated between these types of resistance exercises. We present evidence for these studies and then focus on why eccentric exercise might provide additional benefits over concentric training for T2DM and brain health.

Muscle weakness and low muscle mass are common in people with T2DM [72]. Muscle is one of the most important target tissues for insulin; therefore, people with T2DM will have significant benefits increasing muscle mass in terms of improv-
ing insulin sensitivity. In addition, there are a number of metabolic factors that are associated with T2DM and dementia that have also been shown to respond to resistance training. A 2010 meta-analysis included 13 RCTs that examined the effect of resistance training on parameters related to the metabolic syndrome and dementia such as obesity, HbA1c, and systolic blood pressure, but no effect on total cholesterol (TC), HDL-C, or LDL-C [73]. A further systematic review (9 randomized trials, 372 participants with T2DM) of progressive resistance exercise found a small reduction in HbA1c compared to control, but no difference compared to aerobic exercise [74]. Resistance exercise also increases secretion of myokines including IL-6, BDNF, IGF-1, Irisin, and VEGF, of which some, such as IL-6, cross the blood-brain barrier and may mediate neuroplasticity and anti-inflammatory responses in the brain [75, 76].

Studies have also shown that resistance training may improve cognitive function. Improvements in global and executive cognitive function have been found after a 6-month progressive resistance-training program compared to a sham program in people with mild cognitive impairment [25]. Intensity and frequency of resistance training has also been investigated. Cassilhas et al. compared two different intensities of resistance training (6-months 3 times per week of 50% or 80% of 1RM), finding that both groups improved short term memory, attention, and executive function compared to control [76]. Liu and Ambrose et al. examined whether 12 months of either once per week or twice per week progressive resistance training benefited executive function in older women [77], finding positive effects in both groups compared to a balance and tone group. These results persisted 1 year after ceasing the intervention [78]. However, brain volume was reduced in both groups at 12 months [77]. Interestingly an animal study that compared aerobic and resistance training with a control and sham group [70] reported improved memory performance as measured by the Morris water maze in both training groups. Although hippocampal IGF-1 improved in both the resistance and aerobic groups, hippocampal BDNF/TrkB and β-CaMKII (important for synaptic plasticity and memory consolidation) only improved in the aerobic group, whereas resistance training appeared to work via the IGF-1/IGF-1R and AKT pathways (important in angiogenesis and neuronal survival). This suggests different types of exercise may work via different pathways on the brain, with a combination potentially providing the greatest effect.

### Eccentric exercise

In a recent study [79], we compared eccentric and concentric resistance exercise of the knee extensors in healthy elderly men aged between 60 to 76 y for changes in insulin sensitivity and blood lipid profiles after 12-week training. The exercise consisted of 30–60 eccentric versus concentric contractions of the knee extensors for both legs performed once a week, and the intensity was progressively increased over 12 weeks. After 12-weeks of training, HbA1c, homeostasis model assessment (HOMA) and oral glucose tolerance test (OGTT) showed improvement of insulin sensitivity for the eccentric training group only. Greater decreases in fasting triacylglycerol (TG), TC, and LDL-C, and increases in HDL-C were evident for the eccentric compared to the concentric training group.

In a subsequent study [80], we compared descending stair walking (DSW), a typical eccentric exercise, and ascending stair walking (ASW) for changes in insulin sensitivity and lipid profiles using overweight elderly (≥60 y) women. An elevator was used to take the participants from the 1st to 5th floor for DSW, and the 5th to 1st floor for ASW. DSW and ASW were performed twice a week for 12 weeks by increasing the volume gradually (e.g., 1st week: 2 reps/session, 12th week: 24 reps/session, 1 rep = 110 stairs). The average heart rate during DSW (90 beats/min) was lower than that of ASW (111 beats/min). Decreases in resting glucose, insulin, HOMA, HbA1c, TG, TC, LDL-C, and OGTT (area under the curve), and increases in HDL-C were greater after DSW than ASW.

These preliminary results suggest that eccentric exercises are beneficial to patients with T2DM. If eccentric exercise training is proven to be effective for preventing and treating T2DM, this may also be significant for the brain. It is also important to note that eccentric muscle contractions appear to require more cognitive demand than concentric contractions. If more cognitively demanding exercises benefit the brain more [81], eccentric exercise may be beneficial for brain health too.

### Combination programs

A systematic review and meta-analysis from 2014 compared resistance exercise and aerobic exercise, and concluded that there was no evidence that resistance exercise differs from aerobic exercise in impact on glucose control, cardiovascular risk markers, or...
safety [82]. Using one or the other type of exercise for T2DM may be less important than doing some form of exercise. However, some studies have found doing both forms of exercise may have incremental benefits on glycemic control [83, 84]. Interestingly, a combination of both resistance and aerobic training in older people has also been found to be most beneficial in improving cognition [19]. In rats, both aerobic and resistance training improved learning and spatial memory after 8 weeks, but did so with differing signaling pathways [70], suggesting a combination of these types of exercise might provide the most benefit. It is important to note that with all forms of exercise, without progression of intensity and volume over time, the effects of exercise plateau. In athletes, periodization, which involves progressive cycles of various aspects of training during a specific period, is often used to reach peak performance. These concepts should be applied to clinical populations.

It would also be interesting to investigate whether the combination of physical exercise with cognitive training would add additional benefit to the brain in T2DM, although this has been unsuccessful when combined with resistance training in people with MCI [25] or with aerobic exercise in people with cognitive complaints [27]. It is possible that the timing of exercise may be important before carrying out a cognitive training program. (e.g., exercise may prime the brain to learn), but this has not been examined in long term studies.

WHAT IS THE EVIDENCE FOR A BENEFIT OF EXERCISE FOR BRAIN HEALTH IN T2DM?

The Fremantle Diabetes Study showed that any exercise was associated with 74% lower odds of cognitive decline in older people with T2DM (odds ratio 0.26, 95% CI: 0.09–0.73) [85]. There are few RCTs examining this topic, but emerging evidence is promising. One small trial (n = 28) of exercise in people with glucose intolerance (not necessarily T2DM), found aerobic training over 6 months improved executive function (Cohens f = 0.36–0.39), but not memory [86]. In the LIFE trial, exploratory post-hoc analysis found that in people with T2DM (n = 415), 24-month moderate intensity exercise (walking, strength, flexibility, and balance training program) compared to health education resulted in better scores on the Modified Mini Mental Status Examination (mean intervention effect 0.114 SD, 95% CI 0.007, 0.222) and HVLT-D (0.208, 95% CI 0.03, 0.387), but not executive function (0.103, 95% CI –0.019, 0.233) [87]. A definitive trial is now required with cognition as a primary outcome measure and comprehensive measurement of potential mechanisms. An additional topic to take the field forward will be to determine who might benefit from exercise in those with T2DM. Recent reviews have outlined how exercise may not benefit all people with T2DM, or there may be variability in response to exercise [88, 89]. Possible factors to be explored include specific genes such as APOE4, duration or severity of diabetes, baseline metabolic or vascular risk factors, medication use, and skeletal muscle transcriptional profiles [90]. Such information could assist in individualizing exercise programs designed to improve brain health.

Overall, there is observational evidence that physical activity reduces the risk of dementia in the general population, but evidence is mixed from RCT for an effect of exercise on preventing cognitive decline. Potential reasons for mixed results may be the heterogeneous populations studied, or that healthy individuals have little to gain. However, examining the benefits of a progressive exercise program of sufficient intensity in T2DM raises the exciting possibility that exercise also has the potential to preserve brain health in this high-risk group for dementia. Studies of exercise with cognitive outcomes, in people with T2DM (Australian and New Zealand Clinical Trial Registry number 12614000222640) or other at risk populations such as those with mild cognitive impairment (EXERT NCT02814526) or hypertension (rrAD –NCT02913664) will continue to advance the field in terms of who might benefit from exercise and the potential underlying mechanisms. Animal studies will also be important in better understanding the mechanisms and actions of exercise on the brain in T2DM with the hope of developing additional therapeutic interventions [45].

CONCLUSION

Dementia is a devastating disease of older age, currently with no cure. T2DM is a high-risk group for dementia that is important to target for preventative interventions. We have provided an overview of the evidence that exercise may be an important intervention that addresses multiple mechanisms, including vascular and metabolic risk factors, and improved...
neuronal health. Further studies are necessary to examine the question as to whether exercise can preserve cognitive function in people with T2DM. Furthermore, identifying the most optimal type and dose of exercise to prevent and treat T2DM related dementia is important, as well as whether all or only some people with T2DM will benefit. It is no doubt that performing regular physical exercise is good for cardiovascular health, with promising evidence that exercise might also be good for T2DM related brain health.

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