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Executive Functions abilities in Person with Type 2 Diabetes: A Systematic Review

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A serious health issue is the rising number of individuals with Type 2 diabetes. Cognitive declines have been linked to type 2 diabetes, according to numerous systematic evaluations. But because of the wide range of approaches, standards, and outcomes among various evaluations, it is challenging for researchers to compile a comprehensive picture. In older adults, type 2 diabetes mellitus has been associated with cognitive decline and a higher risk of dementia. The impact of diabetes on cognition in younger people is less well understood. Examining potential disparities in executive function between middle-aged type 2 diabetic patients and healthy controls was the aim of this systematic review. The specific purpose of this systematic review is to examine the nature and existence of the association between executive functions and Type 2 diabetes among middle- aged individuals by examining cross-sectional studies to confirm any indication of a potential causal relationship between these variables. The search for studies comparing type 2 diabetes and cognitive function in patients under 65 to healthy controls was conducted using electronic databases and lists of references from chosen papers. The criteria for inclusion were met by six studies. In various areas of executive function, patients underperformed compared to controls. These executive domains differed in the direction of linkage, though. According to the findings, middle age may be the onset for cognitive decline associated with diabetes rather than being limited to older adults. It is imperative that healthcare systems prioritize the early identification and treatment of diabetes-related cognitive decline.

Keywords*:* Cognitive decline, middle aged, older adults & Type 2 Diabetes

A considerable portion of the global population suffers from type 2 diabetes mellitus (T2DM), a chronic illness that is common. 462 million people worldwide—or 6.28% of the total population—are thought to have type 2 diabetes (Khan et al., 2020). Diabetes is known to raise the chance of dementia and cognitive decline (Mayeda et al., 2013; Allen et al., 2004). According to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, “one’s ability to plan, initiate, sequence, monitor, and inhibit complex behavior” (DSM-IV), EF entails a wide range of advanced cognitive tasks. In the face of distraction, complexity, and stress, executive, or cognitive control, talents enable us to inhibit established behaviors, strategically focus attention, and compose our thoughts. Each element of EF may mature at a different age depending on how quickly it develops throughout childhood and adolescence (Diamond, 2013). To properly carry out these activities, EFs including organizing resources, planning and starting actions, controlling urges, and focusing attention are needed. EFs can become severely weakened as DM advances, which might worsen symptoms even further. It’s

unclear, yet, how EFs and diabetes are related. We cover the relationship between EFs and diabetes in this review, covering physiological, behavioral, psychological, and hereditary aspects in addition to hyper- and hypoglycemia.

The best times for cognitive performance are in early adulthood (De Luca et al., 2003). Declines can start as early as 20 or 30 years old. These declines can occur at any time during adulthood and include verbal and visuospatial memory (Murre et al., 2013), working memory (Park et al., 2002; Hartshorne et al., 2015), face processing (Ghisletta et al., 2012; Parl et al., 2002), reasoning (Salthouse, 2009), and speed of processing (Ghisletta et al., 2012; Parl et al., 2002). Regarding when cognitive capacities peak and decay, there is a great deal of variability.

The first evidence of a link between diabetes and cognitive decline dates back to 1922, when neuropsychological tests were used to compare the cognitive abilities of diabetes patients with those of healthy controls (Miles & Root, 1922). Though it is now generally known that type 2 diabetes increases the risk of dementia and cognitive impairment in older adults (Biessels et al., 2006; Cheng et al., 2012), it is still unclear if diabetes has an impact on cognitive abilities even in middle age. Although the intricacy of the Type 2 diabetes syndrome is widely known, efforts to identify the underlying cause of the disease's cognitive declines are hampered. Diabetes is related with a higher prevalence of conditions like hypertension, hyperlipidemia, macrovascular disease, and depression, all of which may independently be linked to cognitive decline.

Only in middle age is type 2 diabetes a substantial risk factor for dementia; in fact, the correlation between type 2 diabetes and dementia becomes much weaker after the age of 65 (Knopmam et al., 2018; Berg et al., 2006). Although research has demonstrated that type 2 diabetes in midlife can have cognitive repercussions up to 20 years later, it is unclear at what age cognitive deficits in type 2 diabetics first appear. Notably, there aren't many effective preventative strategies available for those with type 2 diabetes in their middle years (Briggs et al., 2020). There is a dearth of information on which midlife type 2 diabetes patients are most vulnerable, and knowing this information could be vital to the creation of these strategies.

There are extremely few or none that concentrate exclusively on middle-aged individuals and old age individuals, despite a plethora of reviews and studies on older patients with diabetes and a variety of conclusions. The purpose of this systematic review is to shed light on the connection between type 2 diabetes and executive abilities in individuals 80 years of age or younger in order to raise awareness and enhance treatment of the cognitive decline associated with diabetes. Finding potential variations in the most prevalent cognitive domains between middle-aged patients with type 2 diabetes and healthy controls was the specific goal.

Method

In order to perform this review, the author adhered to the current standards for conducting systematic reviews of the literature using "Preferred Reporting Items for Systematic Reviews and Meta-Analyses."

Selection of Studies

An electronic method was used to conduct the literature search. The databases "PubMed," "Science Direct," and "PLOS One" were used to find English-language publications involving human subjects that were released between January 1, 2000, and March 30, 2024. For the purpose of finding the pertinent publications, a mix of search

terms and key boolean phrases, specifically "type-2 diabetes" and "executive functions" or "executive dysfunctions," were used in the searches. By reviewing the citations and abstracts of each study, it was possible to avoid duplication of effort.

The following were the exclusion standards: (1) The article is not accessible in the English language. (2) research on pharmaceuticals; (3) research on interventions; (4) research on animals; (5) case studies; (6) letter, statement, viewpoint, poster, or only abstract accessible; (7) executive functions that were not the subject of the investigation (for example, the study solely looked at how neurophysiological, neuroanatomical, and neurobiological functions were involved in diabetes); (8) The study only looked at dementia or mild cognitive impairment; (9) cognitive abilities not evaluated via a conventional neuropsychological technique; (10) a review or meta-analysis; (11) based on the mean and standard deviation (SD) or age not known, the age of diabetic patients over 65.

Results

Study Selection and characteristics

After scanning three major databases, the total number of articles found was 1,223. 657 unique papers were located, of which 16 passed the title and abstract screening and were deemed relevant. Ten articles were excluded during the full-text screening process because they did not meet the inclusion criteria, (Figure 1). Some research used the same sample participants as other reviews, hence not included; some studies excluded because of the participants with diabetes and depression; three used criteria for depression that was not present at the time of the study; two measured cognitions as an exposure rather than an outcome; two limited the sample to individuals with high cognitive functioning; two did not compare the exposure groups; and one did not include a diabetic participant.

Data Extraction and Management

The required information was separately gathered by the author from the studies: The study design and sampling method, the year of publication, the author(s), the sample sizes, and demographic information about the patient and control groups (such as age, education, and gender distribution), diabetes-related factors (such as glycated hemoglobin (HbA1c) and the length of the disease, and the use of neuropsychological methods. The executive functions contained techniques for assessing mental flexibility, planning, inhibition, and abstract reasoning. The analysis did not include tests that were not categorized. The most thorough article was included and the neuropsychological data were only utilized once in a study involving many papers based on the same people. Data were only extracted for the diabetes and healthy control group in studies where more than two groups were compared.

Table 1. Study Characteristics

Authors	Year	Sample Size	Country	Age Range	Gender	StudyDesign	TestsPerformed
Alkethiri et al.	2021	79	Saudi Arabia	30- 65	Male &Female	Cross- Sectional	CANTABMMSE
Cosway et al.	2009	78	Edinburgh	40-65	Male & Female	Cross -Sectional	NARTRPMAVLT
Nazaribadie et al.	2014	62	Isphahan	35- 60	Male & Female	Cross- Sectional	WCST
Sola et al.	2023	56	Finland	30-65	Male & Female	Cross- Sectional	Tower of London (ToL) Phonemic

							Fluency: P-A-S Semantic Fluency: animal
Dyer et al.	2020	152	Dublin	35-65	Male & Female	Cross- Sectional	MoCACANTAB
Casares et al.	2014	50	Spain	45-65	Male & Female	Cross- Sectional	Trial Making Test & Stroop Test

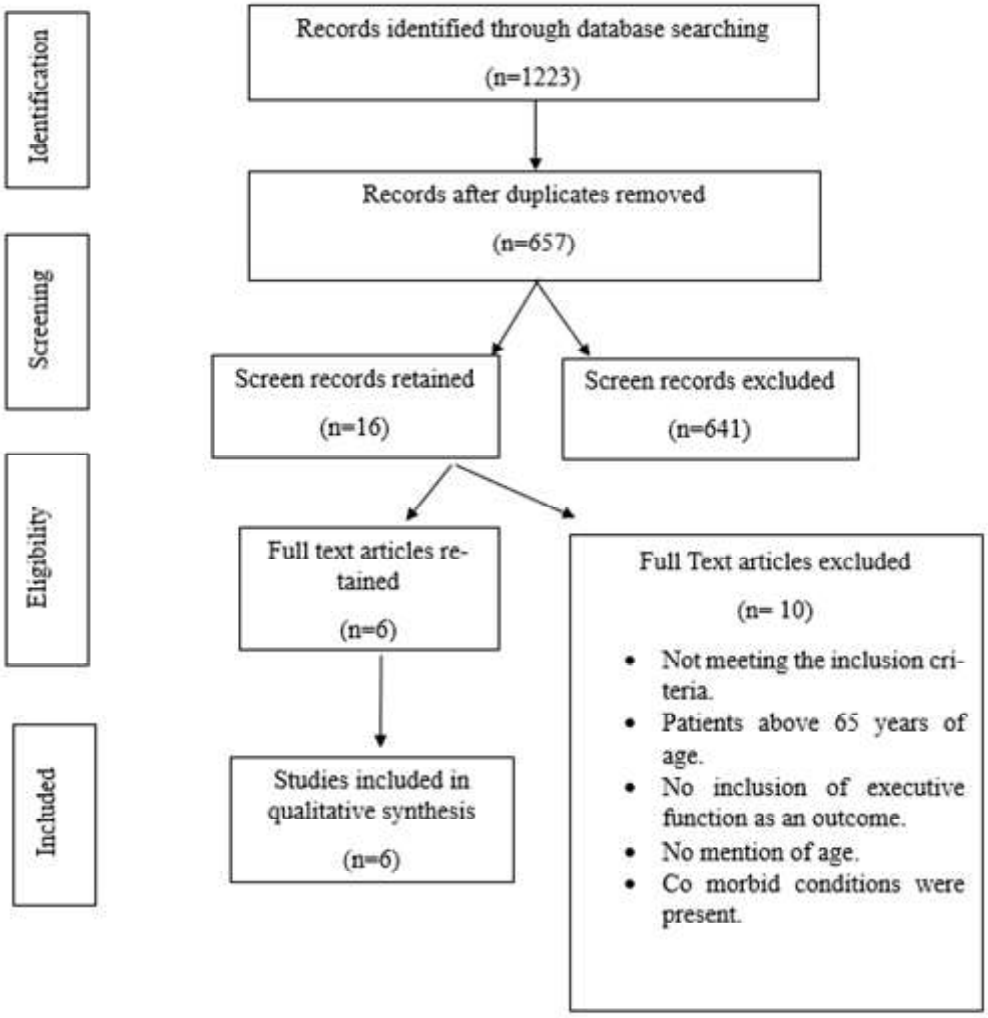

Fig 1. PRISMA Flow Diagram

Discussion

This systematic review looked at the executive abilities of middle-aged people with type 2 diabetes in comparison to healthy controls. In every executive function test, patients tended to do worse than controls. The domains of executive function i.e., inhibition, shifting, decision making and updating showed the biggest standardized mean differences between the groups. There were also notable distinctions observed in overall perception/construction, and attention and memory. The findings support earlier meta-analyses and reviews, which

primarily involved older individuals, and show that planning is among the cognitive domains most affected in type 2 diabetes patients (Awad et al., 2004; Monette et al., 2014; Palta et al., 2014; Reijmer et al., 2010; Van den Berg et al., 2009). The observation aligns with earlier findings as well (Palta et al., 2014; Reijmer et al., 2010; Sadanand et al., 2015; Vincent & Hall, 2015). Though the results were statistically significant in both instances, a somewhat greater effect was discovered in the subdomain measuring inhibition, mental flexibility, planning, and abstract reasoning than in the verbal fluency subdomain.

In light of the results on the patients' worse performance in executive functions, it is possible to interpret the significant impacts observed in the domains of working memory and attention/concentration as being consistent. According to Alvarez and Emory (2006) and Diamond (2013), attention and working memory are also believed to play a part in executive functions, which explains why all three of these domains are so closely related. According to Tomlin and Sinclair (2016), maintaining a healthy diet, exercising, setting and achieving treatment goals, and adhering to medication are just a few of the executive function-related skills that patients with diabetes must possess. As a result, the clinical significance of these patients' significantly lower performance levels should not be overlooked. The domains of executive functioning did not show a significant correlation between age and effect size.

In every tested executive function, the overall performance of the patients was surprisingly worse than that of the controls. When evaluating the results, though, a few things need to be taken into account. Cross-sectional and case-control studies appear to have bigger impact sizes than population-based and longitudinal studies, according to some data obtained by Monette et al. (2014). Given that the majority of the studies in this systematic review were cross-sectional in nature, it's likely that the performance disparities between the groups have been exaggerated. However, it's also likely that younger ages are when the consequences of diabetes on cognitive abilities become more noticeable. For instance, diabetes has been linked in some studies to greater relationships with cognitive functions in younger individuals than in older individuals. This finding may be due to the fact that aging and increased morbidity also affect cognitive functions in older non-diabetic controls (Van Eersel et al., 2013; Winkler et al., 2014). The perspective aligns with research indicating that type 2 diabetes does not correlate with a faster pace of cognitive decline; rather, cognitive decline may begin earlier in the course of the illness. (McGrimmon et al., 2012). Nonetheless, opposing viewpoints do exist (Reijmer et al., 2010).

This study has the advantage of being the first to examine executive functioning in middle-aged individuals with type 2 diabetes in a systematic manner. Also, this study has considered the effect of comorbidities. As such, it offers a valuable foundation for further research in this field. There are a few restrictions on this systematic review i.e., generalization was challenging due to the small number of research considered. Another obstacle to generalization is the fact that participants in the studies came from various cultural backgrounds and the studies were conducted in different nations. However, this can also be considered as a strength of the work, as the inclusion of research from several nations increases the systematic review's external validity.

From a societal perspective, the findings of this study are quite significant. The results suggest that we might anticipate a higher incidence of cognitive impairments in the working age population as well, given

that the prevalence of diabetes is rising quickly and in younger age groups globally (International Diabetes Federation, 2015). Thus, additional study is required to validate these findings and provide insight into cognitive symptoms in the initial phases of type 2 diabetes. More research should examine how cognitive symptoms appear at various ages and stages of diabetes. It is plausible that the correlation between diabetes and cognitive decline may differ based on age in specific cognitive domains, as per the findings of this study.

Conclusion

Conclusively, the findings of this investigation indicate that cognitive symptoms associated with type 2 diabetes are not exclusive to the elderly; rather, they may manifest as early as middle age across multiple cognitive domains, including executive skills. It is imperative that healthcare systems prioritize the early detection and management of cognitive symptoms associated with diabetes mellitus, and acknowledge cognitive decline as a plausible consequence of the disease.

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