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NEUROPSYCHOLOGICAL UNDERSTANDING OF EXECUTIVE FUNCTIONS AND DEMENTIA IN ELDERLY WITH DIABETES MELLITUS TYPE 2

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Abstract: Introduction: Executive Functions (Fes) and Dementia in the elderly with Type 2 Diabetes Mellitus (DM2) are important public health issues in the world because they are directly linked to the quality of life, independence, ability to plan activities of daily living, social relationships and leisure of these individuals, although it needs more studies. **Aim:** to describe and analyze scientific articles on the relationship between EFs and Dementia in elderly people with DM2, point out evidence, and promote in-depth and useful information about the implications, mechanisms, and results of DM2 in aging and worsening of EF deficits and dementia. **Methods:** A bibliographic search was carried out in databases such as PubMed, Lilacs, Scielo, and Scopus, using keywords, "dementia", "type 2 diabetes mellitus" "Executive Functions" and "Neuropsychology". Articles in English and Portuguese were used, without determining publication period, containing data on the author(s) and year, type of study and sample, objective(s), and main results. **Results:** DM2 impairs EFs in elderly people and contributes to the progression of Dementia. This neuropsychological dysfunction affects neurocognitive, sensorimotor, behavioral, emotional, and social skills. **Conclusion:** There is a significant relationship between EF deficits and dementia in the elderly with DM2. More studies are needed to elucidate such relationships. Early interventions are suggested to delay the onset and control of DM2, to prevent some of its adverse effects on EFs and worsening of dementia. Neuropsychological diagnosis of EFs in the elderly with DM2 is indicated to propose neuropsychological rehabilitation and better quality of life in these patients.

Keywords: Dementia; Type 2 Diabetes Mellitus; Executive Functions; Neuropsychology.

INTRODUCTION

Executive Functions (EFs) and dementia in the elderly with DM2 are relevant disorders due to their prevalence and impacts on the health and quality of life of these populations in the world with increasingly longer life expectancy. For Cristofori I and colleagues (2019), EFs are part of a set of cognitive and behavioral processes, such as verbal reasoning, problem-solving, planning, sequencing, sustained attention, resistance to interference, use of feedback, multitasking, cognitive flexibility and the ability to respond to new stimuli. Structural changes within the brain in people with DM2 cause white matter lesions, subcortical and subcortical ischemic changes, and intracerebral atrophy that present clinically as impaired memory, disorientation, and decreased processing speed (Blackwood et al., 2019; Guarino et al., 2019; Guarino et al., 2020; Choi et al.,2020; Theodosiou et al., 2022).

Studies by Cansino et al., 2018 and Sakul et al., 2018 show that EFs are also compromised in chronic diseases such as diabetes, emphasizing that EF deficits with increasing age, potential factors such as body mass index (BMI), and intake of processed foods and alcohol are indirectly involved in this process via the cardiovascular system.

The Diabetes Atlas published by the International Diabetes Federation (IDF, 2021) reports that 537 million adults worldwide are living with diabetes – and this number is expected to increase to 643 million in 2030 and 783 million in 2045; In Brazil, 15.7 million adults live with diabetes, generating high health expenditures, since it is already the third largest country in the world, with estimated costs equivalent to USD 42.9 billion.

Even more, Chatterjee, Khuntiand, and Davies (2017) refer in their article that in Brazil, DM2 is responsible for more than 90% of patients with diabetes and leads to microvascular and macrovascular complications that cause deep psychological and physical suffering for patients and caregivers. Nearly a third (32%) of people living with diabetes in Brazil are undiagnosed and at risk of serious illness, which leads to complications such as heart attack, stroke, kidney failure, blindness, and lower limb amputation.

DM2 patients have shown cognitive impairment attributable to their disease. Both hypoglycemia and hyperglycemia have been implicated as a cause of cognitive dysfunction, although the pathophysiological mechanisms underlying these complications are not very well understood and need further research.

Symptoms such as decreased psychomotor speed, EFs, verbal and working memory, processing speed, complex motor functioning, visual retention, and attention are very common in elderly people with DM2. Notably, the world scientific literature points out that patients with Dementia and DM2 tend to have an almost twice higher risk of neuropsychological dysfunctions and brain damage than individuals without a diagnosis of diabetes, in particular, impairments in certain tasks related to EFs, which indicates a possibility of brain pathology (Luria et al., 1973; Rucker et al., 2012; Vincent, Corita and Hall, 2015; Sadanand and Balachandar, 2016; Callisaya, 2019; Cerezo et al., 2018; Guarino et al., 2019; Peña-González, 2020; Backeström, 2020; Teixeira et al., 2020.

Importantly, people with diabetes are at greater risk of cognitive decline, to the detriment of the metabolic and vascular disorders of the disease that affect brain function, due to prolonged exposure associated with other potentially harmful factors, which leads to irreversible cognitive declines over time, a consequence of the aging process, which can progress to dementia, both vascular dementia, and Alzheimer's dementia, according to Nici and Hom (2018).

DM2, as a chronic medical condition, largely depends on the patient's self-care and the management of their condition to achieve optimal control. Declines in the cognitive domains of memory and EFs result in sequelae associated with the general mismanagement of DM2. Furthermore, poor management of blood glucose levels in the form of hypoglycemia increases the risk of cognitive dysfunction, confusion, dizziness, and poor coordination, which contributes to the emergence of injuries and falls in the elderly (Callisaya et al., 2019; Thabit et al., 2012).

Thus, to understand the possible presence of cognitive, emotional, behavioral, and social impairments, this study aims to verify the characteristics of the main empirical studies, indexed in the period from 2000 to 2022, which focus on the relationship between EFs and dementia in elderly people with DM2, by a need to contribute with a deepening of useful information on the mechanisms and results of why some diabetic patients have a decline in these neuropsychological functions, since it has a significant impact on activities of daily living, worsening of dementia and mortality. As DM2 progresses, EFs can become significantly impaired, which can further exacerbate symptoms. However, the link between EFs, DM2, and dementia is unclear.

METHODS

The methodological design of this study was characterized by a literature review. According to Casarin et al. (2020), this type of study aims to synthesize the scientific knowledge produced and consolidated it into different themes. Thus, the bibliographic search was performed in the following databases: PsycINFO, PubMed, Biological Abstracts, Medline, Web of Science, Science Direct, and Virtual Health Library. These bases were chosen because they are the main ones on the researched subject. The keywords used were: Diabetes Mellitus Type 2, elderly, executive functions, cognitive deficits (Type 2 diabetes, old or older, diabetes cognitive functions, diabetes type 2 elderly, cognitive flexibility). The search was carried out between the years 2002 and 2022 and the selection of articles followed the following inclusion criteria: (a) longitudinal studies and/or case-control studies (experimental group and control group), open studies (experimental group,) and cohort, review articles; (b) samples made up of individuals over 60 years of age and with a clinical diagnosis of DM2; and (c) studies containing cognitive functions as an outcome variable. Exclusion: (a) they were published outside the period of interest, and (b) studies composed of heterogeneous samples regarding the pathology or that did not aim to verify the impact of DM2 on executive functions in the elderly. Finally, the references of the articles found were evaluated, aiming to identify previous studies.

DIABETES MELLITUS TYPE 2

DM, for Guyton and Hall (2006), is a metabolic syndrome that belongs to a heterogeneous group of dysfunctions in the mechanism of carbohydrate metabolism, presenting in common the increase in blood glucose. This increase, in turn, is the result of defects in insulin action and insulin secretion, or both conditions simultaneously.

Insulin resistance (IR) according to Freeman and Pennings (2021) and Deacon (2019) predates the development of DM2 by 10 to 15 years and results in a compensatory increase in endogenous insulin production. Therefore, high levels of endogenous insulin are associated with IR and result in weight gain, which in turn accentuates IR. The authors describe that IR is primarily an acquired condition related to excess body fat, although genetic causes have also been identified. The authors emphasize that the metabolic consequences of IR can result in hyperglycemia, hypertension, dyslipidemia, visceral adiposity, hyperuricemia, elevated inflammatory markers, endothelial dysfunction, and a prothrombotic state.

Punthakee et al. (2012) cited that insulin (I) is one of the main hormones produced by the ß cells of the pancreas and, like its receptors, is present in several tissues of the body, including the central nervous system. In this environment, it crosses the blood-brain barrier and is capable of interfering with brain function by modulating local metabolism, neuronal growth, and differentiation, synaptic transmission, and memory and learning formation, therefore, it seems logical that insulin is related to cognitive health.

Umegaki (2019) points out that (IR) in the brain may be involved in cognitive impairment or DM-related dementia, as these elderly patients are frail, have renal dysfunction, low adherence to treatment, high risk of developing hypoglycemia, which in turn can induce cognitive dysfunction, which carries a high risk of dementia.

DM is highly prevalent throughout the world and has caused a significant number of deaths among the population. Key Global Findings from the 10th Edition of the Atlas of Diabetes in the Year 2021 report that this pathology is a significant global challenge to the health and well-being of individuals, families, and societies. According to data from these surveys (IDF, 2021), 537 million adults (20-79 years) are living with diabetes - 1 in 10. This number is expected to increase to 643 million in 2030 and 783 million in 2045. More than 3 in 4 adults with diabetes live in low- and middle-income countries. Diabetes is responsible for 6.7 million deaths in 2021 - 1 every 5 seconds. Diabetes has caused at least

$966 billion in healthcare spending a 316% increase over the past 15 years. 541 million adults have glucose intolerance (IGT), which puts them at high risk for DM2. DM2 is the most prevalent diabetes subtype, accounting for approximately 90% of cases (Chen et al., 2011; Hu and Jia, 2018).

Two main pathophysiological mechanisms characterize DM2: insulin resistance, especially in skeletal muscle and liver, and defective insulin secretion from the pancreas (Chatterjee and Mudher, 2018). However, not all disease-causing pathways are fully understood, as DM2 is a complex disorder resulting from an interaction between genes and the environment.

In this sense, the pathophysiology of DM2, as pointed out by Milech, Oliveira, and Vêncio (2016), involves complex interactions between genetic predisposition and environmental risk factors. As is known, there is a close relationship between obesity/overweight and the risk of DM2. The distribution of body fat also influences the risk of disease, with abdominal obesity being the variety associated with the highest risk. Other known risk factors include a sedentary lifestyle, hypertension, dyslipidemia, a history of gestational diabetes, and age.

Furthermore, it is important to note that Luna et al (2021) also describe biomarkers or risk factors for cognitive decline in diabetic patients, classifying them into three aspects: serum molecules or relevant complications, changes in functional or metabolic by neuroimaging tools and genetic variants. They also cite factors related to impaired glucose metabolism, insulin resistance, inflammation, comorbid depression, micro/macrovascular complications, adipokines, neurotrophic molecules, and Tau protein, which present significant changes in diabetic patients with cognitive decline. In addition, age, height, obesity, diastolic blood pressure, smoking, chronic kidney disease, vascular disease, low HDL cholesterol, high levels of triglycerides and glycosylated hemoglobin (HbA1c) is associated with an increased risk of neurological complications in patients with DM, especially polyneuropathy.

Research on diabetes, cognitive impairment, glucotoxicity, and dopaminergic dysfunction, carried out by Pignalosa et al (2021) shows that the neurotransmitter dopamine (D) plays an important role in cognitive function, as poor control of diabetes results in glucotoxicity, causing complications of multiple systems and organs, with consequent cognitive decline in patients with diabetes.

Interrupted neuroplasticity and impaired energy metabolism in DM2 have severe brain complications, according to Rucker, McDowd, and Kluding (2012), as there is strong evidence that elderly people with this disease have deficiencies in the planning, coordination, sequencing, and monitoring of cognitive operations, collectively known as EFs. Although poorly understood, disorders in the EFs can contribute to gait abnormalities and increased risk of falls, functional impairments, and disabilities associated with DM2 (Cuevas, 2017).

DEMENTIA

Dementia or Major Neurocognitive Disorder Maior (TNM), according to the new edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V, 2015), is a common neurological condition that affects many people in old age (Gale, Acar and Daffner, 2018). However, the main limitation of DSM-5 is that it requires intellectual deficits to be severe enough to impair social or occupational functioning. It therefore necessarily draws an arbitrary line between insanity and the lack of it. In clinical settings, patients often go through stages of intellectual decline, including cognitive deficits that occur

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with normal aging, mild cognitive impairment (CCL), and early dementia.

Ramsey and Arnold (2022) and Marques Dias (2017) states that Dementia is a chronic and progressive encephalic pathology. It is characterized by several deficiencies of acquired superior cortical functions, such as memory, thinking, orientation, comprehension, calculation, ability to learn, language and judgment. Also, decline in intellectual capacity and cognitive impairments accompanied or preceded by losses, in varying degrees, of emotional control, social conduct, and motivation.

Thus, the accurate diagnosis of dementia remains a challenge for health professionals, as mentioned by Lam et al (2019), since there is no definitive diagnostic test to identify it, but they point out the importance of this pathology being detected at an early stage, indicating that timely assessments are carried out to initiate appropriate therapy with patients able to participate in management decisions. Another point highlighted by the authors refers to the fact that the initial step in the evaluation of a patient with suspected dementia should be to obtain a focused history of cognitive and behavioral alterations, followed by a complete physical examination. Delirium, depression and MCI should be considered in the differential diagnosis of memory impairment. In addition, many useful screening tools for a diagnosis are now available for dementia, such as neuroimaging.

In the diagnosis of dementia, as Gale, Acar e Daffner (2018) must include risk factors, neurological, neuropsychiatric, and primary medical conditions. The authors state that neurodegenerative dementias, such as Alzheimer's dementia (AD) and Mild Cognitive Deficit (MCI) are more common in the elderly, while traumatic brain injuries and brain tumors are more common in younger adults.

Concerning the anatomical bases involved in the diagnosis of dementia, Towsend (2011) and Bazarella (2010) describe that these can be classified into cortical, subcortical, and white matter dementia. The first is characterized by the incidence in the cerebral cortex and by impairment in specific domains of cognition, perception, and language (aphasia, agnosia, acalculia, apraxia). On the other hand, subcortical dementias present damage to deeper brain structures that will influence the cortex. Difficulty in language with limitation in the speed of communication and the ability to find words and slow repetition is common, as well as the presence of motor signs and memory impairments.

Among specific potentially modifiable risk factors for dementia, Livingston et al. (2020) and Falk et al. (2019) describe risk factors in early life (education), middle age (hypertension, obesity, hearing loss, traumatic brain injury, and alcohol misuse), and later in life (smoking, depression, physical inactivity, social isolation, diabetes, and air pollution), although some factors of advanced age, such as depression, have a bidirectional impact and are also part of the prodrome of dementia.

The aforementioned authors also describe that approximately 40% of all cases of dementia can be explained by these risk factors. They also point out two possible mechanisms of protection against dementia, such as: reducing neuropathological damage or increasing and maintaining the cognitive reserve. The latter is influenced by early life factors, such as a high level of education, while risk factors in middle age and late-life can trigger neuropathological damage. Treating hypertension and diabetes, quitting smoking, reducing mid-life obesity and air pollution, and preventing head injury are interventions that protect against cerebrovascular damage and the neuroinflammation cascade associated with amyloid pathology. In this sense, elderly people in good physical health can bear a greater burden of neuropathological damage without cognitive impairment. Thus, culture, poverty, and inequality are important obstacles and drivers of the need for change in cognitive reserve (CR). There is also the fact that the elderly is more vulnerable to illness because they are more prone to events such as bereavement, the decline in socioeconomic status such as retirement, or a disability. All of these factors can result in social isolation, loss of independence, loneliness, and psychological distress (Livingston et al., 2020; Falk et al., 2019).

About sex and dementia, Falk et al. (2019) reveal in their research that women are at greater risk of developing dementia and living longer with the disease after its onset. Furthermore, Livingston et al. (2020) assert that older women are more likely to develop dementia than men of the same age, probably in part because, on average, older women had less access to education than older men. Also, Chatterjee et al. (2016) cite in their study that the magnitude of the increased risk of diabetes in Vascular Dementia (VD) was 18% higher in women than in men, possibly linked to selective survival and longevity in women.

On the other hand, Fages-Masmiquel et al (2021) carried out a cross-sectional study in a sample of 1,048,956 people aged 65 years or older on " The effect of age and gender on factors associated with dementia" and the results suggest that the association between medical history of cerebrovascular disease, Parkinson's, depressive disorder or hyperthyroidism and dementia was more pronounced in men, whereas the inverse association between coronary disease, heart failure or smoking, and dementia was significant only in women. A stronger association was seen in younger age groups for most risk factors, but hypertension, coronary heart disease, heart failure, or smoking were negatively associated among older age groups. The authors concluded that gender and age condition the association between risk factors and dementia.

The course of the dementia illness for Almeida et al. (2014) varies between 5 and 10 years and the reduction in life expectancy is around 50%. In addition to impairing the biological functioning of the individual, Lopes and Cachioni (2013) point out that dementia also affects the social side, since the lack of knowledge about the general conditions of the disease leads to prejudices that affect the patient's family, causing an increasing burden on the elderly and the family, in addition to representing an enormous financial cost for the health system.

The multimorbidity, according to Sharma et al (2018) is a major challenge in dementia, not only because people have increased rates of other illnesses, but also because it is particularly difficult to organize care, since the EFs responsible for planning, and controlling actions, memory, etc., are impaired, with important cognitive deficits, which prevent the elderly with dementia from informing their family members or professionals about their symptoms, following self-care plans. These difficulties make them more likely to forget to drink and eat, thus increasing the rates of falls and infections, hospitalizations, and consequent mortality, since they seek little help from primary care, as well as the lack of preparation and knowledge of their family members.

EXECUTIVE FUNCTIONS

Although the term "executive functions" has been used more frequently over the last 15 to 20 years, it has deeper historical roots. Several authors note the important contribution of the Russian neuropsychologist A.R. Luria for the formation of its scientific interest in the study of processes of activity regulation from positions of neuropsychology and roles of the frontal lobes of the brain (Shallice, 1982; Uehara et al., 2013).

The neuropsychologist, Alexandr Romanovich Luria (1966, 1973) mentioned the term FEs in an article published in 1968 (Karpov, Luria & Yarbuss, 1968). Based on clinical findings, he proposed a model of brain functioning composed of three functional units. This complex brain system would be mediated by neuroanatomical and functionally hierarchical regions that, when working together, would regulate all our behaviors and mental processes. In this context, the first unit would regulate basic physiological functions, such as cortical tone, wakefulness, and heartbeat, associated with subcortical structures; The second unit, is related to the posterior areas of the brain, which include the parietal, temporal, and occipital regions, would be responsible for obtaining, analyzing and storing information through visual modalities, auditory and tactile and finally, the third unit would exercise the functions of programming, regulation, and verification of mental activities, comprising, mainly, the frontal lobes.

From the point of view of neurological development based on specific developmental stages related to the phases of greater cortical maturation of the EFs, Luria (1983), points out stages that were thought to interact with environmental stimuli supported by the cultural-historical theory of Vygotsky. Thus, for the author, the consequence of the interaction between neurological development and environmental stimuli would result in more efficient cortical functioning related to skills such as language, attention, memory, intelligence, and EFs. These higher, integrating mental functions (language, memory, perception, etc.) manage task-oriented behavior. Still, second Luria, the EFs are connected to the frontal lobe, having the function of programming, verification, control, and execution of the behavior and, also, supervision, control, and integration of the other cerebral activities

Thus, Luria contributes to a more interconnected view of brain functioning, contrary to the postulate of phrenologists – isolated and "locatable" mental faculties–, then Luria describes the brain and mental processes as an integrated system. This notion of functional unity is central to his work, being a milestone in the understanding of executive processes, and still influences contemporary neuropsychological approaches.

Therefore, there are several definitions of EFs, however, the descriptions have some points in common. The EFs present gradual development, with maturation according to the ontogenetic development, and in childhood, they are not fully developed, important changes occur until the end of adolescence. These changes happen thanks to neuroplasticity, that is, the ability of the nervous system to change in terms of function or structure in response to external or internal environmental influences (Cristofori, Cohen-Zimerman and Grafman; 2019; Allain, Etcharry-Bouyx, Verny, 2013; Baddeley, 2012; Luria, 1983,1973).

But also, Best and Miller (2010), Cipolotti et al (2015) Keller et al (2015) emphasize that the development of EFs begins in the first year of life and develops mainly between 6 and 12 years of age. After complete maturation, EFs remain stable until the onset of senescence, being one of the first functions affected by the aging process, mainly working memory and information processing speed.

EFs in DM2 have been investigated by authors such as Huizinga et al (2006) e Hull et al (2008) mainly in terms of three basic skills: Inhibitory Control; Working Memory, and Cognitive Flexibility; Inhibitory control is the ability to inhibit strong inclinations to perform a given task or to inhibit responses to distracting stimuli that interrupt the course of action. Working memory, also known as working memory, corresponds to the brain's ability to assimilate information as we perform certain tasks and Flexibility is the ability to think of different strategies to reach the same goal. In addition to these basic FEs, Lezak (2005) points out that patients with affected frontal areas often have problems with initiative and motivation and are incapable of planning goals and objectives, as well as designing action plans for the desired objective.

Executive skills allow us to change our mindset quickly and likewise allow us to adapt to different situations, at the same time, it has the ability to inhibit inappropriate behavior, as well as create a plan, initiate its execution, and persevere with a task until its conclusion. They also measured the ability to organize our thoughts in a goal-oriented manner, therefore essential in everyday life (Cerezo-Huerta, Yáñez-Téllez, Aguilar-Salinas, 2018; Moheet et al., 2015).

A meta-analysis carried out by Botond Antal et al (2022) showed that both aging and DM2 cause changes in executive functions, such as working memory, learning, thought flexibility and changes in brain processing speed. However, people with diabetes had an additional 13.1% decrease in executive function on top of age-related effects, and their processing speed decreased by more than 6.7% compared to age-matched people without diabetes. Their meta-analysis of other studies also confirmed this finding: people with DM2 had consistently and markedly lower cognitive performance compared to healthy subjects who were the same age and had similar education.

In this way, the EFs are understood as elaborate mental processes, whose apex occurs, in terms of phylogenesis, in the human being, being an ability exclusively of our species. These neurobehavioral capabilities allow the individual to plan, execute and monitor a sequence of actions aimed at a goal; are crucial and depend on the integrity of the frontal lobes, namely the dorsolateral, orbitofrontal and prefrontal cortex, as well as their connections (Peña-González et al., 2020; Pelimanni et al., 2019; Vincent et al, 2015; Sadanand S, Balachandar R, Bharath S, 2016; Allain, Etcharry-Bouyx, Verny 2013; Schroeter et al, 2012).

On the other hand, deficits in EFs or dysexecutive syndrome can be seen in difficulties with solving problems associated with new and complex material, difficulties in determining relevant information from irrelevant, planning, organizing, and responding adequately to situations in which mental flexibility is required, activities that are impaired in the elderly. For these reasons, many everyday acts in the lives of elderly people with DM2 and Dementia can be extremely complex with regard to the executive control of their performance. Propositive acts or directed towards an end; how planning, monitoring, and suppression of internal and external influences can be diverted from the actions of the pursued objective. Likewise, executive dysfunction in the elderly/has been associated with impairments in gait and functional abilities, deficits that are more broadly implicated in falls, loss of independence and, ultimately, institutionalization and mortality (Blackwood et al, 2019).

In this line of thought, Thabit et al (2009), studied the relationship between diabetes self-care and the importance of patient self-monitoring in the daily management of their diabetic condition, comparing two different measures of EFs in an elderly population with type 2 diabetes mellitus (DM2). The results indicate that elderly people with DM2 may have the syndrome dysexecutive and this EF impairment may impact self-care in this group.

BRAIN CHANGES IN THE ELDERLY WITH DM2, EXECUTIVE DYSFUNCTIONS, AND DEMENTIA

With advancing age, hemodynamic changes can be expected throughout the brain, being more pronounced in the frontal, temporal and occipital lobes. Furthermore, frontal lobe atrophy depending on age, as well as reduced connectivity between frontal regions and subtentorial territories, has also been described (Steffener, Habeck, Stern, 2012).

A large cross-sectional cohort was performed by Botond Antal et al (2022) in the United Kingdom using neuroimaging exams with the aim of evaluating the relationship between typical brain aging and that observed in individuals between 50 and 80 years of age with DM2. The results showed that the neurocognitive impact of DM2 suggests a marked acceleration of normal brain aging. Scientists have shown that normal brain aging is accelerated by approximately 26% in people with progressive DM2 compared to individuals without the disease; disease duration was associated with increased neurodegeneration. The results suggest a neurometabolic component to brain aging and also indicate that, by the time DM2 is formally diagnosed, there may already be significant structural damage to the brain, thus reinforcing the need for early assessments to detect diabetes-associated changes in the brain.

Neuroimaging methods according to Riederer et al (2017) led to the identification of potential neural correlates of neurocognitive changes, related to DM2, both structural, functional, and metabolic disorders in the brain, such as global and regional atrophy, white matter hyperintensity, altered functional connectivity and alterations in neurometabolic levels.

Recent research carried out on DM2 and global brain atrophy, demonstrated loss of brain volume in patients with diabetes similar to or up to three times the atrophy rate of normal aging, being more pronounced in the regions around the ventricles, such as the subcortical gray matter or the white matter regions, this is because the ventricles are less sensitive to segmentation errors due to the relatively high signal contrast and the smooth border between brain tissue and cerebrospinal fluid (Biessels et al., 2020; Mankovsky, 2018; Biessels et al, 2014).

Nonetheless, Espeland et al (2013) postulate that diabetes is associated with smaller brain volumes in the gray matter but not in white matter, as well as increased volumes of ischemic lesions throughout the brain.

Also, Roy et al (2020) show in their research that patients with DM2 have brain damage in regions that are involved in the control of cognition, anxiety, and depression, and these tissue changes are associated with deficits in EFs.

In turn, Pignalosa et al (2021) when studying patients with, DM2, showed that gray matter loss is present in the prefrontal areas, hippocampus, amygdala, insular, cingulate, cerebellum, caudate, basal forebrain, and thalamus, and white matter loss is evident in the frontal and temporal regions. In addition, magnetic resonance imaging also revealed more frequent cerebral infarcts in individuals with DM2.

So, from the point of view of the neurobiology of the EFs, we find affirmations in Goldberg (2002) which says that the EFs would be totally mediated by the frontal lobes, this region being of important adaptive value for the individual, facilitating the management of other cognitive skills, such as the conductor of an orchestra or the general of an army. The cortical regions involved are the Dorsolateral circuit; Orbitofrontal circuit and Anterior cingulate circuit.

ASSOCIATION DM2, EFS AND DEMENTIA IN THE ELDERLY

The prevalence of DM2 and dementia for Ninomiya (2019;2014); Chatterjee, Khunti and Davies (2017); Trikkalinou, Papazafiropoulou and Melidonis (2017) increases with age, being a significant influencing factor for dementia, especially those related to Alzheimer's dementia (DA).

Impaired performance on a variety of executive tasks has been reported in older adults with DM2 for Hoyos CM (2021), Allain P, Etcharry-Bouyx F, Verny C. (2013); Baddeley, A.D. (2012); increased risk of executive decline related to gait difficulties in the elderly by Thabit et al (2012). In the same line of thought, Sadanand et al (2016), in a systematic review showed that logical memory, phonemic fluency, and processing speed are affected in elderly people with DM2, being a harmful factor in certain cognitive subdomains, making the person vulnerable to subsequent dementia. A recent meta-analysis performed by Luna et al (2021) revealed that DM2 has more significant effects on information processing speed, planning, mental efficiency, and verbal learning.

Another prospective study carried out by Marneras et al (2020), revealed that patients with DM2 have cognitive deficits in several domains with a significant impact on QVRS, compared to healthy participants. On the other hand, Vincent and Hall (2015) in a meta-analytical review presents results that indicate a small but reliable association between DM2 and decreases in EFs, both in verbal fluency, mental flexibility, inhibition, working memory, and attention. Illness duration significantly moderated the effect of DM2 status on EFs.

On the other hand, a longitudinal cross-sectional analysis with 14.444 participants, aged between 35-74 held in Brazil by Teixeira et al (2020) suggests a significant association between diabetes and decreased performance in memory, language, and executive functions (attention, concentration, and psychomotor speed) in this Brazilian population with a distinct epidemiological profile (Cerezo-Huerta, Yáñez-Téllez and Aguilar-Salinas, 2018), studied the cognitive impairment associated with DM2 and the interaction between the Therapeutic Adherence Factors (TAF). The authors concluded that there are specific difficulties in EFs in patients with DM2 that are influenced by demographic and disease factors.

Furthermore, Junquera et al (2020) when assessing executive dysfunction and as a potential early predictor of mild cognitive impairment progression (CCL) for dementia in clinical Alzheimer's syndrome (SCA) and functional impairments in instrumental activities of daily living (AIVD). The authors concluded that CCL with dysexecutive phenotype significantly predicts conversion to dementia in SCA one year later. Exchange skills and verbal fluency should be assessed in patients with CCL to assess the risk of future dementia.

Also, Karvani et al (2019) point out in their review several emerging evidence that cognitive impairment can be a complication related to diabetes mellitus, such as a higher risk of cognitive decline, metabolic disorders, and vascular disease that affect brain function and aging. Neurocognitive impairment compromises performance in cognitive domains such as verbal and non-verbal memory, immediate and delayed memory, FEs, attention, visuospatial and psychomotor performance, information processing speed, semantic knowledge, and language skills

Although McCrimmon, Ryan, and Frier

(2012) show a distinctive feature regarding cognitive dysfunction in DM2, as people with this disorder often perform poorly on measures of learning and memory, the disorders are associated with mental and motor slowing and decreases of similar magnitude in measures of attention and EFs. Also, neural slowing increased cortical atrophy and microstructural abnormalities in white matter tracts. Obesity in DM2 in all age groups may result in a substantial increase in the prevalence of diabetes-related cognitive dysfunction.

On the other hand, Rostamian et al (2019) state that worse performance on EFs and memory tests is associated with all-cause mortality, and cardiovascular and non-cardiovascular in the elderly. This association is independent of risk factors and cardiovascular disease, brain structural abnormalities, and cerebral blood flow.

CONCLUSIONS

This research shows important evidence between DM2, deficits in EFs, and dementia, indicating the negative reflexes in the functional abilities of activities of daily living, social relations, and leisure of the elderly because these pathologies have common pathological characteristics, including inflammation, changes in insulin signaling or vascular damage, in addition to cognitive, behavioral and emotional impairments.

Diabetic people are at greater risk of cognitive decline, to the detriment of the metabolic and vascular disturbances of the disease, which affect brain function due to prolonged exposure associated with other potentially harmful factors, as a consequence of the aging process, which can progress to dementia, both vascular dementia and Alzheimer's dementia.

As the elderly represent a large part of the population with DM2, the spectrum of complications tends to increase, since cardiovascular and neurological complications have been associated with deficits in the EFs, by the increased risk of cognitive and physical decline, falls and depression, nosological entities commonly found in the human aging process.

Because they are fragile patients, with difficulties in adhering to the self-care recommendations proposed for the management of the pathology, with regard to the domains of blood pressure, lipid and glucose control, polypharmacy, adequate use of medication, type of diet, elderly people with DM2 may not guarantee the same benefits proven in younger individuals, in addition to the chance of leading to risk situations, such as hypotension and hypoglycemia.

We suggest neuropsychological assessments of EFs in elderly diabetics, early psychoeducational interventions to delay the onset and better control of DM2 in order to prevent some of its adverse effects on brain functioning and progression of dementia, as well as further research in collaboration with workers in the field of health and neuropsychology is recommended.

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