https://repository.uaeh.edu.mx/revistas/index.php./MJMR/issue/archive

Mexican Journal of Medical Research ICSa

Biannual Publication, Vol. 13, No. 25 (2025) 30-36

ISSN: 2007-5235

Mild Neurocognitive Disorder: Clinical Manifestations and Treatment

Deterioro cognitivo leve: Manifestaciones clínicas y tratamiento

Jesús Serrano Ruíz [a]

Abstract:

The World Health Organization (WHO) estimates that there are 50 million elderly people who have a condition related to cognition; this figure is expected to increase in incidence in the coming years. Although it is true that Mild Cognitive Impairment (MCI) is not considered pathological, it is the intermediate stage between normal aging and the presence of some major cognitive alteration. Currently there are no treatments for mild cognitive impairment (MCI), however, there are therapeutic measures with positive results such as Cognitive Stimulation (CS) and Transcranial Direct Current Stimulation (tDCS) to prevent the appearance of symptoms. serious. This review aims to explore the therapeutic measures used in elderly people with MCI.

Keywords:

Mild cognitive impairment, epidemiology, treatment

Resumen:

La Organización Mundial de la Salud (OMS) estima que existen 50 millones de personas de la tercera edad que tienen algún padecimiento relacionado con la cognición, se prevé que esta cifra aumente su incidencia en los próximos años. Si bien es cierto que el Deterioro Cognitivo Leve (DCL) no se considera patológico, si es la etapa intermedia entre el envejecimiento normal y la presencia de alguna alteración cognitiva mayor. Actualmente no existen tratamientos para el deterioro cognitivo leve (DCL), sin embargo, se cuenta con medidas terapéuticas con resultados positivos como la Estimulación Cognitiva (EC) y la Estimulación Transcraneal de Corriente Directa (tDCS) que ayudan en la prevención de la aparición de sintomatología grave. Esta revisión, tiene por objetivo explorar las medidas terapéuticas que se utilizan en las personas de la tercera edad que presenta DCL.

Palabras Clave:

Deterioro cognitivo leve, epidemiologia, tratamiento

INTRODUCTION

It is estimated that the number of people living with dementia will triple by 2040, going from 57.4 million to 152.8 million.[1] In the United States, it is estimated that suffering from a Neurocognitive Disorder has an annual cost of $590.78 US for mild dementia and US$25,510.66 for severe dementia.[2] In the case of Neurocognitive Disorders (NCD), it is important to highlight that, from the onset of mild symptoms such as The case of Mild Cognitive Impairment (MCI) is disabling from the first manifestations, for this reason the objective of this work is to know both pharmacological and non-pharmacological preventive treatments for the prevention of MCI. In the case of MCI, its study is essential, since it is in an intermediate phase between normal aging or pathological aging.[3] MCI manifests itself as a set of alterations in basic cognitive functions, that is, in orientation spatial, language, visual recognition, as well as the reduction of mnemic function. This condition is also usually accompanied by behavioral changes.[3] MCI is considered a precursor to dementia and is usually located in an intermediate stage between normal aging and Alzheimer's type dementia. It is a reality that pharmacological treatments have not had the results that were expected, hence the importance of exploring new treatments that allow older people to enjoy health and, above all, a good quality of life.[4]

EPIDEMIOLOGY OF NEUROCOGNITIVE DISORDERS

World statistics

[a] Corresponding author, Universidad Autónoma del Estado de Hidalgo, https://orcid.org/ 0000-0002-0525-6852, Email: jesus_serrano@uaeh.edu.mx

Received: 04/03/2024, Accepted: 14/05/2024, Postprint: 09/08/2024, Published:DD/MM/AAAA

DOI: https://doi.org/10.29057/mjmr.v13i25.12425

MCI is not a disease typical of the elderly, since there are different diseases that can cause cognitive deterioration; however, there is a much higher prevalence in people between 60 and 65 years of age.[5]

In Latin America, the global prevalence is 11% of older people suffering from some type of dementia. Regarding sex, a significant difference is observed: in women this prevalence is 6%, while in men it is 4%. Likewise, differences were found between the rural and urban population. In the case of men in rural communities it is 1%, while in urban places it is 5%. On the other hand, in women it is still higher than in men, both in rural communities and in urban communities, representing 7% in urban communities and only 2% in rural communities.[6]

In a systematic review with meta-analysis carried out by Prince, Bryce, Albanese, Wimo, Ribeiro and Ferri in 2013, it was found that the standard proportion of people over 60 years of age varied between 5% and 7% in most regions of the world, with a highest rate in Latin America 8.5% and considerably lower in the four subregions of sub-Saharan Africa 2%-4%. It is estimated that in 2010, approximately 35.6 million people had dementia worldwide, and this number is expected to almost double every 20 years, reaching 65.7 million in 2030 and 115.4 million in 2050. In 2010, 58 % of all people with dementia lived in low- or middle-income countries, and this proportion is projected to increase to 63% in 2030 and 71% in 2050.[7]

National statistics

In recent years, dementia has represented a primary concern for public health due to its global presence, and its significant impact in economic, social and health terms. Despite this, in Mexico there are few reports that are based on formal evaluations and that adopt a clinical approach that uses the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5).[8] The prevalence that exists in Mexico it is 7.3% and an incidence of 27.3 (1000 people/year) for Alzheimer's Disease (AD).[9]

At the national level, there are surveys that provide important data on the cognitive status of older people. First there is the Health Wellbeing and Aging Survey (SABE). This survey was applied in the period from 2013 to 2015 at the national level in the following states of the Mexican Republic: Coahuila, Colima, Durango, State of Mexico, Guanajuato, Hidalgo, Michoacán, Morelos, Querétaro, San Luis Potosí, Tlaxcala, Yucatán and Veracruz. In the area related to cognitive state, Folstein's Mini-mental state examination instrument was applied, where the cut-off line to consider an older adult as suspected of cognitive impairment was a score equal to or less than 12 points.[10]

In Table 1 it can be seen how the highest prevalence of symptoms of cognitive impairment is in the State of Mexico with 22% followed by Coahuila with 18.8%, Michoacán with 18.5%, Guanajuato with 16.2 and at the end of the table, San Luis Potosí with 2.9%, Tlaxcala with 5.6% and Durango with 6.2%.[10]

There is also the National Survey on Health and Aging in Mexico (ENASEM), which evaluates orientation through five specific questions. The data obtained from the survey revealed the following: in an age group of 58 years and older and older, 94.3% correctly answered what day of the week it was. Likewise, 90.6% correctly identified the month in which they are located, the federal entity of residence, with 85.7 percent. The lowest percentages of correct answers were for the day of the month, with 67.9%, and the time of the interview, with 67.1%.[11]

Tabla 1. *Prevalence of Cognitive Impairment in Mexico.*[10] *Results of the Health, Wellbeing and Aging Survey ≥60 age.*

State	Percentage of memory impairment	Men	Women
Estado de México	22%	41%	59%
Coahuila	18.8%	40.64	59.4%
Michoacán	18.5%	38.3%	61.7%
Guanajuato	16.2%	25.4%	74.6%
Querétaro	14.6%	38.3%	61.7%
Morelos	13.6%	39.8%	60.2%
Veracruz	12.8%	36.9%	63.1%
Yucatán	12.7%	34.3%	65.7%
Colima	9.5%	38.5%	61.5%
Hidalgo	6.7%	30.3%	69.7%
Durango	6.2%	34.6%	65.4%
Tlaxcala	5.6%	No data	No data
San Luis Potosí	2.9%	42.7%	57.3%

State statistics

In the state of Hidalgo, two studies have been carried out in the municipalities of Actopan and Tlahuelilpan. In the first, it was found that approximately 16% of the population had a score below average. It is important to note that in this study the Mini Mental test was not used as is common, but rather the Cognitive Abilities Screening Instrument (CASI) was used.[12] In the second study the results showed a significant increase, With a percentage of 40.9% of people presenting probable cognitive impairment, Fosltein's Minimental was used to evaluate cognitive impairment.[13]

MILD COGNITIVE IMPAIRMENT

The term Mild Cognitive Impairment (MCI) or as it was previously known: benign senile forgetfulness, age-related memory impairment or age-related cognitive decline, mild cognitive impairment (MCI) did not have a clinical description, it was Reisberg et al.[14] in the 1980s, he placed this entity at level 3 of compatible functioning, describing it as follows:

"Objective functional impairment of sufficient severity to interfere with complex occupational or social tasks (ADL-C). The patient, for the first time, forgets important appointments; From a psychomotor point of view, they can get lost in unknown places, although they do not have difficulties in performing routine tasks (ADL-I)".[15]

In the nineties Petersen et al.[15] developed the first clinical criteria in 1997, which were listed as follows: (1) memory complaint, preferably corroborated by an informant; (2) objective memory decline for age and education; (3) largely normal general cognitive function; (4) essentially normal activities of daily living; and (5) no dementia. The same authors in 2004 expanded the criteria for MCI and proposed two subtypes: amnesic (which includes memory impairment) and non-amnestic (alteration of other cognitive domains).[15,16] The aforementioned criteria follow still valid, but by including the non-amnestic type, the alteration can refer to any cognitive domain. One of the points to consider for the diagnosis of MCI is that the complaint must preferably be evaluated with neuropsychological tests that corroborate the clinical information. If the evaluation determines a deficit in any of the cognitive functions, we can determine that it is MCI. If the cognitive domain that is altered is memory, we will speak of amnestic type MCI and in addition no other altered domain is found, the diagnosis of amnestic MCI, single domain, is made; If in the evaluation it turns out that other domains (executive, visual-spatial or language) are altered, it is called multiple-domain amnestic MCI; If memory is not affected, it is determined whether there is a single altered domain (single-domain non-amnestic MCI) or several (multiple-domain non-amnestic MCI).[16,17]

The DSM-5 encompasses the term major and minor Neurocognitive Disorder (NCD), these criteria are similar to those proposed by Petersen et al., the manual mentions that NCD are cognitive alterations that were not present in the individual at the time. moment of birth, in childhood or adolescence, so it represents an acquired decline compared to a previous level of functioning.[18] The diagnostic criteria for it are the following:The diagnostic criteria for the DSM-5 are as follows:

Diagnostic Criteria for Mild Neurocognitive Disorder[18]

A. Evidence of moderate cognitive decline compared to the previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual motor skill, or social cognition) based on:

1. Concern in the individual himself, in an informant who knows him or in the clinician, because there has been a significant decline in a cognitive function and.
2. A modest impairment in cognitive performance, preferably documented by a standardized neuropsychological test or, failing that, by another quantitative clinical evaluation.

B. Cognitive deficits do not interfere with the ability to be independent in daily activities (e.g., you maintain complex instrumental activities of daily living, such as paying bills or following treatments, but you need to make greater effort, or resort to compensation or adaptation strategies).

C. Cognitive deficits do not occur exclusively in the context of delirium.

D. Cognitive deficits are not better explained by another mental disorder (e.g., major depressive disorder, schizophrenia).[18]

The importance of timely detection of aMCI lies in the fact that it has been observed that people who suffer from mild amnestic cognitive impairment usually develop a Neurocognitive Disorder due to Alzheimer's disease.[4]

Clinical features

On the other hand, although some other mental disorders compromise cognitive performance (such as bipolar disorders or schizophrenia), the present group (TNCs) only considers those whose main characteristics refer to those of the cognitive type [18,19] and whose symptomatology is explored considering the domains established in the DSM-5[18] which, depending on the clinical threshold presented, determine the diagnosis, as well as the level and specification of the subtype.[18-20]

The first domain, Complex Attention, includes the evaluation of the maintenance of attention over time (continuous attention) and with discrimination of external stimuli and distracting factors (selective attention), as well as the feasibility of carrying out two tasks in sync (divided attention). The evaluation of Executive Function is carried out taking into consideration the capacity for planning, decision making, working memory (retention of information in a short time, for manipulation), feedback (implementation to solve a problem), inhibition (ability to carry out a solution that involves greater effort) and cognitive flexibility (ability to alternate between two concepts or tasks).[18]

Regarding the learning and memory domain, both immediate memory (which can be evaluated within working memory) and recent memory (which involves the encoding of new information) are evaluated. In the most severe cases, alterations in semantic, autobiographical and implicit memory are observed.

Regarding language, the expressive capacity of the language is assessed (including the ability to name objects, through identification, fluency or phonemes), grammar and syntax, and understanding of the language. Visual perception, vasocondtrictive ability (coordination of vision and manipulation of objects), perceptual motor skills (use of movement based on perception), praxis (execution of learned movements or use of objects) and gnosis (perceptual integration of recognition and knowledge), are the subdomains belonging to the Perceptual Motor Skills themselves.[18]

The last domain considered in the DSM-5 is Cognition social that encompasses emotion recognition and theory of mind (ability to consider experience or psyche other thoughts, desires and intentions). In general, in all domains, the significant difficulty or impossibility in carrying out these tasks on one's own, in contrast to the implication of a greater effort or notable changes in their execution, is what determines the severity with which the domain is compromised; In turn, as previously mentioned, the formation of the level of execution of this function will integrate, as appropriate, the respective diagnoses of this group of deficits.[18]

In addition to the degree of decline in the domains, the presence of apathy and/or depression in patients suffering from TNCs has

been pointed out by different investigations[20,21] they are also, in themselves, risk factors for the development of TNCs[19] and entities related to negative consequences or worse prognoses in the progression of these deficits. The importance that the identification of these symptoms acquires also represents a challenge for clinicians in order to be able to differentiate them pertinently, in order to implement a specialized intervention that becomes central to the management of these deficits.[20,21]

Finally, it seems relevant to mention that although the neuronal circuits involved in the development of apathy and depression in TNCs are different, a possible explanation for the presence of the different symptoms is the existence of a cholinergic deficit, which is also possibly associated with to other behavioral and psychological symptoms of dementia, such as: irritability, agitation, psychosis, sleep disorders, anxiety, dysphoria, hallucinations, aberrant motor behavior and delusions, such relevance and the symptoms themselves suggest being compromised by the type of deficit that has developed by the patient and its etiology.[22]

Risk factors associated with Cognitive Impairment in Older People

Risk factors in old age refer to those that accelerate the aging process and increase the chances of having MCI. These factors can be divided into two: Modifiable and non-modifiable risk factors. Among the modifiable risk factors are healthy lifestyles that affect the prevention of diseases such as: diabetes, hypertension, cholesterol levels, obesity, smoking, alcohol, a sedentary lifestyle and depression.[3]

One of the risk factors has to do with demographic aspects. After the age of 65, the risk of suffering from some cognitive impairment doubles every 5 years. In terms of gender, there are no studies that reflect that there is a higher prevalence in men or women. Some studies also refer to economic factors, access to health and education issues that play an important role due to the cognitive reserve that people can generate throughout their lives.[4]

Non-modifiable risk factors are those that cannot be changed, for example, age and genetics. Some studies have shown that there is a relationship between the ApoE4 genotype and cognitive impairment, and it is also associated with a higher risk of arteriosclerosis. and vascular cognitive impairment due to problems in cholesterol transport.[3]

MCI can be attributed to extrinsic factors linked to aging, for example, age-dependent diseases with cerebral repercussions such as cerebrovascular disease, hypertension, diabetes, endocrinopathies, psychiatric pathology, sociocultural isolation, sensory alterations. There are also intrinsic factors of the individual such as brain functional and structural reserve, genetic endowment, and the degree of adaptation to changes during life.[3]

In patients with MCI, the presence of accumulations of beta-amyloid protein and tau proteins, the same as those observed in Alzheimer's disease, have been identified; In other cases, there are microscopic accumulations of a protein called Lewy bodies, related to Parkinson's disease. Likewise, the presence of transient strokes or reduced blood flow through the blood vessels of the brain have been present in studies of people with MCI.[4]

At the brain level, neuroimaging studies allow us to observe a decrease in the size of the hippocampus (area involved in memory), an increase in the size of the ventricles (spaces filled with fluid in the brain), and a reduced use of glucose in the brain has also been identified. key brain regions.[4]

TREATMENTS FOR MILD COGNITIVE IMPAIRMENT

Pharmacotherapy

When talking about pharmacological treatment in mild cognitive impairment, it must be clear that the treatment does not aim to cure or eliminate the symptoms that occur. The goal is to slow or stop the severity of the symptoms. The earlier pharmacological therapy is started, the course of the disease will be less aggressive than in people who start late treatment.[22]

It is important to clarify that the treatment mentioned below is specifically for the treatment of mild cognitive impairment due to Alzheimer's disease.

Firstly, we have Acetylcholinesterase Inhibitors (AChI), which have shown good results in mild and moderate cognitive impairment, slowing cognitive and functional symptoms, allowing people to maintain their independence. IACh inhibit the degradation of acetylcholine in the synaptic cleft, allowing the active substance of the drug to act more quickly and stimulate the postsynaptic receptors for a longer time. Among the side effects of this type of medication are: dizziness, vomiting, nausea, diarrhea, loss of appetite, bradycardia, urinary retention, among others.[22,23]

The medications that have been studied the most are Donepezil, Ribastigmine and Galantamine, the first of which has been shown to have better results in mild and moderate cognitive impairment; however, it has not shown clinically significant results in severe stages of cognitive impairment. The therapeutic dose of donepezil is 10 mg daily before going to sleep in a single dose. At the beginning of treatment, only 5 mg is used, which will progressively increase up to 10 mg. There are special cases where the dose is increased up to 20 mg, however, this leads to greater side effects.[22,23]

Rivastigmine acts on the cerebral cortex and the hippocampus, bioavailability will depend on the dose. There are two ways to administer it orally and transdermally, in the case of oral administration it shows gastrointestinal side effects, unlike transdermal administration where there is greater tolerability by patients.[24] Treatment is individualized, however, generally starting with 3 mg, increasing the dose every 3 or four weeks until reaching a dose of 9-12 mg daily. Oral administration is suggested to be two doses per day, with food and in the case of the transdermal route it is applied only once a day and, as in the oral route, it begins with the lowest dose of 4.6 mg until reaching at the dose of 13.3 mg per day.[22,25]

Finally, Galantamine, which acts as a reversible inhibitor of acetylcholinesterase, is administered orally in two doses per day.

Treatment begins with 8 mg daily, with a gradual increase so that at the end of the fourth week it increases to 16 mg. The clinician will have to evaluate if there is improvement in symptoms; if no therapeutic response to the drug is observed, the dose can be increased to 24 mg per day. Like the two previous medications, the most common side effects are: loss of appetite, vomiting, nausea, diarrhea, abdominal pain, etc.[22,26]

Some studies have carried out clinical trials in which Donepezil and Memantine are combined for the treatment of advanced stages of cognitive impairment of the Alzheimer type; however, they did not demonstrate clinically significant effects in any cognitive domain, nor in functional symptoms, nor in the caregiver overload.[24]

It is important to mention that in the case of older people, the way to ensure compliance with treatment is to simplify the administration regimens, reducing the number of doses per day and the method of administration, since it has been observed that older people who require administration of several doses per day, their adherence to treatment is much lower than people who have fewer doses per day.[27]

PREVENTIVE MEASURES FOR MILD NEUROCOGNITIVE DISORDER

Cognitive Stimulation

Some studies show that Cognitive Stimulation (CS) is a protective factor for the prevention of cognitive symptoms in old age; said stimulation also impacts the cognitive reserve of the subjects. The CS, in addition to having an important role in learning and memory processes, is considered one of the main prevention strategies for the development of Neurocognitive disorder.[28]

CE refers to a set of activities designed to preserve and improve cognitive functioning. It is achieved through exercises that address memory, attention, concentration, language, reasoning, and control. In other words, CE is a multidomain stimulation. CE is frequently carried out in a group and training is carried out in the different cognitive domains. Generally, these types of interventions do not focus solely on a single cognitive domain, but rather the different exercises or activities are multidomain, this is because people's cognitive functioning is not used in isolation and cognitive functions are They find themselves constantly interacting in the daily lives of the subjects.[3,4]

CE is used for the prevention of cognitive deterioration and not as a rehabilitation tool, its objective is aimed at either preserving or improving the cognitive functioning of the different cognitive domains of older people.[28] For Madrigal, CE should improve cognitive functioning in older people, in such a way that they have a positive impact on the quality of life, for this reason interventions must compensate and promote adaptation in the social environment in which older people find themselves.[29] Just as two cognitive domains interact Among themselves, cognition and affectivity also go hand in hand, which is why an improvement in mood has been noted in patients who receive some cognitive training.[30]

In a systematic review study that was carried out in 2017, articles were reviewed from 2001 to 2017. of the studies that were reviewed, it was found that in 98% of them positive results and an increase in cognitive capacity were obtained, increasing in this way the independence and quality of life of older adults.[31] The studies presented vary in the period of application of cognitive stimulation, on average the time is between 7 and 12 weeks, that is, from two to 4 months. As additional information, it was found that the 30 studies carried out are cross-sectional studies. Therefore, carrying out this type of studies increases the autonomy of older people, as well as increases their quality of life.[32]

Transcranial Direct Current Stimulation in the Treatment of Mild Cognitive Impairment

Recently, work has begun using neuromodulation techniques, which consist of the depolarization of the neuron. This depolarization is carried out by passing low-intensity electrical impulses, resulting in the excitation or inhibition of the neuron. Among the neuromodulation techniques that are currently being used is transcranial direct current stimulation (tDCS), which has been used to treat psychiatric and neurocognitive conditions. Considered non-invasive techniques, they consist of the application of small electrical impulses (usually between 0.5 and 2 mA) through two electrodes with positive and negative charges that are placed on the scalp and through which direct and constant electrical current passes. The electric current penetrates the cerebral cortex, reaching the cortical and subcortical layers, having an expiatory response from the neuron, increasing neuronal plasticity.[33]

Within the literature, different randomized clinical trials have been found showing the benefits of using tDCS, such as Murugaraja et al.[34] where the results show that tDCS is safe and potentially beneficial in combating cognitive deficits in patients with mild cognitive impairment. Another randomized, double-blind clinical trial in older adults with MCI and who underwent tDCS has shown that it can significantly improve executive function in MoCA and performance in Trail Making Test Version A and B (TMT-A/B).[32] Likewise, tDCS has been seen to improve visual sustained attention, spatial WM, and visual memory assessed using digital neuropsychological tests.[34,35]

According to the evidence reviewed, tDSC is considered a safe technique.[36] In different clinical trials, adverse effects considered mild have been reported, such as: feeling itching, burning or tingling at the application site during or minutes after, headache and fatigue. There are several predisposing factors that increase the risk of local side effects such as high skin impedance, small and dry electrodes, incorrect electrode position and contact with the skin, as well as an allergic predisposition.[37]

Among the different studies with tDCS that have been carried out, we find those carried out by Manor et al.[37], who carried out randomized, double-blind clinical trials in older adults with MCI and who underwent tDCS, demonstrating that it can significantly

improve executive function. in MoCA and performance in Trail Making Test Version A and B (TMT-A/B).[38]

CONCLUSIONS

Although it is true that the results of the different investigations that have been carried out demonstrate that both CE and tDCS are effective for the prevention of some major cognitive alteration, it is important to mention that the objective of both CE and tDCS are not curative, and that its effectiveness is measured by the reduction of mild symptoms or by the fact that it does not progress to more serious stages. According to a recent systematic review carried out by da Silva et al., the combination of tDCS+CT does not seem to enhance the effects of tDCS essentially due to the variability of protocols.[36] The above represents a challenge that consists of verifying whether there is a significant benefit from the synergistic application of two stimulation interventions to treat aMCI, whether cognitive interventions and neuromodulation techniques, or interventions that contemplate three types of intervention to evaluate the efficacy and effectiveness of the treatments together.

REFERENCES

[1] GBD 2019 Dementia Forecasting Collaborators. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. Lancet Public Health. 2022; 7(2): e105-25.

[2] Mattap SM, Mohan D, McGrattan AM, Allotey P, Stephan BC, Reidpath DD, Siervo M, Robinson L, Chaiyakunapruk N. The economic burden of dementia in low- and middle-income countries (LMICs): a systematic review. BMJ Glob Health. 2022; 7(4): e007409.

[3] Cerezo K. Trastornos neurocognitivos en el adulto mayor: evaluacion diagnostico e intervencion neuropsicologica. Ciudad de México: Manual Moderno; 2019.

[4] Jurado MA, Mataró M, Pueyo R. Neuropsicología de las enfermedades neurodegenerativas. Barcelona: Síntesis; 2013.

[5] Lövdén M, Fratiglioni L, Glymour MM, Lindenberger U, Tucker-Drob EM. Education and Cognitive Functioning Across the Life Span. Psychol. Sci. Public. Interest. 2020; 21(1): 6-41.

[6] Ribeiro F, Teixeira-Santos AC, Caramelli P, Leist AK. Prevalence of dementia in Latin America and Caribbean countries: Systematic review and meta-analyses exploring age, sex, rurality, and education as possible determinants. Ageing Res. Rev. 2022; 81: 101703: PMID: 35931410; PMCID: PMC9582196.

[7] Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. Alzheimers Dement. 2013 Jan; 9(1): 63-75.e2.

[8] Reyna Carrizales ML, González Rubio MV, López Esqueda FJ, González González GR, editores. Demencias, una visión panorámica Temas derivados del V Simposio de Medicina Geriátrica realizado el 5 y 6 de septiembre del 2014. San Luis Potosi: Editorial Universitaria Potosina; 2014

[9] Sosa-Ortiz AL, Acosta-Castillo I, Prince MJ. Epidemiology of dementias and Alzheimer's disease. Arch Med Res. 2012; 43(8): 600-8.

[10] CENAPRECE [Internet]. Cuidad de México: Centro Na cional de Programas Preventivos y Controles de Enfermedades; 28 de Julio de 2015 [cited 2024 april 6]. Encuesta SABE. Available from: http://www.cenaprece.salud.gob.mx/programas/interior/adulto/envejecimiento/EncuestaSABE.html

[11] INEGI [Internet]. Ciudad de México: INEGI; 2021 [cited 2024 april 6]. Encuesta nacional sobre salud y envejecimiento en México (ENASEM) y encuesta de evaluación cognitiva1 2021. Available from: https://www.inegi.org.mx/programas/ecenasem/2021/#:~:text=La%20Encuesta%20de%20Evaluaci%C3%B3n%20Cognitiva%20para%20la%20ENASEM%20tiene%20el,estudios%20similares%20a%20nivel%20mundial.

[12] Rodríguez-Camacho MA, Bernal Hernández J, Villalva Sánchez AF, Salgado Ceballos H, Guzmán Cortés, JA. Cognición, depresión y estado funcional en adultos mayores de una comunidad rural de Actopan-Hidalgo, México. Neuropsicol. Lat. Am. 2022; 14(2): 32-41.

[13] López-Nolasco B, Austria-Reyes A, Santander-Hernández JJ, Maya-Sánchez A, Cano-Estrada EA. Nivel de deterioro cognitivo del adulto mayor de la comunidad de Tlahuelilpan, Hidalgo, México. Rev.Enferm.Neurol. 2021; 20(1): 45-8.

[14] Reisberg B, Ferris SH, de Leon MJ, Crook T. The Global Deterioration Scale for assessment of primary degenerative dementia. Am J Psychiatry. 1982; 139(9): 1136-1139.

[15] Petersen RC, Smith GE, Waring SC, Ivnik RJ, Kokmen E, Tangelos EG. Aging, memory, and mild cognitive impairment. Int. Psychogeriatr. 1997; Suppl. 1: 65-9.

[16] Petersen RC. Mild cognitive impairment as a diagnostic entity. J. Intern. Med. 2004; 256(3): 183-94.

[17] Cespón J, Galdo-Álvarez S, Pereiro AX, Díaz F. Differences between mild cognitive impairment subtypes as indicated by event-related potential correlates of cognitive and motor processes in a Simon task. J. Alzheimers Dis. 2015; 43(2): 631-47.

[18] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-5-TR. Washington: American Psychiatric Publishing; 2022.

[19] Organización Mundial de la Salud. [Internet]. Ginebra: Organización Mundial de la Salud enero 2024 [cited 2024 march 12] Clasificación Internacional de Enfermedades, undécima revisión (CIE-11). Available from: https://icd.who.int/browse/2024-01/mms/en

[20] Miller DS, Robert P, Ereshefsky L, Adler L, Bateman D, Cummings J, et al. Diagnostic criteria for apathy in neurocognitive disorders. Alzheimers Dement. 2021; 17(12): 1892-904.

[21] Lanctôt KL, Ismail Z, Bawa KK, Cummings JL, Husain M, Mortby ME, et al. Distinguishing apathy from depression: A review differentiating the behavioral, neuroanatomic, and treatment-related aspects of apathy from depression in neurocognitive disorders. Int. J. Geriatr. Psychiatry 2023; 38(2): e5882.

[22] Mahmoudi R, Novella JL, Laurent-Badr S, Boulahrouz S, Tran D, Morrone I, et al. Cholinergic Antagonists and Behavioral Disturbances in Neurodegenerative Diseases. Int. J. Mol. Sci. 2023; 24(8): 6921.

[23] Vaz M, Silvestre S. Alzheimer's Disease: Recent treatment strategies. Eur. J. Pharmacol. 2020; 15;887:173554. PMID: 32941929.

[24] Deschle F. Donepecilo y memantina para la enfermedad de Alzheimer moderada a severa. Neurol. Arg. 2012; 4(4): 236-9.

[25] Cruz Jentofta AJ, Hernández B. Manejo terapéutico con rivastigmina en pacientes con enfermedad de Alzheimer de leve a moderadamente grave en condiciones de práctica clínica habitual. Estudio ENTERPRISE. Neurología. 2014; 29(1): 1-10.

[26] Carretero Colomar M. Medicamentos de vanguardia. Galantamina. Offarm. 2023;22(8): 140-2.

[27] Priao L, Gasco L, Mauro A. Transdermal treatment options for neurological disorders: impact on the elderly. Drugs Aging 2012; 23(5): 357-75.

[28] Gómez-Soria I, Iguacel I, Aguilar-Latorre A, Peralta-Marrupe P, Latorre E, Zaldívar JNC, et al. Cognitive stimulation and cognitive results in older adults: A systematic review and meta-analysis. Arch. Gerontol. Geriatr. 2023; 104: 104807.

[29] Jara Madrigal M. La estimulación cognitiva en las personas adultas mayores. Rev. Cúp. 2008; 22(2): 4-14.

[30] Bilyk E, Ventura AC, Cervigni M. Caracterización de la producción científica iberoamericana sobre intervenciones en la prevención del Deterioro Cognitivo en adultos mayores. PSIENCIA. 2015; 7(2): 383-96.

[31] Orejarena-Ballestas M-C, Quiñonez-Pérez AM, Marín-Gutiérrez A. Estimulación cognitiva para pacientes con trastorno neurocognitivo mayor por enfermedad de alzheimer: revisión sistemática. Búsqueda 2017; 4(19): 208-26.

[32] Davicino NA, Muñoz MS, Barrera ML, Donolo D. El rol psicopedagógico en la Estimulación Cognitiva de pacientes con Demencia tipo Alzheimer. Rev. Chil. Neuropsicol. 2009; 4(1): 6-11.

[33] Gomes MA, Akiba HT, Gomes JS, Trevizol AP, de Lacerda ALT, Dias ÁM. Transcranial direct current stimulation (tDCS) in elderly with mild cognitive impairment: A pilot study. Dement. Neuropsychol. 2019; 13(2): 187-95.

[34] Murugaraja V, Shivakumar V, Sivakumar PT, Sinha P, Venkatasubramanian G. Clinical utility and tolerability of transcranial direct current stimulation in mild cognitive impairment. Asian J. Psychiatr. 2017; 30: 135-40.

[35] Andrade SM, Machado DGDS, Silva-Sauerc LD, Regis CT, Mendes CKTT, de Araújo JSS, et al. Effects of multisite anodal transcranial direct current stimulation combined with cognitive stimulation in patients with Alzheimer's disease and its neurophysiological correlates: A double-blind randomized clinical trial. Neurophysiol. Clin. 2022; 52(2): 117-27.

[36] Stonsaovapak C, Hemrungroj S, Terachinda P, Piravej K. Effect of Anodal Transcranial Direct Current Stimulation at the Right Dorsolateral Prefrontal Cortex on the Cognitive Function in Patients With Mild Cognitive Impairment: A Randomized Double-Blind Controlled Trial. Arch. Phys. Med. Rehabil. 2020; 101(8): 1279-87.

[37] Manor B, Zhou J, Harrison R, Lo OY, Travison TG, Hausdorff JM, et al. Transcranial Direct Current Stimulation May Improve Cognitive-Motor Function in Functionally Limited Older Adults. Neurorehabil. Neural Repair 2018; 32(9): 788-98.

[38] da Silva ER, Rodrigues Menezes IR, Brys I. Effects of Transcranial Direct Current Stimulation on Memory of Elderly People with Mild Cognitive Impairment or Alzheimer's Disease: A Systematic Review. J. Cent. Nerv. Syst. Dis. 2022; 14: 11795735221106887.