International Journal of Geriatrics and Gerontology

OPEN ACCESS

Wilson Astudillo A et al. Int J Geriatr Gerontol 7: 164.

www.doi.org/10.29011/2577-0748.100064

www.gavinpublishers.com

GAVIN PUBLISHERS

Review Article

On the Etiology and Characteristic of Pain in the Elderly Suffering from Dementia

Wilson Astudillo A[1], Luis C Alvaro G[2], Antonio Salinas M[3], Michael Silbermann[4*], Zemilson Bastos Brandao[5], John Comba M[6], Carmen Mendinueta A[7]

[1]Neurologist, Chair Palliativos Sin Fronteras (PSF),San Sebastian, Spain.

[2]Neurologist Universidad del País Vasco Hospital de Basurto, Bilbao, Spain

[3]Paliativist.Radiotherapist Hospital Universitario Virgen de la Candelaria, PSF Spain, Tenerife

[4]Technion- Israel Institute of Technology, Haifa, Israel

[5]Anaesthetis. Rede D´oR Sao Luis de Hospitales, Brasil PSF Brasil

[6]Pathologist Hospital Universitario Donostia, PSF Spain,San Sebastian

[7]General physician, PSF Spain San Sebastian, Spain

***Corresponding author:** Silbermann M. Technion- Israel Institute of Technology, Haifa, Israel.

Citation: Astudillo AW, Alvaro GLC, Salinas MA, Silbermann M, Brandao ZB, et al. (2023) On the Etiology and Characteristic of Pain in the Elderly Suffering from Dementia. Int J Geriatr Gerontol 7: 164. DOI: 10.29011/2577-0748.100064

Received Date: 16 August, 2023; **Accepted Date:** 01 September, 2023; **Published Date:** 08 September, 2023

Abstract

Unaddressed pain poses a significant problem for individuals with dementia, resulting in substantial distress and unnecessary suffering. The main causes of pain in dementia patients are reviewed. Some of them overlap with those faced by other patients, while others are distinct due to the specific neuropathological transformations inherent to dementia. These changes often modify the way pain is perceived, anticipated, and physically responded to. Consequently, diverse pain experiences and altered anticipatory and motor reactions can arise. It is imperative to enhance research, training, and the comprehension of pain management among healthcare practitioners, specifically concerning patients with dementia.

Keywords: dementias, pain pathways, causes, behavioural disorders, pathological changes.

"There is nothing in man of a more fragile nature than memory, since it is affected by illness, injury and even fear". Plinio, the Elder. First Century

Introduction

Pain is underestimated and undertreated mostly in elderly in all settings of care, but also in middle aged man and women [1,2]. Its prevalence increases with age affecting 25 % y 83% of the elderly living in the community and up to 80 % living in nursing homes experience chronic pain[3,4]. Dementia patients are also commonly affected by acute and chronic pain, which is often unrecognized and undertreated due lack of recognition and of insight that may mean that patients with dementia fail to report pain. Aphasia also could lead to problems expressing pain. It is estimated that between 20% and 50% of with moderate to severe dementia suffer from chronic pain [5,6]. Likewise , Landi [7] found that individuals with dementia had a 20 % lower probability of receiving analgesics for daily pain than those with normal cognition and Morrison and Siu [8] found that after hip surgery, dementia patients received only one-third as much opioid analgesics as those with normal cognition. Pain can be accompanied by disability, sleep disturbances, reduced mobility, weight loss, depression, anxiety, and behavioral and emotional disturbances [1-3]. Its persistence causes unnecessary suffering, compromises functionality and quality of life, and contributes

to the progressive decline of the physiological reserve with age and to frailty [9]. Caregivers often face difficulties in identifying it, due to insufficient education in pain management, limited use of pain assessment tools and resistance to use opioids and non-pharmacological measures [5]. This situation reveals the need for improved research, training and understanding of pain among caregivers of dementia patients.

Common Pain Problems in the Elderly and In Dementia Sufferers

Dementia is defined by the American Psychiatric Association as "an irreversible mental state characterized by a decrease in intellectual function, personality change, impaired judgment, and often a change in affect" [10]. It is a clinical diagnosis that requires memory impairment to be present along with at least one of other associated impairment, such as aphasia, apraxia, agnosia , or deterioration of executive function (planning, initiating, sequencing, monitoring, abstract thought) ,and complex behaviours [9,11,12]. The high number of physical assaults on staff working in dementia wards, may be related to unidentified and unmanaged pain and often results in antipsychotic medication rather than person-centered care [13].

An essential aspect of dementia is that the cognitive impairment represents a change from baseline. With most of the dementia syndromes, the change is gradual and progresses over time [12]. Dementias tend to become more prevalent after the age of 65, many sufferers share the acute or chronic persistent pain that accompanies the elderly. Thus, Mitchel et al. (14) followed for 18-month elderly people with severe dementia and found that pain to be the third most common cause of distress, affecting 39% of all cases, preceded by agitation in 54% and dyspnea in 46%. All pain cases require a complete clinical history delineating factors that could reduce or exacerbate it [1-3,11,15].

Pain is classified as acute- associated with trauma or injury or chronic (lasting longer than 3 months. (Table1) presents common diseases and causes of pain in the elderly [1,2,11,16]. In acute pain, the most important causes are traumatic and inflammatory while in chronic pain are musculoskeletal pathology including previous injuries and areas of surgery, history of rib or limb fractures, cranial trauma or surgery, herpes zoster and treatments (anticholinergics, benzodiazepines, opioids, antipsychotics and antihypertensives, statins, chemotherapy), etc. If there has been gastric surgery, vitamin B12 deficiency may be suspected, and in case of frequent headaches, chronic use of analgesics. Other medical conditions, like cancer, heart disease or kidney disease, can cause pain. The different types of pain: nociceptive, neuropathic, visceral or mixed can be more difficult to assess. Frailty and dementia may increase the risk of medication-related harms and change goals of care. Caregivers may not realize the disease has worsened because patients cannot verbally express how they are feeling. Swelling or other symptoms may not be easily noticed if the person is bedridden. Mental pain can be exasperated by dementia. Patients may experience significant loss or grief, even when confused or disoriented. This can lead to social, spiritual or emotional pain, which is felt physically like other types of pain [5].

Table 1: Common Causes of Pain in Old Age and Dementia [11,14-18]

Arthritis Osteoarthritis	Intracranial hypertension
Gout and pseudogout	Spinal stenosis
Osteoporosis	Seronegative spondyloarthropathies
Claudication	Fibromyalgia
Decubitus ulcers	Low back pain from many causes
Constipation	Primary headaches (tension, advanced or early stage of dementia) and excessive use of painkillers. Temporal arteritis, cervical osteoarthritis, depression, subdural hematoma, water and electrolyte disorders
Gastro-esophageal reflux	Muscle cramps
Previous fractures	Peripheral neuropathies, postherpetic neuropathy (PHN)
Thrombosis	Muscle spasticity
Tumors	Angina
Urinary tract infections	Prolonged immobility

L.C. Alvaro [17] and Mesioye A. [18] consider that there are several red flags that should always be assessed in this age group as follows: (a) herpes zoster, which can cause pain before and after the rash. Neuropathic pain is quite common and is eight times more common in people over 50 than in younger people [19]; (b) temporal arteritis, which causes headache, pain in the limbs, or proximal limb stiffness and weakness; (c) minor o major trauma, which can go unnoticed and cause chronic pain such as rib fractures, head injuries, subdural hematomas, severe osteoporosis ; (d) nocturnal or rest bone pain, indicating a possible tumor of inflammatory or infectious origin, with fever, chills, night sweats , urinary tract infection, recent instrumentation, i.e., spondylodiscitis; e) unexplained weight loss, loss of bladder and bowel, significant acute sensory deficit o motor weakness, and (f) acute limb ischemia due to fibrillation, or arteriosclerosis with pain in walking due to arterial obstruction.

For Galicia-Castillo and Weiner [1], there are four common, overlooked painful conditions in the elderly: myofascial pain syndrome (MPS), chronic low back pain, spinal stenosis, and chronic diffuse pain. Myofascial pain syndrome is described as pain, numbness, and paresthesia in the neck, shoulders and other areas, with trigger painful myofascial points (TrPs) and distant radiation, resembling entrapment neuropathy with pain in any area [20]. It usually occurs after direct trauma to the sacroiliac and

gluteal region [1,20,21] and are very common in a wide variety of conditions. It is accompanied by altered gait, sacroiliac, and lumbar and hip pain and behaves like a radiculopathy with muscle dysfunction where patients complain of severe pain in the buttocks radiating to the leg and foot.

Chronic low back pain is multifactorial. It accounts for 80% of all pain and is associated with multiple physical and psychological factors such as myofascial, sacroiliac joint syndrome, hip osteoarthritis, and/or anxiety or depression. Imaging tests should be ordered if there is a history suggestive of fracture, infection, or tumor. A majority (95%) of the elderly have degenerative disc or lumbosacral joint pathology that is often unrelated to pain.

Lumbar spinal stenosis (congenital or acquired narrowing of the spinal canal) usually presents as pain, paresthesia, and weakness in the legs and calves during prolonged standing or walking (neurogenic claudication), with spasms and pain in the back. In most cases, spinal stenosis is asymptomatic. It is necessary to identify claudication and treat contributory factors such as being overweight before referral for surgery. Caudal or lumbar epidural blocks with local anesthetic and corticosteroids are effective. Surgery is indicated in pain that does not respond to treatment [21]. Chronic diffuse pain is associated with osteoporosis or osteoarthritis and is a very frequent cause of disability. One can see that half of the patients with progressive neuromuscular disease report moderate to severe pain and that degenerative arthropathies are the second most common chronic condition after hypertension in 50% of the elderly and are accompanied by stiffness and pain in up to four joints [1,11,20,21].

Chronic pain affects some of the same areas of the brain that are affected by AD. The changes occur in the area called locus coeruleus and affect norepinephrine. Its effective management should consider not only the underlying pathology but also the most prevalent comorbidities and drug interactions that might contribute to the pain and its implications.

Pain Pathways and the Expression of Pain Experience

Pain according to the IASP is “an unpleasant sensory or emotional experience associated with, or resembling that associated with, actual or potential tissue injury [22].”The current IASP definition acknowledges that although tissue injury is a common antecedent to pain, pain can be present even when tissue damage is not discernible. This definition encompasses the objective part of pain, related to physiological aspects, as well as the subjective part, i.e., the affective or reactive emotional charge that qualifies the suffering associated with pain. It is valid for patients with mild dementia but as it progresses their difficulties in expressing the experience of pain increase [14,15,18,23,24].

Both neuropathological an neuroimaging studies have describe interconnected brail areas that are important intermediation of pain processing. Painful stimuli reach the brain via two pathways: the lateral system, where the sensation of pain (in its sensory-discriminative-intensity aspects) travels through the anterolateral part of the spinal cord via the lateral spinothalamic bundles, until it reaches the hypothalamus, thalamus, and somatosensory cerebral cortex, and the slower medial conduction system, which is located in the medulla oblongata and periaqueductal midbrain to the cingulate cortex and terminates diffusely in the frontal and limbic lobes. The latter is responsible for the motivational-affective, cognitive-evaluative aspects of pain memory (unpleasant feelings) and its autonomic neuroendocrine responses (need references for all these statements). The cortical projection areas of the medial nociceptive pathway are strongly affected by the neuronal deposits characteristic of Alzheimer’s disease 9,17-Overlap of the two systems might occur in the insula [5, 17, 22] (figure 1)

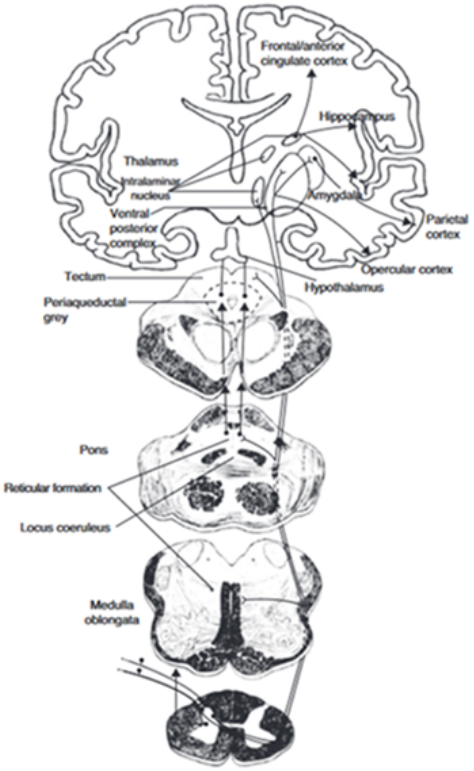

Figure 1: The lateral and medial pain pathways [17]

Figure.1 Schematic of the efferent pathways of the lateral pain system, which project from the ventral posterolateral nucleus of the thalamus to the primary parietal cortex, and schematic of the efferent pathways of the medial pain system, which reach numerous cortical areas and the hypothalamus, according to the more complex aspects of pain perception that they transmit.

This may explain the alterations in the mental experience of pain in this condition. For L.C. Alvaro [17] and Price [22],

the prefrontal cortex, anterior cingulate cortex, perisylvian areas, hippocampus, and hypothalamus are the areas responsible for the cognitive, evaluative, emotional, memory, and autonomic response dimensions of painful experiences. They are prepared to neutralize or defend it through the coordination of the cognitive-evaluative and the strictly sensory component of pain. The connections of the medial pain system with the limbic system, especially the amygdala and those of the hypothalamus, play a central role in aversive behaviors and in autonomic and neuroendocrine responses [17]. The periaqueductal gray matter (PGS) decreases pain by facilitating the secretion of endogenous opioid derivatives [17, 25-27].In demented patients there is less response to analgesic treatments with absence of the placebo effect. Consequently, higher doses of analgesics are necessary in cases of AD [26].

Types of Dementia and Pain

Dementia is a very common pathology over the age of 70, so it is to be expected that many people with dementia will suffer from pain. The most obvious and serious effect of dementia in chronic pain is its inability to relay subjective pain information accurately; otherwise, there is the possibility that chronic pain may be ignored, undertreated, or assumed to be nonexistent. Pain intensity and number of localized pain complaints bear small but significant negative impact to cognitive impairment [14,15].

The nature of chronic pain in dementia might be altered due to neuropathological changes that are involved and affects some of the same areas of the brain by AD, which in turn can alter pain perception and consequently might compromise anticipatory reactions and motor avoidance responses. Pain among nonverbal elderly or severely cognitively impaired individuals usually is expressed in the form of stereotypical pain behaviors, such as moaning, whimpering, withdrawal, restlessness, guarding, and protective postures. It is likely that the dementia process affects nociception and cognition and that the emotional components of pain overlap with the behavioral components in severe dementia, as shown in Table 2.

Table 2. Dementia and pain [11]

Effect on nociception	The dementia process damages the nervous system and can have a direct effect on pain pathways. It may decrease, increase, or alter pain sensation.
Effect on pain cognition	Dementia impairs all aspects of cognition, from memory to the conceptualization of pain.
Effect on emotional response to pain	Dementia can damage appropriate emotional responses and can have effects as varied as indifference or disinhibition.

Dementia lesions are placed in the nociceptive pathways and accordingly pain may have different clinical features than those in the non-demented population. As dementia progresses, do does the likelihood that patients are experiencing pain. For this reason, the painful experience becomes different and distinctive for every lesional type. The lateral nociceptive pathway (lateral thalamic nuclei and primary parietal cortex), which is in charge of the primary pain perception, is preserved in dementia. Thereafter, the shear painful perception, including pain intensity and threshold, remains unmodified [11,17]. Distinctly, the medial pain pathways are affected by dementia lesions in several cortical projection areas, including areas of expectation and integration of experience (prefrontal), memory (hippocampus), and autonomic and motor defense (amygdala, periaqueductal gray matter, hypothalamus). In this pathway are included: the intralaminar thalamic nuclei, the pons (locus ceruleus: LC), the mesencephalon (periacueductal grey substance: PGS), the hypothalamus (paraventricular nuclei, mamilary tuberculum) and different areas of the parietal (primary, secondary, operculum), temporal (amigdala, hyppocampus) and frontal (anterior cingular: ACC) [9,19,22-27]. As a consequence, the kind of pain evoked by these areas will be compromised and affect cognitive assessment, the mood and emotion inherent to pain, the pain memory or the autonomic responses are modified in dementia [28].

The medial regions of the temporal lobe (hippocampus and amygdala) are responsible for pain memory. The orbitofrontal cortex is crucial to the anticipation inherent in the placebo effect and locates the site of the painful stimulus. In a recent article in Nature Neuroscience, using surgical implants, scientists have recorded electric fluctuations in the orbitofrontal cortex, an area involved in emotion regulation, self-evaluation and decision making [24]. The anterior cingulate cortex is important for perceiving both acute and chronic pain. Neurodegeneration also affects brain structures involved in the inhibitory control of pain, such as the raphe nucleus, the mesencephalic periaqueductal gray matter (MGP), the vegetative nervous system, and the intralaminar nucleus [17,22,24], influencing aversive and neuroendocrine pain behaviors. The main subtypes of dementia as related to pain, are the following:

Alzheimer's disease (AD) is characterized by extracellular deposits of beta-amyloid and neurofibrillary tangles formed by tau protein that accumulate in the cytoplasm of neurons and axons and loss of neurons [9]. The neuropathological changes are predominantly in the temporal and parietal cerebral cortex and hippocampus. As a result there is a reduction in the anticipatory and avoidance responses and also a flattening of the autonomic responses [9,18,25]. These are essentially secondary to the degenerative changes in the medial temporal (pain memory) and anterior cingular: ACC (cognitive and mood aspects) areas. Memory loss in older Alzheimer patients can be characterized

by decrements in all three levels of memory: sensory register, short-term, and long-term memory. It accounts for 60 %–80% of all dementias. In the mild to moderate forms, perception, pain threshold, and touch are relatively preserved [9,17]. Due to dysfunction of cortical connectivity, there is impaired integration of information, with particular impairment of the ability to combine incoming stimuli and analyze them simultaneously in different cortical areas to produce a coherent response, although the ability to analyze each feature separately is retained [17,23]. Further, in AD cases structures associated with pain perception, including the cognitive component, memory formation and with the vegetative autonomic response, patients require stronger stimuli to elicit equivalent autonomic responses as compared with controls. For example, blood pressure and heart rate are not altered except when the pain is very acute [17]. Thus, patients developed a distorted mental experience of pain, leading to varying degrees of pain impairment that differ from the simple parietal sensory of the lateral pain pathway and the parietal cortex S1 and SII, which are usually less affected. They feel the pain, but do not anticipate it, remember it, or avoid it by withdrawal or autonomic defense [17,22,23,25,26].

Vascular dementia or multi-infarct dementia (MID) (10%-20%) is the second most common type of dementia caused by multiple ischemic –hypoxic brain lesions or haemorrhagic cerebrovascular, cortical, or subcortical lesions, affecting both gray and white matter and resulting in cortical, subcortical, and hippocampal-hypothalamic disconnection [9]. Multiple lacunar infarcts or deep white matter changes related to chronic isquemia may cause a subcortical dementia [9,30]. MID has been associated with slightly higher pain prevalences. They can cause hyperactivity of the hypothalamic-pituitary-adrenal axis and increased painful emotional responses, similar to hyperpathia, such as cortico-subcortical deafferentiation pain due to disruption of normal sensory stimuli reaching the brain secondary to the white matter lesions, whereby the brain tends to create its own sensory experiences, as in phantom limb pain [9,17] or post stroke central pain. The consequence is the presence of hyperpathy and hyperalgesia. Patients experience more “felt” and vivid pain, both in intensity and in the variety of forms, which may explain, for example, why they have more headaches months or years after a stroke or more central neuropathic pain. Unlike AD, there is no suggestive evidence of a decreased pain threshold.

Dementia with Lewy bodies (DLB) is the third most common cause of dementia, Pathologically ,it is part of the spectrum of synucleopathies, characterized by neuronal deposition of synuclein, leading to the formation of Lewy bodies(abnormal alpha-synuclein clamps). In this kind of dementia, there is a slowly progressive cognitive decline, accompanied by vivid hallucinations, motor features of parkinsonismo and fluctuating cognition with pronounced variations in attention and alertness. Reduced perception of pain and distress, is characterized by fundamental alteration in the parasylvian area [9,17,23,25,29] with naming loss than in AD, although they share some of the topography of the pathological deposits, more in posterior areas in MDI than in Alzheimer’s disease. Postural instability, difficulty in walking and falls are their most important motor manifestations.

Mixed dementia: This is a combination of two or more types of dementia because most sufferers have a vascular element and AD components that are difficult to quantify. Vascular changes are considered often as the trigger to AD symptoms; therefore, control of vascular risk factors is important for reducing the impact of AD and other dementias.

Frontotemporal dementia (FTD) is a rare form of dementia that tends to occur before the age of 60. It is associated with abnormal amounts or forms of the tau and TDP-43 proteins. Frontal and lateral temporal atrophy in FTD are greater than in AD, with less flow in prefrontal cortex, orbitofrontal cortex, the insula and perisylvian areas as seen in SPECT or PET imaging scans. As a result, there is a reduction in the cognitive-evaluative component of the painful experience, so that the expression of pain is milder. It is possible that patients with FTD have an increase in pain threshold. It is linked to the above mentioned affective-emotional component, which is responsible for a higher tolerance to pain and for a lesser pain sensation [9,17,22].

Parkinson’s and Huntington dementias (PD) often are accompanied by dementia in the last stages of the disease. Advanced Parkinson’s present with tremors, rigidity, bradykinesia, and gait disturbances. Several pain syndromes exist in these cases, and it is linked to early lesions of the locus ceruleus or PGS, which reduce its prominent antinociceptive action through several peptides. There is a Lewy Bodies pathology in areas of the brain important for pain processing [9]. Dysfunction of these areas which is very common [17], and may improve with levodopa therapy. However, erratic pain in different areas, with poor response to L-dopa adjustments, and even more common than those of other origins (joint, inflammatory, systemic, etc.). The lack of facial expression may lead to a reduction in the external expression of pain, as in the case of FTD as described above.

In the demented patients in general there is a lack of expectation to analgesic treatments and an absence of the placebo effect, consequently higher doses of analgesics are necessary [17,26].

Conclusions

Pain in dementia patients is fairly common but is usually is poorly recognized and under-treated due as dementia progresses, the persons ´s ability to communicate their need becomes difficult to notify it or interpreting their pain as the lack of appropriate education of further training and interest among the care givers and professionals. Next to easy self-report measures, observational

instruments are necessary in clinical practice. These kind of pain increase with age and they have unique characteristics due to neuronal damage that affects the pain pathway in dementia. Persistent, untreated pain can promote a progressive worsening of dementia and its suffering. It needs more research and training for a better understanding of the problem. The management of pain in dementia requires a more complex multidisciplinary approach involving patient, family and health personnel.

References

1. Galicia-Castillo M. Weiner D. (2023) Treatment of chronic non-cancer pain in older adults. UpToDate.
2. Dougherty J, Sgrillo J, Swan El (2011) Assessing and addressing pain. In. Palliative care for advanced Alzheimer´s and Dementia, edited by Gary A-. Martin, and M. S. Sabbagh, Alzheimer´s Association. Springer Publishing Company. N.Y, 2011, 83-92.
3. Bieu R, Kulas J. (2019) Pain in dementia. In: Handbook on the Neuropsychology of Aging and dementia. Edited by I.D. Ravdin HI, Katzen. Springer nature Switzerland. _20 :311-318.
4. Achterberg W, Gambassi G, Finne-Soveri H, Liperoti R, Noro A, et al. (2010) Pain in European long- term care facilitys: cross national study of Findland, Italy and Netherlands. Pain 148:70-74.
5. Mayo Clinic on Alzheimer´s disease and other dementias(2023). Mayo Clinic Press.
6. Jensen-Dahm C. (2021) Assessment and management of pain in patients with dementia. In Management of patients with dementia. 179-200.
7. Landi F, Onder G, Cesari M, Gambassi G, Steel K, et al. (2001) Pain management in frail, community- living elderly patients. Arch Intern Med, 161:2721– 4.
8. Morrison RS, Siu AL. (2000). A comparison of pain and its treatment in advanced dementia and cognitively intact patients with hip fracture. J Pain Symptom Manage, 19:240–8.
9. Widera E, Talebreza S, Bernacki R. (2021) Dementia. In: Oxford Textbook of Palliative Medicine, Edited by N.I. Cherny, M.T. Fallon, Kaasa S., Portenoy T, Currow, D. Sixth Edition, 987-999.
10. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR) APA Press, (2013) Washington, DC.
11. Watson N, Campbell R. Vallath N, Ward S. Wells J. (2019) Oxford Handbook of Palliative Care. Third Edition, Oxford University Press, 607-611.
12. Larson EB. (2023) Evaluation of cognitive impairment and dementia. UpToDate.
13. Morgan DG, Stewart NJ, D'Arcy C, Forbes D, Lawson J. (2005) Work stress and physical assault of nursing aides in rural nursing homes with and without dementia special care units. Journal of Psychiatric and Mental Health Nursing.12:347–58.
14. Mitchel SL, Teno JM, Kiely DK, Shaffer ML, Jones RN, et al. (2009) The clinical course of advanced dementia. N. Engl. MJ Med. 361:1529-1538.
15. Gloth FM. (2011) Assessment. Handbook of pain relief in older adults. Springer. 5:15-26.
16. Herr LA, Mobily PR. (1991) Complexities of Pain assessment in the elderly. Clinical considerations J Gerontol Nurs.17:12-19.
17. Álvaro González LC. (2015) El neurólogo frente al dolor en la demencia. Neurología. 30:574- 585
18. Mesioye AS. Cordts G. (2019) Pain Assessment in older adults. In: Effective treatments for pain. Edited by G.A Cordts, P.J. Christo.13-24 Springer Nature.
19. Alaba J, Arriola E, Navarro A, González MF, Buiza C, et al. (2011) Demencia y dolor. Revista de la Sociedad Española del Dolor, 18:176-186.
20. Donnelly JM, Fernandez de las Peñas C, Finnegan M, Freeman JL. Travell, Simons & Simons' Myofascial Pain and Dysfunction: The Trigger Point Manual, (2018) 3ed.
21. Waldman S. (2003) Atlas de síndromes dolorosos frecuentes. Elsevier España.
22. Price DD. (2000) Psychological and neural mechanisms of the affective dimension of pain. Science, 288:1769-72.
23. Braak H, Braak E. (1991) Neuropathological staging of Alzheimer changes. Acta Neuropathol, 82:239-59.
24. Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, et al. (2020) The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises Pain.161:1976-1982.
25. Sherder EJA, Sergeant JA, Swaab DF. (2003) Pain processing in dementia and its relation to neuropathology. Lancet Neurol, 2:677-86.
26. Benedetti F, Arduino C, Costa S, Vighetti S, Tarenzi L. et al. (2006) Loss of expectation-related mechanism in Alzheimer´s disease makes analgesic therapies less effective. Pain.121:133-44.
27. Cotrufo T. y Ureña J. M. El Cerebro y las emociones.(2022). Neurociencia & Psicología. EMSE EDAP. España.
28. Runwai P. (2023) Scientists find brain signals of chronic pain. Nature Neuroscience, May 22.
29. Mori E. (2002) Impact of subcortical ischemic lesions on behavior and cognition. Ann NY Acad Sci. 977:141-8.
30. Fisher S.E, Burgio LD, Thorn BE, Hardin JM. (2006) Obtaining self-report data from cognitively impaired elders: methodological issues and clinical implications for nursing home pain assessment. Gerontologist 46:81-88.