

Topical review

Pain in dementia

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1. Introduction

Age is the highest risk factor for both dementia and pain. With the aging of the population in many countries, the number of older persons with dementia suffering from pain will increase substantially in the next decades. Dementia and pain are complex phenomena, considering the different subtypes of dementias (for example, Alzheimer's disease: AD, vascular dementia: VaD, fronto-temporal dementia: FTD, and Parkinson's disease (PD) with dementia: PDD) and the various ways in which pain may express itself (nociceptive pain, neuropathic pain, and central pain). The subject of this review is whether patients with dementia experience and express pain in the same way as those without dementia. Clinical and experimental pain studies emphasize upon an urgent need for reliable pain assessment in both communicative and non-communicative patients. The more reliable pain assessment, the more effective is pain treatment. It is striking that the treatment of pain in patients with dementia has received the least attention so far; this topic will be highlighted upon in the final part of the review.

2. Clinical pain studies in dementia

Clinical studies suggest that undertreatment of pain in patients with dementia is common. In one study, patients with dementia (subtype not otherwise specified, NOS) recovering from hip fracture surgery received only 1/3 the amount of morphine sulphate equivalents administered to non-demented adults and 76% of patients with dementia had no standing order for post-operative analgesia [20]. In another study, only 33% of AD patients received appropriate analgesic medication compared to 64% of non-demented adults [27]. This was true for non-steroidal anti-inflammatory drugs (NSAIDs) and other classes of analgesics (opiates and acetaminophen), even though the treating physicians judged the need for pain relief to be equivalent in the two groups. Nearly 40% of PD patients have chronic pain related to their underlying movement disorder ('PD-pain'), but they are much less likely to consume anal-

gesics for this pain [21]. After adjusting for osteo-articular co-morbidities, PD patients were twice as likely to have chronic pain as a comparison group. Treatment of pain in PD patients with dementia (PDD) has been little studied so far.

Conversely, if assessments using either self-report, observational pain scales or proxy nurse ratings [17,26] suggest that there is a reduction in pain prevalence and severity in patients with AD, VaD, and mixed dementia (features of both AD and VaD), one can argue that undertreatment does not exist as those who indicate less suffering from pain, presumably need less pain medication. This appears not to be the case, however. Patients on a psychogeriatric ward where pain prevalence and intensity were found to be lower than on a somatic ward, received less pain medication than patients on the somatic ward, even when these pain parameters were matched [1]. The risk for undertreatment of pain is further enhanced in non-communicative patients with white matter lesions (WMLs), as WMLs may cause an increase in the suffering from pain due to de-afferentiation (central pain) [28]; WMLs are characteristic of subcortical ischaemic vascular dementia (SIVD), a subtype of VaD [25], but may also occur in AD, FTD, and PD [19,28,29].

Taken together, the available literature, though sparse, suggests that pain may not be adequately treated in patients with dementia. This is not so surprising while considering the complexity of reliable pain assessment and effective pain treatment in this population.

3. Experimental pain studies on dementia

Could an observed decrease in pain experience in patients with dementia be caused by altered pain processing related to neurodegenerative changes? With advancing age there are significant and widespread losses in the peripheral and central nervous systems involved with pain processing, including both afferent transmission pathways and endogenous descending inhibitory control systems [10]. The presence of a dementing illness likely adds further deficits in central pain processing pathways.

The direction in which the pain experience is altered in dementia varies with the pain parameter under investigation. In patients at an early to moderate stage of AD, VaD, and mixed dementia, an

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increased nociceptive reactivity has been observed in facial responses to pain [18] and nociceptive motor reflexes pain measures [14–16]. Adding to this perspective, it was observed by fMRI that patients in an early stage of AD showed greater pain-related activity in the known cerebral pain networks [8]. Since the deterioration of cognitive and linguistic capacities renders the verbal pain report more and more invalid, conclusions from this source of evidence have to be drawn with caution but ought nevertheless to be mentioned. Patients in an early to moderate stage of AD, VaD, and mixed dementia consistently rate weak pain stimuli similarly to controls [10,14,15]. Pain threshold studies, which by definition use weak pain stimuli, also show patients in an early to moderate stage of AD not to be different from healthy control subjects [2,3]. Pain-related brain potentials evoked with weak stimuli did not appear markedly altered in AD patients in a moderate stage of the disease [10]. However, the more severe the cognitive impairment, the more pronounced the difference in pain experience between demented and non-demented populations. For example, in AD patients, the lower the cognitive function, the lower the anticipatory heart rate responses to a noxious event [3] and the higher the pain tolerance [2]. Although pain tolerance can be tested in an experimental setting, it does not represent the suffering from *chronic* pain, which is characterized by lack of control, and its impact on function and mood. In chronic pain, the role of the prefrontal cortex is well known [28]. In PD patients with dementia (PDD) it is hypothesized that Lewy bodies and Lewy neuritis in the prefrontal cortex are responsible for a decline in suffering from chronic ‘PD-pain’ [29]. Decades ago, bilateral frontal lobotomy was used in a final attempt to control refractory trigeminal post-herpetic neuralgia [30]. Although spontaneous complaints of pain decreased, the patient reported pain as unchanged when asked.

4. Pain assessment

Clinicians often believe that those with cognitive impairment feel and experience less pain, although the evidence presented earlier suggests that this may not be the case. But the way in which the pain sensation is interpreted by the older person may impact the expressions of pain (e.g. vocalizations, facial expressions, body movements, activities and behaviors) and how those are interpreted by the observer. Herein lays the challenge of assessment.

Based on an assumption that pain conditions are similarly painful in those that can and cannot self-report, recommended procedures for identification of pain in this population have been posited by the expert panels [11,22]. Because self-report has been established as the gold standard for determining and rating pain severity and many persons with dementia are able to self-report, attempts to obtain this directly from the older persons is a recommended first step. Valid and reliable pain assessment tools in cognitively impaired older persons include simple verbal descriptor scales, pain thermometers, and facial pain scales [13]. However, when efforts to establish reliability indicate that the report is not reliable, other methods must be used. For example, observations of key behaviors (e.g. grimacing or guarding) can be made directly by the health care provider or gathered through report of surrogates (e.g. family and caregivers). Evidence suggests that the association between patient reports and surrogate reports is strong for the presence of pain but not strong for reporting of pain severity. A number of reviews have been completed [12,32] and a detailed evaluation of psychometric properties and utility are available for tools published in English at <http://prc.coh.org/PAIN-NOA.htm>. A final step in the process is the use of an analgesic trial to help validate if potential behavioral indicators of pain do respond to analgesic treatment.

5. Pain treatment

There are very few studies in the literature on pain treatment in older persons with dementia. Adequate pain control in patients with dementia depends on good pain evaluation and may express itself in an improvement in behavior and activities of daily life [6], as verbal communication about pain is not reliable anymore. Social interaction and well being of patients with moderate-to-severe dementia (not further specified) improved after administration of acetaminophen, 3 g/d, during one month [7]; acetaminophen is the most frequently prescribed analgesic medication, followed by NSAIDs and opioids. Serious adverse effects and drug–drug interactions are, however, potential because of multiple diseases and polypharmacy associated with old age [23]. Pharmacokinetic changes alter the metabolism and the elimination of the drugs. Chronic use of acetaminophen and NSAIDs may increase the risk for hepatotoxicity and gastric bleeding/renal insufficiency, respectively [24]. During the use of opioids, increased sedation and cognitive dysfunction develop easily, with side-effects like constipation and urinary retention [22]. For ‘PD-pain’, pain related to the underlying movement disorder, antiparkinsonian drugs appear to be effective [21]. On the other hand, neuroleptics that induce extrapyramidal syndromes may provoke pain [9]. Antidepressants and antiepileptic drugs, used for neuropathic pain, have numerous well-described side effects. Start slow and go slow is the motto in geriatrics, but the benefit–risk ratio of any analgesic treatment must also be kept in mind and further studied in older persons with dementia.

Expectation-induced analgesia may be affected by dementia. The prefrontal lobes play a key role in both pain processing and analgesic responses. More specifically, prefrontal regions are typically activated in complex cognitive tasks, appealing to executive functions [5], as well as in placebo-induced expectation of analgesia [31]. Interestingly, it has been shown that the placebo component of an analgesic treatment is disrupted in AD patients whose prefrontal executive functions are impaired [4]. As expectation/placebo-related mechanisms and specific effects of analgesic therapies show additive effects, the impairment of prefrontal executive control may lead to lower responsiveness to analgesics. The potential disruption of placebo mechanisms in any kind of pathological condition with the involvement of the prefrontal lobes, as occurs in FTD and VaD [28] should alert us. More research is needed to determine if there is a need to revise analgesic treatments in demented patients in order to compensate for the loss of placebo-related analgesia. Finally, the possible synergy of drug treatment with non-pharmacological approaches should not be neglected. Although little has been studied so far in the context of pain and dementia, a broader holistic approach in the care of this vulnerable population is warranted.

6. Conclusions

- Findings from clinical and experimental pain studies do not suggest that pain is less frequent and intense even if no longer reported. To the contrary, it is likely that any sign of pain (verbal or via behavioral markers) made in the presence of marked cognitive impairment requires even greater attention and a more proactive treatment response.
- The impact of dementia on pain processing varies in direction and quality, depending on the type of pain, neuropathology and stage of dementia.
- There is a high risk for undertreatment of pain in dementia, particularly in non-communicative patients with white matter lesions, but also in demented patients who report less prevalent and intense pain.

- Assessment of the cognitive status of the patient is crucial to learn which pain assessment tools are appropriate and the extent to which the patient will be able to comply with the suggested pain treatment regimens.
- A clinically relevant question that remains unanswered is whether acute and chronic pain require different behavioral assessment strategies when dementia is present.

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