CHAPTER 15

Pain perception in dementia

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Introduction

There is an estimated 35 million people with dementia across the world. 'Dementia' designates a broad category of brain neurodegenerative diseases that are accompanied by long-term loss of cognitive ability in memory functioning, attention, executive functioning, orientation, language and other cognitive domains, as well as by changes in mood and behaviour. These cognitive and affective changes increase along the course of dementia and severely impact a person's daily functioning. The most common type of dementia is Alzheimer's disease. Other common forms are vascular dementia, frontotemporal dementia and Lewy body dementia. Given that prevalence rates of dementia are tightly linked to aging, demographic changes in the coming decades and the increasingly aging population will lead to a substantial growth in the number of people affected by dementia and in the scale of the challenge of providing appropriate treatment and care for all of them. Pain presents a great challenge in the treatment of patients with dementia. The prevalence of pain, and especially of chronic pain, is strongly related to age, hitting the oldest population the hardest: prevalence rates above the age of 85 years are of 70 per cent (Helme and Gibson, 2001). Given these circumstances, it is clear that pain is probably very common among people suffering from dementia. However, because such patients (especially those in the advanced stages of the disease) are often unable to use self-report to communicate their suffering, their pain is often overlooked, and therefore remains untreated (Scherder et al., 2009). For a long time the topic of pain in dementia has been overlooked; but in the last two decades clinicians and scientists have started to conduct research on the prevalence (Takai et al., 2010) and assessment (Hadjistavropoulos et al., 2007; Herr, 2011) of pain in older people with dementia and on the challenges related to its treatment in this population and have stressed the severe consequences of undetected and untreated pain (AGS Panel, 2009; Gloth, 2011). Persistent pain has been associated with a progressive decline in functional and mental capacity (Moriatry, McGuire and Finn, 2011), in social interaction (Lin et al., 2011), in quality of life (Cipher and Clifford, 2004), in appetite (Bosley et al., 2004) – as well as with sleep (Giron et al., 2002) and behavioural disturbances

such as agitation, depression and anxiety (Husebo et al., 2011). Given these severe conse-quences, it is a pressing issue to improve our understanding of how dementia impacts pain processing and how pain can be assessed and treated in this vulnerable patient group.

On the basis of previous reviews made in our group (e.g., Husebo et al., 2012), we give here an overview of the literature on pain and dementia – including of basic research that investigates how pain processing and pain responses are affected by the disease. Our overview also summarises pain assessment and treatment recommendations for these individuals.

Experimental perspective

When research on pain and dementia started in the late 1990s, some believed that patients with dementia reported less pain simply because their neurodegenerative decline made them less sensitive to pain. In order to investigate how the pain system itself might be altered across the evolution of dementia, experimental studies are necessary. So far, there have been several studies that used experimental pain in patients with dementia (these were mostly patients with Alzheimer´s disease) and assessed changes in pain thresholds, pain tolerance, pain reflexes and supra-threshold responses. Applying experimental pain has the advantage of making it possible to gain complete control over the noxious stimulus and, in the process, to disentangle that stimulus from the assessable pain responses. Experimental pain is usually induced by means of thermal, electrical or pressure stimulation.

In an assessment of pain thresholds, each individual has to indicate when a stimulus starts to become painful. When carrying out this process in patients with dementia and in healthy controls, most studies found no differences in threshold levels between the two groups (Benedetti et al., 1999; Benedetti et al., 2004; Gibson et al., 2001; Jensen-Dahm et al., 2014; Lints-Martindale et al., 2007). Likewise, patients with dementia and controls were found to rate supra-threshold pain intensities – that is, situatons where stimuli were lying above the pain threshold – as equally painful (Cole et al., 2006; Jensen-Dahm et al., 2014; Kunz et al., 2007; Kunz et al., 2008). When pain tolerance is under investigation, each individual has to indicate when a stimulus starts to become unbearably painful. Here the findings were more contradictory: there was evidence for increased (Benedetti et al., 1999), decreased and unchanged tolerance levels in patients with dementia (Jensen-Dahm et al., 2014). An interesting approach has been chosen by Jensen-Dahm et al. (2014), who reported not only on changes in pain psychophysics in patients with dementia but also (in parallel) on the psychometric quality of their data. Their findings clearly suggest that the pain threshold, pain tolerance and supra-threshold pain ratings were as reliable in patients with mild degrees of dementia as they were in healthy controls. Thus we can conclude from these studies that sensitivity to low and moderate noxious stimuli seems unchanged in patients with dementia, but it remains unclear how pain tolerance is affected.

Some authors have argued that it might be more appropriate to assess pain responses that are independent of the patients' ability to give self-reports of pain, in view of the decline in their cognitive abilities (Kunz et al., 2007). Such a response is the nociceptive flexion reflex (NFR/RIII) – a physiological, polysynaptic reflex allowing for noxious stimuli to elicit an

appropriate withdrawal response. The NFR threshold has been shown to be highly correlated with the subjective pain threshold (at least in cognitively unimpaired individuals); in consequence, it is believed to have the potential to serve as a non-verbal assessment tool for pain sensitivity. This reflex has been assessed in one study, and its threshold was found to be significantly decreased in dementia; this could point to an increase in pain processing, at least at the spinal level (Kunz et al., 2008). Moreover, when looking at brain responses to pain in patients with dementia, functional magnetic resonance imaging (fMRI) studies showed that brain activity in response to noxious stimulation is preserved and even elevated in patients with dementia by comparison to healthy controls (Cole et al., 2006). Another type of response that is independent of the patients' ability to give self-reports of pain is the autonomic response (e.g., heart rate, skin conductance). Studies showed a decline in autonomic responsiveness in patients with dementia (Kunz et al., 2008; Rainero et al., 2000). However, given that dementia is known to be accompanied by dysfunctions of the autonomic system even at its earliest stages, the autonomic response might not be a valid pain indicator in this patient group.

In conclusion, although the empirical findings on pain processing in patients with dementia are partly contradictory, most of them seem to suggest that the processing of experimentally induced pain is not diminished in patients with mild to moderate forms of dementia. When intepreting these findings, one has to keep in mind, however, that they come from, and are representative of, patients with only mild to moderate degrees of cognitive impairments. Most of the patients included in the studies were still able to use language in order to provide pain thresholds and pain tolerance estimates, as well as self-report ratings of their pain – an ability that declines rigorously in moderate to severe stages of dementia. We therefore do not know whether or how pain sensitivity might be altered in later stages of the disease. Due to ethical considerations, however, it is difficult to apply experimental pain induction procedures on patients in these severe stages of dementia.

Clinical perspective

Pain prevalence in older individuals with and without dementia

On account of their advanced age, individuals with dementia often suffer from multiple morbidities associated with pain. However, the exact pain prevalence in dementia is unknown, due to the lack of self-report in this patient group. Thus we will report prevalence rates from elderly individuals with and without dementia. Between 45 per cent to 83 per cent of the patients living in nursing homes experience acute or chronic pain, particularly those with moderate to severe dementia. Most of them (about 94 per cent) suffer from persistent pain (3–6 months or more: Miro et al., 2007), which is often located in the musculoskeletal system (Grimby et al., 1999). Chronic musculoskeletal pain affects over 100 million people in Europe and is by far the most common limiting factor that affects activities of the ageing population. Musculoskeletal pain increases the risk of reduced mobility, disability and muscle weakness and reduces the health-related quality of life (Woolf et al., 2004). But pain problems are not related only to movement. About 40 per cent of elderly individuals experience pain in internal organs, head and skin, which is more challenging to quantify (Husebo et al., 2008). Elderly

patients with visceral painful conditions are far more likely than younger adults to present atypical pain responses (Helme and Gibson, 2001). Peptic ulcers, intestinal obstruction, and peritonitis are other visceral conditions, often with reduced or absent abdominal complaints (Helme and Gibson, 2001), and about 45 per cent of older persons with appendicitis do not have typical lower-right quadrant pain as a presenting symptom, by comparison with 5 per cent of younger adults (Wroblewski and Mikulowski, 1991). Living in a nursing home, 53 per cent of the elderly are at risk of developing a pressure ulcer (Horn et al., 2002), and skin diseases found in 95 per cent of the patients were described as constituting one of the most prevalent health problems (Black et al., 2006). Pain in connection with genito-urinary infections is quite often described in elderly patients. Catheter-associated urinary tract infection is the most common nosocomial infection; it accounts for more than 1 million cases every year in American hospitals and nursing homes (NHs) (Tambyah and Maki, 2000). Moreover, orofacial pain also has an incidence rate that increases with age (Koopman et al., 2009; Lobbezoo, Weijenberg and Scherder, 2011); around 30 per cent of the institutionalised elderly have experienced acute dental pain during the preceding year (Gluhak et al., 2010).

In conclusion, pain prevalence rates are high in elderly individuals and there is no reason to believe that these prevalence rates should substantially differ between those with and those without dementia.

Assessment of pain in individuals with dementia

Given the high prevalence of pain in the elderly, a proper assessment of pain by onlookers such as health-care professionals or family members is a prerequisite to successful pain treatment. The task of judging a sufferer's pain appropriately is a very complex one, given that pain is a very personal, private and subjective experience. Whenever older adults in pain also have severe cognitive impairment – which goes along with the loss of language and abstract thinking – the task of appreciating their pain becomes even more challenging. This is the case because one of the most important cues that judges rely on when assessing pain is the patient's self-report; but this self-report is often missing in cognitively impaired patients (Kappesser, Williams and Prkachin, 2006). Accordingly, older adults with dementia, particularly those in advanced stages of the disease, are at a very high risk for being underdiagnosed, and consequently undertreated for pain. Against this background, immense effort has been invested in the development of behavioural pain assessment tools that do not rely on the individual's capacity to provide a self-report of pain (e.g., Herr, Bjoro and Decker, 2006; Zwakhalen et al., 2006). These assessment tools are based on observations of typical behaviour in the patients that might be related to pain, such as vocalisations (e.g., moaning), facial expressions (e.g., grimacing), and body movements (e.g., defense).

There is also strong evidence that behaviours like agitation, pacing or resisting care are related to present pain problems. As stated above, a panel on Persistent Pain in Older Persons convened by the American Geriatric Society (AGS) has recommended that, as a prerequisite to appropriate pain treatment, a comprehensive, disease-specific and individual assessment of a patient's typical pain behaviour be carried out by using a validated pain assessment tool (AGS Panel, 1998). However, the recommendations of the AGS Panel are based on experience

with older adults without dementia. This is of key importance, because in dementia symptoms attributed to neuropsychiatric disturbances may overlap with indicators of pain and thus can make interpretation quite challenging (Herr et al., 2006).

Self-report on pain

As stated before, the validity of self-report ratings might be questionable in patients with dementia, given the decline in language ability throughout the course of this disease. However, self-report might still be an appropriate method for pain assessment in its early stages, when the patient is still able to recognise and verbalise pain (Corbett et al., 2012). Nevertheless, studies that aimed to assess the performance of self-assessment scales (verbal and visual scales, the Faces Pain Scale) found that, whereas patients with mild to moderate degrees of impairment demonstrated comprehension of at least one scale, the comprehension rate decreased drastically in those with moderate to severe impairments (Kaasalainen and Crook, 2004; Pautex et al., 2006). Comprehension was defined as the ability to explain the scale's use and to indicate correctly on it positions for 'no pain' and for 'extreme pain'. Thus the self-report on pain seem to be still valid in mild forms of dementia. However, when the degree of cognitive impairment increases, the self-report seems to become a more and more invalid assessment tool (see Figure 15.1). Clinicians should be aware of this and should not interpret the absence of self-reported pain in a severely demented patient as a valid indicator of a pain-free state.

The facial expression

In the last two decades, more than 30 pain assessment instruments for older persons with dementia have been developed, tested, and reviewed in the literature. Most of these instruments are based on the idea that the patients' acute or chronic pain experience is communicated through changes in facial expression, vocalisation, and body movements (see Figure 15.1). Especially the *facial expression* seems to be one of the most promising non-verbal
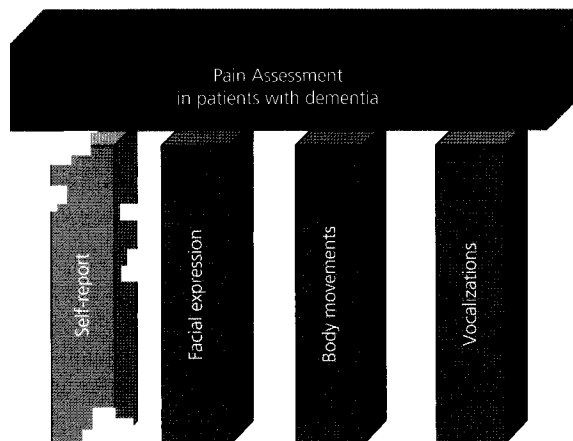

Figure 15.1 Pain assessment in patients with dementia should mostly rely on behavioural categories that are believed to be indicative of the presence of pain (facial expression, body movements and vocalisation), and not so much on self-reports on pain.

pain indicators, given that items relating to it are included in all pain assessment instruments. Interestingly, one of the first instruments developed that try to assess non-verbal behaviour is the Facial Action Coding System (FACS), which focuses exclusively on facial expressions (Ekman and Friesen, 1978). The FACS is based on the anatomical analysis of visible facial movements, which are categorised as action units. Using the FACS, it has been shown that there is a small subset of facial movements that occur in the context of pain; these include narrowing the eye aperture, contracting the eyebrows, lifting the upper lip and closing the eyes (Prkachin, 1992). Patients with dementia show the same subset of facial movements in response to pain as non-demented elderly individuals (Kunz et al., 2007). These findings are very promising: they clearly suggest that the face encodes the experience of pain in a specific way and that this specific encoding does not change throughout dementia.

It is, however, important to point out that, despite evidence that there is a small subset of pain-indicative facial movements, this does not imply the existence of only one facial expression of pain – a uniform and unique 'face', which can be observed at all times and in all individuals. Instead the frequencies of the occurrence of these key movements during pain usually range from 10 per cent to 60 per cent. Therefore the likelihood that all four key facial movements will occur simultaneously – in other words, the likelihood that an individual experiencing pain will display the complete subset or the 'prototypical expression of pain' – is very low. Rather individuals display only parts of this subset, sometimes even blending it with a limited range of other facial movements (e.g., smiling: Kunz, Prkachin and Lautenbacher, 2013). We have recently shown that it might be more helpful to differentiate between *at least three* different facial activity patterns that are displayed in the context of pain and that combine, or are made up of, various facial movements (Kunz and Lautenbacher, 2014). These patterns were (1) a tightening of the muscles surrounding the eyes, with furrowed brows and wrinkled nose; (2) furrowed brows, with a tightening of the muscles surrounding the eyes; and (3) an opened mouth, with a tightening of the muscles surrounding the eyes. These different facial activity patterns all have one facial movement in common, namely the tightening of the muscles surrounding the eyes. This facial movement is indeed the most frequent, and hence possibly the most important movement that occurs during pain.

Pain behaviour rating scales

Observational pain behaviour-rating scales have been developed mostly on the basis of literature reviews and interviews with nursing staff, and – as stated before – they include observational items related to facial expressions, vocalisation, and body movements (see Figure 15.1; Cohen-Mansfield, 2006). Most of these items are assessed by the rater according to frequency, intensity, or presence and absence. The different observational scales differ to a certain extent with regard to the types of items included, the interpretation of the total pain intensity, the scoring method, and the instructions for staff training. In addition, different systems of scoring the presumed pain intensity make the use of these scales challenging and sometimes only suitable for research purposes.

Usually these observational scales are filled out when the patient is at rest (after some minutes of observation); but sometimes patients are observed during activities of daily life (ADL). Recent findings clearly suggest that the observation of the patient at rest may

not disclose the pain, especially chronic pain conditions, and it is now recommended that movement-related pains are better disclosed during ADLs. This idea has already been incorporated into at least four pain behaviour-rating scales, and these scales include instructions for spontaneous or guided movements during the pain observation process (Lefebvre-Chapiro, 2001; Snow et al., 2004; Husebo et al., 2010; Nygaard and Jarland, 2005).

Most of these scales are easy to use but require training and time for proper administration. In the past few years doctors, nurses and other caregivers have been involved in the validation processes. Evaluations of the most promising observational pain assessment scales in patients with dementia indicate that, although a number of tools demonstrate some promising potential, the validity of those scales is still not satisfactory (Villanueva, 2003). A further limitation is that some instruments are not validated for English or are validated for one language only. Another concern is related to the scoring system. To produce a total score, most instruments add up the number of observed behaviours. This means that a higher number of behaviours indicates more pain. However, a patient may be in severe pain even if this pain is manifested only in a few items, for instance in connection with moving a leg or an arm, and the rest of the body is pain-free. Some patients with Parkinson disease, for instance, or in a severely reduced condition would not be able to express enough behaviour to be judged to be in pain. Others, such as patients with Huntington's chorea, may express too much pain even when there is none.

In conclusion, as the severity of dementia is increasing, caregivers should rely less on self-report ratings and more on behavioural indicators of pain. Especially the facial expression seems to be a promising pain indicator. Patients with dementia display the same types of facial movements in response to pain as everyone else; the pain typicalness of their facial expression is not reduced. This implies that facial expressions of pain have the potential to serve as an alternative pain indicator in patients with dementia. With regard to pain behaviour-rating scales, several scales are available. However, the process of validating these scales has only just started. Although first results are promising, future studies are needed to define the most appropriate pain behaviour items – the ones that are able to discriminate between pain behaviours and behaviours related to other aspects and unmet needs in patients with dementia.

Pain treatment for individuals with dementia

Pharmacological management of chronic pain in older persons may be challenging. In 2009, with support from the American Pain Society and the American Academy of Pain Medicine, the AGS Panel revised its previous recommendations on pain management in older adults. The new guidelines include key approaches for safer opioid prescriptions in older adults. However, the current treatment recommendation guidelines, which aim to update the evidence base of the 2002 guidelines, are not yet evidence-based and do not consider the treatment of pain in patients with severe dementia, who often are excluded from randomised clinical trials and pain treatment studies (Corbett et al., 2012).

Although pharmacological treatment with analgesics is the most common form of pain treatment in older individuals, the use of non-pharmacological and alternative treatment should also be considered, given that these treatments have less adverse side effects (Ballard et al., 2011).

Prevalence studies of analgesic drug use in dementia

Traditionally, medications with analgesic effects are classified into three groups: periphery analgesics, such as acetaminophen; non-steroidal anti-inflammatory drugs (NSAIDs); and opioid agents. Even when pain is assessed and recognised, pain management often falls short of prescription recommendations. This seems to be a worldwide challenge, documented by studies from the Netherlands (e.g., Achterberg et al., 2007), Belgium (Elseviers, Vander Stichele and Van Bortel, 2010), England (Closs, Barr and Briggs, 2004), Norway (Nygaard and Jarland, 2005), the United States (Won et al., 2003) or China (Tse, Pun and Benzie, 2005).

In a study of 551 nursing-home residents in North Carolina, only around 50 per cent of the individuals with severe cognitive impairment received pain medications, by comparison with 80 per cent of the cognitively intact cohort ($P < 0.001$), despite a similar rate of pain-related conditions in both groups (Richards and Scott, 2002). Notably, cognitively impaired persons were more likely to be given pain medications 'as needed', while their peers had regularly scheduled analgesics. 'As needed' drug regimens are particularly inappropriate for individuals with moderate to severe cognitive impairment, who are unable to verbally communicate the need for pain relief. A study on the knowledge and beliefs of health-care professionals caring for older adults with dementia in a nursing-home setting found that a large number of the resident professionals thought that patients should only receive analgesics 'when necessary' rather than on a fixed schedule (Cramer et al., 2000).

In addition to the reduced analgesic treatment in patients with dementia, the analgesic effect itself might be reduced in these patients. There is evidence that patients with dementia do not experience a placebo effect (Benedetti et al., 2006). Losing the ability to modulate pain via endogenous placebo-related mechanisms could mean that patients with dementia need a higher dose of analgesic medications for pain relief to be achieved (Benedetti et al., 2006; for a comprehensive overview of this aspect, see Chapter 16 in this volume).

But time is changing. An increasing awareness of pain management in patients with dementia has been recently reported in the Swedish National Study of Aging and Care – Kungsholmen (Haasum et al., 2011). The study analysed the use of analgesics and psychotropics in 2,610 participants aged over 65 and found that 46 per cent of the patients with dementia used at least one analgesic drug, by comparison with 25 per cent of those without dementia. Persons with dementia reported pain less frequently, but the prevalence of pain-related diagnoses was similar to that found in persons without dementia. These findings are very promising, since they clearly suggest that the research findings of the last decades – which reported the undertreatment of pain in dementia – have already impacted the clinical practice and have led to an intensification of pain management in this frail patient group.

In conclusion, after many decades of reduced analgesic treatment for patients with dementia, health-care professionals seem to be better aware of the need for pain management in this patient group. Given that patients with dementia are still excluded from high-quality randomised-controlled analgesic trials, it is difficult to give recommendations for their pharmacological treatment with analgesics. We do know, however, that dementia is accompanied by a loss of placebo effects, which might mean that higher dosages of analgesics are required to treat pain.

Overall conclusion

Advanced age is associated with an increased prevalence of pain and of dementia. Given that the ability to report about pain depends on the patient's memory, expectation, and insight, patients with dementia (who are often limited in these respects) are at high risk for being underdiagnosed and for remaining untreated for pain. In patients with dementia, pain that goes unnoticed may contribute to increasing behavioural disturbances, like agitation and aggression. International recommendations to assess pain have been published and an impressive number of pain behaviour-rating scales have been developed and tested. However, the validity of these scales is still unsatisfactory. It is, moreover, an alarming fact that patients with dementia are still excluded from high-quality trials of pain treatment in older individuals. This underlines the high need for research as well as for excellent concepts for the implementation of pain assessment and pain treatment in elderly individuals with dementia.

Acknowledgement

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