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Chapter 1

Introduction

Undertreatment of pain in dementia

The number of older people is predicted to increase rapidly in industrialized countries within the next years (Anderson and Hussey, 2000). For example, in the United Stated, the proportion of the population aged 65 years or older will increase from 13% in 2010 to more than 20% in 2050 (Vincent and Velkoff, 2010). The most distinct growth will be in the oldest-old age group, i.e. the proportion of people aged 80 years or over will double from 3.7% of the population in 2010 to 7.4% in 2050 (Vincent and Velkoff, 2010). Comparable predictions exist for the Netherlands, i.e. the percentage of people aged 65 and older will increase from almost 14% in 2004 to 24% in 2040, more than 4 million people (De Jong, 2005). In addition, the proportion of people aged 80 years and older will increase from 3% of the Dutch population in 2004 to nearly 8% in 2050 (De Jong, 2005). As aging is the number one risk factor for the development of dementia, the number of people suffering from dementia is predicted to increase rapidly in the next decades as well (Skoog, 2004).

Besides dementia, aging is also a major risk factor for the development of chronic painful conditions, e.g. chronic back or neck pain, arthritis, and joint pain (Tsang et al., 2008). Additionally, also the risk for other diseases, in particular cardiovascular diseases, e.g. diabetes and hypertension, increases with increasing age (Ford, 2001; Varagic et al., 2001). The presence of these cardiovascular diseases increases the risk for lesions in the brain's white matter (Carmelli et al., 1999), which in turn may increase pain experience due to deafferentiation, causing central neuropathic pain (Haanpää and Hietaharju, 2010; Hong et al., 2010). Central neuropathic pain involves cortical and subcortical brain regions that belong primarily to the medial pain system, e.g. the anterior cingulate cortex and insular cortices (Jones et al., 2004). The medial pain system is the system that represents among others the motivational/affective components of pain (Scherder et al., 2003). Indeed, white matter changes are associated with an increase in the affective component of pain (Oosterman et al., 2006). Due to the increasing number of older people (Anderson and Hussey, 2000), the number of older people with dementia suffering from pain will increase in the near future. In addition, this will also increase the number of people living in nursing homes (Eaker et al.,

2002). A major concern with respect to these developments is that people with dementia living in nursing homes are at increased risk for undertreatment of pain (Achterberg et al., 2007; Husebo et al., 2008; Plooij et al., 2012).

An important cause of undertreatment of pain in dementia patients is the difficulty in pain assessment (Herr et al., 2006a). Owing to communicative problems that are present in all major dementia subtypes, e.g., Alzheimer's disease (AD; Taler and Phillips, 2008), frontotemporal dementia (FTD; Reilly et al., 2010), and vascular dementia (VaD; Reilly et al., 2010), the capacity to provide reliable self-report, considered the gold standard in pain assessment, is reduced in dementia patients (Scherder et al., 2009). Alternative and complementary tools for pain assessment in patients with communicative disorders are observational scales (for an overview see Herr et al., 2006b; Zwakhalen et al., 2006a). The main disadvantage of observational scales is that they rely on the interpretation of the observer (Zwakhalen et al., 2006a), and are thus subjective. A factor complicating pain assessment even more might be that although dementia patients are still able to perceive the presence of pain, they may have difficulty understanding the sensation and placing it in context (Scherder et al., 2005). This may partly explain why dementia patients express their pain different than older people without dementia (Herr and Dekker, 2004).

Undertreatment of pain has many negative consequences. In the first place these negative consequences of undertreated pain concern the dementia patients whose pain is undertreated. For example, pain in dementia patients may cause behavioural disturbances and depression, which in turn negatively influence activities of daily living (Cipher and Clifford, 2004). Additionally, undertreated pain may have a negative effect on cognitive functioning, i.e. a decrease in memory (Oosterman et al., 2011; Weiner et al., 2006), attention (Kuhajda et al., 2002), and executive functioning (Karp et al., 2006) has been observed in chronic pain patients, and it has been suggested that pain may increase existing cognitive deficits (Frampton et al., 2003). There is also evidence that untreated chronic pain even causes structural brain damage. More specifically, patients with chronic back pain show a decreased neocortical gray matter volume and

density, especially in the dorsolateral prefrontal cortex (Apkarian et al., 2004; Schmidt-Wilcke et al., 2006).

Besides the dementia patients themselves, undertreatment of pain may also affect the caregiver. As mentioned before, undertreated pain in dementia patients may cause behavioural disturbances (Cipher and Clifford, 2004). Increased behavioural disturbances in dementia patients were predictors of caregiver burden (Coen et al., 1997), and were associated with higher levels of depression and physical symptoms among their caregivers (Baumgarten et al., 1992).

These issues concerning undertreatment of pain in dementia patients indicate that there is a lot to gain for dementia patients when undertreatment of pain is reduced, and form the motivation for this thesis, which has a special focus on undertreatment and on treatment of pain in dementia patients.

Outline of this thesis

This thesis is divided into two parts, i.e. a review section, and a clinical section. Two chapters focus on under-exposed features of undertreatment, i.e. physical inactivity as both a cause and a sign of pain **(chapter 2)**, and the relationship between cognitive functioning and undertreatment **(chapter 6)**. Two chapters focus on alternative methods to assess pain, in order to reduce undertreatment, i.e. autonomic responses to pain **(chapter 3)**, and neuropsychological testing **(chapter 5)**. The remaining two chapters focus on treatment of pain in dementia patients **(chapter 4 and chapter 7)**.

Review section

In the review section, firstly the relationship between physical inactivity and pain in aging and dementia is discussed. Physical activity has many benefits, of which one is the positive effect it has on cognitive functioning in aging (Kramer et al., 1999), as well as in patients with mild cognitive impairment (MCI; Scherder et al., 2005) and in people at risk of dementia (Lautenschlager et al., 2008). Considering this positive effect of physical

activity, it is unfortunate that older persons, in particular those with dementia, show a decrease in the level of physical activity (Westerterp & Meijer 2001, Burns et al. 2008). In patients with dementia, this passivity may be a symptom of apathy (Colling, 2000). However, this physical inactivity may also be caused by pain, as it is known that with advancing age an increase in the number of chronic pain conditions, e.g. osteoarthritis, is strongly associated with a decline in the level of physical inactivity (Issa & Sharma 2006, Tsang et al. 2008). The relationship between physical inactivity and pain in older persons with and without dementia is addressed because awareness of physical inactivity as an expression of pain may contribute to early detection of pain, and hence to reduction of undertreatment **(chapter 2)**.

Chapter 3 is focused on autonomic responses to pain in aging and dementia. As mentioned before, reliability of the use of self-report and observational scales to assess pain in dementia patients is disputable. A more objective method to assess pain that has been used in children and adolescents is the registration of autonomic responses to pain (Storm, 2008). Examples of autonomic responses are changes in skin conductance, changes in blood pressure, or changes in heart rate (Katz and Melzack, 1999). When baseline values are known, autonomic responses can be used to evaluate pain treatment. Studies on autonomic responses in older people with and without dementia are reviewed, in order to investigate whether autonomic responses to pain may contribute to a more reliable pain assessment in these people.

Despite the risk for undertreatment, it is well known that there is a high prevalence of chronic pain in dementia patients, which is suggested to be mainly due to musculoskeletal pain (Baan et al., 2011; Husebo et al., 2010). For example, arthritis, osteoporosis, old fractures, muscle spasm, and contractures have been observed in patients with severe dementia (Husebo et al., 2010). However, next to musculoskeletal pain, also central neuropathic pain is present, and may be by far the most undertreated type of pain in patients with dementia, as the medical staff is less familiar with this type of pain. Appropriate assessment of this type of pain is clinically relevant, as it requires treatment that differs from treatment of other types of pain. In **chapter 4** the possible presence of central neuropathic pain in

dementia is briefly described. Subsequently, assessment and treatment of pain in advanced stages of dementia is addressed, with a special focus on central neuropathic pain.

Clinical section

In the first chapter of the clinical section of this thesis **(chapter 5)** the relationship between pain threshold, pain tolerance and cognitive functioning is examined in healthy adults and older people, in order to investigate whether neuropsychological testing may contribute to pain assessment. Examining this relationship in healthy people is the first step in eventually understanding this relationship in dementia patients. As mentioned before, undertreatment of dementia patients is mainly caused by problems in recognising pain. Next to communication difficulties in dementia, these problems in recognising pain may be partly because although dementia patients are still able to perceive the presence of pain, they may have difficulty understanding the sensation and placing it in context (Scherder et al., 2005). In addition, based on the neuropathology, patients with dementia may even experience an increase in the experience of motivational/affective components of pain, increasing the risk for undertreatment. In other words, the development of reliable motivational/affective pain indicators in patients with dementia would be clinically most relevant. The extent in which a person suffers from the motivational/affective components of pain can be assessed by experimentally examining the person's pain tolerance (Benedetti et al., 1999), which is mediated by the medial pain system (Scherder et al., 2003). As brain areas involved in the medial pain system are also involved in cognitive functioning, a relationship is expected between pain tolerance and cognitive functioning, implying that changes in cognitive functioning may predict changes in pain experience. This knowledge may contribute to more reliable pain assessment, and hence adequate pain treatment.

As stated before, decreased cognitive functioning, resulting in decreased abilities to communicate, contributes to difficulties in pain assessment. Indeed, the prevalence of identified pain decreases with increasing cognitive impairment in nursing home patients (Proctor and Hirdis, 2001). Multiple studies have investigated the relationship between cognitive

functioning and analgesic prescription and administration in patients with cognitive impairment. However, these findings are ambiguous, and in all previous studies participants without a painful condition were also included. In **chapter 6** the relationship between pain medication and cognitive functioning within a group of nursing home residents with dementia and a painful condition will be examined, in order to further unravel the problem of undertreatment of pain.

Finally, the effect of a structured pain assessment intervention, conducted to optimize pain treatment, on the cognitive functioning of dementia patients living in nursing homes will be examined. Rationale behind this chapter is that undertreatment of pain may negatively influence cognitive functioning. For example, in chronic pain patients decreased performance on tests that measure memory (Oosterman et al., 2011; Weiner et al., 2006), attention (Kuhajda et al., 2002), and executive functioning (Karp et al., 2006) was shown. Additionally, it was stated that pain might increase existing cognitive deficits (Frampton et al., 2003). In reverse, it has also been shown that treating pain in chronic pain patients without dementia may improve cognitive functioning (Lorenz and Bromm, 1997; Tassain et al., 2003). The pain observation scale used for the structured pain assessment intervention is the Dutch version of the Pain Assessment Checklist for Seniors with Limited Abilities to Communicate (PACSLAC-D; Zwakhalen et al., 2007). At this moment, the PACSLAC is one of the best methods to assess pain in older people with dementia (Aubin et al., 2007; Zwakhalen et al., 2006b). It is expected that due to the structured pain assessment pain will be detected earlier, resulting in a more effective pain treatment, and stabilizing or even improving cognitive functioning in demented nursing home residents **(chapter 7)**.

Implication and discussion

In **chapter 8** a summary of the thesis is provided and the implications of the previous chapters are discussed.

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