Experiences of pain and associations between pain, disease severity and individual quality of life in people with motor neuron diseases

Ylva Åkerblom
Abstract

Many people with the incurable and often times fatal motor neuron diseases have pain, but there is lack of knowledge about people’s experiences of living with pain. Further, the correlation between pain and their quality of life is not well understood and previous studies have not used individual quality of life (iQoL), namely that people with their own words express what quality of life is. The aim of these studies was to explore the experiences of pain and the association between pain and quality of life in people with MND.

Methods: Study I was explorative about the individual experience of pain, while study II was correlational between pain, pain severity, disease severity and iQoL. Study I was qualitative, whereas study II used both qualitative and quantitative analysis.

Results and conclusions: People with motor neuron diseases experienced pain to have multiple characteristics and impact. However, the results emphasise that the individual experienced some pain characteristics as difficult and that pain could worsen functions that were already affected by the disease. The experience was also that it could be challenging to manage pain. However, the symptom of pain could pass unnoticed in contacts with healthcare professionals (study I). The three most important areas for individual quality of life in both participants with and without pain were: Social relations, followed by Activities for amusement and relaxations, and Being in the outdoor environment. Individual quality of life was noticed to be good regardless of pain. Pain and pain severity were not found to be associated with satisfaction of individual quality of life in patients with motor neuron diseases, neither was disease severity. The results support previous findings, that strong associations between symptoms of MND and iQoL are not obvious. However, this does not infer that pain in people with MNDs should be neglected and undertreated. On the contrary, it seems to be important for healthcare to pay more attention to pain in people with motor neuron diseases and that pain continuously is measured, individually treated and followed. Regardless of whether persons with MND have pain or not, the results point to the importance of healthcare professionals providing support to not only the patient but also the patient’s family and friends, as well as assisting in various forms of relaxing activities and possibility of being in the outdoor environment.

Keywords: Amyotrophic lateral sclerosis, motor neuron disease, pain, quality of life, individual quality of life, qualitative content analysis, pain severity, disease severity.

Ylva Åkerblom, Department of Neuroscience, Äsenlöf: Physiotherapy, BMC, Husargatan 3, SE-752 37 Uppsala, Sweden.

© Ylva Åkerblom 2019
List of Papers

This summary is based on the following papers, which are referred to in the text by their Roman numerals.


Reprints were made with permission from the publisher.
Contents

Introduction ............................................................................................................................. 7

Background ............................................................................................................................ 8
  Motor neuron diseases ............................................................................................................ 8
  Pain and motor neuron diseases .......................................................................................... 9
  Quality of life and pain in people with motor neuron diseases ........................................ 12
  Individual quality of life ....................................................................................................... 13
  The rationale ....................................................................................................................... 13

Aims ........................................................................................................................................... 15
  Specific aims .......................................................................................................................... 15
    Study I ............................................................................................................................... 15
    Study II .............................................................................................................................. 15

Methods ................................................................................................................................... 16
  Design .................................................................................................................................. 16
  Ethical considerations and approval .................................................................................... 16
  Participants and procedures ................................................................................................. 17
    Study I ............................................................................................................................... 17
    Study II .............................................................................................................................. 18
  Data collection ..................................................................................................................... 19
    Pain ..................................................................................................................................... 19
    Individual quality of life ..................................................................................................... 19
    Disease severity .................................................................................................................. 19
    Demographic data .............................................................................................................. 20
  Data management and analysis ............................................................................................. 21
    Study I ............................................................................................................................... 21
    Study II .............................................................................................................................. 21

Results ....................................................................................................................................... 23
  Study I ................................................................................................................................... 23
    The multiple faces of pain .................................................................................................. 24
    The thin line between experience of pain and no pain ....................................................... 24
    The negative effects of pain on role function ..................................................................... 24
    Successfully coping with pain, requiring personal effort and competent engagement .... 25
  Study II .................................................................................................................................... 27
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discussion</td>
<td>31</td>
</tr>
<tr>
<td>Pain in people with motor neuron diseases</td>
<td>31</td>
</tr>
<tr>
<td>Quality of life in people with motor neuron diseases, who have pain</td>
<td>33</td>
</tr>
<tr>
<td>Methodological considerations</td>
<td>34</td>
</tr>
<tr>
<td>Conclusion</td>
<td>36</td>
</tr>
<tr>
<td>Implications and future studies</td>
<td>36</td>
</tr>
<tr>
<td>Svensk sammanfattning (Swedish summary)</td>
<td>38</td>
</tr>
<tr>
<td>Acknowledgements</td>
<td>40</td>
</tr>
<tr>
<td>References</td>
<td>42</td>
</tr>
</tbody>
</table>
Introduction

During my eight years as a physiotherapist at a multidisciplinary Motor Neuron Disease (MND) team in Sweden, I have met several patients and their families and followed them during their disease progression. Patients with MND go through various stages of the disease, both physically and mentally. Their Motor Neuron Diseases (MNDs) might differ a lot, where some with Amyotrophic Lateral Sclerosis (ALS) might have an aggressive disease with rapid progression and short survival and other patients have milder forms of MND with disease progression that is stable for many years and a life that works relatively well. During a patient visit to the multidisciplinary MND team, there is usually a lot of important aspects in the patient and their relatives’ lives that need to be addressed. Since pain usually is not the most central impact in the lives of people with MNDs, the routines for assessing pain might still be overlooked. During my years working as a physiotherapist, I do not recall ever discussing pain at networking meetings with colleagues from other MND teams. Based on my clinical experience with patients living with difficult levels of pain and there being lack of research in this area, a PhD project was designed.
Background

Motor neuron diseases

Motor neuron diseases are disorders and conditions that impact on the cells and the paths of the motor neurons. The loss of the motor neurons leads to different types and degrees of muscle weakness and in some MNDs muscle spasticity and increased reflexes. However, MNDs are not only about the neuromuscular impact. Some of those diagnoses are also considered to be multi-system diseases, with symptoms such as cognitive dysfunction and pain (1-3).

In Europe, Australia and New Zealand, MND is the umbrella concept for the MND diagnoses (4, 5). However, in US or in South America, they use ALS or Lou Gehrig’s disease (2, 6, 7). This difference might result in confusion when evaluating research throughout the world. Most studies of MND are about people with ALS, but as previously mentioned that does not mean all studies are about the diagnosis of ALS.

Amyotrophic lateral sclerosis (ALS) is the most common of the MNDs and generally also the most severe due to its rapid progression. Survival from symptom onset is 3 – 5 years, and respiratory failure is the most common cause of death (6). People with ALS get lesions in both upper and lower motor neurons and paths, which thereby results in symptoms such as paresis and fasciculation in some muscles, simultaneously as spasticity and hyper reflex can appear in others. The progression of ALS results in successive paralysis, with inability to move the body, affecting the person’s swallowing- and speech functions and finally the motor neuron lesions, which impact breathing. People usually get ALS in their 5 – 6th decade (2). The El Escorial is one of the most used diagnostic criteria for ALS and involves clinical findings supported by electrophysiological studies (EMG). Neuroimaging and lab tests are used to exclude other possible diagnoses (8). The incidence for ALS is 2.2/100,000 (9), and the prevalence is around 6/100,0000 (4). In Sweden, 220 – 250 persons get ALS every year, and 750 – 850 people in Sweden are estimated to have ALS (10).

Primary lateral sclerosis (PLS) is another MND; compared to ALS, it primarily has symptoms from the upper motor neuron damage. Common symptoms are spasticity and poor coordination with clumsiness. The prognosis is better
in PLS than in ALS (11). There are also MNDs that mostly affect the lower motor neuron and paths (4). However, people with MND with lower motor neuron damage and those with PLS might end up with ALS (12, 13).

Many different theories about the aetiology in MNDs are discussed, as genetics and environmental factors (2, 14). However, still there is no cure (6). Riluzole seems to prolong life in ALS patients by two to three months (15), and the non-invasive ventilation by approximately a year (1, 16). Invasive mechanical ventilation (IMV) can prolong survival in ALS patients, sometimes for many years. However, there is no documented improvement of quality of life (QoL), and also an apparent risk that patients will develop a locked-in condition (17).

Treatments for MND are mostly symptomatic, like percutaneous endoscopic gastrostomy (PEG), which is enteral feeding tube placement, baclofen for spasticity, exercise for cramps (1) or cough-assist for clearance of bronchial secretions (17). Multidisciplinary care within the MND teams is recommended for those afflicted, as the teams can follow and support the patient throughout the disease period and provide coordinated inter professional care and seek to address the complex needs (17, 18). Despite patients expressing positive opinions about the care of the MND team, the visits can be tiring for the individual. The specialists in the multidisciplinary MND team include diverse healthcare disciplines and social worker (17).

The physiotherapist (PT) in the team assesses the patient’s motor functions and abilities regularly, for instance, the movements indoors and outdoors and use of assisted devices. The PT can provide the patient with different treatments, strategies and aids to facilitate movements and activities (19) or give advice about appropriate exercise level. The PT support can also include treatments to assist the patient to cough or manage pain (20-22). As for the other team members, continuous communication with home-based professionals and the healthcare staff as well as the patient’s family is important (17).

Pain and motor neuron diseases

The definition of pain is ‘An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage’ (23) and can be categorised as acute, subacute (24) or chronic. Chronic pain is defined as pain that lasts or recurs for longer than 3 months (25). In people with MND, the acute and chronic pain are observed and mentioned (3). There is a new diagnostic classification system for chronic pain, which is specified for pain being conceived of as a disease in its own right, chronic primary pain or secondary to a disease (26). With the new diagnostic
classification system, people with MND, who have chronic pain, would be placed under the chronic secondary musculoskeletal pain due to diseases of the nervous system or chronic neuropathic pain. The new system will enable research and treatment for chronic pain to be more specific (27).

The general definition of pain from the International Association for Study of Pain (IASP) (23) was used as inclusion criterion for participants in study I. For people with MND, 15% (28, 29) up to 85% have pain (30-36). However, it is difficult to get any consensus on why they think that pain is mild or severe, or why people with MND feel that pain affects different functions in daily life, even though the pain intensity is not so high (3). There is also no knowledge of these people's thoughts, feelings and experiences of living with pain, as the studies have been quantitatively designed (37). Their pain is not found to be limited to typical sites of the body and can be present in the extremities as well as the neck, shoulders or back (33-36, 38, 39). As mentioned, despite the pain intensity usually being low (30, 34-36, 38, 40), it affects the daily functioning of people with MND (34, 36, 38, 41). Pain can appear in any stage of the disease (3), and the severity of the pain has been noted to be highest both at the beginning and towards the end of the disease in different longitudinal studies (42, 43).

What people with MND perceive as being stressful about pain is not well understood. The intensity of pain might not be the most stressful. Instead, it might be having pain and not knowing how to control it, which causes the major distress in people with MND (35). Despite strong arguments that healthcare should have knowledge about pain as a symptom in people with MND, it is still a neglected symptom (3, 44). Specialist physicians express uncertainty about how to handle pain in MND (35). Guidelines on how to measure and treat pain based on studies of MND would therefore be helpful (17, 45, 46).

The primary causes of pain in people with MND might be pain of neuropathic nature and pain affected by spasticity or by cramps (44). However, there is weak evidence that neuropathic pain affects people with MND (34, 47) despite the anatomical observations (29, 48, 49). Generally, cramps are the most common type of pain in people with MND (44). The secondary nociceptive pain results from tissues, where noxious stimuli have been activated as response to, for instance, skin pressure, inflammatory processes in joints or because of traumatic injuries to the body (50). It would not be surprising if people with progressive muscle weakness had nociceptive pain. However, lack of systematic studies makes it difficult to draw any conclusions, especially as there is no unambiguous correlation between pain severity and disease severity (35, 39, 47, 51-53). Further, the supposed nociceptive pain might in some cases
instead be so-called nociplastic pain (3), on the basis that the person's physiology for pain has been changed, resulting in that normal sensory stimuli can change to a pain response (54).

Alongside the mechanisms behind the pain in people with MND, it is noted that similar to people with musculoskeletal chronic pain (55, 56) and people with other neurological diseases (57), pain and mental status have an association in people with MND (33, 41, 58).

Treatments for pain in people with MND, both pharmacological and non-pharmacological, need to be further investigated in order to assess safety and establish efficacy (3). The pharmacological treatments for people with MND are mainly based on experience rather than reliable data (3, 44). However, there are ethical concerns about designing randomised controlled trials (RCTs) or quasi-RCTs for pharmacological treatments (1). Today, the pharmacological treatment for pain in people with MND follows the 1990 World Health Organisation (WHO) Analgesic Ladder (1). Non-steroidal Anti-Inflammatory Drugs (NSAID) and paracetamol are the most commonly used pharmacological treatment for nociceptive pain. NSAID prevent inflammation without being steroids or corticosteroids, while paracetamol only has the analgesic effect. Opioids are the third alternative for people with MND, who have nociceptive pain. In late stage of disease, opioids are required, especially if pain is associated with symptoms like dyspnoea and poor sleep (3). The recommended treatment for pain, which originates from the neurological system, is pharmacological.

The non-pharmacological treatment is more common and effective for the secondary nociceptive pain, where transcutaneous nerve stimulation, acupuncture and cool packs are used (59). Trying to off-load the painful body part with orthosis, walking aids and mattresses are also used (59), combined with altered techniques in moving (19). Splints can be used to reduce joint contractures in hands and ankles (59). Different movements, especially in a pool, might relieve pain as well as stretching and passive and active range of motion to prevent painful spasticity or axial pain (59). However, there is no systematic review about non-pharmacological treatments (3, 59).

The correlation between pain and QoL in people with MND is difficult to understand as the results from the studies are not clear-cut. There are studies that have shown significant correlation between pain and QoL (33, 51). However, the study by Pizzimenti et al. found that after depression scores were added and controlled for, pain no longer showed any significant correlations with QoL (33). Two other studies did not find any correlation between pain and QoL (40, 60). All these mentioned studies used either predetermined questions to be answered or statements to be commented upon, both regarding QoL (33, 40, 60).
Quality of life and pain in people with motor neuron diseases

In absence of a cure, QoL is important and the primary goal for supporting and caring for people with MND (17). Quality of life is also viewed as a way to measure the adaptation to the disability of severe diseases (61), also for people with MND (62). However, there is no consensus about the definition of QoL (63, 64). The World Health Organisation (WHO) defined the concept as the individuals’ perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns (65). Other descriptions are that it is a subjective and multidimensional perception (63) or the difference between one’s hopes and expectations and present experience (66), which is similar to the definition presented by WHO. In research, different terms have been used interchangeably, as health, happiness, self-esteem, mental health and life satisfaction (67). Regardless, since QoL is subjective, the person him/herself is the best one to assess their QoL (68).

Studies of QoL can be sorted into different QoL concepts (69); thereby, the multifaceted construct might be more stringent, which is important for research (70). Concepts that are usually used are health related quality of life (HRQoL) and global quality of life (GQoL). Health related quality of life refers to the physical, psychological and social domains of health with distinct areas, influenced by the person’s experiences, beliefs, expectations and perceptions (71). Health related quality of life is suitable for studying, for instance, the effects of patients’ medications (69). Global quality of life instead reflects the more overall QoL with multiple dimensions on person’s life and thereby also includes non-medical view of the QoL, such as leisure and religion (72). The individual quality of life (IQoL) is part of the GQoL, but puts greater emphasis on subjectivity, because the person with his or her own words expresses what QoL means to him or her (68, 73).

Health related quality of life is not surprisingly worsened with the progress of the disease in people with MND (74, 75) as well as correlated with their mental health (73). To study HRQoL in people with MND does not seem to be relevant in understanding QoL from a broader perspective (76, 77). I studies about GQoL/IQoL, the person’s QoL instead is stable, despite their diseases getting worse (75, 78-81). In comparison to people with other severe diseases, people with MND seem to have better GQoL/IQoL (82, 83). People with MND have actually been observed to have comparable IQoL with healthy people (80). However, family members of people with MND seem to think their relative has worse GQoL than they actually have (84, 85). The positive attitudes towards their QoL in people with palliative diseases might be explained by the response shift in what people with MND include in their
Common expressed content of what is important for IQoL in people with MND are family, friends and health (75, 79, 86, 87).

**Individual quality of life**

Often used questionnaires for measuring IQoL are: the Patient Generated Index (PGI) (88) and the Schedule for Evaluation of Individual Quality of life – Direct Weighting (SEIQoL-DW) (89). Both PGI and SEIQoL-DW use semi-structured interviews, where the individuals themselves are supposed to freely nominate areas about QoL. Patient Generated Index is focused on what impact the disease has for the IQoL (88), while SEIQoL-DW investigates the IQoL in general (89). The Schedule for Evaluation of Individual Quality of life – Direct Weighting was used in study II.

**The rationale**

Living with a progressive and incurable MND involves much strain physically, psychologically and socially. In addition, many of those affected also have pain. However, previous research makes it difficult to get any consensus on their pain, as well as to get an understanding of what it is like to live with MND and pain. As far as we know, there are no previous studies with personal qualitative interviews about pain in people with MND. Moreover, the correlation between pain and their QoL is not well understood, and studies about pain and IQoL in people with MND seem to be missing. By qualitatively studying how people with MND experience and handle their pain, it is possible to obtain information about pain in its context, i.e. get deeper insight into what the situation is like when participants experience pain and what feelings they have (37). Further, by studying IQoL in people with MND who have pain, there is an opportunity to get another aspect of QoL that might clarify the association between pain and QoL in people with MND. Additionally, by studying the disease severity, it is possible to find out how much of IQoL that is explained by the disease severity.

Accordingly, the studies here are meant to provide an understanding of patients’ experiences of living with pain. This understanding might be useful for treatment and to provide support to people with MND, who have pain; moreover, it can be useful for proactive management of pain and prevention. Extensive knowledge on pain might also be informative for development of pain measures specific for people with MND.

By studying IQoL in those with pain might give important information to clinical healthcare personnel in their support and treatment of those affected.
The results are also intended to be a platform for future studies of explanatory factors for the association between pain and QoL in people with MND.
Aims

The aims of these studies were to explore the experiences of pain as well as the association between pain and QoL in people with MND.

Specific aims

Study I
To explore personal experiences of pain in people with MND.

Study II
To study associations between pain, pain severity, disease severity and IQoL in patients with MND.
Methods

Design

Study I was explorative about the individual experience of pain, while study II was correlational between pain, pain severity, disease severity and IQoL. Study I was qualitative, whereas study II used both qualitative and quantitative analysis. See table 1.

Table 1. Overview of the studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample</th>
<th>Variables</th>
<th>Data collection</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Explorative Qualitative</td>
<td>16 participants</td>
<td>Interview about pain experiences</td>
<td>Interview with an interview guide One occasion</td>
<td>Qualitative content analysis</td>
</tr>
<tr>
<td>II</td>
<td>Correlative Qualitative and quantitative</td>
<td>61 participants completed demographics, IQoL, disease severity 55 of those participants also completed data collection about existing pain and pain severity</td>
<td>IQoL, Disease severity, Existing pain, Pain severity</td>
<td>Interview based instrument Questionnaire Self-reported questionnaire All data collection on one occasion</td>
<td>Qualitative analysis Descriptive statistics Mann-Whitney U-test Spearman’s rho</td>
</tr>
</tbody>
</table>

IQoL = Individual Quality of Life

Ethical considerations and approval

The patients might have had difficulties to refuse participation in the studies. Therefore, it was important to give the patients enough reflection time to decide if they wanted to participate.

Another ethical consideration related to if the participants in study II could be harmed by talking about QoL, where many of them had a life-threatening disease. The data collector needed to be prepared for feelings of sorrow that
might have been aroused. Therefore, it was important that the data collectors had experience working with people with severe diseases and could handle difficult discussions, but also that there was extra support in the MND team for those participants who needed.

Ethical approval was obtained for both studies from the Regional Ethics Review board of Uppsala, Sweden, Dnr 2013/288 (study I) and Dnr 2015/293 (study II). The participants were given written and oral information about the respective studies, and informed consent was obtained from each participant.

Participants and procedures

The participants in studies I and II were two different samples. The participants in study I were recruited from one multidisciplinary MND team. In study II, the participants were recruited from four different multidisciplinary MND teams, where one of the teams belonged to a university hospital, while the others belonged to their county hospital.

The inclusion criteria differed by the fact that in study I, the participants should have pain. Otherwise, the two samples had similar inclusion criteria: they had diagnosis of MND, e.g. either ALS with both upper and lower motor neuron symptoms, PLS with primarily upper motor neuron symptoms or MND with primarily lower motor neuron symptoms. All were supposed to be >18 years old, understand instructions and speak Swedish language. Patients with Kennedy’s disease were excluded, as symptoms of sensory impact and slow progression distinctly differ from other MNDs.

Study I

During the first months of autumn 2013, eligible patients were invited to participate in the study. Seventeen patients were eligible, and sixteen accepted to participate. Based on the participant's wishes, the interviews were conducted either in the hospital or at their home. All interviews were tape recorded.

Before the interview started, demographic data as well as measurements for physical function, the ALS Functional Rating Scale Revised version (ALSFRS-R) and pain, the Brief Pain Inventory Short Form (BPI-SF) were completed. The ALSFRS-R and BPI-SF are presented in study II. An interview guide was used during the interviews, to check that some areas were included in all the interviews. Questions in the interview guide were available as support if the participant did not bring up the subject during the interview. The
questions were designed in a way that stimulated the participants’ own statements and experiences.

Study II
There was a consecutive sampling of the patients, who had their ordinary hospital visit with the MND team during September 2015 to September 2016. In total, there were 154 patients in the four multidisciplinary MND teams during the recruitment period. Ninety-five of these patients met the criteria for inclusion, and 61 were finally included. See figure 1.

Figure 1. Flowchart showing participants in study II
Data collection

Pain
The Brief Pain Inventory – Short-form measures different aspects of pain and is an abbreviated version of the original BPI and measures pain during the past 24 hours (90). In study I, the BPI-SF was used as demographic characteristics of the participants’ pain intensity. In study II, the subscale of presence of pain in 24 h, body regions affected and the pain severity index (PSI) were used. Presence of pain in 24 h is answered dichotomously with “yes/no”. In the part regarding body regions affected, painful areas on the body should be marked. The PSI is established by the subscale of pain severity. The pain severity is rated as worst, least, average, and current pain during the last 24 hours on a numeric rating scale (NRS) from 0 = “no pain” to 10 = “worst pain imaginable” (91). The PSI can thereafter be calculated by the average ratings of worst, average and current pain. An average of 0 – 3 is considered no or mild pain, 4 – 6 as moderate and 7 – 10 as severe pain (92). The internal reliability of pain severity is high (93-99) and valid in many different painful conditions (98, 100-102).

Individual quality of life
A study-specific SEIQoL-DW (64, 89) was used to measure IQoL in study II. To adapt the ordinary SEIQoL-DW for the MND population, the instrument was modified and thereafter called study-specific SEIQoL-DW.

The instrument is a semi-structured interview, where the participants first nominate the most important areas for his/her quality of life. Thereafter, they select five of these areas, which currently are the most important (89). Each of the five areas are then rated regarding how satisfied he/she is with each area. In order for MND participants to manage the rating, as their fine motor skills gradually deteriorate, the instrument was modified in this study. By using a seven-point categorical scale, instead of the visual analogue scale (VAS) that is found in the ordinary SEIQoL-DW (89), all participants with MND, regardless of skills of fine motor function, could rate their satisfaction of their defined areas of IQoL. The response format was: 1= “as bad as could possibly be”, 2 = “very bad”, 3= “bad”, 4= “fairly good”, 5 = “good”, 6 = “very good” and 7 = “as good as could possibly be” (64). For the same reason, the weighting procedure, which is the next step in the ordinary SEIQoL-DW (89), was omitted. The weighting procedure has also been viewed as not having impact on the total index of another version of SEIQoL-DW (103).
SEIQoL-DW seems to be reliable and valid (104) and is seen as having high face validity in people with MND (105).

Disease severity

The ALSFRS-R consists of four subscales of different functions. Each subscale includes three items, ranging from 0 (totally lost) to 4 (normal function) making a total score of 12 for each of the subscales. Lower scores indicate a higher level of dysfunction (106). The ALSFRS-R was used in both study I and study II to describe the participants’ disease severity, but it was also used in the correlation analysis between the disease severity and IQoL in study II. The internal consistency reliability is high (106) and the validity moderate to strong in correlations with HRQoL measure and pulmonary function (106). In order to get better validity for disease severity, the four functions were analysed separately in study II (107).

Demographic data

Demographic data in studies I and II were collected with questionnaires about gender, age, family constellation, occupational status, type of MND diagnosis and time since first symptom of MND. The demographic data in study II also consist of a screening for neuropathic pain (108, 109) and experience of chronic pain before onset of MND with a single question. Information about pharmacological treatment in study II was derived from the participants’ medical record.

The variables and instruments in studies I and II are presented in table 2.
Table 2. Variables and instruments in studies I and II

<table>
<thead>
<tr>
<th>Variables</th>
<th>Study I</th>
<th>Study II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Existing pain</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>PSI</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Disease severity</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>IQoL</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

**Instruments**

<table>
<thead>
<tr>
<th>Instruments</th>
<th>Study I</th>
<th>Study II</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALSFRS-R</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>BPI-SF</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Study-specific SEIQoL-DW</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>DN4-SWE</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

PSI = Pain severity index, IQoL = Individual Quality of Life, ALSFRS-R = the Amyotrophic Lateral Sclerosis Functional Rating Scale - Revised Version, Study-specific SEIQoL-DW = study-specific version of the Schedule for the Evaluation of Individual Quality of Life Direct Version, BPI-SF = The Brief Pain Inventory – Short-form, DN4-Swe = Douleur Neuropathique 4 questions -Swedish version is a screening instrument for neuropathic pain.

**Data management and analysis**

**Study I**

Descriptive statistics were used to describe the demographic data for the participants.

A qualitative content analysis (110) was used to analyse the interviews. After the first author (YÅ) in study I had transcribed the taped interviews, the first and the second authors (YÅ, BJL) read all the interviews and picked out and sorted the areas of the content that covered the aim of the study, e.g. how they presented their pain, the consequences due to pain and their management of the pain. Thereafter, meaning units, sub-categories and/or categories were analysed and concretised. Finally, the two authors discussed patterns of shared meaning across data, creating themes. The analytic process involved a back-and-forth interchange, first between the two first authors and thereafter, with all the authors that were involved for a so called research triangulation (YÅ, BLJ, LZ, PÅ), to increase the credibility. The authors had different specialties and two different professions.

**Study II**

There was a qualitative analytic process to sort the nominated and described areas of IQoL into groups. Four authors in study II (YÅ, LZ, BJL, PÅ) took part in the back-and-forth discussions about the participants’ areas, and agreed on the summarised areas. The content of each area was described qualitatively.
To describe the participants, descriptive statistics were used. Information about the participants’ existing pain was obtained from the BPI-SF (90), where the participant makes marks on an anatomical drawing of a human form to identify where they have pain in different body areas. If they did not have pain, they did not make any marks. Marked body area/s became a yes for existing pain and was the score that was used in the calculations. Pain in the latest 24 h in BPI-SF was also described in the results. Each participant received an IQoL score based on the individual ratings for his/her areas. The IQoL index for the total sample and the separate groups of those with and without pain was calculated using the median of the IQoL scores (103). Descriptive statistics were also used to describe the number of participants with and without pain, respectively, who nominated each area; the level of satisfaction with the area (Md) of participants with and without pain and the level of bulbar, fine motor, gross motor and respiratory function of the participants who nominated the area.

The differences in IQoL scores for participants with and without pain were analysed with Mann-Whitney U-test. Spearman’s rho was used for the correlation calculations between the IQoL score and pain severity (BPI-SF), and between IQoL score and the functions of disease severity, i.e. bulbar function/ fine motor function/ gross motor function or respiratory function (ALSFRS-R).

An alpha level of 0.05 or below was regarded as statistically significant. The analyses were performed using the IBM, Statistical Package for Social Sciences (SPSS) version 24.
Results

Study I

The participants’ characteristics are presented in table 3.

Table 3. Participants’ characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of participants</td>
<td>16</td>
</tr>
<tr>
<td>Gender, n</td>
<td>11/5</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>60 (8.6)</td>
</tr>
<tr>
<td>Family constellation, n</td>
<td></td>
</tr>
<tr>
<td>Married/cohabitant</td>
<td>13</td>
</tr>
<tr>
<td>Single parent</td>
<td>1</td>
</tr>
<tr>
<td>Single</td>
<td>2</td>
</tr>
<tr>
<td>Occupational status, n</td>
<td></td>
</tr>
<tr>
<td>Working full-time</td>
<td>2</td>
</tr>
<tr>
<td>Working part-time</td>
<td>4</td>
</tr>
<tr>
<td>Sickness benefit</td>
<td>4</td>
</tr>
<tr>
<td>Retired</td>
<td>6</td>
</tr>
<tr>
<td>Diagnosis, n</td>
<td></td>
</tr>
<tr>
<td>ALS¹</td>
<td>7</td>
</tr>
<tr>
<td>MND²</td>
<td>7</td>
</tr>
<tr>
<td>PLS³</td>
<td>2</td>
</tr>
<tr>
<td>ALSFRS-R⁴, Md (IQR))</td>
<td></td>
</tr>
<tr>
<td>The bulbar function</td>
<td>11 (3.8)</td>
</tr>
<tr>
<td>The fine motor function</td>
<td>8 (3.5)</td>
</tr>
<tr>
<td>The gross motor function</td>
<td>6 (1.8)</td>
</tr>
<tr>
<td>The respiratory function</td>
<td>11 (3.8)</td>
</tr>
<tr>
<td>BPI-SF⁵</td>
<td></td>
</tr>
<tr>
<td>PSI, mean (SD)</td>
<td>4.2 (1.5)</td>
</tr>
<tr>
<td>Worst pain, Md (IQR)</td>
<td>7.5 (4)</td>
</tr>
</tbody>
</table>

Note. ¹ALS, Amyotrophic Lateral Sclerosis with both upper and lower motor neuron signs and symptoms that were not further classified into the specific El Escorial categories; ²MND, Motor Neuron Disease with lower motor neuron signs and symptoms but were not further classified into the specific El Escorial categories; ³PLS, Primary Lateral Sclerosis with only upper motor neuron signs and symptoms; ⁴ALSFRS, Amyotrophic Lateral Sclerosis Functional Rating Scale Revised version, a 12-item scale that assesses the level of physical function in the five domains of speech, swallowing, fine motor function, gross motor function and breathing. The items of the subscales are rated from 0 (worst) to 4 (best), and each subscale score has the maximum 12; ⁵BPI-SF, Brief Pain Inventory Short Form. Questions 3-5 asked about worst, least and average perceived pain intensity in the last 24 hours, from 0 (no pain) to 10 (pain as bad as you can imagine).
For results of themes, categories, subcategories and participants’ quotations see table 4.

The multiple faces of pain
The theme *The multiple faces of pain* consisted of one category; *Multiplicity of pain perceptions*, and three subcategories; *Multiplicity of pain characteristics and areas, Pain is inconstant during days and nights* and *Pain alters over the course of the disease.*

The pain and discomfort described by the participants varied widely. Some participants experienced intense and severe pain and others mild. Pain could be worse in the beginning of the disease, while others experienced worse pain as the disease progressed. Unpredictable nocturnal pain was described as stressful. However, it was also noted that participants disregarded their pain. The experience of pain and its discomfort could reflect the participant’s total situation with the disease and thereby be reduced. Others failed to disclose their pain to healthcare as they felt it was useless since there was no treatment, like the disease. Participants described not only sensory and bodily pain but also mental anguish, such as being a burden to one’s family or feeling anxiety about the progress of the disease. The presence of pain could be the same or it could change during disease progression. For some participants, the presence of pain could vary several times within 24 hours.

The thin line between experience of pain and no pain
This theme consisted of one category of *Exacerbation of pain*, and six subcategories: *Physical strain, Immobility, Non-adapted equipment causes discomfort, Worrying has a negative impact, Sense of bodily exhaustion, Physical touch is uncomfortable.*

In this theme, the participants described that there were several aspects that worsened their experience of pain, as expressed in the six subcategories above. They also experienced that margins between not having pain and for perceiving pain could be thin.

The negative effects of pain on role function
The theme consisted of eight categories: *Pain restricts physical function, Pain impacts activities of daily living, Pain restricts autonomy, Pain impairs sleep quality, Pain creates powerlessness, Pain results in bad mood, Pain causes fear and anxiety, Pain complicates fellowship and social life.*
Those participants, who experienced negative effects from pain, expressed how it affected them. The individuals described how pain influenced their physical ability negatively, for instance, painful joints, difficulties in using his/her hands. Pain made individuals feel weaker, and some were worried that pain would get worse or start in another body part. Pain affected their ability to perform activities in daily life. One participant described not being able to eat because of pain in the neck, and another participant slept badly because of the pain.

Successfully coping with pain, requiring personal effort and competent engagement

The theme consisted of one category of Strategies to endure pain and eight subcategories: Physical activities and movements, Reduced exertion, Modifying tasks to avoid pain, Adapted medication, Sensory stimulation, Individualised equipment, Acceptance of pain, Competent and available support and advice

Different strategies were used to handle pain, and the participants experienced that the management of pain relief could take a lot of effort.
<table>
<thead>
<tr>
<th>Theme</th>
<th>Category</th>
<th>Subcategory</th>
<th>Quotation</th>
</tr>
</thead>
<tbody>
<tr>
<td>The multiple faces of pain</td>
<td>Multiplicity of pain</td>
<td>Multiplicity of pain characteristics and areas</td>
<td>‘It itches a lot and especially in my eyes, and then it also hurts’ (3).</td>
</tr>
<tr>
<td></td>
<td>perceptions</td>
<td>Pain is inconsistent during days and nights</td>
<td>‘…it happens every other night’ (10).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pain alters over the course of the disease</td>
<td>‘It began two-and-a-half years ago, and there was more pain then’ (9).</td>
</tr>
<tr>
<td>A thin line between</td>
<td>Exacerbation of pain</td>
<td>Physical strain</td>
<td>‘I also have pain in my knee joint because I overstretched it’ (8).</td>
</tr>
<tr>
<td>experience of pain and no</td>
<td></td>
<td>Immobility</td>
<td>‘I have felt pain when I lie very still at night’ (13).</td>
</tr>
<tr>
<td>pain</td>
<td></td>
<td>Non-adapted equipment causes discomfort</td>
<td>‘When I’m sitting and leaning against the backrest, just where the backrest meets my back…that is where it hurts’ (15).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Worrying has a negative impact</td>
<td>‘Sometimes, I’ve maybe felt a gastric ulcer because of my worries about the future. There must be a connection. That’s what I think’ (2).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sense of bodily exhaustion</td>
<td>‘My body is exhausted by the late afternoon/evening and I have screaming pain’ (15).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Physical touch is uncomfortable</td>
<td>‘…massaging a little bit to make it better, but it gets even worse’ (16).</td>
</tr>
<tr>
<td>Pain negatively affects</td>
<td>Pain restricts physical</td>
<td>Pain restricts physical function</td>
<td>‘The pain itself makes you feel weaker. You lose your strength when it hurts’ (16).</td>
</tr>
<tr>
<td>role functioning</td>
<td>function</td>
<td>Pain impacts activities of daily living</td>
<td>‘It is hard to move the head because it hurts in the neck in certain positions, especially when I eat. I need to think, because otherwise it gets even worse’ (2).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pain restricts autonomy</td>
<td>‘I can’t buy groceries by myself. I get pain when picking up groceries’ (11).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pain impairs sleep quality</td>
<td>‘When I sleep, I frequently wake up because of pain’ (9).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pain creates powerlessness</td>
<td>‘You know, I get fed up and give up; I can’t keep asking other people about things that I can’t do myself’ (12).</td>
</tr>
<tr>
<td>Theme</td>
<td>Category</td>
<td>Subcategory</td>
<td>Quotation</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>-----------------------------------------------</td>
<td>--------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Pain results in a bad mood</td>
<td></td>
<td></td>
<td>‘But now it’s getting to where it affects my mood. You get a little touchy when it hurts; you get in a bad mood’ (8).</td>
</tr>
<tr>
<td>Pain causes fear and anxiety</td>
<td></td>
<td></td>
<td>‘It can feel like a little pressure in the chest, here at the side, when I get dyspnoea and it has developed. Then you get worried. Is it going to increase?’ (4)</td>
</tr>
<tr>
<td>Pain complicates fellowship and social life</td>
<td></td>
<td></td>
<td>‘At five or six in the evening, or just after I’ve eaten or something, I’m not able to sit up anymore. My body is just screaming. That makes it hard to have a social life’ (15).</td>
</tr>
<tr>
<td>Successfully coping with pain requires personal effort and competent engagement</td>
<td>Strategies to endure pain</td>
<td>Physical activities and movements</td>
<td>‘Sometimes, I sit up and try to stretch a bit and then after that I am able to go to sleep again’ (14).</td>
</tr>
<tr>
<td></td>
<td>Reduced exertion</td>
<td></td>
<td>‘If that achying pain starts, then I have to rest; I have to lie down’ (12).</td>
</tr>
<tr>
<td></td>
<td>Modifying tasks to avoid pain</td>
<td></td>
<td>‘…shave myself and go on for a while, then I get cramps here and there and have to change hands’ (2).</td>
</tr>
<tr>
<td></td>
<td>Adapted medication</td>
<td></td>
<td>‘Now, I take one pill three times a day, but it’s not enough’ (11).</td>
</tr>
<tr>
<td></td>
<td>Sensory stimulation</td>
<td></td>
<td>‘If I manage to prevent the cramp by pressing on it or lying in a certain position’ (6).</td>
</tr>
<tr>
<td></td>
<td>Individualised equipment</td>
<td></td>
<td>‘I’ll also try the orthosis I got from the occupational therapist. Maybe it’ll provide relief’ (3).</td>
</tr>
<tr>
<td></td>
<td>Acceptance of pain</td>
<td></td>
<td>‘I don’t know what to do, so I just have to accept it’ (9).</td>
</tr>
<tr>
<td></td>
<td>Competent and available support and advice</td>
<td></td>
<td>‘I need to talk about some of them to find out what they are. It depends on whether you can do something about it, like this with the eyes. At home, if I have pain, I ask if I can take a tablet or whether it will disappear’ (3).</td>
</tr>
</tbody>
</table>

**Study II**

Sixty-four percent of the participants were male, and the mean age was 61.9 years (SD 12.3). Most of them had either ALS or MND, with a mean time since first symptom of disease of 5.8 years (SD 7.1). Seventy-four per cent of the participants (of a total number of 55) had existing pain, and 71% of the
participants had experienced pain during the last 24 h. Pain severity was moderate (mean 3.8, SD 2.4), and 59% used pharmacological treatment for pain relief. Thirty-six per cent of the participants had had pain before symptoms of MND.

Nineteen areas were nominated as important for IQoL (table 5), and five of these areas were only mentioned by the participants with pain: *A safe and comfortable home environment, A pet, Hope for the future, Having a philosophy of life* and *Being alone*. Areas of IQoL and satisfaction with each area in participants with and without pain are presented in table 6.

The average satisfaction with IQoL was good in both participants with and without pain, and there was no significant difference between those groups, Md = 5 (25th percentile 4 and 75th percentile 6) and Md = 5 (25th percentile 2.5 and 75th percentile 6), respectively, Mann Whitney U-test U = 249, p = .452. There was also no significant correlation between pain severity and IQoL, Spearman’s rs = -.007, p= .961.

Nor were there any significant correlations between different functions that reflected the disease severity and IQoL: bulbar functions and IQoL rs = .087, p =.505; fine motor functions and IQOL rs = .101, p=.44; gross motor functions and IQOL rs = .181, p=.163; and respiratory functions and IQoL rs = .069, p = .598.

**Table 5.** The individual quality of life expressed by the participants

<table>
<thead>
<tr>
<th>Areas</th>
<th>Description of area content</th>
<th>Examples of patients’ quotations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hope for the future</td>
<td>To have a hope for the future. A belief that things will be sorted out e.g. faith in research</td>
<td>‘Surf on the net regarding the disease - gives hope’ (10).</td>
</tr>
<tr>
<td>Being able to work</td>
<td>Having an occupation with daily routines. A sense of coherence; feeling important and capable at work. Better economy.</td>
<td>‘The work – doing something meaningful’ (15). ‘The work – better economy’ (6). ‘Manage to work, to have something to do’ (59). ‘The work – to be someone and discuss’ (41).</td>
</tr>
<tr>
<td>Get along with daily inconveniences</td>
<td>Being happy about things that work in the daily life and appreciation of being spared from e.g. a cold, pain or other discomforts.</td>
<td>‘To feel pretty good, meaning not too much nausea or too much pain’ (34). ‘To be able to eat without too much problem with mucus’ (22). ‘To not have a cold’ (23). ‘Be able to talk’ (46).</td>
</tr>
<tr>
<td>Being alone</td>
<td></td>
<td>‘Be by myself’ (4).</td>
</tr>
<tr>
<td>Domestic care and family responsibilities</td>
<td>Being able to take care of household chores and the family.</td>
<td>‘Manage the household, which works today, vacuum-clean, dishwasher and washing machine’ (60).</td>
</tr>
</tbody>
</table>

28
<table>
<thead>
<tr>
<th>Areas</th>
<th>Description of area content</th>
<th>Examples of patients’ quotations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Being independent</td>
<td>Being able to decide things by yourself and transport myself.</td>
<td>‘To feel free and make own decisions’ (7).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘The car – a sense of freedom to transport oneself without help’ (16).</td>
</tr>
<tr>
<td>Being physically active</td>
<td>The ability to be physically active.</td>
<td>‘To be able to perform daily exercises’ (40).</td>
</tr>
<tr>
<td>Social relations</td>
<td>Social contacts, relations and interactions that make one feel happy, comfortable and taken care of, also including the possibility to care for other people. The importance of collegial fellowship.</td>
<td>‘To be with my friends, the social part, to laugh and hang around’ (37).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘To feel and give love to my children’ (7).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘The family and my friends – often contact and are close’ (50).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘My marriage – the thoughtfulness and full of fun’ (58).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘The work – the community’ (28).</td>
</tr>
<tr>
<td>Being in good health</td>
<td>Feeling as good as possible.</td>
<td>‘To feel well inside and be in good mood’ (1).</td>
</tr>
<tr>
<td>Being able to travel</td>
<td>The joy of making a journey.</td>
<td>‘Travel and experience other environments and people’ (6).</td>
</tr>
<tr>
<td>The cottage</td>
<td>The sense of peace and satisfaction from being at one’s cottage.</td>
<td>‘My cottage – a sense of happiness and freedom’ (41).</td>
</tr>
<tr>
<td>A pet</td>
<td>The happiness, security and joy that comes with having a pet to care for.</td>
<td>‘My dog – welcoming and happy to see me’ (37).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘The dogs and the cat give me sense of security’ (30).</td>
</tr>
<tr>
<td>Being in the outdoor environ\ment</td>
<td>Activities in the outdoor environment and nature e.g. fishing, berry picking.</td>
<td>‘Walk in the nature with the dog, love the nature’ (47).</td>
</tr>
<tr>
<td>Enjoying good food and drinks</td>
<td>To enjoy and cook good food and drinks, including eating at restaurants.</td>
<td>‘Go to restaurant and eat good food’ (50).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘Cook nice tasting food’ (36).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘The food and wine’ (48).</td>
</tr>
<tr>
<td>Activities for amusement and relaxation</td>
<td>Engagement in hobbies e.g. relaxing activities, entertainment like theatre or sport events, watching TV, reading books, Internet browsing, listening to music, daydreaming, singing, taking photographs.</td>
<td>‘Cross-word to activate the brain’ (56).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘Theatre visit – entertainment’ (9).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘Listen to music’ (18).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘Take pictures to get the perfect picture’ (36).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘Watch sports on TV’ (39).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘Listen to a book’ (48).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘Needlework’ (57).</td>
</tr>
<tr>
<td>Physical contact</td>
<td>Experience of physical contact, body touch and sex</td>
<td>‘Physical contact, body contact’ (33).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘To have sex’ (13).</td>
</tr>
<tr>
<td>A safe and comfortable home environment</td>
<td>Feeling comfortable and secure at home, both indoors and outdoors, for both oneself and others.</td>
<td>‘The home – with its safety and stability’ (39).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘That everyone feel comfort with our home environment’ (27).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘A good house close to nature’ (61).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘A safe home with food for the day, where the wife is cooking’ (26).</td>
</tr>
<tr>
<td>Access to support and aids</td>
<td>Having access to support from health-care, including personal assistance, psychological support and aids.</td>
<td>‘Aids – BiPAP, cough assist, indoor wheelchair facilitates physically and psychologically’ (33).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘That people around me make it possible for me to feel free’ (7).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘That my children can assist me’ (54).</td>
</tr>
</tbody>
</table>

The number in the parenthesis in the column examples of the participants’ quotations, is the code for the participant.
Table 6
Areas of the individual quality of life in those with and without pain and satisfaction with the area

<table>
<thead>
<tr>
<th>Areas†</th>
<th>Participants with/without pain ‡ n (%)</th>
<th>Satisfaction in participants with pain ‡, median (Q1-Q3, min-max)</th>
<th>Satisfaction in participants without pain ‡, median (Q1-Q3, min-max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social relations</td>
<td>35 (85) / 12 (86)</td>
<td>6 (4.5-6.5, 2-7)</td>
<td>6 (4.2-7, 3-7)</td>
</tr>
<tr>
<td>Activities for amusement and relaxations</td>
<td>23 (56) / 4 (28)</td>
<td>5 (4.8-6, 1-7)</td>
<td>3.8 (1-6.2, 1-7)</td>
</tr>
<tr>
<td>Being in the outdoor environment</td>
<td>12 (29) / 7 (50)</td>
<td>5.5 (4-6.8, 3-7)</td>
<td>5 (1-6, 1-6)</td>
</tr>
<tr>
<td>Being able to work</td>
<td>9 (22) / 2 (14)</td>
<td>4 (1.5-5.5, 1-6)</td>
<td>5.5 (5, 5-6)</td>
</tr>
<tr>
<td>Being independent</td>
<td>9 (22) / 4 (28)</td>
<td>4 (2.5-4, 1-6)</td>
<td>4.5 (1.8-5.8, 1-6)</td>
</tr>
<tr>
<td>Being physically active</td>
<td>9 (22) / 2 (14)</td>
<td>4 (2.5-6.5, 1-7)</td>
<td>2 (1, 1-3)</td>
</tr>
<tr>
<td>Access to support and aids</td>
<td>8 (20) / 2 (14)</td>
<td>6 (4.5-7, 2-7)</td>
<td>6.5 (6, 6-7)</td>
</tr>
<tr>
<td>Get along with daily inconveniences</td>
<td>6 (15) / 3 (21)</td>
<td>3.5 (1.8-4.5, 1-6)</td>
<td>3 (2.2-5.2, 2-6)</td>
</tr>
<tr>
<td>A safe and comfortable home environment</td>
<td>6 (15) / 0</td>
<td>6 (5.1-6.2, 4-7)</td>
<td></td>
</tr>
<tr>
<td>The cottage</td>
<td>4 (10) / 2 (14)</td>
<td>6 (5.2-6.8, 5-7)</td>
<td>4 (1, 1-7)</td>
</tr>
<tr>
<td>Being able to travel</td>
<td>4 (10) / 1 (7)</td>
<td>6 (2-7, 1-7)</td>
<td>5 (5-5)</td>
</tr>
<tr>
<td>Being in good health</td>
<td>3 (7) / 4 (28)</td>
<td>6 (2, 2-6)</td>
<td>5.5 (4.2-6, 4-6)</td>
</tr>
<tr>
<td>Enjoying good food and drinks</td>
<td>3 (7) / 2 (14)</td>
<td>6 (4, 4-6)</td>
<td>6.5 (6, 6-7)</td>
</tr>
<tr>
<td>A pet</td>
<td>2 (5) / 0</td>
<td>6.5 (6, 6-7)</td>
<td></td>
</tr>
<tr>
<td>Hope for the future</td>
<td>2 (5) / 0</td>
<td>3.5 (1, 1-6)</td>
<td></td>
</tr>
<tr>
<td>Domestic care and family responsibilities</td>
<td>1 (2) / 2 (14)</td>
<td>4 (4-4)</td>
<td>3.5 (3, 3-4)</td>
</tr>
<tr>
<td>Physical contact</td>
<td>1 (2) / 2 (14)</td>
<td>4 (4-4)</td>
<td>1.5 (1, 1-2)</td>
</tr>
<tr>
<td>Having a philosophy of life</td>
<td>1 (2) / 0</td>
<td>5.5 (5.5-5.5)</td>
<td></td>
</tr>
<tr>
<td>Being alone</td>
<td>1 (2) / 0</td>
<td>5 (5-5)</td>
<td></td>
</tr>
</tbody>
</table>

†Areas = areas important for the participants’ individual quality of life (IQOL). ‡Participants with/without pain (of a total 55) mentioning the area. §Satisfaction in participants with pain = the level of satisfaction with the area in participants with pain (part of the study-specific SEIQoL-DW). ‡Satisfaction in participants without pain = the level of satisfaction with the area in participants without pain (part of the study-specific SEIQoL-DW).
Discussion

Pain in people with motor neuron diseases

Although several studies have been conducted on pain in MND, it is difficult to completely understand pain connected with the diseases. For example, how pain is still an overlooked symptom in healthcare despite many people with MND found to have pain (44), why pain is noted as interfering with several daily activities, despite the level of pain being relatively low (34, 36). In order to better understand, we came to the conclusion that it was important to study how people themselves experience their pain and their perceptions thereof in their daily lives.

The variation of pain characteristics and appearance of pain during the disease progress in study I confirmed findings from previous studies (36, 39, 51). However, pain was also noted to be an overlooked ailment, both by the participants themselves and by staff in healthcare. To our knowledge, under-reporting of pain in people with MND is new information but might be one explanation for why pain seems to be an overlooked symptom in healthcare. The participants described different reasons for why pain was ignored. It became clear that people with MND could avoid disclosing their pain because they thought that pain, as well as the disease, could not be treated. Low interest from staff in healthcare about pain was the second reason for why participants overlooked disclosing their pain. These experiences might have been negative for the participants’ pain. Peoples’ thoughts about resources for coping with something that is stressful is important for their appraisal of the stressor (111). Uncertainty and lack of knowledge about pain in people with MND (35) might be a reason why staff do not have discussions about pain with the patient. The participants' thoughts about treatment for their pain and low interest in having discussions about pain by healthcare staff highlighted the importance of discussing pain at meetings between the healthcare staff and the patient. It further emphasises that the caregiver's approach towards the patient can be a significant factor if the patient mentions his/her pain at all. The final reason for the participants to overlook pain was described as in comparison with the disease itself, i.e. pain was not the worst thing. That mirrors results from another study (112) and illustrates what might be specific for pain in MND.
Pain discomfort for participants in study I were found to vary, where some experienced it as a slight ache with minimal discomfort, while others thought it was very intensive and hard to stand. Episodes with pain breakthrough were described as difficult, especially those that occurred during the night. These experiences have not been acknowledged before. The participants described pain as a stressor. Appraisals of stress arise when environmental demands exceed the individuals’ resources (113). However, studies about pain as a stressor in people with MND are missing. In order to support the individual, it is important to analyse the individual’s specific situation with pain.

The experiences of participants in study I described that there are aspects that increase the risk of having pain, such as movement and immobility (34). However, the descriptions from the participants in study I also revealed other reasons for pain being aggravated and provoked, such as bodily exhaustion, use of badly adapted equipment, worries and even physical touch and small movements and changes in loads. These experiences highlight that treatment for pain needs to be tailored for the individual, but also that healthcare staff need to have good knowledge about the clinical care for MNDs (3); otherwise the management for pain relief might have the opposite effect and instead worsen their pain.

The consequences of pain for people with MND has been documented in several studies using quantitative methods (32, 34, 36). However, descriptions from participants in study I increased the understanding of how pain was experienced and how it affected the individual in the specific situation. Pain was experienced as additionally affecting functions that were already reduced by the disease, for instance, the possibility to eat or walk. Respiratory impact might be possible symptom for many of those with MNDs. In study I, respiratory decline was described as being combined with chest pain. Furthermore, pain caused concerns as to whether it would increase together with breathing difficulties. However, the consequences of pain varied between the participants; also, there were participants, who thought that pain did not affect them so much. The participants’ experiences are important knowledge and show why MND patients’ pain should be minimised. It also emphasises the importance of that pain research need to sort pain secondary to the participants' disorder. Here, the new diagnostic classification system about chronic pain will be helpful (27).

There is a need for clinical research on pain relief in MNDs (3, 45). Today, much of the clinical management of pain relief is pharmacological (114, 115). However, the participants in study I experienced that the pharmacological and non-pharmacological treatments complemented each other, which is supported by previous study (34). The participants’ descriptions indicated reasons
for combining pharmacological and non-pharmacological treatments in clinical intervention studies. In study I, it was also found that participants needed to make efforts to get pain relief. They described the complexity and energy required to find a pain free position, which might be short-lived, requiring them to find a new position. The participants also described how they needed to take a walk or stretch in the middle of night until the pain was milder so they could fall asleep again. This was new insight and underlined the importance of continuously and thoroughly evaluating pain management in healthcare, including finding consequences of different pain management options.

Pain was found to be common among the participants. In study II, 74% of the participants had pain, and 36% had chronic pain before the first symptom of MND. The 36% is higher than the average of chronic pain (18%) for the general population in Sweden (116). The higher percentage might indicate that pain was part of the disease. Stephen et al. has verified that 50% of the patients reported that pain started before symptoms of ALS (35), and it has also been found that MND patients, more frequently than general population, use drugs for neuropathic pain before onset of MND (117). In study II, the prevalence of pain for the participants was, regardless of the mechanisms behind their pain, considerably higher for those with disease of MND compared to those who had chronic pain before the MND symptoms, an increase from 36 to 74%. This is in line with pain being found to be more frequent in people with MND compared to people with other neurological diseases and healthy people (34, 36, 38).

Quality of life in people with motor neuron diseases, who have pain

Satisfaction with IQoL was noticed to be good regardless of pain. There was no significant difference in satisfaction with IQoL between participants with and without pain. The three most important areas described for IQoL for both participants with and without pain were: Social relations, Activities for amusement and relaxations and Being in the outdoor environment, which are all well-known areas from IQoL studies with MND (78, 79, 86). The five areas that were only mentioned by those with pain, A safe and comfortable home environment, A pet, Hope for the future, Having a philosophy of life and Being alone, could not be determined to be real differences of IQoL content in participants with and without pain, or be based on individual factors, as the data were too small.

It became clear that neither the existing pain nor pain severity, as well as the disease severity was associated with the participants’ satisfaction for IQoL in study II.
The results from study I, of varying perceptions of pain and different opinions as to whether pain affected the participants and their lives, might have explained that no differences between existing pain and IQoL were found in study II.

Good coping strategies for pain as well as coping with disease severity might have been other reasons for why there were no associations between pain, disease severity and satisfaction of IQoL in study II. Good IQoL is found to be predicted by coping strategies (62), which strengthened this assumption. People with severe diseases tend to cope with their situation by accepting symptoms and disabilities in order to continue to live (118), but they also focus on things in life that give them QoL and are possible to achieve (119). This kind of coping strategy that reduces or manages emotional distress associated with a stressful situation is called emotional coping strategy (113).

The result showing no correlation between pain severity and IQoL might also be explained by the fact that the intensity of pain in study II might not have been the most troublesome aspect of their pain. It might be having pain and not the intensity that is the deciding factor for how pain is experienced (35). Measuring the correlation between pain intensity and IQoL showed no correlation; however, a correlation might be found with IQoL by studying the circumstances under which pain is experienced, for instance, during the day or night. Another example might be to study the correlation between different characteristics of pain and IQoL. Both pain during the night and the characteristics of unpredictable pain flair-up were described as stressful for participants in study I.

Methodological considerations

Important aspects to get trustworthiness in qualitative research is dependability, credibility and transferability (120). The individual interviews in study I made it possible to get clarifications about what was told, as the interviewer had the opportunity to ask follow-up questions if something was unclear and thereby also strengthen the dependability of the study. The interview-guide in study I was also important for the dependability as it was used to support that no important area was forgotten, complemented with broad and open-ended follow-up questions, if the participant spoke sparsely. To strengthen the credibility of the qualitative results in studies I and II, every step of the qualitative analysis was clearly described as well as descriptions of the area content (study II). To minimise any preunderstandings of the authors affecting the results in both study I and study II, the results were supported with the participants’ quotations, which were presented in both the analysis tables (studies I and II) and in the manuscript (study I). However, complementary individual interviews about QoL, with the participants who had pain (study II), could
have led to supplementary and clarified results. In both studies, researcher triangulation was used, i.e. a collaboration between the researchers to reduce the possibility of biased interpretation of the data (120). Researchers' diverse perspectives and fruitful discussions are positive for credible interpretations of data (120). The authors involved in the researcher triangulation in studies I and II had different backgrounds to increase the credibility of the results.

Since pain in Study I was noted to vary also within 24 hours, study II used existing pain in the calculations instead of pain in the latest 24 h (BPI-SF).

Limitations of the studies also need to be discussed. The participants in study I came from only one MND team, which might have limited the variation of the participants’ experiences and thereby the transferability to other settings. In study II, the participants should preferably have been recruited from a larger numbers of teams and have been more geographically dispersed. The reason for the selection was better accessibility and possibility of financing. However, the transferability to other MND populations was facilitated by the careful descriptions of the participants, the data collection and the analysis in both study I and II (110).

Patients who had no verbal speech were not included in study I. In study II, patients who had no verbal speech could participate if they could express themselves in another way, like via eye-controlled computer. The participants in study I, who had limited speech, need to be considered, as they might not have managed to describe everything they experienced. People with MND, without ability to speak and having pain, need to be studied too, since speech dysfunction is found to be something that people with MND fear (121). The combination of not being able to communicate and having pain might therefore be more stressful, compared to those having speech. It also needs to be considered that the participants in study II had relatively good respiratory function, taking into consideration that they had ALS. Therefore, this might limit the transferability of the results to the whole group of people with MND. In comparison, the participants in study I had slightly worse functions in both respiratory and gross motor function compared to the participants in study II.
Conclusion

- People with MND experienced pain as having multiple characteristics and impact. However, the results emphasise that the individual experienced some pain characteristics as difficult and that pain could worsen functions that were already affected by the disease. The experience was also that pain could be demanding to manage. However, the symptom of pain could pass unnoticed in contacts with healthcare professionals.

- Pain and pain severity were not found to be associated with satisfaction of IQoL in patients with MND, neither was disease severity. The results support previous findings that strong associations between symptoms of MNDs and IQoL are not obvious. Regardless of that, it does not infer that pain in people with MNDs should be neglected and undertreated.

Implications and future studies

Pain in people with MND need more attention from healthcare and should be continuously measured and individually treated and followed. Staff should provide information that it is possible to treat pain, as opposed to the possibility of curing the disease itself.

Healthcare professionals need more knowledge about pain in people with MND.

Regardless of whether persons with MND have pain or not, the results point to the importance of healthcare professionals providing support to not only the patient but also the patient’s family and friends, as well as assisting in various forms of relaxing activities and possibility of being in the outdoor environment, since these areas appear to be important for IQoL in people with MND.

In order for clinicians and patients to more easily register the pain, there is a need to develop and implement pain assessment methods adapted to the MND population.

Further research about pain as a stressor in people with MND is needed, also focusing on people in the severe stage of the disease.
Moreover, to further understand what influences the association between pain and QoL, there is need for research with longitudinal studies.
Motorneuronsjukdomar (Motor Neuron Diseases, MNDs) är neurologiska sjukdomar där motorneuronen och dess banor som styr vår viljemässiga muskulatur successivt förstörs. Förutom den neuromuskulära påverkan, kan vissa av dessa diagnoser medföra en påverkan på fler system med symtom såsom kognitiva nedsättningar och smärta. Amyotrofisk Lateral Skleros (ALS) är den mest förekommande av MNDs och i vanligtvis också den allvarligaste på grund av sitt snabba förlopp. Överlevnaden är 3-5 år och dödsorsaken är ofta orsakad av andningssvikt. ALS har en påverkan på både de primära och de sekundära motorneuronen och dess banor. Detta resulterar i en gradvis muskelförsvagning i vissa muskler och en samtidig okontrollerbar anspänning, s.k. spasticitet, av andra muskler. Primär Lateral Skleros (PLS) är en MND med framför allt spasticitet och koordinationspåverkan av muskulaturen. Personer med PLS har i allmänhet en bättre prognos än personer med ALS. Det finns också MNDs som primärt resulterar i en muskelförsvagning och muskelbortfall, d.v.s. enbart med nedre motorneuron påverkan.

Det finns inget botemedel för personer med MND. Vården inriktas istället på symptomlindring och stöd för de behov som patient och närstående behöver under sjukdomsprogressen. Målsättningen är att uppnå en så god livskvalitet (Quality of Life, QoL) som möjligt för den sjuke och dennes närstående.

Uppemot 85 % av personer med MND har i studier noterats ha smärta. Smärta är i allmänhet relativt låg i sin intensitet, men upplevs ändå inverka på personernas dagliga aktiviteter. Utifrån nuvarande forskning är smärta vid MND inte helt klarlagd och studiers resultat går till viss del isär. Det saknas också studier om hur det dagliga livet ter sig för personer med MND som har smärta. Vidare är det oklart huruvida smärta korrelerar med QoL eller inte. Genom att studera QoL som personerna själva vill beskriva den, s.k. Individuell QoL (IQoL), så finns det möjlighet att få klarhet i om det finns något samband mellan smärta och QoL från perspektivet med IQoL. Denna forskning har inte gjorts tidigare på personer med MND som har smärta.

Syftet med de två studierna var dels att utforska erfarenheterna av smärta liksom att studera sambandet mellan smärta, sjukdomens svårighetsgrad och IQoL hos personer med MND.

Studie I var explorativ med användning av kvalitativ analys. Studie II var en korrelerande studie med användning av både kvalitativ och kvantitativ analys. Deltagarna i studie I kom från ett multidisciplinärt MND team och i studie
II från fyra multidisciplinära MND team. Gemensamma inklusionskriterier i studierna var att deltagarna skulle ha en MND, vara över 18 år samt förstå och kunna uttrycka sig på svenska. I studie I skulle deltagarna dessutom ha smärta. Sexton personer deltog i studie I och 61 i studie II. Datainsamlingen i studie I bestod av djupintervjuer om personernas erfarenhet av smärta. I studie II användes ett intervjubaserat mätinstrument om IQoL och ett självskattningssinstrument om smärta.

I studie I noterades att erfarenheterna av smärta var olika och den hade många olika karaktärsdrag och påverkan. Resultatet understryker dock att individen kunde uppleva vissa smärtegenskaper som svåra och att smärta kunde förvärva funktionsområden som redan var drabbade av sjukdomen. Deltagarnas upplevelse också att smärta kunde vara krävande att hantera. Trots deltagarnas smärta, så kunde den passera obemärkt i kontakterna med sjukvården. Vidare noterades att befintlig smärta och smärtans svårighetsgrad inte var förknippad med IQoL hos patienter med MND, inte heller sjukdomens svårighetsgrad. Resultaten stöder tidigare fynd att associationer mellan symptomen på MND och IQoL inte är tydliga. Emellertid innebär inte detta att smärta hos personer med MND bör försummas och underbehandlas. Istället indikerar resultaten att sjukvårdspersonal behöver mer kunskap om smärta vid MND. Smärta hos personer med MND behöver också få en ökad uppmärksamhet i sjukvården d.v.s. bör mätas kontinuerligt och individuellt behandlas och följas upp. Sjukvårdspersonal bör ge patienten information om att smärtan är möjlig att behandla. Resultatet pekar också på att oavsett om personer med MND hade smärta eller inte, så är det betydelsefullt att stöta relationen mellan patienten, patientens familj och vänner samt uppmuntra till olika former av avkopplande aktiviteter och möjlighet för personen att vara i utomhusmiljö, då dessa områden tycks vara betydelsefulla för personens IQoL. Vidare indikerar studierna på behovet av fortsatt forskning om smärta, inte minst longitudinella studier för att förstå vad som påverkar sambandet mellan smärta och QoL.
Jag skulle vilja tacka personer som varit betydelsefulla under min forskarutbildning och arbetet med min licentiatavhandling. Jag vill särskilt tacka:

Alla patienter som medverkat i studierna och bidragit med sin tid, erfarenheter och tankar. Detta har inte bara gett värdefull kunskap och forskningsdata. Att få träffa er i en annan kontext än den jag är van vid, där ni generöst delat med er av era erfarenheter och, även om det ibland varit utmanande, har visat på en fantastisk vilja att leva. Detta sammantaget gör mig ödmjuk.

Alla personer som bidragit till rekrytering och bedömning av deltagare i studie II. Utan er hade studie II och den longitudinala datainsamlingen under fyra års tid inte varit möjlig att få till. Ett särskilt tack vill jag rikta till Margareta Bovin Larsson, Ingrid Orefeldt, Ann Sundbom, Helena Jensen, Petra Låång, Marianne Skoglund, Ann-Marie Nilsson och Monika Magnusson, som tålmodigt tagit emot min information och önskemål om uppgifter i den longitudinala datainsamlingen, genomfört och slutfört all datainsamling.

Pernilla Åsenlöf, min huvudhandledare för din vetenskapliga kompetens och skärpa i design och analys både verbalt, skriftligt och i de diskussioner vi haft. Det har varit så lærorikt.

Lena Zetterberg, min handledare som inspirerade mig till att hitta ett ämne och som la grunden för utformningen av doktorandprojektet. Tack även för din tillgänglighet och de vetenskapliga diskussioner vi haft.

Dag Nyholm, min handledare för ditt stöd och positiva inställning, dina snabba återkopplingar, kunskap och kommentarer som erfaren forskare.

Birgitta Jakobsson Larsson, medförfattare i båda studierna för att du är en klok medmänniska som står med båda fotterna på jorden. Min kliniska kollega som jag uppskattar på många sätt och förutom din kliniska kompetens av patienter med MND, också har en förmåga att i forskningen ständigt knyta an till det kliniska. Vi har haft många givande diskussioner.
Ingela Nygren, min handledare initialt och medförfattare i studie II, för möjligheten att få starta upp projektet i MND teamet, liksom din kunskap och klokhet inom området MND.

MND-teamet med tidigare och nuvarande medlemmar, för att ni är lätta att samarbeta med och är goda kollegor. Vi har haft många givande diskussioner, men även resor och middagar tillsammans som svetsat oss samman och utvecklat verksamheten.

Verksamhetschefer och avdelningschefer inom verksamhetsområdet, nu senast Rehabilitering och smärtcentrum Akademiska sjukhuset under ledning av Rolf Karlsten, som möjliggjort för mig att vara tjänstledig för att genomföra mina doktorandstudier.


Mina föräldrar, där pappa Lars-Erik gärna diskuterade projektet med mig innan han blev alltför sjuk och Birgitta, ständigt påhejande. Mina syskon Anders, Mats och Åsa, där Åsa alltid funnits som ett stöd och en viktig vän.


Denna licentiatsavhandling har finansierats med anslag från: Vårdforskningsmedel från Uppsala Universitet, ALF och Regionala forskningsmedel från Region Uppsala, Neuroförbundet och Ulla-Carin Lindquist stiftelse.
References


78. Olsson AG, Markhede I, Strang S, Persson LI. Differences in quality of life modalities give rise to needs of individual support in patients with ALS and their next of kin. Palliative & supportive care. 2010;8(1):75-82.
88. Ruta DA, Garratt AM, Leng M, Russell IT, MacDonald LM. A new approach to the measurement of quality of life. The Patient-Generated Index. Med Care. 1994;32(11):1109-26.


118. Anderson M, Asmani M. "You just have to live with it": coping with sickle cell disease in Jamaica. Qual Health Res. 2013;23(5):655-64.


120. Polit DF, Beck CT. Nursing research: principles and methods
