Multidimensional Aspects of Dystonia

Description and Physiotherapy Management

LENA ZETTERBERG
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Abstract

Aims: The overall aim of this research was to increase the knowledge about dystonia by identifying factors that influence self-reported quality of life and health in this disorder and to determine what factors predict disability. A further aim was to develop an objective outcome measure for quantifying the movement dysfunction in cervical dystonia (CD) and evaluate effects of physiotherapy.

Methods: A descriptive correlative design was adopted for study I (n=351), with a questionnaire covering physical activity, satisfaction with treatment, physiotherapy or not, and quality of life and health measured with the Craniocervical Dystonia Questionnaire (CDQ-24) and the Cervical Dystonia Impact Profile, respectively.

In study II a CD group (n=6) was compared with a control group (n=6). Head movements were measured with a motion capture system, and a Movement Energy Index (MEI) was calculated. In study III an experimental single-case design (n=6) was used, with continuous assessments during pre-treatment, intervention and follow-up. Quality of life, measured with CDQ-24, was the primary outcome measure.

A prospective correlative design was applied in study IV (n=179), where data from questionnaires were collected on inclusion and 2 months later. Independent variables were: duration of dystonia, severity of dystonia, pain intensity, catastrophizing, self-efficacy, fatigue, kinesiophobia, depression, anxiety and physical activity; and the dependent variables were the Neck Disability Index and the Functional Disability Questionnaire.

Results: Study I indicated that physical activity and satisfaction with treatment were associated with quality of life and health in dystonia. In study II the groups differed significantly concerning MEI in all movement directions. Mean MEI was significantly higher in patients than in controls. Positive treatment outcomes were reported by all patients in study III, mainly with reduced pain and reduced CD severity during the treatment period. Five of the six patients reported increased quality of life at the 6-month follow-up. Perceived self-efficacy, fatigue, pain intensity and anxiety contributed significantly to disability prediction in study IV.

Conclusion: These investigations have increased the knowledge of dystonia from a multidimensional perspective and the results could be valuable in developing new treatment strategies.

Keywords: disability, dystonia, health, movement analysis, physiotherapy, quality of life

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urn:nbn:se:uu:diva-9417 (http://urn.kb.se/resolve?urn=urn:nbn:se:uu:diva-9417)
To Gustav and Klara
Man måste gå i motlut, om man ska komma upp på fjället.

Norskt talesätt
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This thesis is based on the following papers, which are referred to in the text by their Roman numerals:


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Abbreviations

ADL Activity of daily living
BTX Botulinum toxin
CAT The Catastrophizing Subscale of the Coping Strategies Questionnaire
CD Cervical dystonia
CDIP-58 Cervical Dystonia Impact Profile
CDQ-24 Craniocervical Dystonia Questionnaire
DBS Deep Brain Stimulation
FDQ Functional Disability Questionnaire
FSS Fatigue Severity Scale
HAD Hospital Anxiety and Depression Scale
IPAQ International Physical Activity Questionnaire
MEI Movement Energy Index
MET Metabolic Equivalent
MS Multiple Sclerosis
NDI Neck Disability Index
NRS Numerical Rating Scale
PMR Progressive muscle relaxation
POI Postural Orientation Index
PT Physiotherapy
SES The Self-efficacy Scale
SF-36 Short Form Health Survey -36
TWSTRS Toronto Western Spasmodic Torticollis Rating Scale
TSK Tampa Scale of Kinesiophobia
VAS Visual Analogue Scale
QoL Quality of life
INTRODUCTION

About this thesis

Dystonia has been extensively investigated concerning biomedical aspects such as cause, classification, characteristics, and the effect of botulinum toxin on the motor severity. However, research on the consequences of dystonia for the quality of life and for health and disability in the individual patient is sparse. There is a need to consider dystonia not only from a biomedical perspective but also from a psychological and social point of view. A simultaneous bio-psycho-social perspective of dystonia increases the possibility of viewing this disorder from a multidimensional aspect. A multidimensional perspective of dystonia could increase the understanding of the consequences of the disorder, which could be of value in developing new treatment strategies.

This thesis is based on four empirical studies. The aim of the first study was to investigate a Swedish population with dystonia regarding demographic variables, and to identify factors influencing the impact of different forms of dystonia on self-reported quality of life and health measured with two disease-specific measures (study I; paper I). In the second study (study II; paper II) quantifying the irregular movements of the head in cervical dystonia (CD) was developed by calculating the “Movement Energy Index” (MEI), which is an estimate of the mechanical power and work involved in the movements. The movements were measured with an optoelectronic motion capture system. The objective of the third study (study III; paper III) was to explore the outcome of a physiotherapy program aimed at improving the quality of life of people with CD by 1) reducing pain, 2) improving the patients’ awareness of their postural orientation 3) increasing muscle strength, and 4) reducing the effort required for moving the head and neck. The purpose of the fourth study (study IV; paper IV) was to identify physical and psychological variables that could predict disability in CD.

Characteristics and classification of dystonia

The term dystonia was used for the first time in 1911 as “dystonia musculus-rum deformans”. Today, almost 100 years later, many types of dystonia are recognised, including both primary dystonia and dystonia secondary to an-
other disorder. In 1984 a definition of dystonia was proposed by an Ad Hoc Committee consisting of members of the Scientific Advisory Board of the Dystonia Medical Research Foundation: “Dystonia is a syndrome of sustained muscle contractions, frequently causing twisting and repetitive movements or abnormal posture” (1).

The dystonic movements can occur in almost any part of the body, either when that body part is “at rest” or when it is engaged in voluntary motor activity. Only in severe cases is muscle activity recorded at complete rest (1, 2). The twisting movements of dystonia are characterised by co-contraction of agonist and antagonist muscles and a voluntary movement exacerbates the co-contraction (2). Another characteristic of dystonic contractions is their consistent directionality. Unlike disorders such as chorea, in which it is often impossible to predict which muscles will move next, the movements in dystonia are commonly repeated within the same muscle groups (3). Dystonia is aggravated during voluntary movements and may only be present during specific voluntary actions. Another feature of dystonia is the importance of sensory input in modifying the abnormal muscle contractions; this is called a “sensory trick”. A cutaneous or proprioceptive input near to the affected region may help the patient to re-establish a normal posture or movement (1).

The classification of dystonia is mainly based on three perspectives (1, 4-6): (a) aetiology, (b) age at onset of symptoms, and (c) distribution of body regions affected. The aetiological classification (a) discriminates primary (idiopathic) dystonia from secondary dystonia, where the former is the only manifestation without any identifiable exogenous cause, or any inherited or degenerative disease, and the latter is usually one of several clinical conditions. Dystonia plus syndromes are associated with another movement disorder, such as myoclonus-dystonia. Wilson’s disease is one example of a heredo-degenerative disorder in which dystonia is a prominent sign, amongst other neurological features. Secondary dystonia is secondary to an identified neurological condition such as a brain tumor or Parkinson’s disease. Exposure to neuroleptic drugs, or to chemicals such as manganese, can also result in dystonia.

Various classifications by age at onset of symptoms (b) have been proposed (1, 4-6). This classification is desirable as age at onset is the most important single factor related to the prognosis of idiopathic dystonia. Age at onset is closely related to anatomic distribution. The earlier the onset of the dystonia, the more likely the dystonia will be to become severe and also spread to involve multiple parts of the body.

Classification by bodily distribution (c) is the third way to classify dystonia. There are five types of dystonia with different bodily distributions, namely focal dystonia, segmental dystonia, multifocal dystonia, generalised dystonia and hemidystonia. Focal dystonia affects one single body region, and in segmental dystonia contiguous body regions are affected, e.g. cranial
and cervical parts of the body. Examples of focal and segmental dystonia are shown in Table 1. The term multifocal dystonia implies that non-contiguous body regions, e.g. an upper and lower limb, or the cranial part of the body and an upper limb, are affected. Generalised dystonia affects both legs and at least one other body region (usually one or both arms). When an arm and the ipsilateral leg are affected the dystonia is classified as hemidystonia (1, 4-6).

Table 1. Examples of focal and segmental dystonia.

<table>
<thead>
<tr>
<th>Example of dystonia</th>
<th>Affected muscles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blepharospasm (focal)</td>
<td>Muscles of the eyelids</td>
</tr>
<tr>
<td>Cervical dystonia (focal)</td>
<td>Muscles in the neck</td>
</tr>
<tr>
<td>Dystonic adductor dysphonia (focal)</td>
<td>Muscles in the larynx</td>
</tr>
<tr>
<td>Writer’s cramp (focal)</td>
<td>Muscles in the hand, forearm and arm</td>
</tr>
<tr>
<td>Oromandibular dystonia (segmental)</td>
<td>Muscles of the jaw, lower face or mouth</td>
</tr>
<tr>
<td>Meige syndrome (segmental)</td>
<td>Combination of blepharospasm and oromandibular dystonia</td>
</tr>
</tbody>
</table>

With increased awareness of the molecular and environmental causes of dystonia a classification scheme based on different genetic forms has been proposed. To date, at least 13 dystonic syndromes have been distinguished on a genetic basis and their loci are referred to as DYT1 to DYT13 (5).

The prevailing ways of classifying dystonia have all been developed from a biomedical perspective on a one-axis basis. This type of classification might be limiting for the development of treatment meeting the needs of the patients, since the manifestations of dystonia might be dependent on multidimensional factors.

Cervical dystonia is the most common focal dystonia (7, 8). Consequently, most research in dystonia is focused on this form. The symptoms of CD usually begin insidiously, with the patients complaining of a sensation of “pulling” or “drawing” in the neck, or involuntary twisting or jerking of the head (3, 9, 10). CD is also known as torticollis. However, torticollis means a twisted neck, a contracted state of the cervical muscles, which may result from various non-dystonic disorder (10). Torticollis involves rotation only in contrast to deviations caused by CD, which may occur in any single plane or combination of directions. Intermittent or sustained elevation or anterior displacement of the shoulder, most commonly ipsilateral to the direction of the turn or tilt, is also frequently seen (11).

The rotational dystonic movements in CD are mainly produced by the contralateral sternocleidomastoid muscle and the ipsilateral splenius capitis muscle with or without additional involvement of the contralateral splenius capitis muscle. The involvement of the trapezius muscle is observable in CD, in which the head is laterally flexed simultaneously with the ipsilateral sternocleidomastoid and splenius capitis muscles. When the head is pulled backwards it is most often caused by bilateral splenius capitus activity (10).
Tremor is a well-known symptom in CD. It is more common in women, is not always associated with head deviation, and the incidence is higher when neck pain is present (12).

Stress and self-consciousness are reported to be aggravating factors in CD, as also are walking, fatigue and carrying objects. Lying in a supine position, relaxation, sleep and lying on the side may ameliorate the symptoms (13).

Risk factors for primary adult-onset CD are poorly known. Defazio et al. (14) suggest that scoliosis that develops in middle to late childhood or around puberty is associated with CD regardless of age, duration of the disease, other spinal diseases and family history of dystonia.

**Diagnosis**

In view of the lack of specific diagnostic tests, expert observation is recommended for recognising the abnormal movements as dystonic. As mentioned earlier, dystonic movements are patterned. They repeatedly involve the same muscle group, they cause twisting of body parts and they are usually of longer duration than those seen in other disorders. In addition, activation of dystonic movements in remote parts of the body may occur; for example the occurrence of leg dystonia while writing and talking might in turn induce axial dystonia. However, dystonia may also be suppressed by voluntary activity. For example, talking or chewing might suppress eye closure in blepharospasm or jaw opening in oromandibular dystonia (6). Neurophysiological tests such as electromyography are not routinely required when diagnosing dystonia. Structural brain imaging is necessary for screening for secondary forms of dystonia, particularly in the paediatric population, but is not routinely required when there is a definite diagnosis of primary dystonia in adult patients (4).

In order to distinguish between CD and other abnormalities in the neck muscles and to identify the type of CD Benecke et al. (15) have recommended a diagnostic procedure to ensure a correct diagnosis. The procedure mainly consists of an analysis of different positions of the head, avoiding use of compensatory tricks, and evaluation of slow head movements; also, the length of time for which the neutral position of the head can be maintained is recorded.

**Prevalence and cause**

The prevalence of dystonia is difficult to ascertain. Prevalence figures given in the literature vary, partly as a result of differences in study design including the sources of cases and case definitions. Lack of clinical criteria for a
dystonia diagnosis and the absence of a diagnostic test or biomarkers make underdiagnosis and misdiagnosis possible problems (8).

On the basis of the results of service-based and record linkage studies, the prevalence rates among patients seeking medical attention for primary early-onset and late-onset dystonia have been calculated to be 24-50 per million and 101-430 per million respectively. Adjustment for possible underdiagnosis in a given area has resulted in estimates of 600 per million for late-onset dystonia in the overall population in northern England and 3000 per million in the Italian population aged 50 years or more. However, these are only rough estimates and lack sound statistical support (4, 8). In Iceland the prevalence of all types of dystonia has been reported to be 37.1 per 100 000, with the highest prevalence of focal dystonia 31.2 per 100 000 (16). No formal study of the prevalence of dystonia in Sweden has yet been conducted. In the county of Uppsala, with 306 100 inhabitants, 233 patients with dystonia were treated at the Department of Neurology of the University Hospital during 2007.

Among patients with dystonia affecting the cranial-cervical area there is a predominance of women, and in limb dystonia there is a male predominance (7, 17).

Velickovic et al. (18) suspect that there are between 60 000 and 90 000 patients with CD in the United States. The overall prevalence rate of CD in eight European countries (Sweden not included) has been found to be 57 per million. The reported prevalence of primary focal and segmental dystonia in Oslo, Norway is 25.4 per 100 000 (19). In the county of Uppsala, Sweden, with 306 100 inhabitants, 159 patients with CD were treated at the Department of Neurology of the University Hospital in 2007.

The minimum incidence of CD in a multi-ethnic health organisation in Northern California, USA was 0.80 per 100 000 persons per year, which was similar to previous estimates in more ethnically homogeneous populations (20).

There is now increasing evidence that dystonia is a basal ganglia disorder. Lesions of the basal ganglia mostly affect automatic movements that need sensory guidance. In recent studies has been found that dystonia is a result of disturbed sensory-motor integration and lack of inhibitory motor control (2, 3, 21). Primary dystonia is thought to be partly genetic in origin, mainly because of its aggregation within certain families and the identification of specific genetic loci (8).

In some of the patients with adult-onset dystonia the disorder has a genetic link (10). In others, trauma has been implicated as a causative factor, possibly related to painful sensory input that alters neuronal responses in the central nervous system. Frei et al. (22) propose that a complex regional pain syndrome could represent a variant of post-traumatic CD that may develop over time after the initiation of dystonia. O’Riordan (23) assessed a group with post-traumatic CD and found a significantly increased frequency of
lateral flexion of the head, more reported pain and more reported depression compared with idiopathic dystonia. Data suggest that the time that has elapsed after trauma is a determining factor in the clinical presentation (24, 25). Patients with delayed onset of CD after trauma, more than three months, display clinical features at presentation that are indistinguishable from those in idiopathic CD, while those with early onset after trauma, within four weeks, have a distinct presentation characterized by reduced cervical mobility, prominent shoulder elevation, sustained posture, and the absence of involuntary movements, sensory tricks, and a less predictable response to botulinum toxin (BTX) (26).

Multidimensional aspects of dystonia

Cervical dystonia has a negative impact on the quality of life (QoL) compared with an age-matched general population (27, 28). This impact is comparable to that seen in multiple sclerosis (MS), Parkinson’s disease, and stroke. Although some patients with CD have been found to have the best physical score, they scored worse for mental health and emotional role limitation. They also rated their energy and vitality, physical role limitation, and social function significantly worse. In contrast, some patients were able to cope well with CD, with relatively little deterioration in their QoL (29).

Depression is a recurrent documented non-motor symptom in CD (27, 28, 30, 31) and has been found to be strongly associated with poor QoL in persons with CD in several cross-sectional studies (27, 28, 30-32). A positive effect of treatment with BTX has been shown to have a beneficial effect on QoL (27, 28).

Disability has been reported to be one of the main predictors of QoL in dystonia (30). Perceived stigma as a consequence of the physical disfigurement has been found to affect the patients’ social, private, and working lives (33).

The impact on QoL of disease-related characteristics in dystonia, e.g. duration and severity, and personal factors, e.g. gender, age and psychological factors, has not been fully explored, and the findings are inconsistent (27, 30).

Fatigue is reported to be a major contributor to disability in other neurological disorders such as Parkinson’s disease (34) and MS (35). The main characteristics of fatigue are enhanced perception of effort and limited endurance in sustained physical and mental activities (36). Dystonia is not documented as a neurological disorder associated with fatigue. However, fatigue is listed as a factor with an aggravating effect on the severity of dystonia (13).

Fatigue and energy are related concepts. Energy refers to both positive and negative aspects in daily life and may be connected with perceived
health, while fatigue describes only the deficit in energy level and is thereby a problematic phenomenon (37). Energy is the capacity to perform work, and when involved in the production of work it is called kinetic energy (38, 39). Analysis of human movement in terms of energy provides essential information. It is important to assess whether a movement is performed in the most energy-efficient way possible, especially if the person is already functioning at the limit of his/her ability (38). The impression has been obtained at the physiotherapy (PT) clinic that after treatment with PT and/or BTX, patients with CD may find it less demanding to carry out voluntary movements with the head compared with before treatment. The use of an energy concept could possibly capture the subjective feeling of an easier way to perform the active movements.

Physical inactivity may have severe consequences for health and QoL, and frequent physical activity is thus important for the health of an individual (40). Physical activity is defined as any body movement, produced by skeletal muscles, that results in energy expenditure (41). Significant health benefits can be obtained by including moderate-intensity aerobic (endurance) physical activity for a minimum of 30 minutes five days each week, or vigorous-intensity aerobic physical activity for a minimum of 20 minutes three days each week. Physical activity reduces the risk of premature mortality in general, and of coronary heart disease, hypertension, colon cancer, and diabetes mellitus in particular. Physical activity also improves mental health and is important for the health of muscles, bones and joints (40).

Pain is a major source of disability and a factor influencing QoL in CD patients (9, 28, 42, 43). The high incidence of pain distinguishes CD from all other types of focal dystonia. The pain is commonly described as tiring, radiating, tugging, aching and exhausting. The common location of the pain in CD is in the neck and upper back, with some radiation up the ipsilateral side of the head and down the ipsilateral arm. However, one-third of the patients do not report pain at all, despite the fact that their dystonia is of equal severity and duration. The motor severity does not seem to correlate with either the duration or intensity of reported pain (42-45). However, the literature concerning pain and its consequences in relation to dystonia is sparse and based on small numbers of subjects.

Research within the area of persistent pain has shown that psychological factors play an important role in the development of disability (46). Some of these factors, e.g. self-efficacy, fear of movement/(re)injury (kinesiophobia) and catastrophizing, are strongly linked to functioning in daily activities and have been identified as important disability-related factors in patients with musculoskeletal pain (47-50). Self-efficacy beliefs determine how people feel, think, motivate themselves and behave in relation to a specific task. For example, people with high assurance in their capabilities approach difficult tasks as challenges to be mastered rather than as threats to be avoided. In contrast, people who doubt their capabilities shy away from difficult tasks,
which they view as personal threats. Accordingly, self-efficacy is the conviction that one can successfully perform a certain task or produce a desirable outcome. A major determinant of self-efficacy is prior mastery experience and physical limitations (51).

Kinesiophobia is defined as an excessive, irrational, and debilitating fear of physical movement and activity resulting from a feeling of vulnerability to painful injury or reinjury (52). Fear and avoidance of activity or movement is related to physical performance and self-reported disability in patients with chronic pain (53, 54).

Catastrophizing is a negative pattern of thoughts concerning experiences and outcome. It is related to pain intensity, disability and psychological distress in patients with chronic pain (55).

Assessment

Several different rating scales have been proposed for facilitating the diagnosis of dystonia or evaluate its treatment. The three scales for estimating the severity of dystonia, namely the Fahn-Marsden Scale (56), the Unified Dystonia Rating Scale (57) and the Global Dystonia Rating Scale (57) all have good reliability, but the Global Dystonia Rating Scale appears to be the easiest to apply (57).

Several rating scales for dystonia are presented in Table 2.

Table 2. Rating scales for dystonia.

<table>
<thead>
<tr>
<th>Rating Scale</th>
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<tbody>
<tr>
<td>Burke-Fahn-Marsden Scale (dystonia) (56)</td>
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<tr>
<td>Unified Dystonia Rating Scale (dystonia) (57)</td>
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<tr>
<td>The Global Dystonia Rating Scale (dystonia) (57)</td>
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<tr>
<td>Tsui Score (CD) (58)</td>
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<tr>
<td>Torticollis Questionnaire (CD) (59)</td>
</tr>
<tr>
<td>Body Concept Scale (CD) (60)</td>
</tr>
<tr>
<td>Functional Disability Questionnaire (CD) (60)</td>
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<tr>
<td>Ways of Coping Checklist (CD) (61)</td>
</tr>
<tr>
<td>Structured Questionnaire (CD) (61)</td>
</tr>
<tr>
<td>Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) (CD) (11)</td>
</tr>
<tr>
<td>Freiberg Questionnaire for Dystonia (CD) (62)</td>
</tr>
<tr>
<td>Craniocervical Dystonia Questionnaire (CDQ-24) (CD and blepharospasm) (63)</td>
</tr>
<tr>
<td>Cervical Dystonia Impact Profile (CDIP-58) (CD) (64)</td>
</tr>
<tr>
<td>Cervical Dystonia Severity Scale (CD) (65)</td>
</tr>
<tr>
<td>Disability questionnaire for patients with cervical dystonia (CD) (66)</td>
</tr>
</tbody>
</table>

CD= Cervical Dystonia

The Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) has been suggested as the current clinician-based outcome measure of choice for
CD. However, Cano et al. (67) concluded that it is clear that none of the existing CD-specific rating scales have been developed and evaluated according to the guidelines recommended by the Scientific Advisory Group of Medical Outcomes Trust, which advocates criteria for health measurement rating scales. Aware of this issue, Cano et al. (64) described the development of a patient-based rating scale for CD named the Cervical Dystonia Impact Profile (CDIP-58) for assessing the health impact of CD. The CDIP-58 and the Craniocervical Dystonia Questionnaire (CDQ-24) are the two measures covering a bio-psycho-social perspective in CD. Up till now, these two instruments have rarely been used in clinical trials as measures of treatment outcome.

The literature also describes other methods than clinical rating scales for quantifying the movement disorder of CD. However, these methods are rarely used in effectiveness studies in the treatment of CD. The velocity of voluntary neck movements seems to be more affected by dystonia than the range of motion as assessed with an electrogoniometer (68). A portable motion analysis system for assessing cervical range of motion is recommended by Carpaneto et al. (69). Kinematics describes movements of the body through space and time, including linear and angular displacements, velocities and accelerations, but without reference to the forces involved (70). Three-dimensional imaging measurement techniques, including optoelectronic systems, have proved to be powerful tools for quantitative assessments of movement in all degrees of freedom. The models for gait analysis have been well established in biomechanical and clinical research and are now applied to detailed diagnosis and treatment planning in patients (71). Galardi et al. (72) measured the head position and voluntary movement in patients with CD, using Fastrack, an electromagnetic system consisting of a stationary transmitter station and four sensors, in a pilot study. However, the most widely used motion capture systems for movement analyses are based on reflective markers and cameras that selectively track the markers.

Treatment

In most patients with adult-onset dystonia there is a focal distribution, and BTX injections are therefore the treatment of choice. In the year 1989, BTX A (formulation Botox) was approved in the United States as a therapeutic agent for strabismus, blepharospasm and other facial nerve disorders. In 2000, Botox and BTX B (Myoblock) were approved as a treatment option for CD. The therapeutic benefit of the toxin is mainly due to its primary mechanism of blocking the release of acetylcholine into the neuromuscular junction, causing local temporary chemodenervation and muscle paralysis (73).
No recommendations can be made regarding prescription of anticholinergic drugs, antiepileptic drugs or antidopaminergic drugs for dystonia. The recommendation for dopaminergic drugs is that levodopa should be initiated and adjusted according to the clinical response following a positive diagnostic trial. Deep brain stimulation (DBS) is long-term electrical stimulation of the globus pallidus internus or the thalamus. When BTX has failed to produce adequate improvement, DBS is considered a good option, particularly for generalised dystonia or CD. Surgical selective peripheral denervation is indicated exclusively in CD. Intrathecal baclofen can be recommended for patients in whom secondary dystonia is combined with spasticity (4).

In a survey study in Sweden (74), patients with dystonia ranked physiotherapy as the second most effective treatment after BTX.

Until now only one controlled study (n=40) has addressed the effect of PT as a complementary treatment to BTX. That study demonstrated that a combination of BTX A therapy with a specific PT programme improved the treatment outcome. The primary outcome measures were the Tsui scale (58), TWSTRS (11), Total Pain Scores (75) and Activity of Daily Living (ADL) (11). The secondary endpoints were the effect of the treatments upon the subsequent dose of BTX and length of the interval between the first and second injection. The association between the two treatment approaches proved effective in controlling the symptoms of CD, decreasing pain and increasing ADL, as well as increasing the effect and lowering the doses of BTX A. The PT programme consisted partly of passive myofascial elongation, massage, stretching, and exercises to improve postural control and strengthen the axial musculature. The relatively small number of subjects in the study reduced the statistical power and consequently the generalisability of the result (75).

Bleton (76) has produced a handbook of PT for cervical dystonia based on clinical experience. Bleton advocates intervention that focuses on activation of the muscle groups opposing the dystonic posture.

Rationale of these studies

The origin of ill-health or diseases must be explained in terms not only of biomedical but also of psychological and social factors. All of these factors are often interdependent, so that one cannot simply treat one to the exclusion of the others. Comprehensive assessment and treatment of all these dimensions is needed in order to reach an effective treatment outcome (77). Hence, to describe a health experience due to a disorder such as dystonia, it is important to collect data on more than one dimension independently and thereafter, to explore associations and causal links between them.

This thesis is based on the need to obtain a better understanding of dystonia, as the knowledge of the psychological and social features of this disor-
der is limited. It was important to conduct our investigations from a multi-dimensional point of view, in an attempt to gain insight into the patients’ perceived QoL, health and disability.

The empirical background of this thesis is the clinical PT setting. The greater part of the literature on the management of CD focuses on pharmacological treatment, even though patients describe PT as an important complement to BTX (74, 78). The literature on PT management in dystonia is remarkably sparse and the clinical physiotherapist is left with few instructions as to which symptoms in CD respond to what treatment approach. The question of the legitimacy of PT in dystonia called for the need of an evidence-based perspective on the use of PT in this disorder. It therefore seemed important to begin the work of developing guidelines for current PT management and to evaluate existing PT treatment for CD.

In research on the outcome of CD treatment a variety of rating scales for evaluation have been used. Criticism has been raised on the grounds that none of the existing CD-specific rating scales has been developed and evaluated following recommended guidelines (67). There is a need for an objective way to assess treatment outcome. The application of an energy concept could be a useful measure for quantification of the movement dysfunction in CD as an objective complement to existing rating scales.
Aims

The overall aim of this research was to increase the knowledge about dystonia, in particular cervical dystonia, from a multidimensional point of view by investigating what factors influence the quality of life and health and also what factors predict disability. A further aim was to develop an objective outcome measure for quantifying the movement dysfunction in CD and to evaluate the effects of physiotherapy on CD.

The specific aims were:

- to investigate a Swedish population with dystonia regarding demographic variables, to identify factors related to the impact of dystonia on self-reported quality of life and health, and to study the impact of different types of dystonia on quality of life and health (study I).

- to characterise the head movements in CD with an optoelectronic system and with use of a movement energy index (study II).

- to explore the outcome of a PT programme aimed at improving the quality of life of people with CD by 1) reducing pain, 2) improving awareness of postural orientation, 3) increasing muscle strength, and 4) reducing the effort of moving the head and neck (study III).

- to investigate the predictive values of the following variables for disability in CD: severity of the dystonia, duration of the disorder, pain intensity, catastrophizing, self-efficacy, fatigue, kinesiophobia, depression, anxiety, and physical activity (study IV).
METHODS

Subjects and designs of studies I-IV

This thesis comprises five different groups of subjects: 351 persons with different forms of dystonia in study I, six patients and six controls in study II, six patients in study III and 179 persons with CD in study IV.

An overview of the characteristics of the subjects of the different studies is presented in Table 3.

Table 3. Characteristics of the subjects in study I-IV. y=years, F=female, M=male, Q1-Q3=quartiles, Md=median. Total TWSTRS* maximum score=85. Tsui scale** maximum score=25.

<table>
<thead>
<tr>
<th></th>
<th>Study I n=351</th>
<th>Study II n=6 patients</th>
<th>Study II n=6 controls</th>
<th>Study III n=6</th>
<th>Study IV n=178</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (y) (SD)</td>
<td>59 (11)</td>
<td>57.8 (6.7)</td>
<td>57.7 (6.4)</td>
<td>48.5 (4.5)</td>
<td>59 (9)</td>
</tr>
<tr>
<td>Gender: F/M</td>
<td>278/69</td>
<td>4/2</td>
<td>4/2</td>
<td>2/4</td>
<td>148/30</td>
</tr>
<tr>
<td>TWSTRS (Md) (Q1-Q3)</td>
<td>Not applicable</td>
<td>37 (27-51)</td>
<td>Not applicable</td>
<td>49 (34-62)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Tsui scale (Md) (Q1-Q3)</td>
<td>Not applicable</td>
<td>11 (7-13)</td>
<td>Not applicable</td>
<td>10 (5-14)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Mean duration of disorder (y)(range)</td>
<td>14 (2-59)</td>
<td>Lacking data</td>
<td>Not applicable</td>
<td>12 (5-25)</td>
<td>15 (1-46)</td>
</tr>
</tbody>
</table>

*TWSTRS (Toronto Western Spasmodic Torticollis Rating Scale) measures motor severity, disability and pain in CD, see page 30.

** The Tsui scale measures the motor severity of dystonia, see page 30.
An overview of the set-up of the studies is presented in Figure 1.

Figure 1. Overview of the four studies.

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design:</strong></td>
<td>Descriptive, correlative and cross-sectional.</td>
</tr>
<tr>
<td><strong>Sample:</strong></td>
<td>351 members with dystonia of the Swedish Dystonia Patient Association.</td>
</tr>
<tr>
<td><strong>Point of assessment:</strong></td>
<td>One point of assessment.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design:</strong></td>
<td>Comparative.</td>
</tr>
<tr>
<td><strong>Setting and sample:</strong></td>
<td>The gait laboratory at the University Hospital in Uppsala, Sweden. Six patients (two men and four women) with CD of different degrees of severity in dystonia and six healthy controls (two men and four women).</td>
</tr>
<tr>
<td><strong>Point of assessment:</strong></td>
<td>Two points of assessment for re-test reliability.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design:</strong></td>
<td>A series of six experimental single-case studies using an A1BA2 design (i.e. baseline no treatment, treatment and follow-up).</td>
</tr>
<tr>
<td><strong>Setting and sample:</strong></td>
<td>The PT department at the University Hospital in Uppsala, Sweden. Six patients (four men and two women) with CD recruited from the waiting list at the PT clinic.</td>
</tr>
<tr>
<td><strong>Point of assessment:</strong></td>
<td>Pre-treatment, during interventions, and at 2-week, 3-month and 6-month follow-up.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study IV (2007-2008)</th>
<th>Focus: Predictive value of physical and psychological variables for disability in CD.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design:</strong></td>
<td>Prospective and correlative design.</td>
</tr>
<tr>
<td><strong>Sample:</strong></td>
<td>179 members with CD of the Swedish Dystonia Patient Association.</td>
</tr>
<tr>
<td><strong>Point of assessment:</strong></td>
<td>Two points of assessments with two months in between.</td>
</tr>
</tbody>
</table>
Study I

A descriptive and correlative cross-sectional design was adopted for this study. A self-administered questionnaire containing instruments for assessment of factors influencing QoL and health, namely CDQ-24 (63) and CDIP-58 (64) respectively, were used for the study.

The questionnaire, with a covering letter explaining the purpose of the study and requesting participation, was sent to 462 members with dystonia of the Swedish Dystonia Patient Association. It was answered by 351 persons giving a response rate of 76 %. Of the respondents, 73 % were women and 18 % were men. The respondents were classified by bodily distribution of symptoms and categorized as having focal, segmental, multifocal or generalized symptoms (79).

Characteristics of the study group in relation to the bodily distribution of symptoms are given in Table 4.

Table 4. Characteristics of the subjects of study I, by bodily distribution of symptoms. M=male, F=female, yr= years, SD=standard deviation.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Focal</th>
<th>Segmental</th>
<th>Multifocal</th>
<th>Generalised</th>
<th>Total sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>56 M/228 F</td>
<td>8 M/27 F</td>
<td>3 M/17 F</td>
<td>1 M/6 F</td>
<td>69 M/278 F</td>
</tr>
<tr>
<td>Age, yr, M (SD)</td>
<td>59 (10)</td>
<td>64 (11)</td>
<td>61 (13)</td>
<td>52 (12)</td>
<td>59 (11)</td>
</tr>
<tr>
<td>Mean duration of disorder, yr</td>
<td>14 (2-59)</td>
<td>13 (3-53)</td>
<td>12 (4-57)</td>
<td>20 (7-48)</td>
<td>14 (2-59)</td>
</tr>
</tbody>
</table>

Study II

This study had a comparative design with comparison of an investigation group with a control group (Table 3). A convenience selection was made to include six patients with CD (mean age 57.8 years, four female and two male) previously admitted to the neurological department at the University Hospital in Uppsala, Sweden. To reduce variance, a procedure of matching age and gender was performed for the six healthy subjects (mean age 57.7 years, four male and two female) in the control group. As the number of subjects was limited, this investigation was considered a pilot study.

Study III

This study (Table 3) consisted of a series of six experimental single-case studies using an $A_1B A_2$-design with continuous assessments during pre-treatment ($A_1$), intervention (B) and follow-up ($A_2$) (80). The duration of the pre-treatment baseline period was 2 weeks with assessments on seven occasions. The PT period was four weeks long with 11 occasions of assessment.
Subsequently there was a two-week follow-up period, with assessments on six occasions. Two additional assessments were made after 3 and 6 months, as long-term follow-up, giving a total of 26 assessment occasions. The patients were assigned to a waiting list of the PT department of the University Hospital in Uppsala, Sweden. The patients were receiving no other medical treatment and had not been treated with BTX for at least 3 months prior to the study. Criteria for inclusion were stated in advance, such as agreeing not to receive occupational therapy or other treatment aimed to improve the dystonia.

Study IV
A prospective and correlative design was used in this study, where data from self-report questionnaires were collected at inclusion and 2 months later.

All 272 members with CD of the Swedish Dystonia Patient Association were invited by mail to participate in this questionnaire study. Completed questionnaires from two points of assessments were received from 179 people, resulting in a response rate of 66 % (Table 3).

Measures and procedures in studies I-IV
The measures used in these studies reflect multidimensional aspects of dystonia. In a general overview of the measures (see Table 5) the biomedical perspective is represented by the Tsui scale and the MEI. The psycho-social perspective is reflected mainly by the CDIP-58, CDQ-24, TWSTRS and the Self-efficacy Scale (SES).
Table 5. Overview of measures used in the four studies.

<table>
<thead>
<tr>
<th>Measures used</th>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical Dystonia Impact Profile (CDIP-58) (64)</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Craniocervical Dystonia Questionnaire (CDQ-24) (63)</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Movement Energy Index (MEI)</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) (11)</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tsui scale (58)</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual Analogue Scale (pain intensity) (VAS) (81)</td>
<td></td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postural Orientation Index (POI)</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Likert scale (effect of BTX) (82)</td>
<td></td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Numerical Rating Scale (severity of dystonia) (NRS) (83)</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>International Physical Activity Questionnaire (IPAQ) (<a href="http://ipaq.ki">http://ipaq.ki</a>)</td>
<td></td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neck Disability Index (NDI) (84)</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Functional Disability Questionnaire (FDQ) (60)</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Self-Efficacy Scale (SES) (85)</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Tampa Scale of Kinesiophobia (TSK) (52)</td>
<td></td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catastrophizing subscale of the Coping Strategies Questionnaire (CAT) (86)</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>The Hospital Anxiety and Depression Scale (HAD) (87)</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>The Fatigue Severity Scale (FSS) (88)</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
</tbody>
</table>

Study I

The respondents received, by mail, one questionnaire covering demographic variables and two questionnaires for assessment of QoL and health, namely CDQ-24 and CDIP-58 respectively.

The demographic variables concerned form of dystonia, gender, age, and duration of the disorder, time before diagnosis, employment, and disability pension as a consequence to dystonia. Questions were also asked about satisfaction with treatment, receiving PT or not, and level of physical activity.

Each questionnaire and envelope was coded with numbers, starting from 1, by one of the authors (LZ). The addresses to the respondents were added on the envelopes by the treasurer of the Swedish Dystonia Patient Association. A reminder was sent out to those who had not answered the first dispatch after one month’s time. Because of the coding process the names and addresses of the respondents were unknown to the authors.

Physical activity was evaluated on a three-graded scale, and referred to the self-rated average level of physical activity during the past week. The level was graded from i) low, which meant being mostly sedentary, ii) mod-
erate, implying physical activity for a minimum of 30 minutes on five
days/week, to iii) high, which meant physical fitness training. The respon-
dents could also add in their own words their experiences of physical activity
despite their dystonia. No formal testing of the scale for reliability and valid-
ity had been performed. Face validity had been ensured through peer reviews
and patient feedback sessions.

The CDQ-24 evaluates QoL in CD or blepharospasm. It contains 24 items
divided into five subscales: “stigma”, “emotional well-being”, “pain”, “ac-
tivities of daily living”, and “social/family life”. The maximum transformed
score is 100. High scores indicate low QoL. Internal consistency reliability is
satisfactory for all subscales (α= 0.77-0.89) and for the total score (α=0.94)
(63).

The CDIP-58 (64) measures the impact of CD on health in eight subscales
divided into three conceptual domains. The subscales “head and neck”, “pain
and discomfort” and “sleep” represent the “symptoms” domain. The sub-
scales “upper limb activities” and “walking” correspond to the “daily activi-
ties” domain and the subscales “annoyance”, “mood” and “psycho-social
functioning” represents the “psycho-social sequelae” domain. The maximum
transformed score is 100. High scores indicate a high impact on health.
Rasch item analyses and psychometric methods have been performed to test
the validity of CDIP-58 (64, 89). This scale has been found to be more sensi-
tive than comparable scales in detecting statistical and clinical changes in
patients treated with botulinum toxin. The time frame is set to the past two
weeks (90).

Study II
The subjects in study II were seated in front of a table with their hands on
the table and feet on the floor. A headband was fastened around the head,
with a laser-pointer pointing forward, attached to the top of the headband. A
cluster of four round-shaped markers was fixed to the back of the headband.
The movements were measured with a ProReflex high-speed, high-
resolution digital optoelectronic motion capture system (Qualisys AB, Gothen-
burg, Sweden) at the University Hospital in Uppsala. The cluster of mark-
ers reflected infrared light from the camera flashes. Six cameras with a cap-
ture rate of 240 Hz were used to measure the position of the reflective mark-
ers. The cameras were positioned on the wall under the ceiling around the
testing area. The images of the markers produced X, Y and Z coordinate
values throughout the measured movement. The system was calibrated to the
volume covering a person sitting at the table and was validated with a person
sitting in the measurement area. The subjects pointed with the laser-pointer
at a cross-shaped target on a white paper screen (140 cm x 80 cm) placed
approximately 80-90 cm in front of the head. The motion procedure started
with the subjects maintaining the beam in the centre of the cross-shaped
target for four seconds. This was followed by six trials, three in each direc-
tion, in which the subjects attempted to track the horizontal black line from
left to right and from right to left (rotation). Three trials followed with
movements in a vertical direction from the top to the bottom (flexion) of the
screen and three trials from the bottom to the top of the screen (extension).
Each of the 12 trials was performed as fast as possible, with sufficient inter-
trial rest. After the recording process, each of the markers was identified in a
Qualisys Track Manager and reviewed to ensure that the markers were
tracked correctly throughout the data capture.

A numerical index, to be described later, named the Movement Energy
Index was then calculated from the optoelectronic data, using custom soft-
ware (“HeadMotion”).

The software calculates the position and orientation of the head and also
the velocity and acceleration of the head movements, and MEI is a meas-
urement that is proportional to the mechanical work required to obtain the
measured movement of the head. To obtain a measure that is more suited for
comparison between subjects, mechanical work needs to be modified to take
into account both the differences in body mass and the differences in the
speed at which the subjects performed the task. We wanted to approximate
the complete work performed by the muscles. A high score indicates a
movement that uses energy in excess of what is needed for the task at hand,
i.e. voluntary movements of the head in the sagittal and horizontal planes.
Test-retest reliability showed no significant differences in patients with CD.
The control group, however, while scoring significantly lower than the CD
group, showed a small decrease from test to retest, indicating a learning ef-
fect. Even if a similar learning effect in the CD patients cannot be ruled out,
it is plausible that the effect would diminish quickly once the patients had
become familiar with the test, the situation, and the personnel. A user man-
ual for the HeadMotion programme version 2.0 is available from one of the
authors (LZ). The clinical routines for using MEI are not fully established,
but their development is in progress.

The patients were initially assessed according to the TWSTRS severity
subscale (11). They were assessed in a seated position, observed in the fron-
tal and lateral view, and instructed to allow the head to move into the spon-
taneous posture. The TWSTRS severity subscale includes ten items for clini-
cian rating, namely: maximum amplitude of excursion, duration factor, ef-
fect of sensory trick, shoulder elevation/anterior displacement, range of mo-
tion, i.e. the ability of the patient to move the head in rotation, lateral flexion
and flexion/extension, and the length of time for which the patient is able to
maintain the head within 10 degrees of the neutral position. In accordance
with the instructions given by Comella et al. (91), the duration component
was measured over a 60-second interval. Each sensory trick was performed
twice.
The TWSTRS is a scale for clinician-rated motor disorder severity and self-rated disability and pain in CD. The total TWSTRS ranges from 0-85, with subscales for severity ranging from 0-35, disability from 0-30 and pain 0-20. High scores on this scale reflect greater levels of motor disorder severity, disability and pain. In a study by Salvia et al. (68), inter-observer reliability for the total score of TWSTRS was excellent ($r_s > 0.99$), and for the disability and the pain scales it was good ($r_s > 0.88$); however, for the motor severity scale the correlation was found to be moderate ($r_s = 0.63$).

The patients were also assessed with the Tsui scale (58). The Tsui scale has four domains and evaluates the amplitude of sustained movements, duration of sustained movements, shoulder elevation and tremor. The maximum total score is 25, representing the worst imaginable difficulty due to the disorder. The inter-observer correlation is considered to be good ($r_s = 0.86$) (58).

Study III
The overarching goal was to improve QoL of the individual patient, mainly by improving his or her awareness of postural orientation, which is defined as “the ability to maintain an appropriate relationship between the body segments and between the body and the environment for a task” (92). The various exercises in the PT programme all together aimed to stimulate not only the biomechanical alignment of the body but also the orientation of the body to the environment. The PT programme consisted of progressive muscle relaxation and muscle training, including exercises of isometric strength and muscle endurance. It also included exercises for stimulating coordination and body perception, as well as muscle stretching exercises. The programme was developed from existing PT regimes for CD at Uppsala University Hospital (Appendix 1).

The main outcome data for dependent variables were collected through CDQ-24, as described in paper I. The secondary outcome measures were TWSTRS, a mechanical Visual Analogue Scale (VAS) for rating current pain in the neck, the Cervical Dystonia Postural Orientation Index (POI) and the MEI, presented in paper II.

The mechanical VAS (81) is a plastic VAS with a sliding marker that consists of a 10 cm long horizontal line, requiring the patient to rate their current pain intensity in the neck. The scale is anchored with endpoints labelled “No Pain” and “Pain as bad as it could be”. High scores on this measure reflect greater levels of pain intensity. One side of the scale, which the patient sees, only lists the pain endpoints. The other side of the mechanical VAS indicates in centimetres how far the patient has slid the marker from the “No pain” end towards the extreme pain end. VAS has been widely used in pain research and displays good construct validity and sensitivity to treatment. The question asked to the patients was “Do you have current pain in your neck and if so, how much according to this scale?”
The POI is a self-rated scale for measuring postural orientation in nine standardized positions, such as standing and sitting, developed by one of the authors (LZ). Each position is rated on a horizontal numerical rating scale ranging from zero to ten. Zero indicates no difficulty in maintaining the position, and ten indicates impossibility of maintaining the position. High scores on this scale (maximum 90 points) reflect increased severity of postural disorientation. No formal testing of reliability and validity of the scale has yet been undertaken. Face validity has been ensured through peer-review and patient feedback sessions.

The pain intensity measured with VAS, the severity of dystonia measured with TWSTRS, and the postural orientation scored on POI were measured three times per week during all phases of the treatment period and once at follow-up at 3 and 6 months. The head movements measured with MEI were carried out once a week during all phases. Quality of life scored on CDQ-24 was performed once at pre-treatment baseline, once after completion of treatment, once 2 weeks after treatment and once at 3 and 6 months of follow-up.

Study IV

The subjects received on two occasions, 2 months apart (measure 1 and measure 2), by mail, one questionnaire covering different physical, psychological and social aspects in relation to CD. The procedure of the distribution followed that in study I.

One numerical rating scale (NRS) (81) were used for screening perceived “hindrance in daily life due to dystonia” as a descriptive variable for the study group. The scale was defined as 0 = no hindrance to 10 = total hindrance.

Perceived “effect of the latest botulinum toxin injection” was measured on a Likert scale, where 1 = great improvement and 7 = great deterioration. These scales were specifically developed for the study (82).

In order to cover a wide range of questions, a disease-specific measure for CD and a general measure for patients with neck pain were used as dependent variables for disability, namely the Functional Disability Questionnaire (FDQ) (60) and the Neck Disability Index (NDI) (84) respectively.

The FDQ is a 27-item scale which measures the impact of CD on activities of daily living (ADL). Questions are asked about the extent to which CD affects the engagement in and performance of a sample of activities at the present time, such as dressing/undressing, use of public transport, and drinking from a cup. Each item is rated on a 5-point scale (0 = not applicable; 1 = not at all affected to 4 = severely affected). The total scores were used in this study. High scores indicate a higher level of functional disability (60).

The NDI measures disability and consists of 10 items scored from 0 (no disability) to 5 (severe disability), with a maximum score of 50. The items
measure, for example, various functions of neck pain, headache, personal care, work, and recreational activities. The total scores were used in this study. The score obtained can be multiplied by 2 to produce a percentage score. High scores indicate a higher level of disability. The time frame is not defined (84).

The independent variables in the study were:

1) Two NRS was used for screening perceived “Pain intensity” and “Severity of dystonia” where 0 = no pain/minimal severity to 10 = worst imaginable pain and /worst imaginable severity. The scales were specifically developed for the study.

2) The Catastrophizing subscale of the Coping Strategies Questionnaire (CAT). This attempts to measure negative self-statements, catastrophizing thoughts and ideation in patients with chronic pain. Six 7-grade scales, where 0 = never and 6 = always, are used. Examples of statements in the scale are: “It is terrible; it feels as if it will never be better” and “It feels as if I can’t continue like this”. The maximum score is 36, which represents frequently occurring negative thoughts (86).

3) The Self-efficacy Scale (SES). This measures perceived self-efficacy in performing common daily activities such as disposing of the rubbish, concentrating on something, shopping, playing party games, eating at a restaurant, watching TV, meeting friends, washing clothes, and going to the movies. The response format consists of 20, 11-grade numerical rating scales, where 0 = not at all confident and 10 = very confident. The total score is calculated. The maximum score is 200, which represents total confidence in performing daily activities. The time frame is not defined (85).

4) The Fatigue Severity Scale (FSS), which measures perceived energy level and reflects the severity of fatigue. The FSS contains nine statements rated on a Likert scale, ranging from 1 = strong disagreement to 7 = strong agreement. Examples of the statements are: “Fatigue interferes with my physical functioning”, and “Fatigue interferes with my work, family, or social life”. The FSS score is the mean of all statement scores and the maximum score is 7. High scores indicate an increased severity of fatigue (88).

5) The Tampa Scale for Kinesiophobia (TSK). This measures fear of movement and (re)injury on a 17-item 4-grade Likert scale where 1 = strongly disagree and 4 = strongly agree. The scale contains statements such as “I’m afraid that I might injury myself if I exercise” and “It’s really not safe for a person with a condition like mine to be physically active”. A total score is calculated (after inversion of the individual scores of items 4, 8, 12 and 16) and ranges from 17 to 68. Higher scores indicate an increased fear of movement (52).

6) The Hospital Anxiety and Depression Scale (HAD), which is a questionnaire with two 7-item subscales for depression and anxiety respectively. Statements in the scale for depression include “I still enjoy the things I used to enjoy” and “I can laugh and see the funny side of things”. Two of the
statements for anxiety are “worrying thoughts go through my mind” and “I feel tense or wound up”. Each question is answered on a 4 point scale (0-3) and the possible scores range from 0 to 21. High scores point to anxiety and depression (93).

7) The International Physical Activity Questionnaire (IPAQ) which measures self-rated physical activity. The questionnaire covers all types of physical activities whether they are occupational or carried out during transportation, household chores or leisure time. The questionnaire collects information on time (i.e. number of sessions and average time per session) spent walking and in moderate- and vigorous-intensity physical activity on weekdays and weekend days, but only those sessions that last 10 minutes or more. The minutes are multiplied by the number of days and then multiplied by the appropriate metabolic equivalent value (MET). One MET represents an individual’s energy expenditure while sitting. Data are summed within each item and expressed as MET-minutes per week according to the IPAQ scoring protocol, version 2.0 (http://www.ipaq.ki) The protocol was followed, with one exception: if only days per week were reported without accompanying minutes per day, the minutes per week were truncated to zero, and not excluded as suggested in the protocol (94).

Selection of the measures was based on recognised reliability and validity for chronic conditions, although not for CD, recommendations in the literature, and previous experience with respect to feasibility for people with CD (60, 86, 88, 95-100).

Data analyses in studies I-IV

The statistical methods used in the four studies are presented in Table 6.

Table 6. Overview of statistical methods used in the four studies.

<table>
<thead>
<tr>
<th>Method</th>
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<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
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Study I

In order to obtain complete data sets the mean subscore was used to substitute for occasional missing items. Descriptive statistics illustrate demographic variables of the study population. Reported results in which figures did not add up to 100 % indicated the proportion of the respondents that did not answer the question.

Kruskal-Wallis tests were performed to study relationships of different forms of dystonia to QoL and health as measured with CDQ-24 and CDIP-58 respectively. To assess associations between some variables and impact of dystonia on QoL and health, the Mann-Whitney U-test was used for dichotomous variables, Spearman Rank correlation for continuous variables and the Kruskal-Wallis test for variables involving more than two categories. Multiple linear regression analyses were performed with the total score of CDQ-24 and the mean score for each of the three conceptual domains in CDIP-58 as dependent variables.

Study II

Data analyses for determining MEI were based on the mean values of the repeated movements in each direction. For comparison between the patient and control group, mean values were calculated from the movements in both test and retest. For the test-retest comparison, mean values were calculated separately for each of the two occasions. Comparison of the mean MEI values for each subject and each movement direction between the two groups was made with the Mann-Whitney U-test. For the test-retest comparison the Wilcoxon Signed-Rank Test was used.

Study III

Data related to dependent variables in each patient were plotted in graphs and visually interpreted with regard to trend changes and variability between phases (80). A linear regression analysis was used to test the significance in trend changes: from baseline to treatment and from treatment to follow-up. The regression lines for MEI had to be interpreted with caution because of the fewness of the occasions when this measure was assessed. The Wilcoxon Signed-Rank Test was used for comparing the outcome of CDQ-24 between phases.

Study IV

To obtain complete data sets, the mean scale score in individual subjects was substituted for occasional missing items. Non-systematic missing data amounted to less than 15 % in all measures.
None of the variables deviated from a univariate normal frequency distribution except for physical activity and catastrophizing. A transformation of scores to standard scores was considered. However, we decided to keep the original scores because of potential difficulties in interpretation.

Bivariate analyses with Pearson product moment correlation were performed to study associations between possible predictive independent variables and the dependent variable disability as measured with NDI and FDQ. No multicollinearity among the set of the possible predictive variables was identified (r<0.7). Correlations r>0.2 and p values ≤0.05 were considered meaningful for inclusion in the subsequent analyses.

Two multiple regression analyses were run to assess proportions of explained variance in disability. Collinearity statistics revealed normally distributed uncorrelated residuals with the possible predictive variables in the multiple regressions analysis.

The analyses of the non-respondents to the questionnaire sent on the second occasion, who thus provided data only on the first occasion (n=20), were performed with the Mann-Whitney U-test.

A two-sided p value of ≤ 0.05 was adopted as statistically significant.

All statistical analyses were carried out in the Statistical Packages for the Social Sciences, version 13.0, (SPSS Inc., and Chicago, Illinois, USA).
RESULTS

Study I
Demographic variables
A total of 73 % of the respondents were female and the mean age was 59 years (SD 11, range 27-85 years). A majority (75 %) had focal dystonia, 10 % had segmental dystonia, 5 % multifocal dystonia and 2 % generalised dystonia. The median duration of dystonia was 14 years (range 2-59 years). In the present study 54 % of the respondents stated that they were physically active at a moderate intensity level (40). Forty-six percent of the respondents experienced satisfaction with their treatment. Physiotherapy had been received by 46 % of the respondents and the scores of that group on CDQ-24 and CDIP-58 indicated a worse QoL as well as a higher impact on health compared with the group that had not received PT.

Craniocervical Dystonia Questionnaire (CDQ-24)
Bivariate analyses identified seven factors related to QoL as measured with the total score of CDQ-24: age (p<0.037), gender (p<0.001), employment (p<0.001), disability pension as a consequence of dystonia (p<0.001), received PT or not (p<0.009), satisfaction with treatment (p<0.001), and physical activity at a high level (p<0.001).
A subsequent multivariate regression model with the above mentioned factors included was significantly associated with QoL as measured with the total score of CDQ-24 (R² 0.30, F (7, 294) = 17.95, p=0.001). This indicated that 30 % of the variance in QoL was explained by the model. The B regression coefficient showed that “satisfaction with treatment” and “physical activity” was associated with QoL as measured with CDQ-24.

Cervical Dystonia Impact Profile (CDIP-58)
“Symptoms” subscale
Bivariate analyses identified five factors that could affect health in patients with dystonia as measured with the symptom subscale score of CDIP-58: gender (p<0.014), disability pension as a consequence of dystonia (p<0.001),
received PT or not \((p<0.016)\), satisfaction with treatment \((p<0.001)\) and level of physical activity \((p<0.001)\).

A multivariate regression model with inclusion of the above mentioned factors significantly predicted the influence of the above factors on dystonia’s impact on health as measured with the mean value of the symptom subscale of CDIP-58 \((R^2 0.21, F (5, 297) =15.75, p=0.001)\). This indicated that 21 % of the variance in health as reflected by symptoms from the head and neck, pain and discomfort, and sleep, was explained by the model. “Physical activity” and “satisfaction with treatment” contributed most to the association with the symptom subscale.

**“Daily activities” subscale**

Further bivariate analyses identified six factors that could affect health in dystonia patients as measured with the daily activities subscale of CDIP-58 measuring: gender \((p<0.001)\), employment \((p<0.001)\), disability pension as a consequence of dystonia \((p<0.001)\), received PT or not \((p<0.001)\), level of physical activity \((p<0.001)\), and satisfaction with treatment \((p<0.001)\).

A multivariate regression model with inclusion of the above mentioned factors included significantly predicted the factors’ impact of dystonia on health as measured with the subscale for daily activities of CDIP-58 \((R^2 0.35, F (7, 292) =22.96, p=0.001)\). This indicated that 35 % of the variance in health as reflected by symptoms from upper limb activities and walking was explained by the model. Being physically active was most strongly associated with this subscale.

**“Psychosocial Sequelae” subscale**

Additional bivariate analyses recognised five factors that could affect health as measured with the psychosocial symptoms subscale of CDIP-58: gender \((p<0.001)\), disability pension as a consequence of dystonia \((p<0.001)\), received PT or not \((p<0.006)\), level of physical activity and satisfaction with treatment \((p<0.001)\).

Finally, a multivariate regression model including the above mentioned factors significantly predicted their impact on health as measured with the subscale for psychosocial symptoms of CDIP-58 \((R^2 0.16, F (5, 294)=10.2, p=0.001)\). This indicated that 16 % of the variance in health as reflected by symptoms concerning annoyance, mood and psychosocial functioning was explained by the model. “Satisfaction with treatment” was most highly associated with the psychosocial subscale.

In summary, being physically active and satisfied with the treatment given were the variables most associated with an experience of health.
Study II

The movement energy index varied between 0.004 and 0.65 when the patients tried to keep their head in the centre position, and between 0.06 and 3.99 for the active movements. In the control group, the index varied between 0.001 and 0.008 in the centre position and between 0.04 and 0.55 for the active movements. In conclusion, the results indicated a significant difference between the groups concerning MEI in all movement directions ($p<0.01$). The mean MEI was significantly higher in the patients than in the controls.

There was no significant difference in the mean values of MEI for all movement directions between test and re-test in the patients. However, there was a significant difference in the mean MEI between test and re-test in the healthy subjects ($p<0.05$), with a higher mean MEI value in the test than in the re-test.

Study III

The results from the six subjects are described in detail in paper III, and the following is a brief summary of the effects of the PT programme.

Patient 1 displayed positive changes in trend between follow-up and treatment for VAS and TWSTRS. Patient 2 displayed positive changes in trends between pre-treatment and treatment for VAS and POI and a negative change in trend between follow-up and treatment for TWSTRS. Patients 3 and 4 showed negative changes in trends between follow-up and treatment for VAS and TWSTRS, and patient 5 also showed a negative change in trend for the scores on TWSTRS between follow-up and treatment. Patient 6 displayed positive changes in trends for VAS and POI during treatment compared with the pre-treatment period. During follow-up, changes in trends were observed for VAS and TWSTRS in comparison with the scores during treatment.

In summary, positive treatment outcomes were reported by all six participants, mainly concerning reduction of pain and severity of the symptoms during the treatment period. Five of the six participants reported an increase in QoL at the 6-month follow-up, as measured on CDQ-24 and shown in Table 7.
Table 7. Total non-transformed scores from the Craniocervical Dystonia Questionnaire (CDQ-24) in the six patients. Maximum point = 96 for each patient at pre-treatment (Pre), post treatment (Post), and follow-up at 2 weeks (F1), 3 months (F2), and 6 months (F3).

<table>
<thead>
<tr>
<th>Patient</th>
<th>Pre</th>
<th>Post</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
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<tbody>
<tr>
<td>1</td>
<td>62</td>
<td>41</td>
<td>46</td>
<td>29</td>
<td>43</td>
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<td>48</td>
<td>29</td>
<td>23</td>
<td>40</td>
<td>46</td>
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</table>

Study IV

The scores of NDI and FDQ answered on the second occasion correlated significantly with data for seven independent variables provided on the first occasion, as shown in Table 8.

Table 8. Correlations (r) between possible predictive variables for disability in cervical dystonia and disability scores measured with the Neck Disability Index (NDI) and Functional Disability Questionnaire (FDQ) two months later.

<table>
<thead>
<tr>
<th>Variables</th>
<th>NDI</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>FDQ</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p value</td>
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<td></td>
<td>r</td>
<td>p</td>
<td></td>
<td></td>
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<tr>
<td>Pain intensity</td>
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<td>&lt;0.001</td>
<td>0.5</td>
<td>&lt;0.001</td>
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<td></td>
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<tr>
<td>Catastrophizing</td>
<td>0.3</td>
<td>&lt;0.001</td>
<td>0.4</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Self-efficacy</td>
<td>-0.7</td>
<td>&lt;0.001</td>
<td>-0.6</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Fatigue</td>
<td>0.5</td>
<td>&lt;0.001</td>
<td>0.5</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Kinesiophobia</td>
<td>0.3</td>
<td>&lt;0.001</td>
<td>0.3</td>
<td>&lt;0.001</td>
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<tr>
<td>Depression</td>
<td>0.3</td>
<td>&lt;0.001</td>
<td>0.4</td>
<td>&lt;0.001</td>
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<tr>
<td>Anxiety</td>
<td>0.3</td>
<td>&lt;0.001</td>
<td>0.4</td>
<td>&lt;0.001</td>
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Neck Disability Index

The multivariate regression model significantly predicted disability as measured with NDI (adjusted R² 0.52, F(7, 147)=25.14, p=0.001). This indicated that 52 % of the variance in disability was explained by the model.

Perceived self-efficacy, fatigue, and pain intensity contributed significantly to the prediction of disability.
Functional Disability Questionnaire

The multivariate regression model significantly predicted disability as measured with FDQ (adjusted $R^2 = 0.46$, $F(7, 149) = 19.76$, $p = 0.001$). This indicated that 46% of the variance in disability as measured with FDQ was explained by the model.

Perceived self-efficacy, pain intensity, anxiety and fatigue contributed significantly to the prediction of disability.
DISCUSSION

Principal findings

The results of the four studies described in this thesis contribute to the base of knowledge concerning dystonia from a multidimensional point of view. First, the impact of dystonia on QoL and health was found to be related to the level of physical activity and satisfaction with treatment. Second, perceived self-efficacy explained a significant proportion of the variance in disability in CD. Third, the objective measure MEI was found to be a useful tool for quantifying movement dysfunction in CD. Further, one of the effects of physiotherapy in CD was to improve QoL in the individual patient.

Relations between the factors considered in the studies

Dystonia has not received the attention in research that has been devoted to other neurological disorders. The burden of treatment on the health services is probably considerable, as also is the impact of the disorder on the patient. This thesis addresses multidimensional aspects of the influence of dystonia from a bio-psycho-social perspective and highlights the need for adequate assessment of the effects of dystonia and the outcome of treatment.

It would seem that patients with dystonia are at risk of limitation of activities and of participation restrictions by factors such as reduced QoL, a subjective feeling of ill-health and increased disability, which partly may have their origin in additional emotional reactions such as anxiety and depression, maladaptive cognition (such as catastrophizing), and physical deconditioning (due to decreased physical activity).

It is now widely acknowledged that the personal burden of illness cannot be described fully by measures of a disease status. Studies indicate that CD has a profound impact on QoL (27-29, 32). Although CD usually is non-progressive, its effect on the health status is comparable to that of progressive conditions that are clinically considered to be of greater severity (29).

The results of study I indicated that in patients with dystonia the level of physical activity partly showed the highest association with QoL and health. However, as shown in study IV, physical activity did not predict disability. A reason for this result could be that when psycho-social variables such as
self-efficacy, catastrophizing and anxiety were added to the model, physical activity did not remain as one of the main predictive variables.

Almost 50% of the study participants in study I claimed that they were not physically active to the recommended degree. No other study has included level of physical activity as a factor possibly associated with QoL and health in dystonia, and the results cannot therefore be compared with those former studies including patients with dystonia. However, physical deconditioning due to decreased physical activity may constitute an additional health problem for the dystonia patients. This might be a supplementary deficit and may possibly increase the patient’s disability.

The subjects in study IV were calculated to have a median (25th – 75th percentile) MET-min/week of 918 (297-2316), which must be considered low in comparison with the reported values of 1905 MET-min/week (592-4455) for men aged 55-74 and 1417 MET-min/week (594-2855) for women of the same age group in a general population (94). The persons with dystonia were thus less physically active than a general population, irrespective of gender.

Satisfaction with treatment was also associated with QoL and health in dystonia, as found in study I. Some of the 40% who were not satisfied with their treatment mainly stated that they needed more PT given by a physiotherapist with knowledge of dystonia. This desire for more PT indicates a need for more controlled studies to verify the positive subjective effect of PT.

It was concluded from the findings in study IV that non-motor symptoms such as self-efficacy, fatigue, pain intensity and anxiety explained a significant proportion of the variance in disability. The subjects in study IV had a mean self-efficacy score of 127 (SD 39) out of 200, which may be compared with the mean score of 146 (SD 37) in patients with musculoskeletal pain (101), indicating a lower level of self-efficacy in daily activities in patients with CD than in those with musculoskeletal pain.

The respondents in study IV scored a mean value of 5 (SD 2) out of 7 on the Fatigue Severity Scale. When a comparison was made with results of a study by Krupp et al. (88), the scores from the participants in study IV were found to be as high as for patients with multiple sclerosis (mean 4.8). Krupp et al. (35) also reported a mean score of 2.3 for healthy adults which meant that the patients with CD had higher perceived fatigue than the healthy individuals (88).

When considering these results it is obvious that CD might include additional non-motor problems which demand a multidimensional approach in studies of this disorder.

Pain intensity was another variable explaining the variance in disability in CD in study IV. The intensity of pain in CD is highly variable, but it has been estimated that about two-thirds of the patients need analgesics to control the pain some time during the illness (102). The results of study IV
showed the perceived level of pain intensity among the respondents to be “fairly difficult”, with a mean value of 5 out of 10 (SD 2).

Several studies indicate that the care of patients with CD should not be focused solely on reducing the severity of the motor disorder. The treatment should also include care of the psychological well-being of the patient, since anxiety and depression have been shown to be the strongest predictors of QoL in CD (27-30, 32). Anxiety was one variable predicting disability in study IV and the respondents scored a mean value of 8 (SD 4) out of 21 on the Hospital Anxiety and Depression Scale (HAD). A score of 8 to 10 is considered to suggest the presence of a mood disorder (103). However, depression was not found to predict disability in study IV.

When comparing data from studies I and IV with results from studies of corresponding neurological disorders and/or a general population, it is concluded that patients with dystonia may be burdened with additional emotional disorders such as anxiety, maladaptive cognition such as low self-efficacy in daily activities, and further physical deconditioning due to decreased physical activity.

Usefulness of movement analysis

The result of study II indicated that MEI could be a useful measure for the quantification of movement dysfunction in CD and thus an objective outcome measure that could supplement existing scoring systems based on clinical judgement. Movement analysis has great possibilities for use as an outcome measure in clinical research, especially as the optoelectronic camera systems are becoming more readily available in clinical settings. Our method of investigating and analysing active movements with the neck muscles has great potential. Clinical rating scales such as TWSTRS focus on the severity of the disorder, while MEI focuses in addition on the performance of active movements. This difference means that MEI can be used as a complement to existing clinical rating scales and thereby capture the results of treatment in a wider perspective and hence rule out threats to internal validity in clinical trials.

The next step is to use and test MEI on subjects with other disorders related to the neck muscles, such as whiplash disorders and Parkinson’s disease, to expand the field of application of MEI. The reliability and validity of this measure also needs to be ensured. The clinical routines for using MEI are not fully established but will be further developed in future studies.

The MEI quantifies the dystonic movements from a biomedical perspective and so far it is not known whether this measure can capture changes that are important for the patients themselves. However, it is important to collect data from a biomedical aspect as well as from psychological and social per-
spectives independently. This objective measurement may be useful as a supplement to the clinical assessment of the individual patient.

Consideration of the physiotherapy treatment

There has been only one well-designed and controlled study concerning physiotherapy in CD (75). Most patients seek benefit from numerous therapies, especially PT, despite limited evidence of their ability to reduce the severity or pain caused by dystonia.

A majority of the dystonia respondents in study I expressed a need for more PT. The greater number of participants with CD, 54.4 %, had tried PT at some time during the last two years and were to some extent satisfied with the effect of the treatment (mean score 5.7 out of 10 on NRS). This should be compared with perceived results of injections with BTX (mean 5.8 out of 7). However, the range of results varied for both forms of treatment, indicating that some respondents were extremely satisfied and some were not satisfied at all with the treatment. Further investigations concerning these experiences of PT and injections of BTX are needed.

Physical prerequisites for movements, i.e. muscle strength, endurance, coordination, mobility and balance, are traditionally targeted in PT and one study indicates its positive effects in CD (75); this was also shown in study III. A multidimensional approach with integration of the physical prerequisites for PT but also with psychological dimensions, such as targeting of self-efficacy, might help the patients to move towards a state of optimal health despite dystonia, in addition to medical treatment such as injections of BTX.

The positive results achieved during the PT and the decreasing effect as measured at the 6-month follow-up, also indicate a need for self-management strategies to help the individual patients to maintain the positive effect achieved during treatment.

There is no “best PT treatment” for patients with dystonia. It may therefore be critical to examine possible treatment processes that will predict the outcome. Higher self-efficacy predicted better functioning and less reported pain in a group of low back pain patients participating in a rehabilitation programme (85). Jahanshahi and Marsden (60) state that patients with CD have a negative body concept and exhibit high levels of functional disability, which points to the need of a cognitive-behavioural intervention approach. In a study of patients with persistent musculo-skeletal pain it was shown that treatment targeting activity, motor behaviour and cognition was more beneficial than physically based exercise treatment alone (101).
Methodological considerations

Study participants

The study participants are not representative of all individuals with dystonia in Sweden. However, the response rates in studies I and IV must be considered high (76 %) and moderate (66 %) respectively, and thus the study represents the accessible population with dystonia in Sweden to an acceptable extent. The Swedish Dystonia Patient Association (http://www.dystoni.com/) has estimated the prevalence of dystonia to be 2700 in Sweden, but this has not been verified.

The participants in studies I and IV were all members of the Swedish Dystonia Patient Association. Membership in an organization related to a diagnosis may indicate that the responses obtained were from individuals who were less depressed and more active, and thus more interested in answering a questionnaire. However, the distribution among forms of dystonia in study I corresponded to the distribution of patients with dystonia treated at the Neurological Department of the Uppsala University Hospital in 2007.

The patients in studies II and III were selected by convenience to constitute a study sample with dystonia of varied severity, and different ages and genders, to match the general population with dystonia.

Design and procedure

A correlative design was used in study I and partly in study IV. The purpose of a correlative design is to examine relationships between variables in a population rather than to test a theory. It is therefore crucial that the sample is representative of the population being studied (104). As discussed above, the participants in study I (n=351) and in study IV (n=179) were recruited from the Swedish Dystonia Patient Association and thus must be considered to correspond to the population with dystonia in Sweden. At present, no other means of including a large study group with dystonia in Sweden than through the Patient Association is available.

The second crucial aspect of the correlational design concerns the measurement instruments used (104). In studies I and IV data were collected through questionnaires. The two instruments used in study I as dependent variables, CDQ-24 and CDIP-58, had demonstrated reliability and validity for the population under study (63, 89, 90). However, the instrument used in an attempt to measure physical activity, which was one of the independent variables in study I, was developed for the study and hence might have lacked the desirable reliability and validity to ensure the internal validity of the result.
In the majority of the published studies addressing QoL in dystonia, SF-36 was used as the primary outcome measure (27-29, 31, 32). Cano et al. (105) suggest that the SF-36 scores should be reported and interpreted with caution, on account of large floor and ceiling effects in some subscales. For this reason two disease-specific measures for QoL and health, respectively, were included in study I.

A comparative design was applied in study II and the critical objective of this design was to determine whether or not the groups differed with regard to MEI values (104). The generalisability of the results in study II was limited, since the samples were small, and thus the study was considered a pilot study.

The experimental single-case design as used in study III offers a systematic approach for the study of new and not previously investigated interventions and their effects. Single-case designs allow rigorous assessment of the efficacy of treatment in the individual subject, which can be useful in the early stages of group research as a means of generating pilot data before the treatment is applied in a study with a more costly large-scale group design (106). It would have been preferable to have longer periods of additional assessments in study III in order to demonstrate more clearly any causal relationships and to strengthen the internal validity of the results. Specifically, an extended pre-treatment period would have given a better picture of the status of each patient prior to the intervention. However, for practical reasons, the preferred guidelines of the design could not be completely followed.

Study IV had a prospective design, to establish the relation between antecedent events and outcome. The loss of subjects from measure 1 to measure 2 in study IV was one weakness of the design, limiting the sample size in the result. However, the attrition in measure 2 must be considered to be low, n=20 out of 179 responses in measure 1. In addition, the studies in which predictive variables of QoL and disability in dystonia have been identified (27, 30) have had cross-sectional designs, which might have decreased the strength of the predictive values obtained.

Internal validity
Attemps to achieve internal validity were made in the present studies. Kazdin (80) has suggested several threats to internal validity. Those relevant to the studies described in this thesis are testing, instrumentation and selection biases. Practice or familiarity with the test may have influenced the performance in the repeated testing and on two occasions of testing in studies III and IV respectively. To avoid this effect, the scores for the questionnaires answered earlier (study III) were not revealed to the participants beforehand. However, the use of continuous assessments over time is one of the key characteristics of the experimental single-case design (study III) (i.e., continu-
ous assessments over time, baseline assessments prior to the intervention, preferably stability of performance, and the use of different phases). The continuous assessments are one prerequisite if the design is to demonstrate causal relations and rule out implausible threats to validity (80).

The threat of instrumentation bias to internal validity was ruled out in studies II and III by a study protocol which was strictly followed during the assessment period. Standardized questionnaires were used partly in all of the present studies, and were administered and scored according to the instructions for each measure. However, TWSTRS is partly a clinician-based outcome measure and the patients in study III were rated three times a week for eight weeks. The possible threat to internal validity which this could have entailed was avoided by the fact that an experienced physiotherapist performed the rating.

A selection bias may have contributed to the result in study II. However, the population with CD is limited in the area where the study was performed, and thus restricted the study to a methodological pilot study.

Reliability of measures

The overall selection of the measures was based on their recognised reliability and validity in chronic conditions, recommendations in the literature, and previous experience with respect to feasibility for people with dystonia in general and CD in particular (60, 86, 88, 95-100). However, further studies are required to increase the validity of the instruments in dystonia.

The sparse existence of well tested dystonia rating scales implies limitations. Cano et al. (67) has claimed that the existing CD-specific rating scales such as TWSTRS and the Tsui Scale have not been developed with use of recognised techniques of rating scale construction, have not been evaluated properly and do not measure the wider impact of CD from the patients’ perspective. Reliability and validity analyses are confined to inter-rater reliability and construct validity (11). Cano et al. (64) created a patient-based rating scale that assesses a comprehensive range of important areas related to the impact of CD on health, namely the CDIP-58, which was used in study I. However, the items as well as the calculation procedure are extensive, which may prohibit its use as routine in a clinical setting.

The CDQ-24 total score was used in studies I and III. The questionnaire captures changes in the patients’ well-being, which are not reflected in clinical rating scales of dystonia severity. The CDQ-24 meets psychometric requirements such as reliability, validity, and sensitivity to change (63). However, the lack of use of CDQ-24 as an outcome measure in clinical treatment trials could be a threat to internal validity in the studies in which it is used.

The self-constructed scales for physical activity and postural orientation (POI) used in studies I and III, respectively, may lack important psychomet-
ric properties. However, face validity had been ensured through peer reviews and patient feedback sessions.

Physical activity was measured with IPAQ in study IV. The IPAQ instrument has been shown to overestimate self-reported time spent in physical activity (107). This might indicate that the responders in study IV were even less physically active than appeared from the result of the study. Physical activity was measured in two different ways in studies I and IV, respectively. It is true that the activity level was self-rated in both questionnaires, but in study I this was a 3-graded scale developed for the study and in study IV IPAQ was used. The 3-graded scale in study I indicated three “levels” (low-moderate-high) of physical activity, which was not the case in the IPAQ measure. This difference in the measures could be an additional reason for the non-predictive value of physical activity in paper IV.

The outcome measures in study IV were mainly chosen with the purpose of investigating psychological and social factors related to CD that have not previously been investigated in relation to this disorder. The application of a general instrument may be inappropriate for or irrelevant to some specific problems in CD. However, by using general measures it is possible to compare results from other patient groups and thus make the impact of CD more evident.

Summary and clinical implications

The studies described in this thesis were based on a multidimensional view of dystonia. Variables such as physical activity and satisfaction with treatment were identified as being associated with QoL and health in individuals with dystonia. Further, self-efficacy, fatigue, pain and anxiety were found to predict disability in CD. In addition, a potentially useful measure for quantification of the movement dysfunction in CD was developed, namely the Movement Energy Index, and some effects of a PT programme for CD were evaluated. However, further investigations with prospective controlled trials are necessary to assess the value of PT in patients with CD, and future systematic replications are also required to study the generality of the findings.

The results of this research have expanded the knowledge on dystonia from a bio-psycho-social perspective and have therefore increased the understanding of the multidimensionality of this disorder which could be valuable in developing new treatment strategies.

The findings demonstrated in these studies have several clinical implications. Health-care professionals dealing with dystonia patients need to promote physical activity, as this has been shown to have an impact on QoL and health in patients with this disorder. Health-care professionals should also ask the patients about their satisfaction with the treatment received and offer additional treatment such as PT by a physiotherapist competent in dystonia.
An additional conclusion of relevance is that there is a need for health-care professionals to assess the level of self-efficacy in daily activities, the amount of fatigue, and the levels of pain intensity and anxiety in the individual patient, since these factors have been shown to be of importance for disability in CD. A further clinical implication of the findings is that MEI may be valuable as an objective measure of the response to treatment and for comparing the effectiveness of different therapies.

**Future studies**

Several suggestions may be made for future studies, and the following summarises the most immediate research questions that need to be answered.

The literature on PT for dystonia is remarkably sparse. There is a need to continue to develop the PT and evaluate its effects. Based on the present studies, the next research question to be addressed is whether self-efficacy, fatigue, pain intensity and anxiety have a causal relation to disability. This question should be studied in a prospective controlled trial where these factors are targets of PT treatment. Further, it is important to assess the value of physical activity, since this is a factor related to QoL and health in dystonia.

There is also a need to develop and test the ability of a screening instrument to identify subgroups among patients with dystonia with a high or low risk of disability. The purpose of the screening procedure would be to enable clinicians to allocate patients to the right type of treatment, e.g. injections of BTX alone or of BTX complemented with PT focusing on physical exercises or PT that also emphases psychological factors such as self-efficacy.

It would seem important to carry out a methodological study in a large group of subjects with the aim of ensuring the reliability and validity of MEI for its use in a clinical setting and as an outcome measure in clinical trials.
Physiotherapy in Cervical Dystonia

The programme includes progressive muscle relaxation (PMR), and exercises for isometric muscle endurance and dynamic strength, co-ordination, balance, body perception, and muscle-stretching. The programme consists of four phases.

Phase 1

On the first day of the programme the physiotherapist explains the set-up of the whole programme. The patient is interviewed concerning relevant medical, physical and psychosocial information and an individualized physical examination is carried out. The intervention begins with a session of PMR according to the method of Jacobson and this continues twice a day during the first week. The main objective of the PMR is to alleviate pain, increase the subjective body perception and achieve muscle relaxation in general. The programme for the PMR is modified for each individual patient in order to find a position in which the treatment can be carried out as comfortably as possible. The patient tries to strain a chosen muscle and subsequently relax that muscle. Once the relaxation exercises are being well performed, the physiotherapist encourages the patient to practice them on his/her own.

Phase 2

In phase 2, exercises for increasing isometric muscle endurance and dynamic strength in the neck muscles are introduced. Both exercises are carried out with the patient in a standing position and also in a supine, prone and lateral position lying on a board, which is leaning against a wall-bar (height 83 cm). An example of an exercise aimed to achieve isometric muscle endurance in the neck muscles in a supine position is active pressing of the back of the head down onto the surface for approximately 5 seconds. An example of a dynamic exercise in a lateral position is active lateral flexion of the head while lying on a board, which is resting against a wall-bar. An illustration of how the training can be accomplished while standing in a walking position is when the patient has a rubber tube (Latex 4.0 x 1.0) fixed at eye level on a wall-bar and placed around the forehead while he/she performs weight transfers backwards and forwards. A starting point with 5x3 repetitions is a common introduction to these exercises.
Phase 3
Phase 3 comprises exercises aimed at improving co-ordination, balance, body perception and postural orientation. The goal of the exercises is to incorporate these different aspects and may be exemplified by an exercise with a ball of medium size. While walking in different directions the physiotherapist bounces the ball in altered directions to the patient. The patient is encouraged to automatically turn the head towards the ball (in order to be able to see and catch it) and grasps the ball with both hands. Exercises for promoting balance are carried out on different surfaces and on balance plates. Attempts to improve body perception in a sitting, standing and walking position are made with manual, verbal and visual guidance. For instance the physiotherapist places a hand on the patient’s shoulder and instructs her/him to “lower your shoulder” while sitting in front of a mirror. The exercises also focus on equilibrium of the pelvic position in addition to symmetry of the position of the feet and head. In this phase exercises for increasing the dynamic strength of the trunk and upper extremities with machine equipment are added.

Phase 4
In the fourth phase active muscle-stretching exercises are introduced for the neck muscles, for the muscles involved in scapular movements and for the muscles of the spine, trunk and legs according to the needs of the individual patient. The physiotherapist prolongs the stretching and increases the number of repetitions as required.

In addition
The PT programme has a cumulative design. The number of repetitions and the types of exercises that are added from one phase to another will vary according to each individual’s needs as decided by the physiotherapist.
Dystoni är en neurologisk motorikstörning som yttrar sig i form av ofrivilliga kramper och spänningar i olika muskler i kroppen. Dessa kramper och spänningar kan resultera i kraftiga felställningar av ex. nacken, benen eller en hand, beroende på vilka musklar som är drabbade. Om kramperna drabbar nackens muskulatur kan huvudet ofrivilligt vridas åt sidan och det kan vara mycket svårt för personen att vrida huvudet i motsatt riktning. Förutom de motoriska svårigheterna kan den person som har dystoni även drabbas av bland annat smärta och depression. Likaledes kan livets dagliga aktiviteter såsom att klä på sig, handla eller promenera vara svåra att utföra.

Den mest verkningsfulla behandlingen för att lindra symtomen är injektioner med botulinum toxin A i den påverkade musklern. Sjukgymnastik vid dystoni är ofta efterfrågad och uppskattad samt omnämnd som det näst viktigaste behandlingsalternativet eller som komplement till botulinumtoxinet.

Dystoni är en kronisk sjukdom som oftast drabbar vuxna och den är något vanligare hos kvinnor. Enligt en studie genomförd i åtta olika länder i Europa finns 152/1 000 000 personer med dystoni. Det finns inga studier om prevalens av dystoni i Sverige. Vid neurologmottagningen på Akademiska sjukhuset i Uppsala behandlades 233 personer med dystoni år 2007.


Den tredje studiens syfte var att beskriva och utvärdera sjukgymnastisk behandling vid cervikal dystoni. Sex personer med olika motorisk svårighetsgrad av cervikal dystoni deltog i sjukgymnastisk behandling under fyra veckor. Behandlingsperioden var uppdelad i fyra olika faser där den första fasen innehöll avspänning och den andra fasen inriktades mot träning av nackens muskulatur. Balans, koordination och kroppskännesnemod var fokus i den tredje fasen och i den fjärde fasen var inriktningen slutligen töjning av framför allt nackens och överkroppens muskulatur. Deltagarna mättes med avseende på motorisk svårighet, smärta, aktivitet i dagliga livet, postural orientering och energiförbrukning i nackens muskulatur inledningsvis tre gånger/vecka under två veckor före behandlingen startade, tre gånger/vecka under pågående behandlingsperiod samt under två veckor direkt efter avslutad behandling. Därefter skedde mätningar vid ett tillfälle vid tre respektive sex månader efter avslutad behandling. Deltagarna skattade även sin upplevelse av livskvalitet före och efter behandlingen. Resultatet var att de flesta deltagarnas motoriska symtom förbättrades, smärtan reducerades, den posturala orienteringen förbättrades och rörelseenergin i nackens muskulatur minskade under det att behandlingsperioden pågick. Vid uppföljningen efter sex månader var nästan samtliga värden lika som vid starten av behandlingen men förutom värdet för livskvalitet vilket fortfarande var bättre än vid behandlingens början.

Den fjärde studiens syfte var att identifiera vilka faktorer som kan prediktera aktivitetsbegränsning vid cervikal dystoni. Ett frågeformulär skickades ut vid två tillfällen, med två månaders mellanrum, till samtliga medlemmar med cervikal dystoni i Svensk Dystoniförening. Deltagarna ombads svara på deras upplevelse av aktivitetsbegränsning i dels ett diagnosspecifikt instrument för cervikal dystoni och aktivitetsbegränsning och dels i ett generiskt instrument för nacksmärta och aktivitetsbegränsning. Dessutom anmodades deltagarna svara på frågor om grad av tilltro till sin egen förmåga i vardagliga situationer, katastrofankar, rörelserädsla, nivå av fysisk aktivitet, fatigue, smärta, depression och ångest. Slutsatsen blev att de faktorer som mest predicerade aktivitetsbegränsning var tilltro till sin egen förmåga i vardagliga situationer samt smärta.
Sammanfattningsvis har studierna i denna avhandling visat att utifrån ett multidimensionellt perspektiv var nivå av fysisk aktivitet och upplevelsen av att vara nöjd med sin behandling faktorer som är förknippade med god livskvalitet och hälsa vid cervikal dystoni. Movement Energy Index kan vara ett passande mått för att beskriva och mäta energiåtgången samt rörelsestörningen vid cervikal dystoni och därmed vara användbart vid utvärdering av olika behandlingsmetoder. Sjukgymnastisk behandling vid cervikal dystoni har positiv effekt framförallt under pågående behandling och med bestående positiv effekt på livskvalitet sex månader efter avslutad behandling. Slutligen visar denna forskning att tilltrot till den egna förmågan i vardagliga situationer samt upplevelse av smärta är de faktorer som kan predicera aktivitetsbegränsning hos personer med cervikal dystoni.
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REFERENCES


A doctoral dissertation from the Faculty of Medicine, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine. (Prior to January, 2005, the series was published under the title “Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine”.)