
**Characterization of Sub-Acute
and Chronic Low-Back Pain in
Activities of Daily Living Using
Linear and Nonlinear Tools**

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PhD Thesis by

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Characterization of sub-acute and chronic low-back pain in activities of daily living using linear and nonlinear tools

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The dissertation is based on the following peer-reviewed articles referred to by their Roman number in the text.

- Study I: Svendsen JH & Madeleine P. Amount and structure of force variability during short, ramp and sustained contractions in males and females. *Hum Mov Sci* 2010; 29(1): 35-47.
- Study II: Svendsen, JH, Samani A, Mayntzhusen K & Madeleine P. Muscle coordination and force variability during static and dynamic tracking tasks. *Hum Mov Sci* 2011; 30(6): 1039-51.
- Study III: Svendsen JH, Svarrer H, Læssøe U, Vollenbroek-Hutten M, Madeleine P. Standardized activities of daily living in presence of sub-acute low-back pain. A pilot study. *J Electromyogr Kinesiol* 2012; (Epub ahead of print) doi: 10.1016/j.jelekin.2012.08.006.
- Study IV: Svendsen JH, Madeleine P & Vollenbroek-Hutten M. Influence of chronic low-back pain on biomechanical and cognitive factors during standardized activities of daily living. *In preparation*.

This thesis has been submitted for assessment in partial fulfillment of the PhD degree. The thesis is based on the submitted or published scientific papers which are listed above. Parts of the papers are used directly or indirectly in the extended summary of the thesis. As part of the assessment, co-author statements have been made available to the assessment committee and are also available at the Faculty. The thesis is not in its present form acceptable for open publication but only in limited and closed circulation as copyright may not be ensured.

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Preface

The present study was carried out at Centre for Sensory-Motor Interaction (SMI), Aalborg University, Denmark, and Roessingh Research and Development (RRD), Enschede, the Netherlands in the period from 2009 to 2012.

I am most grateful to all co-authors for their contributions and for a fruitful collaboration. Especially, I wish to express my gratitude to Professor Pascal Madeleine and Miriam Vollenbroek-Hutten for their supervision and guidance to my projects. I would also like to thank all my colleagues at Centre for Sensory-Motor Interaction for providing a friendly, inspiring and competitive research environment. Further, I thank Dr. Heine Svarrer and Dr. Daan Wever for helping with inclusion of the specific patient groups in study III and IV. And a big thank you to all the participating volunteers, low-back pain patients and healthy subject, for showing patience and cooperating in the experiments of this PhD project.

Finally, I would like to thank my lovely family who have supported me, encouraged me, and travelled with me to complete this project.

List of abbreviations

LBP: Low-back pain

ADL: Activities of daily living

COP: Center of pressure

SEMG: Surface electromyography

CSQ: Coping strategy questionnaire

FABQ: Fear-avoidance beliefs questionnaire

ESR: Erector spinae - right

ESL: Erector spinae - left

EAOR: External abdominal oblique - right

EAOL: External abdominal oblique - left

RMS: Root mean square

NRMS: Normalized root mean square

SD: Standard deviation

CV: coefficient of variation

SaEn: Sample entropy

NMI: Normalized mutual information

ANOVA: Analysis of variance

Introduction

Low-back pain

At some point in a lifetime, everybody experience musculoskeletal pain, with the low-back region being one of the major sites for pain occurrence [Breivik et al, 2006]. Lifetime prevalence of low-back pain (LBP) is reported up to 84% [Airaksinen et al, 2006]. The musculoskeletal pain can be due to e.g. an injury or soreness after heavy work. In major part of cases, after treatment or just rest, the muscles recover and no further complications are present. But for some individuals, an acute injury can progress into a chronic musculoskeletal disorder, and specifically LBP is a widespread burden upon society, as the monthly prevalence is reported to be up to 40% in the working population [Nachemson, 2004]. The high prevalence of LBP results in major costs for healthcare, but also in the loss of productivity. In fact, only 7% of costs due to LBP incidences are directly from healthcare, where the remaining costs are related to productivity loss [van Tulder et al, 1995].

Acute LBP most times develops spontaneously from muscle strains during daily life [Hall et al, 1998], and depending on physical activity symptoms vary. Physical demands in daily living activities like manual lifting, bending are risk factors of LBP [Hartvigsen et al, 2001; Hoogendoorn et al, 1999; Waddell and Burton, 2001]. LBP can be painful and spreads towards the thighs, but in majority of cases, the condition will recover [Waddell, 1987; Waddell, 1996].

As a model of acute LBP, experimental induced pain has been used to analyze the influence of LBP on movements and motor control. It is a controlled way of inducing pain to mimic clinical conditions. However, the effect of experimental LBP has shown to vary in dynamic exercises, where the immediate effect of LBP does not show alterations in movements, but mainly as changes in muscular activation [Arendt-Nielsen et al, 1996; Lamothe et al, 2004]. The perception of experimental induced pain also differs from clinical acute pain in pain location and quality [Madeleine, 2010]. Further, cognitive aspects cannot be studied in experimentally induced muscle pain.

Sub-acute LBP

From the amount of patients that experience acute LBP, approximately 80-90 % recovers within 6 weeks. After the first six weeks of LBP, the pain turns into a sub-acute stage and the recovery rate decreases substantially [Waddell, 1996]. In sub-acute LBP findings have shown, that a decline in physical activity compared with the period before the LBP onset is disabling and associated with fear of movement/(re)injury [Verbunt et al, 2005] as proposed in the fear-avoidance model [Vlaeyen et al, 1995]. Furthermore, the classification of sub-acute LBP has been of interest, as the sub-acute behavior has shown to not only last for up till 3 months, but also in ongoing pain for up to 6 months [Pengel et al, 2002].

Chronic LBP

Within stages of chronic LBP, the cause of pain sensation and disability within chronic stages is much more widespread, with both biomechanical [Lehman, 2004] and pain-related cognition [Kusters et al, 2011] influenced by the ongoing pain perception. In society chronic LBP is a major problem with an estimated lifetime prevalence of up to 23%, where 12 % is immobilized by the pain [Airaksinen et al, 2006]. The rest of the chronic LBP patients carry on with daily living activities despite the pain.

The development of LBP and how it turns into a chronic condition is undisclosed, but it is widely accepted, that both physical demands and cognitive variables play a role [Waddell and Burton, 2001] and that the chronification is a dynamic interplay by cognition and physical characteristics [Weiser and Cedraschi, 1992].

Disability, pain and the interference with daily living activities

LBP is disabling and it reduces the ability to perform physical activity. Furthermore, LBP also interferes with ordinary daily life activities throughout acute, sub-acute and chronic LBP stages [Bakker et al, 2007; Spenkeliink et al, 2002; Verbunt et al, 2005]. Simple everyday tasks like

walking, trunk flexion or stand to sit are complicated by the present pain.

Subjects with LBP may have increased co-contraction of spinal muscles, which may increase the risk of spinal tissue injury [Ferguson et al, 2004]. Studies have shown that repetition of tasks, sustained load and flexed posture can induce neuromuscular disorders of the lower back [Ben-Masaud et al, 2009; Parkinson et al, 2004]. The role of posture as a risk factor for LBP is controversial and current guidelines suggest that there is limited evidence for posture as a risk factor for LBP [Burton et al, 2006]. However, some postural factors in working life and ADL are considered to influence postural exposure. Namely cumulative effects of duration [Parkinson et al, 2004], trunk range of motion [Hoogendoorn et al, 2000] and frequency of trunk flexion are considered to be the three main influences of postural exposure [Solomonow et al, 1999].

The presence of pain or fear-avoidance behavior associated with pain is suggested to alter movements in LBP patients, as an adaptive strategy to reduce pain by restricting trunk movements [Watson et al, 1997b]. Potentially a restriction like this could also be seen at other levels of movements with altered movement patterns in e.g. lower extremities.

In general, the influence of cognition in the presence of pain, and especially chronic pain, is an important aspect in the limitation of movement, including basic activities of daily living. The fear-avoidance model and the avoidance-endurance model suggest that coping strategies influence physical functioning and in that manner maintain the chronic pain stage. A limitation of activity has been associated by findings of fear of movement/(re)injury and this pain-related fear is often more dominant than the pain severity itself [Crombez et al, 1999; Vlaeyen et al, 1995]. The fear-avoidance model proposes that fear-related pain emerges when patients experience the pain as threatening which typically can be catastrophizing thoughts [Vlaeyen and Crombez, 1999]. From this concept of fear-related pain and the following limitation of pain, two behavioral responses are suggested, which are confrontation and avoidance. By confronting daily living activities despite the pain, fear may be reduced and the adaptive response may promote recovery from the painful

condition. This adaptation takes in to account that no somatic pathology is present. Counter to confrontation is avoidance a maladaptive strategy which leads to physical inactivity due to the fear of increased pain and disability [Vlaeyen et al, 1995; Vlaeyen and Crombez, 1999]

Assessment of physiological characteristics and relation to pain

Classical approaches in research of human movements often use common linear assessment where kinematic and kinetic data of several trials are averaged to summarize time series in some overall outcome parameters. Such approaches resulting in overall mean values and range of movements may mask important alterations of motor and movement variability. [Stergiou et al, 2006]

Variability in human movements and performance of tasks is a natural and important feature of human behavior. The variability arises from the motor output which is an inherent variable. Motor output is the result of neural commands, muscle contractions and torques from synergistic and co-contracting muscles, and during adaptation to sensory input, variability arises. In a task which requires stable performance, variability may be regarded as noise in the sensorimotor system [Fitts, 1954; Schmidt et al, 1979; van Beers et al, 2004]. But variability can also be useful in expressing how the neuromuscular system is adapting the required force output in relation to sensory input due to inherent properties [Latash et al, 2002; Madeleine et al, 2008b; Madeleine, 2010]. Thus, from that perspective, the assessment of motor and movement variability can enhance our understanding of motor control in e.g. population suffering from LBP.

Linear and nonlinear variability

The classical approach to delineate motor performance and variability is by the use of standard linear method with computation of e.g. mean and variance of physiological variables [Madeleine et al, 2008b; Slifkin and Newell, 1999]. A linear approach like this reflects the magnitude of variability, but it does not describe structural changes in motor variability. These dynamic changes

in motor variability are not obtained through linear computation, which makes it insufficient in motor control studies [Madeleine et al, 2011a; van Emmerik and van Wegen, 2002]. By the use of nonlinear approaches, complex structures inherent in the biomechanical variability can be outlined [Harbourne and Stergiou, 2009], and a broader insight to variability can be reached. In movement analysis nonlinear approaches have been introduced, and as an addition to linear measures it can be used to reveal motor control strategies [Latash et al, 2002; Morrison et al, 2007].

The use of variability and time-dependent structure of variability have been limited in musculoskeletal pain studies, but recent results have indicated, that pain decreases motor variability [Madeleine et al, 2008a]. Additionally it is found, that the impact of acute and chronic pain on motor variability seems to be opposite oriented [Madeleine et al, 2008b; Madeleine, 2010].

Loss of complexity hypothesis

In painful or pathophysiologic conditions, it has been suggested, that a loss of complexity in physiological recordings can be observed due to decreased functionality of adaptation of the motor control mechanisms to unpredictable changes [Lipsitz and Goldberger, 1992]. In static contractions the hypothesis has been confirmed [Lipsitz and Goldberger, 1992; Madeleine et al, 2011a; van Emmerik and van Wegen, 2002], but for dynamic exercises an increase of complex output of a physiological system is proposed [Vaillancourt and Newell, 2002].

Muscular activation and recruitment

In LBP, changes in the muscular control are present, and depending on the task the changes appear as altered patterns of muscle recruitment of the trunk [Hodges, 2001; van Dieen et al, 2003].

Altered trunk muscle recruitment is reflected in an increased use of antagonist muscles to stabilize

the lumbar spine [van Dieen et al, 2003] and changes in the recruitment synergies of trunk muscles [Hodges, 2001; Mehta et al, 2010]. During daily living activities, altered coordination of lumbar-hip muscles for LBP patients in a sit-stand and stand-sit test is found [Shum et al, 2005; Shum et al, 2007]. Also in the trunk muscles deviating activity are pronounced for LBP patients during dynamic tasks reflecting basic activities of daily living [Sheeran et al, 2012; Watson et al, 1997a].

Supplementary to identifying muscular activation and ratios, functional connectivity between synergistic muscles can be revealed by mutual information detecting linear and nonlinear dependencies between time series [Jeong et al, 2001; Kojadinovic, 2005]. Within assessment of functional connectivity of trapezius muscle sub-divisions it has provided valuable information [Johansen et al, 2012; Madeleine et al, 2011b]. How the functional connectivity is altered due to the changed muscle recruitment is yet to be investigated, but a decrease in synergistic effect is plausible due to potential imbalance in trunk muscle activation [Silfies et al, 2005].

Aims of the study

The overall aim of this study was to characterize the influence of LBP during activities of daily living throughout sub-acute and chronic pain stages. Analysis of movements and muscular activation was of main interest together with influence of cognitive factors. The combination of physiological and cognitive parameters was achieved to provide a basis for exploring interplays of cognitive aspects in relation to motor control in LBP patients.

From this main aim, 3 sub-aims were derived;

- The initial sub-aim was to establish a set of analytic methods in order to assess performance and motor variability in group comparisons and during dynamic exercises.
- Secondly, the aim was to investigate how patients with sub-acute LBP differed with respect to controls in movements and muscle activation during standardized tasks representing daily living activities.
- And finally, the aim was to investigate chronic LBP patients and how they differed in respect to controls during standardized tasks representing daily living activities.

In the two latter sub-aims, the relationships between cognitive aspects and the measures of motor performance were also explored.

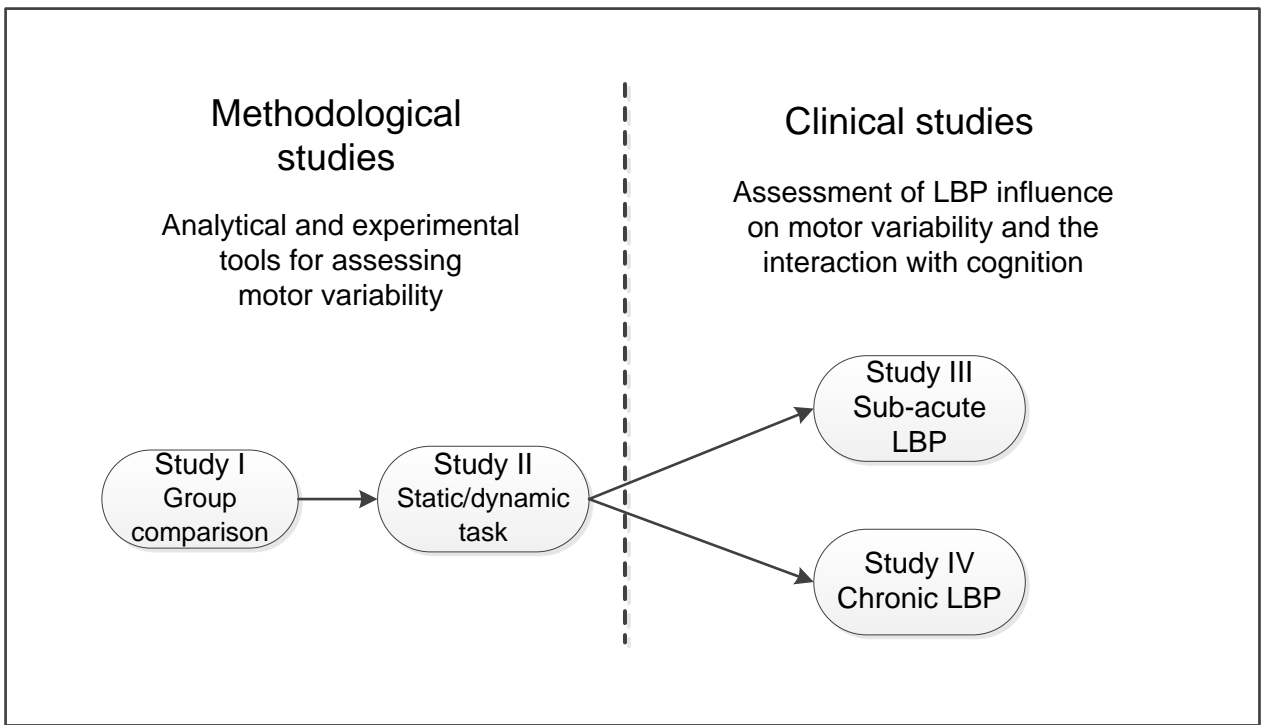


Figure 1: Overview of the studies in the project

Methods

Subjects

A total of 80 subjects participated in the four studies. From this total, 24 LBP patients were recruited for study III and IV (12 in in each study). In study I and II, only healthy volunteers participated, and for study III and IV, groups of healthy volunteers were included to match the LBP groups on gender, age and body mass index at a group level. Anthropometric characteristics can be found in table 1. In study III, sub-acute LBP patients were recruited by rheumatologists at Aalborg Hospital, Denmark, and in study IV, Specialists in rehabilitation from Roessingh Rehabilitation Center, Enschede, the Netherlands, carried out the initial recruitment. Prior to final inclusion to the studies, LPB patients were instructed by phone or letter, and again asked if they wanted to participate. Inclusion criteria for LBP patients in both study III and IV were: an age between 18 and 70, free of any known psychiatric disturbances, and non-pregnant. Besides the inclusion criteria, LBP patients had to be able to conduct normal daily life routines. In study III, the period for LBP had to be less than 6 months, which was defined for this study as being sub-acute LBP. In study IV, the LBP period had to exceed 6 months of duration, defined as chronic LBP in this project. Healthy volunteers consisted of staff and students from Aalborg University and Roessingh Research and Development, together with relatives.

Table 1. Anthropometric data from participants in studies I-IV.

	Study I		Study II	Study III		Study IV	
Groups	Females (N = 10)	Males (N = 10)	One group (N = 12)	LBP (N = 12)	Controls (N = 12)	LBP (N = 12)	Controls (N = 12)
Males/females, N	0/10	10/0	8/4	9/3	9/3	7/5	7/5
Age (years), mean (SD)	25 (4)	26 (3)	27 (4)	39 (10)	38 (10)	47 (15)	44 (19)
Body mass index (kg/m ²), mean (SD)	23 (2)	23 (1)		25 (3)	24 (2)	26 (3)	26 (4)

All the studies were approved by the local ethical committees (N-20070004; N-20100006; NL36455.044.11). Informed consents were obtained from all participants.

Procedures

Study I and II in this PhD project acted as methodological precursors to gain insight in how data processing techniques could be used in respectively group comparison [I] and within dynamical exercises on both kinetic and muscle activation data [II]. As experimental frame, static elbow flexion [I] and static and dynamic wrist contractions were used [II]. Study I was set up to be a group comparison study in static condition, and study II a comparison of tasks i.e. static and dynamic

tasks.

Methods and procedures gained in the methodological studies were then implemented in the 2 last studies, to assess motor control in LBP patients. Study III and IV were carried out as case-control studies and in both studies participants (LBP patients and healthy controls) were instructed to do three dynamic tasks representing daily living activities. The tasks were: i) a repeated sit-stand-sit task, ii) repeated trunk flexion task, and iii) a box lifting task of each 30 s duration. Before entering the experimental procedures, LBP patients were asked to fill in 2 questionnaires to address their fear avoidance beliefs and coping strategies, with respect to the LBP present.

Measurements

Pain intensity

Current pain intensity was measured on a numeric rating scale ranging from 0 to 10, where 0 indicated no pain and 10 indicated worst imaginable pain. During the studies, no pain was induced to any of the participants, so the only pain present, was the LBP for the patient.

Again, rating of pain intensity is highly subjective and the outcome should be handled with cautiousness. During longer sessions with experimental recordings, it is important to measure the pain intensity throughout the session, as it might change over time.

Kinetic recordings

For study I and II a 3 dimensional force transducer (FS-6, AMTI, Watertown, MA, USA) was used to collect data from the elbow flexion tasks and the wrist contractions. For these studies, subjects had to reach a certain force output, and continuous feedback was give on a monitor. The forces were sampled at 500 Hz and filtered low pass filtered (10.5 Hz).

For study III and IV, subjects were positioned on force plates (AMTI, Watertown, MA, USA) when performing the requested tasks. From the force plate, ground reaction forces from body movements were recorded, and center of pressure (COP) displacements during the tasks calculated.

Kinematic recordings

For study III and IV, motion capture was used to quantify joint angles of the ankles, knee, hip, and the overall trunk angle. In study III a QTM 8-camera motion capture system (Qualisys AB, Sweden) was used, and in study IV, a VICON 6-camera motion capture system (VICON 370, Oxford metrics Ltd., Oxford UK) recorded the 3-dimensional kinematics. For the purpose of these studies, both systems were more than sufficient.

To extract the joint angles, reflective markers were placed on the subjects at anatomical landmarks. The placement of markers varied slightly between the 2 studies, due to the difference in systems.

- In study III, the marker placement was as it follows: Markers used to calculate bilateral angles for the ankle were markers at: 1st and 5th metatarsal, calcaneus and four markers in a cluster at the tibia. For bilateral knee angles, the markers were: four markers in a cluster at the tibia, four markers in a cluster at femur and a marker at the lateral epicondyle. For bilateral hip angles, the markers were: four markers in a femur cluster, one marker at the greater trochanter, anterior superior iliac spine, posterior superior iliac spine and iliac crest. Overall trunk angle was calculated from markers bilateral at posterior superior iliac spine, acromion and a marker at L5.
- Marker placement for study IV. Bilateral angle of the ankle: Markers at 1st and 5th metatarsal, calcaneus, fibula and a marker on the tibia 1/3 of the distance between fibula and lateral epicondyle. Bilateral knee angles: Markers at the tibia (1/3 of the distance between fibula and lateral epicondyle), lateral epicondyle, and femur (approx. 1/3 of the distance

between lateral epicondyle and anterior superior spine (ASIS). Bilateral hip angles: Markers at femur, ASIS, iliac crest, and posterior superior spine (PSIS). For the overall trunk angle, marker placements were: PSIS, a marker at L4 and acromion.

Surface electromyography (SEMG)

To record muscle activity in the studies, bipolar SEMG was used. Surface electrodes were aligned on abraded ethanol-cleaned skin along the direction of the muscle fibers with an inter-electrode distance of 2 cm. Electrode placement for study II was at the extensor carpi ulnaris muscle (ECU), the extensor carpi radialis muscle (ECR), the flexor carpi ulnaris muscle (FCU) and the flexor digitorum superficialis muscle (FDS) of the forearm. For study III and IV electrodes were placed bilateral at the erector spinae (ES) and external abdominal oblique (EAO). At EAO, electrodes were located approx. 15 cm lateral to the umbilicus, and at ES approx. 3 cm lateral from the midline at L3 level on the largest muscle mass found by palpation. For study II and III, SEMG recordings were sampled at 2000 Hz and band pass filtered with cutoff frequencies at 5 and 500 Hz. In study IV, sampling frequency was 1000 Hz and a similar band pass filtering as the previous studies.

Questionnaires

To quantify cognitive behaviors during the presence of pain, questionnaires can be used as a valid tool. Two questionnaires were used during study III and IV, the fear-avoidance belief questionnaire (FABQ) and the coping strategy questionnaire (CSQ). The FABQ is a 16 item questionnaire, and each item is a statement like e.g. “my pain is caused by physical activity” which has to be rated on the 7 point Likert scale, where 0 corresponded to “completely disagree” and 6 to “completely agree”. From this questionnaire, 2 sub-scale can be derived, fear-avoidance beliefs during physical activity, and fear-avoidance beliefs during work.

The CSQ is a 44 item questionnaire which also has to be answered on a 7 point Likert scale. In the

questionnaire the answers have to be given in respect to how the subject acts in the presence of LBP. The extremes of the Likert scale, 0 and 6, corresponds to “never do” and “always do”, respectively. An example of a statement in the CSQ is “I worry all the time about whether it will end”. The questionnaire included 44 items, from which 6 sub-scales of cognitive coping were derived. The sub-scales were: diverting attention, reinterpreting pain sensations, coping self-statements, ignoring pain sensations, increasing activities, praying and hoping, and catastrophizing.

When pain is present, it can affect the cognitive behavior and how patients cope during daily life situations. To be able to quantify these altered patterns of cognition can be helpful in the assessment of the patients. On the other hand, answers in the questionnaires are subjective, and it is important to highlight the importance of the answers to the patients.

Analyses

Root mean square (RMS)

Due to its stochastic properties, SEMG can be estimated by the probability function. Estimators like mean and variance can be computed. RMS displays the variance in the time series, and has been presumed to be the maximum likelihood estimator of SEMG [Hogan and Mann, 1980]. Moreover, RMS measures the amplitude or energy of the signal, giving a clear physiological interpretation. It is computed as:

$$RMS = \sqrt{\frac{1}{N} \sum_{i=1}^N x(i)^2}$$

where $x(i)$ is the time series to calculate RMS from, and N is the number of data points in the time series. In group comparisons, a normalization of the RMS is preferred, as subject dependent factors like skin thickness, subcutaneous fat layer and muscle strength influences the EMG recorded at the

surface of the skin. In study II, maximal voluntary contractions (MVC) were recorded and maximum RMS was used for normalization. However, in study III and IV MVC was not feasible due to sub-acute and chronic LBP, so normalization of RMS was performed with maximum RMS computed from a submaximal condition, i.e. quiet erected standing.

Variability measures

To address the first aim of the present PhD study, analytical methods were implemented to quantify variability (Studies I and II). The size of variability in the time series from kinetic and kinematic recordings, statistical measures like standard deviation (SD) and coefficient of variance (CV) are common tools. SD reflects the absolute size of variability, and CV is the relative variability. These statistical measures are linear means, and do to simplicity, often used for variability quantification. SD is calculated as:

$$SD = \frac{1}{N} \sqrt{N \sum_{i=1}^N x^2(i) - \left(\sum_{i=1}^N x(i) \right)^2}$$

Where $x(i)$ is the time series to calculate SD for and N the number of data points. CV is a normalization of SD with respect to the mean and is calculated as: $CV = \frac{SD}{mean}$.

In study I, the size of variability from force outputs was estimated by both SD and CV. To get a valid measure of size of variability from CV, the error of performance needs to be low. In study I a target force had to be reached, which enabled the use of CV, but it was also demonstrated, that in tangential directions, where the force fluctuated around zero, CV was inappropriate due to division by zero.

To access nonlinear time-dependent structure of variability in the time series, entropic computations is useful, as the output value directly expresses the tendency towards recurrent patterns within the

time series. Time dependent structure reveals deterministic and stochastic organization of the neurophysiological system and the degree of complexity of a signal is typically associated with the number of system elements and their functional interactions [Heffernan et al, 2009; Jordan and Newell, 2004; van Emmerik and van Wegen, 2002]. Throughout the studies [I-IV], sample entropy (SaEn) was computed for this purpose. Studies I and II served as primordial steps to the use of linear and especially non-linear methods confirming the potential of such approaches in the clinical studies. SaEn expresses the complexity of the recorded signal excluding self-matches [Kuusela et al, 2002; Lake et al, 2002; Richman and Moorman, 2000]. To compute SaEn the time series $x(i)$ with $i = 1 \dots N$ has to be divided into $N - m + 1$ vectors $u(i)$ of the state space: $u_i = x_i, x_{i+\tau}, x_{i+2\tau}, \dots, x_{i+(m-1)\tau}$, where m are the embedding dimension and τ the time lag (set to 1). Then, the distance d is calculated as the maximal distance d between each vector in the state space. The first $N - m$ vectors are considered and the conditional probability is not estimated in a template manner [Richman and Moorman, 2000]. It means that i is never equal to j when the distance d between $u(i)$ and $u(j)$ are computed.

$$d(u_i, u_j) = \max_k |u_{i+k} - u_{j+k}|,$$

$$\text{with } 1 \leq j \leq N - m \text{ and } i \neq j$$

Now, Φ^m_r representing the average of natural logarithm of the probability of matches C^m_i is computed as:

$$\Phi^m_r = \frac{1}{N - m} \sum_{i=1}^{N-m} C^m_i$$

Finally, SaEn representing the negative logarithm of the relationship between the probabilities that two sequences coincide for $m+1$ and for m points is computed as:

$$SaEn(m, r, N) = -\ln \frac{\Phi^{m+1}_r}{\Phi^m_r}$$

SaEn depends on the embedding dimension m , the tolerance distance for similarity r and the number of data points N .

The output is a unitless, non-negative number where lower values indicate a more regular signal and higher values a more complex signal. SaEn was computed for SEMG [II, III, IV], kinetic [I-IV] and kinematic [III, IV] time series. Throughout the studies [I-IV], the embedding dimension m was set to $m = 2$ to enable a more consistent estimation of time-dependent structures in the signals [Lake et al, 2002], and the tolerance distance r was set to $r = 0.2 \times SD$. The setting of these variables was based on human movement studies [Vaillancourt and Newell, 2000].

As methodological precursors, study I and II revealed the usability of both linear and nonlinear techniques to access the size and time-dependent structures of variability to outline group and task differences in control processes and compensatory mechanisms influencing variability in static and dynamic tasks.

Muscle connectivity

Between time series of recorded EMG, the dependency or shared information between the time series can be computed by normalized mutual information (NMI). Compared to linear correlations of the time series (cross-correlation), NMI also detects nonlinear dependencies.

The average amount of information contained in the EMG signal X is the entropy H defined as:

$$H_X = - \sum_{x_i} p_X(x_i) \log p_X(x_i) ,$$

where $p_X(x_i)$ is the probability that an EMG measurement will find the system in the i^{th} element of the bin, and $p_X(x)$ is the normalized histogram of the distribution of values observed for the measurement x . Sixty four bins were used to construct the histogram to estimate the density function. Given a measurement x_i drawn from the EMG set $X = \{x_i\}$, and y_j drawn from the EMG

set $Y = y_j$ representing a muscle pair, mutual information is defined as [Jeong et al, 2001]:

$$MI_{XY} = \sum_{x_i, y_j} p_{XY}(x_i, y_j) \log \frac{p_{XY}(x_i, y_j)}{p_X(x_i) p_Y(y_j)},$$

where $p_{XY}(x_i, y_j)$ is the joint probability density for the EMG measurements of X and Y . Mutual information was estimated over 500 ms non-overlapping epochs between muscle pairs. From the last equation, mutual information appears always to be non-negative and zero if and only if X and Y are stochastically independent. However, the upper bound depends on signals entropy rendering comparisons between samples unreliable. Thus, a normalized version of the mutual information was implemented and defined as:

$$NMI_{XY} = \frac{MI_{XY}}{\min(H(X), H(Y))}$$

As the mutual information detected is normalized, outcome of the NMI computations are between 0 and 1, where 0 is no dependency between time series at all, and 1 reflects complete connectivity. Furthermore, $NMI_{XY} = 1$ if and only if X and Y are functionally independent [Kojadinovic, 2005].

For this project, computations of NMI were applied for study II, III, and IV. In all studies SEMG from four muscles was recorded and used as input to the computations. EMG time series from the muscles were paired in six combinations and for all six pairs, NMI was computed.

Questionnaire data extraction

From the questionnaires of cognitive assessment different sub-scales of fear-avoidance and coping strategy were selected. FABQ items were used for two sub-scales (fear avoidance during physical activity and work). CSQ items were used for six sub-scales (diverting attention, reinterpreting pain sensations, coping self-statements, ignoring pain sensations, increasing activities, praying and hoping, and catastrophizing). From the 7-point Likert scale in the questionnaires, the maximum

score for the sub-scale of fear avoidance beliefs during physical activity would be 24 (four items), and during work 42 (seven items). In the CSQ sub-scales maximum values would be 36 (six items in each sub-scale). For internal reliability test, Cronbach's α was calculated within each sub-scale [Cronbach, 1951]. Only sub-scales with $\alpha > 0.7$ were considered reliable and were used for further analysis.

Due to the exploratory purpose of the questionnaires and outcome, the main focus for the use of coping strategies and fear-avoidance beliefs was in the association with outcome of biomechanical and physiological measures. To quantify relationships between cognitive factors and SEMG and biomechanical parameters, Pearson's correlation was applied [III, IV].

Statistical analysis

One-way ANOVAs were used with groups as factor in 3 of the studies [I, III, IV]. In study I dependent variable was endurance time. In study III and IV, dependent variables were SD and SaEn for the kinetic recordings; RMS, NRMS, SaEn and NMI of the SEMG; mean, SD and SaEn for kinematic recordings. In study II two-way ANOVAs was performed with factors task and direction and the deviation from target force, NMI SD and SaEn as dependent variable. In study I a 3-way ANOVA with factors group, contraction level/contraction time and force direction and dependent variables: Error of performance, SD, CV and SaEn was performed.

Pearson's correlation (r_p) was applied in study III and IV to quantify the relationship between averaged CSQ and FABQ subscales (catastrophizing, ignoring pain sensation, fear avoidance during physical activity and work) with acceptable internal reliability (Cronbach's $\alpha > 0.7$), and group-significant SEMG and biomechanical parameters. Significant level in all statistical analyses was set to be $p < 0.05$. For group comparisons, there is always a risk of type 2 error and with limited amount of subjects in groups, the risk increases. With mainly characteristic purposes, the inclusion of participants for the studies in the PhD project was limited to a reasonable number

which was able to demonstrate the effect in each study. Still, type 2 errors may occur, as groups in especially study III and IV reflected average patients seeking help for LBP.

Specifications of studies

The four studies of this project differed in the use of methods and settings. In table 2 the properties of the studies are summarized to give an overview of where different analyses were deployed.

Table 2. Specification of performed studies in the current PhD project

	Study I	Study II	Study III	Study IV
<i>Variability measures (Used for kinetic and kinematic recordings)</i>				
SD	X	X	X	X
CV	X			
SaEn	X	X	X	X
<i>SEMG analysis</i>				
RMS		X	X	X
SaEn		X	X	X
NMI		X	X	X
<i>Others</i>				
Questionnaires of cognitive aspects			X	X

Discussion

Linear and nonlinear techniques were initially implemented and evaluated (Studies I & II). Then, these methods were used to address motor control in sub-acute and chronic LBP patients during ADL (Studies III & IV). Finally, cognitive aspects were investigated, and the interplay with biomechanical and muscular activation parameters was explored. During standardized activities of daily living, sub-acute LBP differed from matched control in terms of muscular activation patterns, whereas chronic LBP was associated with changes in both kinematics of lower extremities and activation patterns of trunk muscles. A transition from altered abdominal muscle activation in sub-acute LBP to changes in the painful muscles at the chronic stages seems to occur, with an overall loss of functional connectivity between trunk muscles. This is also reflected by transitions into restricted movements in the chronic stage, shown by less complexity in joint angles. In table 3, main findings the trunk flexion task for sub-acute and chronic LBP are reported. The following section mainly deals with motor variability changes. Further, for both sub-acute and chronic LBP, correlations of biomechanical and cognitive factors were found underlining the potent association of cognition and motor control.

Effect of LBP on muscle activation during ADL

It has been hypothesized that dysfunctional trunk muscle recruitment is associated to the limitation of physical function [Hodges and Richardson, 1996]. In this PhD project, muscle activation of the trunk at painful sites of the lower back and non-painful antagonist abdominal muscles was investigated for both sub-acute and chronic LBP patients. Compared to matched controls, a decreased level of activation was found for sub-acute LBP patients in the abdominal muscles during a trunk flexion task [III]. In a comparable task for chronic LBP patients, no such finding for muscle activation was found [IV]. A potential imbalance within activation level of trunk muscles to stabilize the spine could take place in antagonist muscles for sub-acute LBP patients due to

compensatory mechanisms [Oddsson and De Luca, 2003]. The greater exposure of muscle activation may increase the risk of spinal tissue injury in subjects with LBP [Ferguson et al, 2004].

Table 3. Significant findings in the trunk flexion task for sub-acute [III] and chronic low-back pain (LBP) patients. Analyses showing significant findings: Normalized root mean square (NRMS), sample entropy (SaEn) and normalized mutual information (NMI). Muscles recorded from: Right erector spinae (ESR), left erector spinae (ESL), right external abdominal oblique (EAOR) and left external abdominal oblique (EAOL). Directions of significant findings: medial-lateral (ML) direction.

	Sub-acute LBP	Chronic LBP
Muscle activity pattern		
NRMS of EAOL	-	No dif
SaEn of EAOL	+	No dif
SaEn of ESR	No dif	+
NMI of ESR-ESL	-	-
NMI of ESL-EAOR	No dif	-
NMI of ESL-EAOL	No dif	-
NMI of EAOR-EAOL	-	No dif
Kinetic recordings		
SaEn in ML direction	No dif	-
kinematics Recordings		
SaEn, ankle	No dif	-
SaEn, trunk	No dif	-

+: Higher for LBP patients compared with controls

-: Lower for LBP patients compared with controls

Additional to computation of the magnitude of muscular activation (RMS), insight to complex structures of motor variability of the SEMG was obtained by the use of nonlinear analysis. Entropy measures derived from chaos theory can be used for this purpose [Rathleff et al, 2011; Sung et al, 2010]. Within acute LBP, motor variability is reported to be an important factor for recovery [Moseley and Hodges, 2006]. Increased complexity (SaEn) of motor variability was found for abdominal muscles in sub-acute LBP patients [III]. This finding confirms the alteration of antagonist muscle activation reported above. In chronic LBP patients, increased complexity of the

muscle activity pattern was also found, but contrary to the group of sub-acute LBP, the increase was within painful erector spinae muscles of the lower back [IV]. A change in activity pattern seems to occur between the two groups of LBP patient, and these subtle changes may not be seen as a positive trend towards recovering from LBP, despite higher complexity of physiological systems is associated with healthier functionality [Costa et al, 2002]. Vaillancourt et al (2002) hypothesized that during dynamic rhythmic tasks such as ADL (e.g. repetitive bending), injury would cause an increase in movement complexity while a decrease will be seen during tasks with an static (isometric) contraction. If this also includes complexity of muscle activation is unclear, but the difference in complexity orientation may indicate that SEMG and Kinematics quantified by sample entropy may represent two different constructs in chronic LBP in agreement with Vaillancourt et al. (2002) and Rathleff et al (2011).

Further information about muscle activation for LBP patients, demonstrated that coordination of trunk muscles during the ADL tasks were reduced compared with controls [III, IV]. A decrease in functional connectivity among left and right erector spinae found for both the LBP groups can be interpreted as a lack in coordination of muscle recruitment, which could lead to lumbar instability or lower bodily awareness. The lack of coordination was most likely more pronounced for the chronic LBP patients, with decreased functional connectivity not only among lumbar muscles, but also within coordination between lumbar and abdominal antagonist muscles [IV]. A reduction in lumbar stability has been associated with LBP, and the importance of coordination between the different muscles acting on the stabilization has been highlighted [Cholewicki et al, 1997; Lamothe et al, 2006; Panjabi, 1992]. The alterations in synergistic actions of the trunk muscles may represent a motor control pattern that can have important consequences for continued dysfunction and chronic pain [Silfies et al, 2005].

Effect of LBP on biomechanical parameters during ADL

The reported differences for motor variability between the studies of sub-acute and chronic LBP patients were also expressed within the analyses of biomechanical measures. Movement variability computations for sub-acute LBP patients resulted in no difference from control group [III]. For the limited duration of LBP (0-6 months) it is possible that the tasks did not demand enough effort to enable discrimination among the groups, and a narrow approach with only using kinetic and kinematic analyses for detecting alteration in sub-acute LBP patients may not be suitable.

On the contrary, chronic LBP patients demonstrated more regular movements compared with controls [IV]. In contrast to the sub-acute LBP group, chronic LBP patients differed in SaEn for both the trunk flexion and stand-to-sit task with less complex movement patterns of postural control and joint angles (ankle, knee, and overall trunk angles) compared with controls. More regular movements for chronic LBP patients could be the result of a more rigid coordination of trunk muscles due to LBP. The different results for sub-acute and chronic LBP groups is in line with previous findings acknowledging a diminished coordination of trunk muscles to be the result of an ongoing pain [Lamoth et al, 2004; Lamoth et al, 2006; Madeleine, 2010]. These findings are in agreement with the loss of complexity hypothesis describing a decrease in complexity in presence of diseases [Madeleine and Madsen, 2009; Madeleine et al, 2011a; Vaillancourt and Newell, 2002].

Interactions between biomechanical behavior and cognition

When measuring biomechanical features from patients with clinical pain conditions, the interaction influence of cognition is an important part to understand the movement deviations [Descarreaux et al, 2007; Grotle et al, 2004]. But within correlations with specific task, the findings of interplays between biomechanical parameters and cognitive aspects are very sparse.

A decrease in physical activity due to LBP is suggested to be associated with cognitive aspects besides the pain experience [Hasenbring, 2000; Verbunt et al, 2005; Vlaeyen et al, 1995]. The interaction of catastrophizing and muscle activity is in line with previous findings for chronic LBP

patients [van der Hulst et al, 2010a]. This supports the existence of a guarding mechanism which has previously been found for patients with chronic pain [van der Hulst et al, 2010b], and now also to some extent in this case of sub-acute pain. For chronic LBP patients [IV], coping strategies as catastrophizing and praying and hoping correlated intensively with different biomechanical parameters. The overall finding shows that the two coping strategies correlate negatively with complexity of joint angles and also slightly with complexity of posturography. With catastrophizing being categorized as a maladaptive strategy in pain coping, the negative association with movement complexity indicates that increasing thoughts of catastrophizing (and praying and hoping) lead to subtle restrictions in movement which can be classified as simple ADL. Furthermore, the same maladaptive coping strategies are associated with complex structures of muscular activation of painful muscles, but opposite to the movements, the correlation is positive.

No comparative findings were made between study III and IV, but a negative correlation between functional connectivity and catastrophizing [IV] again outlines the changes in trunk muscle coordination from sub-acute to chronic LBP stages, since a positive association was found for the study sub-acute LBP [III].

Conclusions

Subtle changes in movements and muscle activation pattern were found characterizing LBP in relation to ADL. In study III, changes in abdominal SEMG was found while in study IV, both kinematics, kinetic and EMG changes were reported underlining the importance of the pain status, i.e. sub-chronic/chronic. This is in agreement with what has been reported in terms of size of variability in neck-shoulder disorders [Madeleine et al, 2008b; Madeleine, 2010]. The present thesis has contributed to new knowledge concerning motor variability during ADL in LBP, enabling to benchmark variability in relation to pain stage. In sub-acute LBP non-painful abdominal muscles showed more complex activity pattern. This was followed by decreased functional connectivity among lumbar and abdominal muscle pairs, which speaks for an altered control of trunk the

stabilization. The influence of LBP in the chronic stage also revealed changes in muscle activation patterns together with less complex movements of the trunk and lower extremities.

The exploration of the interplay between biomechanical variables and cognitive factors showed a distinct presence and correlation with coping strategies in both sub-acute and chronic LBP, with maladaptive catastrophizing interacting strongly. This shows an important role of cognition in the assessment of clinical pain, and related biomechanical outcomes. The used of motor variability assessment in LBP and exploration of cognitive interaction in this project, can serve as a platform for future studies in prevention and handling of clinical LBP.

Perspectives

In the present study, all recordings of ADL were performed as standardized tasks in biomechanical laboratories for the benefit of comparison between studies. In real life, tasks will not be so restricted, so for correct interpretation of the results, similar studies need to be carried out in LBP patients' daily environment, while performing their usual ADL. Further studies with larger sample size are warranted to enable a more overall generalization of the associations between biomechanical and cognitive parameters reported here.

Additionally, a longitudinal study is required to assess the LBP patients from the time they report pain and through pain stages. This approach will give a direct comparison of pain stages and behavior of motor variability can be outlined. Furthermore, the association between biomechanical and cognitive parameters could be enhanced by evaluating cognitive adaptations relative to each performed ADL [Kusters et al, 2011].

English summary

Low-back pain (LBP) is a major burden on society with a monthly prevalence of 40%. LBP is found to influence activities of daily living (ADL), but still no clear characterization is established to delineate how ADL is influenced by LBP.

The influence of cognition has shown to be substantial and in sub-acute and chronic LBP coping strategies and the fear of pain is considered to be one of the major cause for sustained pain and alterations in motor control and movements.

Even though LBP influences the activity level of daily routines, the use of classical approaches to outline the influence of biomechanical measures may not be sufficient to detect subtle changes in motor control. Variability of movement patterns in LBP has received little attention. Further, it has been regarded as purely random fluctuations of biomechanical measures. However, the assessment of the time-dependent structures of variability in biomechanical measures can be used to get insight to motor control which can reveal changes of ADL where gross movement deficits will not necessary take place. In this PhD, variability is used to characterize the influence of LBP in ordinary ADL. Furthermore, associations with cognitive factors are explored to outline how it can be revealed in the motor control.

Initially, linear variability and nonlinear time-dependent structures of variability were outlined and evaluated to access deviations in motor control. In the following studies of standardized ADL, sub-acute LBP influenced muscle activity in non-painful abdominal muscles, with more complex activity pattern. This was followed by decreased functional connectivity among lumbar and abdominal muscle pairs, which speaks for an altered control of trunk stabilization. The influence of LBP in the chronic stage also revealed changes in muscle activation patterns together with less complex movements of the trunk and lower extremities.

Exploration of the interplay between biomechanical variables and cognitive factors showed a

distinct presence and correlation with coping strategies in both sub-acute and chronic LBP, with maladaptive catastrophizing interacting strongly. This shows an important role of cognition in the assessment of clinical pain, and related biomechanical outcomes. The use of motor variability assessment in LBP and exploration of cognitive interaction in this project, can serve as a platform for future studies in prevention and handling of clinical LBP.

Dansk sammenfatning

Lændesmerter (LS) er en stor byrde for samfundet med en månedlig prævalens på 40%. LS har vist sig at påvirke daglige gøremål (DG), men stadig er der ikke etableret nogen klar karakterisering for at beskrive, hvordan DG er påvirket af LS.

Indflydelsen af kognition har vist sig at være betydelig, og i sub-akutte og kroniske LS anses coping strategier og frygten for smerte for at være en af de væsentligste årsager til vedvarende smerter og ændringer i motorisk kontrol og bevægelser.

Selvom LS påvirker aktivitetsniveauet af daglige rutiner, er brugen af klassiske tilgange til at beskrive indflydelsen af biomekaniske målinger ikke tilstrækkeligt til at påvise små ændringer i muskelkontrollen. Variabilitet af bevægelsesmønstre i LS har fået begrænset opmærksomhed.

Yderligere er det blevet betragtet som rent tilfældige udsving i biomekaniske målinger. Dog kan klarlægning af tidsafhængige strukturer af variabilitet fra biomekaniske målinger bruges til at få indsigt i muskelkontrollen, som kan afsløre ændringer af DG hvor ændringer i større bevægelser ikke nødvendigvis finder sted. I denne PhD bruges variabilitet til at karakterisere indflydelse af LS ved almindelige DG. Endvidere undersøges forforbindelser med kognitive faktorer for at skitsere, hvordan det kan blive afsløret i muskelkontrollen.

Indledningsvis blev lineær variation og ulineære tidsafhængige strukturer af variabilitet beskrevet og evalueret til at få indblik i afvigelser i motorisk kontrol. I de følgende studier af standardiserede DG, påvirkede sub-akut LS muskelaktiviteten i ikke-smertefulde mavemuskler, vist ved mere komplekse aktivitetsmønstre. Dette blev suppleret af nedsat funktionel konnektivitet blandt lænd- og mavemuskelpar, hvilket taler for en ændret styring af torso stabilisering. Indflydelsen af LS i den kroniske fase, viste også ændringer i muskelaktiveringsmønstre sammen med mindre komplekse bevægelser af kroppen og nedre ekstremiteter.

Undersøgelse af forbindelsen mellem biomekaniske variabler og kognitive faktorer viste en tydelig tilstedeværelse og korrelation med coping strategier i både sub-akut og kronisk LS, med maladaptiv

katastrofetænkning værende kraftigt forbundet. Dette viser en væsentlig rolle af kognition ved karakterisering af klinisk smerte, og beslægtede biomekaniske målinger. Brugen af motorvariabilitet til vurdering af LS og udforskning af kognitiv interaktion i dette projekt, kan tjene som en platform for fremtidige undersøgelser i forebyggelse og håndtering af kliniske LS.

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