Identifying Low-Back Stabilization in Low-Back Pain

and the Influence of Tactile Information

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Preface

Depending on where you live and what you do, your chances of getting low-back pain (LBP) are between 60 and 90 percent. Some cases of LBP are caused by structural failures like a collapsed disc or by trauma that damages the spine. However, the majority of LBP is diagnosed as "non-specific", a medical euphemism for problems whose causes are poorly understood. Despite decades of intense research, we remain tragically ineffective at diagnosing, preventing and treating LBP. Many experts therefore conclude that LBP is a nearly inevitable consequence of evolution's unintelligent design of the human lumbar spine, which has cursed the human lineage ever since we stood up about 6 million years ago.

But is this conclusion true? LBP is one of the most common causes of disability today. Nowadays, we have painkillers, heat pads and other largely ineffective ways to alleviate back pain, but imagine how a serious back injury would have affected a Paleolithic hunter-gatherer. Even if our ancestors simply suffered through the pain, it would probably have lessened their ability to forage, hunt, take care of their children and other tasks that affect reproductive success. Natural selection is therefore likely to have selected individuals whose backs were less susceptible to injury. This may also explain why humans today only have five lumbar vertebrae, one fewer than early hominins such as Homo erectus. Perhaps the lumbar spine is a much better adapted structure than we realize. If so, then might it be that our bodies are not well adapted to the novel ways in which we use them? Unfortunately, LBP is such a complex, multifactorial problem that intense efforts to find simple answers about why it occurs and how to prevent it have been frustratingly inconclusive. Studies designed to associate LBP with specific causal factors have mostly failed to reveal any smoking guns.

A normal, healthy back needs to have a considerable degree of flexibility, strength and endurance. However, one of the more impressive feats, something most people are not aware of or don't appreciate, is the complexity of neuromuscular control required to stabilize the spine during activities of daily life. There is quite a body of research showing that neuromuscular control of the lumbar spine is affected in patients with LBP and exercise therapy targeting neuromuscular control seems to be effective in some patients. However, our understanding of the neuromuscular control of the human spine is still very limited and the majority of patients are still out of luck. A better understanding of the neuromuscular control of the lumbar spine might be a good bet in improving diagnostics, treatment and prevention of LBP. This is where my thesis begins…

Chapter 1

Introduction

Low-back Pain

Chronic non-specific low-back pain (LBP) is a common health problem in Western society, affecting 40-60% of the adult population annually (Loney and Stratford, 1999). Of the Dutch adult population, 27% suffers from LBP at any given time (Picavet and Schouten, 2003) and about 10% suffers from chronic LBP (van den Hoogen et al., 1997). The associated medical expenditure as proportion of total medical expenditure is high and places a substantial burden on society (Dagenais et al., 2008; Martin et al., 2008). In the Netherlands, the total costs (sick leave, medical costs and disability compensation) associated with LBP are around 4 billion euros (Slobbe et al., 2006). The bulk of the costs associated with LBP are due to patients developing chronic problems (Von Korff, 1994).

The majority of patients attending to the general practitioner for LBP recovers fairly quickly without specific treatment. However, relapses are common, with 60-75% of the patients relapsing within one year (Pengel et al., 2003; van den Hoogen et al., 1997). In a relatively large minority (10%), LBP develops into a chronic problem persisting even one year after the first visit to the general practitioner (van den Hoogen et al., 1997). The primary cause of LBP remains unknown in most patients, as only 10% receives a specific diagnosis (Waddell, 1996).

Several risk factors are designated to be involved in the development of LBP. These factors vary from personal risk factors such as age, gender and body mass (Hooftman et al., 2004; Leboeuf-Yde, 2004), via psychosocial risk factors as stress and social support (Hartvigsen et al., 2004; Hoogendoorn et al., 2000), to physical risk factors related to the mechanical loading of the spine (lifting and sustained flexed or twisted spine posture)(Coenen et al., 2013; Kumar, 1990). However, evidence of a causal relationship between these risk factors and LBP is weak (Bakker et al., 2009; Van Tulder et al., 2006). Furthermore, neuromuscular control (Macedo et al., 2009; van Tulder et al., 1997), pain sensitization (Roelofs et al., 2008; Staal et al., 2009) and pain-related fear (Scascighini et al., 2008; van Tulder et al., 2001) have been identified as general prognostic factors for chronicity of LBP. Most common treatments focus on one or several of these prognostic factors and there is some evidence that exercise therapy targeting neuromuscular control is effective in treating patients with chronic non-specific LBP (Macedo et al., 2009). However, a large number of patients does not respond to treatments that target a single factor, whether it is neuromuscular control (Macedo et al., 2009), pain sensitization (Roelofs et al., 2008; Staal et al., 2009) or pain-related fear (Scascighini et al., 2008; van Tulder et al., 2001). This limited treatment success is

often attributed to lacking diagnostic possibilities to determine individual treatment targets (Scascighini et al., 2008; van Tulder et al., 2000; van Tulder et al., 2001).

Neuromuscular control is often targeted in conservative therapy for LBP and there seems to be some evidence for its treatment success (Macedo et al., 2009). However, the effect size remains small. Furthermore, the changes in trunk muscle control that have been shown to occur with LBP (Cholewicki et al., 2005; MacDonald et al., 2009; van Dieen et al., 2003b) are diverse and complex, with evidence of both increased and decreased excitability, depending on the individual, the muscle and the circumstances (Hodges and Moseley, 2003; van Dieen et al., 2003b). These changes in neuromuscular control may cause pain and pain recurrence, due to tonic muscle activity (Roland, 1986) or by negatively affecting spinal stability (Hodges and Moseley, 2003; MacDonald et al., 2009). On the other hand, changes in neuromuscular control might also be protective against pain and re-injury by stabilizing the spine (van Dieen et al., 2003a) and limiting range of motion and velocity of movement (Lund et al., 1991). All in all, sub-populations of LBP patients may show different and opposite changes in neuromuscular control, possibly unrelated to the initial cause, that suggests there might be clinically relevant sub-groups (Dankaerts et al., 2006).

Low-back Stabilization

In order to get insight into the complex neuromuscular control of the low-back, static postural stabilization might be a good starting point, as one might argue that this is a prerequisite for control during more dynamic tasks (such as lifting, walking, reaching). Low-back stabilization involves a complex biomechanical system that counteracts the downward pull of gravity on the large mass of the upper body while it balances on top of the lumbar vertebrae which, in turn, balance on the sacrum. The human spine is not structurally stable and without musculature it would buckle under the weight of the upper body during upright posture (Bergmark, 1989; Crisco and Panjabi, 1991; Franklin and Granata, 2007). To prevent the spine from buckling, sufficient spinal stiffness is a necessity and can be provided by intrinsic components, comprising passive tissues (ligaments, vertebrae, fascia), agonist-antagonist muscle co-contraction and reflexive components (muscle activation initiated by feedback from one or multiple sensory organs). As increasing spinal stiffness by utilizing only one component has drawbacks (continuous muscle co-contraction is energetically costly; reflexes may

lead to instability due to the presence of time-delays), it is generally thought that intrinsic and reflexive components work together in low-back stabilization. However, whether this actually occurs and how these components interact with each other is still unknown.

Sensory Information

The reflex contribution to trunk stabilization depends on the presence of adequate sensory feedback in the form of proprioceptive feedback from muscle spindles and Golgi tendon organs (GTOs), vestibular feedback, visual feedback and, as discovered recently, tactile feedback. How tactile feedback affects the control of trunk posture will be the primary topic of the second part of this thesis, and will not be considered in the first part.

Proprioceptive Feedback

Proprioceptive reflexes are generated by the combined feedback from muscle spindles (information of muscle lengthening and lengthening velocity) and GTOs (information on muscle force). Both contribute to the muscular response to trunk posture and movement (Figure 1).

Vestibular Feedback

Vestibular reflexes are generated by feedback from the two vestibular organs, located in each inner ear in the head. Specialized components of the organs provide information on the tilt, angular velocity and acceleration of the head. The vestibular organs provide information on the location and movement of the trunk (Figure 1) as well as head movement relative to the trunk.

Visual Feedback

Visual reflexes are generated by feedback from the eyes that register the location and velocity of the head and trunk in space (Figure 1).

Actuators

There are many muscles located in the lumbar region, often classified in relation to their specific function and/or location. The total number of muscles considerably exceeds the number of muscles needed to maintain static equilibrium. This enables stability in an arbitrary choice of posture while the nervous system can independently distribute the load across the different muscles. However, little is known about how this is achieved, a fact that hampers our ability to model and simulate spinal stability in detail. A useful point of view, described by Bergmark (1989), is to make a distinction between a local and a

global system of muscles. The local system consists of deep muscles that lie close to the spine, and have their insertion and origin (or both) at lumbar vertebrae whereas the global system consists of superficial muscles with their insertion and origin on the pelvis and thoracic cage. Due to the small moment arms and limited number of vertebrae spanned, the local system is thought to be primarily involved in stabilization of the vertebrae relative to each other and appears to be essentially independent of the external load on the body. In contrast, the global system has large moment arms, spans the entire lumbar spine and is therefore better equipped for stabilization of the trunk relative to the pelvis, a central topic of this thesis.

Controller

Sensory information is integrated and used to generate muscle activation patterns to stabilize the trunk by the nervous system or, in system identification terms, the controller. To circumvent the incredible complexity of the controller, the approach applied throughout this thesis views the controller largely as a "black box".
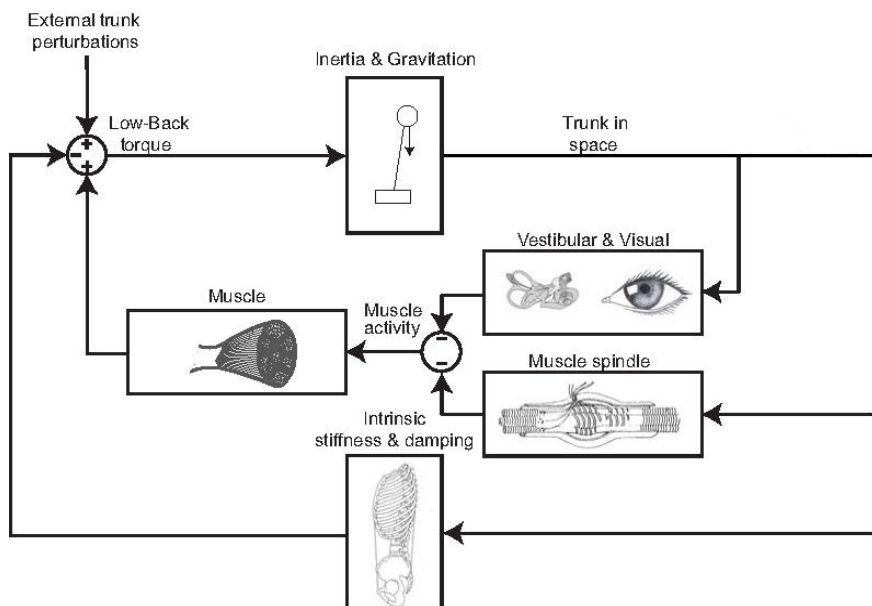
Figure 1:
The low-back stabilization model as used in this thesis. The lumbar spine is described as an inverted pendulum. The upper body mass is subjected to inertial forces, gravitation and low-back torques resulting in trunk movement. The upper body mass is stabilized using intrinsic stiffness and damping and reflexive behavior. Reflexes include muscle spindle reflexes and the vestibular and visual feedback. The reflexive information is sent to the muscles, generating low-back torques and therefore closing the loop.

NeuroSIPE – project QDISC

NeuroSIPE (Neurophysiological System Identification and Parameter Estimation) is a consortium of Dutch medical universities, technical universities and industrial companies with the aim to develop and apply diagnostic tools for diverse neurological disorders using system identification and parameter estimation (SIPE) techniques. Within the NeuroSIPE consortium, project QDISC (Quantitative Diagnosis of Impaired of Spine Control) is a collaboration between the VU University Amsterdam, VU University Medical Center Amsterdam, Delft University of Technology, along with Motek Medical, TMSi, McRoberts, and MOOG as industrial partners and the Military Rehabilitation Center Aardenburg, Rehabilitation Center Heliomare and Rehabilitation Center Amsterdam (Reade) as collaborating rehabilitation centers. The QDISC project aims to quantitatively assess the neuromuscular control of the trunk in patients with chronic non-specific low-back pain.

Problem Definition & Research Questions

At present, analysis of neuromuscular control impairments in LBP patients and the underlying causes is hampered by lack of an objective and reliable methodology. Furthermore, how different tasks and conditions influence the low-back neuromuscular control strategy is not well understood. Improving our understanding of low-back stabilization in healthy individuals and studying the differences between healthy subjects and LBP patients may, after a reliable methodology has been established, contribute to improved diagnostics and better treatment for those with chronic non-specific low-back pain.

The aim of this thesis is to advance the understanding of the neuromuscular control in low-back stabilization and to gain insight into the interaction between low-back stabilization and low-back pain. To achieve this goal, three main research questions were formulated:

1. Can the intrinsic and reflexive contributions to low-back stabilization be determined reliably?
2. How does low-back stabilization modulate between different conditions and task instructions?
3. How does low-back stabilization differ between healthy subjects and LBP patients?

Since the experimental methods applied throughout this thesis (see paragraph below) imply that the subject is in contact with an external object (the pushing-rod applying the external perturbation), the second part of this thesis will deal with the following research questions:

1. Does tactile information on the back interact with sensory feedback from other sources (i.e. does it lead to sensory reweighting)?
2. Does sensory reweighting occur with a moving source of tactile information?
3. Does tactile information interact with sensory feedback even when the source of tactile information is moving in an unpredictable manner?

To answer these questions, new experimental protocols had to be developed.

Research Methods

System Identification of Low-back Stabilization

System identification techniques are commonly used to investigate postural control of e.g. the neck (Guitton et al., 1986; Forbes et al., 2013), arm (van der Helm et al., 2002; de Vlugt et al., 2006; Schouten et al., 2008), leg (Hunter and Kearney, 1982; Kearney et al., 1997; Abbink et al., 2004; Mugge et al., 2007) and also the low-back (Goodworth and Peterka, 2009). The purpose of these techniques is to obtain a model of the system under study by analyzing the dynamic relationship between an input signal (position, force) and output signal (force, position, electromyography). Frequency response functions (FRFs) describe the magnitude (gain) and timing (phase) of the output signal with respect to the input signal and provide a linear approximation of the system dynamics in the frequency domain.

Due to the presence of sensory feedback, the human neuromuscular control system is inherently closed-loop. This poses a challenge, as it is impossible to determine the origin of a signal. For example, a movement could be initiated voluntarily or be the result of a reflexive response. To overcome this challenge, an external perturbation (providing a known independent origin) is used to estimate the human dynamics and reflexive pathways (Figure 1). This method (joint input-output approach, van der Kooij et al. (2005)) is used throughout this thesis to determine low-back stabilization.

External perturbations can be classified as transient or continuous. Transient perturbations can be used to determine the state of the system at the onset of the perturbation. However, the repetitive and often predictable nature of these perturbations may lead the response to be confounded by voluntary activation. Continuous signals, on the other hand, can be designed to be unpredictable, which minimizes voluntary activation and isolates the reflexes. The applied system identification techniques assume the system to be linear, while in actuality the human neuromuscular control system is highly nonlinear. This necessitates the perturbation to result in small deviations around an equilibrium point to minimize nonlinear contributions, which can easily be achieved with continuous perturbations. Finally, continuous perturbations can have power at selected frequencies (i.e. a multi-sine) which, with respect to transient perturbations or continuous perturbations containing all frequencies, allows for higher power at the selected frequencies resulting in a better signal to noise ratio. Throughout this thesis, a multi-sine was used exclusively as external perturbation.

Physiological Modeling of Low-back Stabilization

To further the understanding from the experimental data, a model approach was used to translate the system identification results into more intuitive measures. Since the primary focus of this thesis is on overall low-back stabilization, a rather simple mechanical model describing an inverted pendulum in combination with a lumped reflexive component was used in order to avoid unnecessary model complexity.

Sensory Manipulations

The second part of this thesis investigates the interaction between tactile information and other sensory sources. To this end, different sources of sensory information were manipulated, to detect changes in the relative contribution of those sources to the control of trunk posture.

Proprioceptive Manipulation

Muscle vibration is an experimental technique that is often used to manipulate the afferent information from muscle spindles (Brumagne et al., 1999; Claeys et al., 2011). A vibrator attached over the muscle belly vibrates either constantly or intermittently at a fixed frequency. The vibration results mainly in activation of Ia-afferents, which causes illusions of lengthening and reflex and voluntary responses to counteract the perceived motion (Goodwin et al., 1972; Roll et al., 1989).

Vestibular Manipulation

Galvanic vestibular stimulation (GVS) is a non-invasive experimental technique that is commonly used to probe the vestibular function. An electric current is applied via electrodes placed over the mastoid processes behind each ear. The applied current results in changes (increased or decreased depending on the pole of the electrode) in the firing rate of the vestibular nerve (Goldberg et al. 1984). The modulation of the afferent firing rate caused by the stimulus induces an artificial sense of motion. This perceived motion is accompanied by compensatory muscular responses and whole-body postural adjustments (Nashner and Wolfson, 1974; Britton et al., 1993; Fitzpatrick and Day, 2004).

Visual Manipulation

There are multiple ways in which visual information can be manipulated but simply closing the eyes is the most straightforward and easy way and was therefore used throughout this thesis.

Aims and Outline of this thesis

All chapters, with the exception of **Chapter 1** (Introduction) and **Chapter 10** (Epilogue), are considered to be autonomous and individually readable, since the contents have been written as journal articles.

In part one of this thesis, the first chapters (2-5) establish a reliable methodology for studying low-back stabilization in healthy subjects. The aim of **Chapter 2** is to systematically review the literature on methods for assessment on trunk stabilization. **Chapter 3** aims to identify low-back stabilization using system identification techniques and to quantify the contribution of co-contraction and reflexes. **Chapter 4** determines the test-retest reliability of the methods developed in Chapter 3. **Chapter 5** uses the experimental methods to investigate the role of posture and vision in low-back stabilization.

In Chapter 6, the methods developed in chapters 2-5 will be applied to a group of LBP patients. The aim of **Chapter 6** is to compare the low-back neuromuscular control of LBP patients to healthy subjects and to identify sub-groups of patients with an unique pattern of motor control deviations relative to the healthy participants.

In the second part of this thesis (Chapters 7-9), the central topic is the influence of tactile information on trunk control. In **Chapter 7**, the aim is to investigate

whether tactile information on the back influences the sensory feedback from other sources (i.e. leads to sensory reweighting). In **Chapter 8**, the aim of Chapter 7 is extended to include a moving source of tactile information. Finally, the aim of **Chapter 9** is to investigate whether an unpredictably moving source of tactile information influences the contribution of other sensory feedback.

Chapter 1

Chapter 2

Methods for assessment of trunk stabilization: a systematic review

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Abstract

Trunk stabilization is achieved differently in patients with low back pain compared to healthy controls. Many methods exist to assess trunk stabilization but not all measure the contributions of co-contraction and reflexes simultaneously. This may pose a threat to the quality/validity of the study and might lead to misinterpretation of the results. The aim of this study was to provide a critical review of previously published methods for studying trunk stabilization in relation to LBP. We primarily aimed to assess their construct validity to which end we defined a theoretical framework operationalized in a set of methodological criteria which would allow to identify the contributions of co-contraction and reflexes simultaneously. In addition, the clinimetric properties of the methods were evaluated. 133 articles were included from which four main categories of methods were defined; upper limb (un)loading, moving platform, unloading and loading. 50 of the 133 selected articles complied with all the criteria of the theoretical framework, but only four articles provided information about reliability and/or measurement error of methods to assess trunk stabilization with test-retest reliability ranging from poor (ICC 0) to moderate (ICC 0.72) . In conclusion, there is a need for standardization and clinimetric evaluation to contribute to a higher quality of research and enable better comparisons to be made between studies.

Introduction

Trunk stabilization can be defined as maintaining control over trunk posture and movement, in spite of the disturbing effects of gravity and external and internal perturbations. Trunk stabilization is dependent on the passive (osteoligamentous), active (muscular) and neural sub-systems that contribute mechanically and in terms of acquiring and processing information to guide mechanical responses (Cholewicki and McGill, 1996). Stabilization of the trunk is required to control trunk movement during daily activities like standing, sitting, walking (MacKinnon and Winter, 1993; van der Burg et al., 2005), and can be limiting in performing precise arm and hand functions (Kaminski et al., 1995; Pigeon et al., 2000). Importantly, it has been hypothesized that inadequate trunk stabilization could contribute to low-back pain (LBP) through high tissue strains and/or impingements (Panjabi, 1992a; Panjabi, 1992b).

Trunk stabilization is achieved differently in patients with low back pain (LBP) compared to healthy controls. These differences in trunk control have been interpreted as cause of the persistence of LBP (Hodges et al., 2009; MacDonald et al., 2010), and were even shown to be prospectively associated to LBP incidence (Cholewicki et al., 2005). Specifically, several studies have indicated longer reflex delays after an external mechanical perturbation of trunk posture in LBP patients than in controls (Magnusson et al., 1996; Radebold et al., 2000). In apparent contrast, higher trunk stiffness, i.e. a higher mechanical resistance to such perturbations has also been reported (Hodges et al., 2009). The latter is probably explained by findings of increased co-contraction of trunk musculature in patients compared to controls (van Dieën et al., 2003). This has been interpreted as an adaptive response to enhance control over trunk movement and therewith prevent pain (Lund et al., 1991; van Dieën et al., 2003). In fact, increased trunk stiffness through co-contraction could explain the longer delays found. With increased stiffness, the same mechanical disturbance will cause a smaller and slower deviation of trunk posture. Consequently, the disturbance would be perceived later and cause a slower and smaller increase in excitatory drive of the trunk musculature, resulting in an apparent increase in reflex delays. So paradoxically, the finding of an increased delay could actually reflect a functional, adaptive response to enhance trunk stability.

The above indicates that the contributions of co-contraction (intrinsic stiffness) and reflexes to trunk stabilization need to be assessed jointly. This is possible using system identification techniques, which apply some form of external (often

mechanical) perturbation and measure responses such as the trunk kinematics and trunk muscle EMG, from which properties of the stabilizing system, such as the intrinsic stiffness and reflex delays are estimated. Many different methods using such an approach have been reported. However, not all of these appear equally suitable. For example, not all take into account the intrinsic and reflexive contributions simultaneously. Furthermore, setups in some studies allow movement corrections in multiple joints (e.g. ankle, knee and hip), due to which experimental effects or between-group differences cannot be ascribed solely to the trunk.

To support interpretation of previous literature and to optimize methods for studying trunk stabilization in relation to LBP, we aimed to provide a critical review of previously published methods. We primarily aimed to assess their construct validity, to which end we defined a theoretical framework operationalized in a set of methodological criteria. This theoretical framework comprised the two criteria as introduced above as well as the criteria based on the requirement to allow for linear system identification, since a wide range of well-established techniques is available for this. The criteria are further detailed in the methods section. In addition, the clinimetric properties of the methods were evaluated, to assess their potential value in a clinical setting.

Methods

Theoretical framework

To evaluate the methods found in the literature, a theoretical framework was defined. In the introduction, two major criteria were already introduced: 1) the necessity of being able to jointly assess intrinsic and reflexive contributions to trunk stabilization and 2) the necessity to study the trunk in isolation.

To be able to assess the intrinsic and reflexive contributions to trunk control jointly through linear identification techniques, the method has to meet the following criteria:

Unpredictable Disturbances must be unpredictable, since the presence of feedforward control to an expected perturbation renders it impossible to quantify reflexive and intrinsic components. System identification techniques assume a closed loop between the output forces and movements and the control input, e.g. the movement occurring upon perturbation of a static posture is assumed to be the basis for reflex inputs. When voluntary movements through feedforward control occur, this obviously would lead to a misinterpretation. To prevent feedforward control, an unpredictable perturbation should be used.

Known Disturbance To allow for system identification, the disturbance should be known (in terms of amplitude and timing). It is important to note that the disturbance is defined as the external input, which should be distinguished from the contact force between a device applying a perturbation and the subject, as this results from an interaction between device and subject.

Perturbation Type To permit the use of linear identification techniques, the disturbance should result in small fluctuations around a fixed working point, i.e. it should not entail large force differences and should not result in a large trunk displacements. To obtain sufficiently reliable information in spite of the limited trunk displacement and hence low signal to noise ratio, repeated perturbations are necessary. The perturbation should, therefore, not be a single impulse or step perturbation but preferably a multisine, repeated impulse or pseudo-random binary signal.

Force Control When perturbations are applied directly to the trunk, a force controlled perturbation instead of a displacement controlled perturbation should be used. With a fixed trunk

displacement relative to the pelvis, the subject is unable to exert any influence over the resulting perturbation. Therefore, the subject will not be motivated to perform and it has been observed that subjects reduce their efforts to counteract position controlled perturbations already after several seconds (de Vlugt et al., 2003a; de Vlugt et al., 2003b).

The following criteria should be met to study the trunk in isolation:

Pelvic restraint   The pelvis of the subject should be restrained, forcing motion at the level of the spine, i.e. this assures that motion does not occur solely at the level of the pelvis.

Point of application   The application of the perturbation should occur at the trunk or at the pelvis.

These criteria will be used to assess the construct validity of the methods found in the literature.

Literature identification

To identify relevant literature, we conducted a comprehensive search in PubMed and Embase from the beginning of the database up to September 2014. To be inclusive, we used a broad search as outlined in Appendix 1. Only articles written in Dutch, German or English were included. Animal and cadaveric studies were excluded. No restrictions were applied to study design. Additionally, a snowball technique was applied by scanning the reference sections of all selected articles for potentially relevant articles that were not retrieved in the original search.

Study selection

Eligibility of studies was determined independently by two researchers. First, the studies were selected on the basis of title and abstract. If uncertainty remained, the full text was reviewed. When discrepancies occurred between reviewers, the justifications for inclusion or exclusion of these articles was discussed until

consensus was reached. The publications were included according to the following criteria: 1) trunk stabilization was studied; 2) external mechanical perturbations were applied; 3) measurements included trunk kinematics and/or trunk muscle EMG.

Data extraction and assessment of methodological quality

The following data were extracted from the included articles: author, year of publication, and perturbation technique. The construct validity of the methods was assessed independently by the two researchers with use of the theoretical framework as described above. When discrepancies occurred between reviewers, the justification for scoring on the set of methodological criteria was discussed until consensus was reached.

If the objective of an included article comprised clinimetric assessment of reliability and/or measurement error of methods to assess trunk stabilization, the methodological quality of the study was assessed by the 2 reviewers using box B and C of an adapted version of the the COnsensus-based Standards for the selection of Health Measurement INstruments (COSMIN checklist (Terwee et al., 2012), see appendix 3).

Results

Results of the search

A total of 133 articles were included (see Fig. 1 for a flowchart of the search and selection procedure).
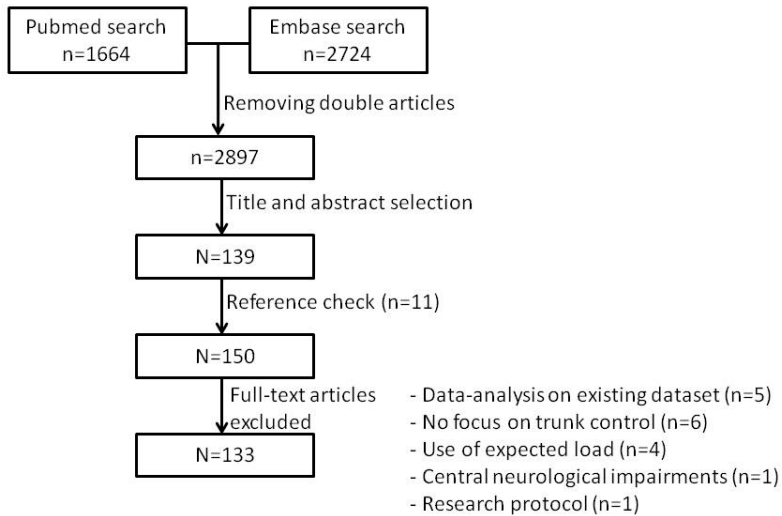
Figure 1:
Flowchart of the search strategy.

Categorization

Four main categories of perturbation methods were distinguished from the included articles; trunk loading, trunk unloading, moving platform and upper limb (un-)loading (see table 1). Loading perturbations involve pushes or pulls applied at the upper back, thorax or pelvis. Unloading perturbation methods use a horizontal force applied to the subject's thorax, upper back or pelvis by a cable from which a load is suspended and unexpectedly released. Alternatively, the subject applies a force, often controlled through visual feedback, on a cable that is unexpectedly released. During moving platform perturbations, subjects sit or stand on a platform, which is translated or tilted. Finally, in the upper limb (un)loading experiments the subjects stand while holding an empty receptacle in which a load is dropped. In some studies, the arms of the subjects are attached to a wire with a load on the other end which is suddenly dropped, resulting in a sudden force. In one setup, subjects hold a weighted box, which is suddenly pulled upward by a cable. In another setup, subjects hold a balloon attached to a load; popping the balloon results in sudden unloading.

Table 1: Overview of studies included with assessment of validity based on the criteria listed in the methods section. An X denotes that the study complies with the accompanying methodological criterion.

Author (year)	Unpredictable	Known disturbance	Perturbation Type	Force control	Pelvic restraint	Point of application
Trunk loading						
Andersen et al. (2004)	X	X	Step	X	X	X
Bazrgari et al. (2011a)	X	X	Impulse	-	X	X
Bazrgari et al. (2011b)	X	X	Impulse	-	X	X
Bazrgari et al. (2012)	X	X	Impulse	-	X	X
Bazrgari et al. (2009)	X	X	Step	X	X	X
Borghuis et al. (2011)	X	X	Impulse	X	-	X
Carlson et al. (1981)	X	-	Step	X	-	X
Chiang and Potvin (2001)	X	X	Step	X	X	X
Cresswell et al. (1994)	X	X	Step	X	-	X
van Drunen et al. (2013)	X	X	Multi-sine	X	X	X
Dupeyron et al. (2010)	X	X	Impulse	X	X	X
Eriksson Crommert and Thorstensson (2009)	X	-	Step	X	X	X
Essendrop et al. (2002)	X	X	Step	X	X	X
Gardner-Morse and Stokes (2001)	X	X	Single sine wave	X	X	X
Gilles et al. (1999)	X	X	Step	X	-	X
Granata et al. (2005)	X	X	Multi-sine	X	X	X
Granata et al. (2004a)	X	X	Impulse	X	X	X
Granata et al. (2004b)	X	-	Step	X	-	X
Hendershot et al. (2013)	X	X	Pseudorandom binary step	-	X	X
Hendershot et al. (2011)	X	X	Pseudorandom binary step	-	X	X
Herrmann et al. (2006)	X	-	Impulse	X	-	X
Hjortskov et al. (2005)	X	X	Step	X	X	X
Hodges et al. (2009)	X	X	Step	X	X	X

Kim et al. (2013a)	X	X	Step	X	X	X
Krajcarski et al. (1999)	X	X	Step	X	X	X
Lariviere et al. (2010)	X	X	Step	X	X	X
Lawrence et al. (2005)	X	X	Step	X	X	X
Lee et al. (2006)	X	X	Pseudorandom binary step	X	X	X
Magnusson et al. (1996)	X	X	Step	X	X	X
Masani et al. (2009)	X	-	"Impulse", manually applied	X	-	X
McGill et al. (1989)	X	-	"Impulse", manually applied	X	-	X
McMulkin et al. (1998)	X	X	Step	X	-	X
Miller et al. (2013)	X	X	Pseudorandom binary step	-	X	X
Miller et al. (2010)	X	X	Impulse	X	X	X
Moorhouse and Granata (2005)	X	X	Multi-sine	X	X	X
Moorhouse and Granata (2007)	X	X	Step	-	X	X
Navalgund et al. (2013)	X	X	Step	X	X	X
Omino and Hayashi (1992)	X	-	Step	X	-	X
Parcero (2000)	X	X	Step	X	X	X
Pedersen et al. (2004)	X	X	Step	X	X	X
Pedersen et al. (2007)	X	X	Step	X	X	X
Pedersen et al. (2009)	X	X	Step	X	X	X
Rietdyk et al. (1999)	X	-	"Impulse", manually applied	X	-	X
Rogers and Granata (2006)	X	X	Multi-sine	X	X	X
Santos et al. (2011)	X	X	Step	X	X	X
Skotte et al. (2004)	X	X	Step	X	X	X
Stokes et al. (2006)	X	X	Single sine wave	X	X	X
Stokes et al. (2000)	X	X	Single sine wave	X	X	X
Thomas et al.	X	-	Step	X	X	X

(1998)						
Thomas et al. (1999)	X	-	Step	X	X	X
Thrasher et al. (2010)	X	X	"Impulse", manually applied	X	-	X
Vera-Garcia et al. (2006)	X	X	Step	X	X	X
Vera-Garcia et al. (2007)	X	X	Step	X	X	X
Vette et al. (2014)	X	X	Impulse	X	-	X
Wilder et al. (1996)	X	X	Step	X	X	X
Trunk unloading						
Brown and McGill (2009)	X	-	Step	X	X	X
Brown et al. (2006)	X	X	Step	X	X	X
Carlson et al. (1981)	X	-	Step	X	-	X
Cholewicki et al. (2002)	X	X	Step	X	X	X
Cholewicki et al. (1999)	X	X	Step	X	X	X
Cholewicki et al. (2010a)	X	X	Step	X	X	X
Cholewicki et al. (2010b)	X	X	Step	X	X	X
Cholewicki et al. (2005)	X	X	Step	X	X	X
Cholewicki et al. (2000)	X	X	Step	X	X	X
Eriksson Crommert and Thorstensson (2008)	X	X	Step	X	X	X
Kim et al. (2013b)	X	X	Step	X	X	X
Magnusson et al. (1996)	X	-	Step	X	X	X
Marshall et al. (2009)	X	X	Step	X	X	X
Radebold et al. (2000)	X	X	Step	X	X	X
Radebold et al. (2001)	X	X	Step	X	X	X
Reeves et al. (2005)	X	X	Step	X	X	X
Reeves et al. (2009)	X	-	Step	X	X	X
Moving platform						
Blomqvist et al. (2014)	X	X	Step	X	-	-
Boudreau et al. (2011)	X	X	Impulse	X	-	-

Carpenter et al. (1999)	X	X	Step	X	-	-
Carpenter et al. (2005)	X	X	Impulse	X	-	-
Chen et al. (2014)	X	X	Step	X	-	-
Cort et al. (2013)	X	X	Step	X	X	X
Cote et al. (2009)	X	X	Impulse	X	X	X
Diener et al. (1988)	X	X	Impulse	X	-	-
Dobosiewicz (1997)	X	X	Step	X	-	-
Farahpour et al. (2014)	X	X	Step	X	-	-
Forssberg and Hirschfeld (1994)	X	X	Step	X	-	X
Goodworth and Peterka (2009)	X	X	Pseudorandom ternary step	X	X	X
Goodworth and Peterka (2010)	X	X	Pseudorandom ternary step	X	X	X
Gruneberg et al. (2004)	X	X	Step	X	-	-
Henry et al. (1998)	X	X	Impulse	X	-	-
Henry et al. (2006)	X	X	Impulse	X	-	-
Horak et al. (1989)	X	X	Impulse	X	-	-
Horak and Nashner (1986)	X	X	Impulse	X	-	-
Horak et al. (1990)	X	X	Impulse	X	-	-
Huang et al. (2001)	X	X	Impulse	X	-	-
Inglis et al. (1994)	X	X	Impulse	X	-	-
Jacobs et al. (2011)	X	X	Impulse	X	-	-
Jones et al. (2012)	X	X	Impulse	X	-	-
Kamper et al. (1999)	X	X	Step	X	-	X
Keshner et al. (2004)	X	X	Impulse	X	-	-
Keshner et al. (1988)	X	X	Impulse	X	-	-
Mok and Hodges (2013)	X	X	Step	X	-	-
Newcomer et al. (2002)	X	X	Impulse	X	-	-

Notzel et al. (2011)	X	X	Impulse	X	-	-
Oddsson et al. (1999)	X	X	Impulse	X	-	-
Parnianpour et al. (2001)	X	X	Impulse	X	-	-
Perret and Robert (2004)	X	X	Step	X	-	-
Preuss and Fung (2008)	X	X	Impulse	X	X	X
Sayenko et al. (2012)	X	X	Step	X	-	-
Zedka et al. (1998)	X	-	Step	X	X	X
Upper limb (un)loading						
Aruin and Latash (1995)	X	X	Step	X	-	-
Brown et al. (2003)	X	-	Step	X	-	-
Dupeyron et al. (2013)	X	-	Step	X	-	-
Gregory et al. (2008)	X	-	Step	X	-	-
Grondin and Potvin (2009)	X	-	Step	X	-	-
Hodges et al. (2001)	X	-	Step	X	-	-
Hwang et al. (2008)	X	-	Step	X	-	-
Lavender and Marras (1995)	X	-	Step	X	-	-
Lavender et al. (1993)	X	-	Step	X	-	-
Lavender et al. (1989)	X	-	Step	X	-	-
Lavender et al. (2000)	X	X	Step	X	-	-
Lee et al. (2011)	X	-	Step	X	-	-
Leinonen et al. (2002)	X	-	Step	X	-	-
Leinonen et al. (2003)	X	-	Step	X	-	-
MacDonald et al. (2010)	X	-	Step	X	-	-
Mannion et al. (2000)	X	-	Step	X	-	-
Marras et al. (1987)	X	X	Step	X	-	-
Mawston et al. (2007)	X	-	Step	X	-	-
McGill et al. (1989)	X	-	Impulse, manually applied	X	-	-
McMulkin et al. (1998)	X	X	Step	X	-	-

Mok et al. (2011)	X	-	Step	X	-	-
Moseley et al. (2003)	X	X	Step	X	-	-
Mullington et al. (2009)	X	X	Step	X	-	-
Ramprasad et al. (2011)	X	-	Step	X	-	-
Ramprasad et al. (2010)	X	-	Step	X	-	-
Shu et al. (2007)	X	-	Step	X	-	-
Sung and Park (2009)	X	X	Impulse	X	-	-
Sung et al. (2004)	X	X	Impulse	X	-	-
Voglar and Sarabon (2014)	X	X	Step	X	-	-
Wagner et al. (2005)	X	X	Step	X	-	-
Wilder et al. (1996)	X	-	Step	X	-	-

Fifty of the 133 included articles described a method that complied with all methodological criteria (see table 1). All methods complied with the "unpredictable" criterion. In all but 7 studies, force control was used. None of the upper limb (un)loading articles met with the "pelvic restraint" and "point of application" criteria.

Trunk loading perturbations
Among the 55 articles describing trunk loading perturbations, 32 complied with all criteria (see table 1). Ten articles did not comply with the "known disturbance" criterion, predominantly due to unknown onset of perturbation (i.e. timing). All but seven articles complied with the "force control" criterion. In 13 articles, the pelvis was not restrained. And all articles complied with the "point of application" criterion. Four types of perturbations were applied: in 14 studies, an impulse was applied, in 30 a step, in four a pseudorandom binary step, in three a single sine wave and in four a multi-sine.

Trunk unloading perturbations
Of the 17 articles describing trunk unloading perturbations, 13 complied with all criteria (see table 1). Four articles failed to comply with the "known disturbance" criterion while one did not restrain the pelvis. All studies applied step perturbations.

Moving platform perturbations

Five out of 35 articles describing moving platform perturbations complied with all criteria (see table 1). In one study, the timing of the disturbance was not known due to manual application of the perturbation. In only six articles, the pelvis was restrained. In 27 articles subjects stood on the platform and therefore these did not comply with the "point of application" criterion. Two types of perturbations were applied: in 15 articles a platform translation was applied, which equals a force impulse on the subject, while in the remaining 20, platform rotations/tilts were performed, which equals a step perturbation .

Upper limb (un)loading

Because all perturbations in this category were applied to the upper limbs, none of the 31 articles complied with the "point of application" criterion (see table 1). Furthermore, none of the methods described used a pelvic restraint. For 21 articles, the perturbation was unknown due to an unknown timing. Three studies applied impulse perturbations while the others applied step perturbations.

Clinimetric assessment

Reliability was tested in three of the included studies (Hodges et al., 2009; Santos et al., 2011; Voglar and Sarabon, 2014) and one study which used data from 2 previously published studies (Hendershot et al., 2012). Measurement error was tested in three studies (Hendershot et al., 2012; Santos et al., 2011; Voglar and Sarabon, 2014). Hendershot et al., (2012) described a sudden-loading task with standing subjects, who wore a wooden or plastic harness attached to a servo-motor, which applied pseudorandom binary anterior-posterior position perturbations. Within-day reliability, between-day reliability and measurement error were calculated for both harnesses. For both the wooden and plastic harness, the within-day reliability of trunk stiffness (0.84 and 0.90 respectively) and effective mass (0.91 and 0.95 respectively) were good (Portney and Watkins, 2000). Reflex gain (0.55 and 0.85), maximum reflex force (0.65 and 0.85) and timing of maximum reflex force (0.84 and 0.86) were found less reliable and within-day reliability was found superior to between-day reliability (mean ICC 0.42, range [0.19-0.72]). The plastic harness also seemed consistently more reliable than the wooden version.

In the study by Santos et al. (2010), subjects were seated with their pelvis restrained. A sudden load was applied via a cable connected to a load cell and attached to a harness worn by the subjects. Three different ways of analyzing the

reflex latencies and amplitudes were used. Reliability of the method was poor to moderate (ICC 0-0.62).

Hodges et al. (2009) applied sudden loading in a semi-seated position via a cable attached to a thorax harness. Reliability was assessed in 10 subjects. For forward perturbations, the ICC's for stiffness, damping and mass were moderate at 0.67 (range [0.12-0.91]), 0.72 (range [0.20-0.92]) and 0.67 (range [0.12-0.91]) respectively. For backward perturbations, the ICC's for stiffness, damping and mass were poor to moderate at 0.60 (range [0.00-0.88]), 0.57 (range [-0.43-0.87]) and 0.31 (range [-0.36-0.77]) respectively.

In Voglar et al. (2014), postural reflex delays to unexpected loading and unloading of the arms were assessed in a standing unrestrained position. The response of five trunk muscles was evaluated, for which a good intra-session (ICC = 0.79, range [0.56-0.96]) and moderate (ICC = 0.64, range [0.43-0.84]) inter-session reliability were reached.

The methodological quality of these four articles was assessed with use of Box B and C of the COSMIN checklist (Appendix 3). Hendershot et al., (2011) scored 'good', Santos et al., (2010) ´fair´ and Voglar et al., (2014) "poor" on both methodological qualities (see table 2 for the results). Hodges et al., (2009) scored "poor" on reliability.

Table 2: Scores of the COSMIN-criteria. E = Excellent, G = Good, F = Fair, P = Poor. For a further explanation of the different criteria of the COSMIN-list, see appendix 2.

Reliability Critera	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10	B11	B12	B13	B14	Total
Hendershot et al., (2012)	G	G	G	E	E	E	G	E	E	E	G	-	-	-	*G*
Santos et al., (2010)	G	G	F	E	E	E	G	E	E	E	G	-	-	-	*F*
Hodges et al., (2009)	G	G	P	E	E	E	G	E	E	E	G	-	-	-	*P*
Voglar et al., (2014)	G	G	P	E	E	E	G	E	E	E	G	-	-	-	*P*
Measurement Error Criteria	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11				Total
Hendershot et al., (2012)	G	G	G	E	E	E	G	E	E	E	E				*G*
Santos et al., (2010)	G	G	F	E	E	E	G	E	E	E	E				*F*
Voglar et al., (2014)	G	G	P	E	E	E	G	E	E	E	E				*P*

Discussion

The aim of the present study was to provide a critical review of previously published methods for studying trunk stabilization in relation to LBP. Many different methods exist but many fail to comply with all the criteria of the theoretical framework as formulated in the methods section. The identified methods were categorized into four categories: upper limb (un)loading, moving platform, unloading and loading. Most methods that complied with all the criteria of the theoretical framework were found in the loading and unloading categories. Only a few articles from the moving platform category and none of the upper limb (un) loading complied with all the criteria.

One of the major problems with upper limb (un)loading is the point of application. When the perturbation is delivered through the hands/arms, the true extent of the perturbation to the trunk (i.e. timing and amplitude) is unknown. Therefore, studying trunk stabilization through upper limb (un)loading is not the most appropriate method.

Applying the perturbation by a moving/tilting platform is only suitable if the pelvis of the subject is restrained in either a seated or a standing position. However, applying the perturbation in a standing position has some drawbacks. For example, Goodworth & Peterka (2009) applied perturbations to standing subjects through a sideways tilting platform, but had to discard a large part of their measurements, due to the inability of many subjects to keep their knees locked. Bending of the knee(s) made the extent of the perturbation to the trunk due to the moving platform unknown.

Many of the methods applying trunk unloading perturbations complied with all the methodological criteria. However, the use of a step perturbation is inherent to unloading and has two potential drawbacks. First, to reach the desired level of reliability, either many trials or high levels of pre-load (% MVC) are required. The combination of many trials and high pre-loads might not be feasible, especially not in LBP patients, who might not be able to produce many repetitions with high force levels without pain. The second potential drawback of step perturbations is the difficulty in making the perturbations truly unpredictable. Unloading often occurs within a certain time period after reaching a desired level of pre-load. However, if this time period is short, subjects are still able to anticipate on the perturbation by ,for example, co-contracting. Therefore, to negate this possibility, long periods of uncertainty must be included. These long periods of uncertainty

coupled with high levels of pre-load can be exhaustive and might not be feasible when studying certain patient populations.

Of the methods applying trunk loading perturbations, many complied with all the methodological criteria. However, when applying loading perturbations, the perturbation should not be delivered manually by the experimenter (by e.g. dropping a weight). This makes the timing of the perturbation (i.e. the onset) uncertain, in turn, making estimates of reflex delays impossible and/or inaccurate. Putting a force sensor between the dropped load and the subject may not be sufficient as this is a measurement of the interaction between the subject and the load, where the force sensor introduces noise into the estimation of the onset of the perturbation. Among the methods using loading perturbations, different perturbation types were applied: single sine waves, step, impulse and pseudorandom binary perturbations and multi-sines. Single sine waves are only appropriate when the period of the sine wave is shorter than the shortest muscle reflex delay and when the onset of the sine wave is unpredictable. Otherwise, subjects are able to respond voluntarily and the reflexive and voluntary activation are no longer distinguishable. Both step and impulse perturbations are suitable but require sufficient power (i.e. large perturbation forces) and/or many repetitions for sufficient reliability. These potential drawbacks can be circumvented with either a pseudorandom binary signal or with multi-sines, where trials can last as long as needed, without becoming predictable. A drawback of multi-sines and pseudorandom sequences is the "unnatural" nature of the task, as the perturbation is continuous and never occurs from an unperturbed initial condition. An added benefit of multi-sines is that power can be selectively included (at selected frequencies).

Only four of the included articles performed a clinimetric assessment by determining the reliability of the method and only two of those complied with all the methodological criteria (Santos et al., 2010; Hodges et al., 2009). The ICC was used as a measure of reliability and ranged from poor (ICC 0) to moderate (ICC 0.72). Besides these studies on reliability, nothing is known about the other clinimetric properties.

Considering the methodological criteria and the arguments outlined above, only a limited selection of articles describe methods that can be recommended, both in the trunk loading (Granata et al., 2005; Lee et al., 2006; Moorhouse and Granata, 2005; Rogers and Granata, 2006; van Drunen et al., 2013) and in the moving platform category (Cort et al., 2013; Cote et al., 2009; Preuss and Fung, 2008).

None of these articles include a clinimetric evaluation and it is therefore recommended that future research focusses on determining the reliability and other clinimetric assessments of these methods.

Several limitations of this review have to be discussed. Beside the ever present publication bias, a certain amount of selection bias may be present as well. However, a snowball procedure was applied to minimize this effect. Furthermore, there is a wide variety of clinimetric assessments that are important when evaluating the quality of an instrument (e.g. internal consistency, content validity, structural validity, responsiveness) that we have not addressed. We have mainly focused on the construct validity for it is the overarching concern of validity research, subsuming all other types of validity evidence. Finally, one of the included studies (van Drunen et al., 2013) was performed by researchers from the same research group as the authors of the current review. Therefore, a certain amount of bias cannot be excluded.

In conclusion, because of the wide variety in methods and the lack of validation and reliability studies, it is difficult to compare studies and the interpretation in terms of the underlying mechanisms of trunk stabilization is limited. Therefore there is a need for standardization and clinimetric evaluation. When considering construct validity, in line with the methodological criteria as outlined in the methods section, we propose a method where the trunk is studied in isolation, i.e. the pelvis is restrained and the perturbation is applied directly to the upper body, either through the trunk or pelvis. Furthermore, the perturbation should be unpredictable, force controlled and completely known (in terms of amplitude and timing). Finally, the perturbation should result in small fluctuations around a fixed working point. To obtain sufficient reliability, a multi-sine, repeated impulse or pseudorandom binary signal is preferred. Hopefully, a higher standardization of methods to study trunk control will contribute to a higher quality of research and enable better comparisons to be made between studies.

Appendix 1. Search strategy

Search conducted in PubMed and Embase on September 1st, 2014:

((perturbat*[tiab] OR "sudden load*"[tiab] OR "quick release"[tiab] OR "external load*"[tiab] OR "Unload*"[tiab] OR "moving platform" [tiab] OR "moving surface" [tiab]) AND (Human OR Adult OR adults OR Patient OR patients OR Healthy control* OR Healthy subject* OR "Humans"[Mesh]) AND ("Back"[Mesh] OR spine[tiab] OR spines[tiab] OR spinal[tiab] OR paraspinal[tiab] OR "low back"[tiab] OR "posture"[tiab] OR "postural"[tiab] OR "motor control"[tiab] OR "Spine"[Mesh:noexp] OR "Intervertebral Disc"[Mesh] OR "Lumbar Vertebrae"[Mesh] OR "Sacrum"[Mesh] OR "Thoracic Vertebrae"[Mesh]))

Appendix 2. COSMIN-list (Box B and C)

Box B. Reliability: relative measures (including test-retest reliability, intra-rater reliability and intra-rater reliability				
Design requirements	excellent	good	fair	poor
1. Was the percentage of missing items given?	Percentage of missing items described	Percentage of missing items NOT described		
2. Was there a description of how missing items were handled?	Described how missing items were handled	Not described but it can be deduced how missing items were handled	Not clear how missing items were handled	
3. Was the sample size included in the analysis adequate?	Adequate sample size (≥50)	Good sample size (25-49)	Moderate sample size (15-24)	Small sample size (<15)
4. Were at least two measurements available?	At least two measurements			Only one measurement
5. Were the administrations independent?	Independent measurements	Assumable that the measurements were independent	Doubtful whether the measurements were independent	Measurements were NOT independent
6. Was the time interval stated?	Time interval stated		Time interval NOT stated	
7. Were patients stable in the interim period on the	Patients were stable	Assumable that patients	Unclear if patients	Patients were NOT

construct to be measured?	(evidence provided)	were stable	were stable	stable
8. Was the time interval appropriate?	Time interval appropriate		Doubtful whether time interval was appropriate	Time interval NOT appropriate
9. Were the test conditions similar for both measurements?	Test conditions were similar (evidence provided)	Assumable that test conditions were similar	Unclear if test conditions were similar	Test conditions were NOT similar
10. Were there any important flaws in the design or methods of the study?	No other important methodologi cal flaws in the design or execution of the study		Other minor methodologi cal flaws in the design or execution of the study	Other important methodologi cal flaws in the design or execution of the study
Statistical methods 11. for continuous scores: Was an intraclass-correlation coefficient (ICC) calculated?	ICC calculated and model or formula of the ICC described	ICC calculated but model or formula of the ICC not described or not optimal. Pearson or Spearman correlation coefficient calculated with evidence provided that no systematic change has occurred	Pearson or Spearman correlation coefficient calculated WITHOUT evidence provided that no systematic change has occurred or WITH evidence that systematic change has occurred.	No ICC or Pearson or Spearman correlations calculated
12. for dichotomous/nominal/or dinal scores: Was kappa calculated?	Kappa calculated			Only percentage agreement calculated
13. for ordinal scores: Was weighted kappa calculated?	Weighted Kappa calculated		Unweighted Kappa calculated	Only percentage agreement calculated

14. for ordinal scores: Was the weighting scheme described?	Weighting scheme described	Weighting scheme NOT described		

Box C. Measurement error: absolute measures				
Design requirements	excellent	good	fair	poor
1. Was the percentage of missing items given?	Percentage of missing items described	Percentage of missing items NOT described		
2. Was there a description of how missing items were handled?	Described how missing items were handled	Not described but it can be deduced how missing items were handled	Not clear how missing items were handled	
3. Was the sample size included in the analysis adequate?	Adequate sample size (≥50)	Good sample size (25-49)	Moderate sample size (15-24)	Small sample size (<15)
4. Were at least two measurements available?	At least two measurements			Only one measurement
5. Were the administrations independent?	Independent measurements	Assumable that the measurements were independent	Doubtful whether the measurements were independent	Measurements were NOT independent
6. Was the time interval stated?	Time interval stated		Time interval NOT stated	
7. Were patients stable in the interim period on the construct to be measured?	Patients were stable (evidence provided)	Assumable that patients were stable	Unclear if patients were stable	Patients were NOT stable
8. Was the time interval appropriate?	Time interval appropriate		Doubtful whether time interval was appropriate	Time interval NOT appropriate
9. Were the test conditions similar for	Test conditions were similar (evidence	Assumable that test conditions	Unclear if test conditions were similar	Test conditions were NOT similar

both measurements?	provided)	were similar		
10. Were there any important flaws in the design or methods of the study?	No other important methodological flaws in the design or execution of the study		Other minor methodological flaws in the design or execution of the study	Other important methodological flaws in the design or execution of the study
Statistical methods 11. for CTT: Was the Standard Error of Measurement (SEM) of Limits of Agreement (LoA) calculated?	SEM, SDC, or LoA calculated	Possible to calculate LoA from the data presented		SEM calculated based on Cronbach's alpha, or on SD from another population

Box B (Reliability) and Box C (Measurement error) of the COSMIN-list. In question B3 and C3 the needed sample size was adjusted for this study.

Chapter 2

Chapter 3

Identifying intrinsic and reflexive contributions to low-back stabilization

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Abstract

Motor control deficits have been suggested as potential cause and/or effect of a-specific chronic low-back pain and its recurrent behavior. Therefore, the goal of this study is to identify motor control in low-back stabilization by simultaneously quantifying the intrinsic and reflexive contributions. Upper body sway was evoked using continuous force perturbations at the trunk, while subjects performed a resist or relax task. Frequency response functions (FRFs) and coherences of the admittance (kinematics) and reflexes (sEMG) were obtained. In comparison with the relax task, the resist task resulted in a 61% decrease in admittance and a 73% increase in reflex gain below 1.1 Hz. Intrinsic and reflexive contributions were captured by a physiologically-based, neuromuscular model, including proprioceptive feedback from muscle spindles (position and velocity). This model described on average 90% of the variance in kinematics and 36% of the variance in sEMG, while resulting parameter values were consistent over subjects.

Introduction

Low-back pain (LBP) is a common disorder, which affects 40-60% of the adult population annually in Western Europe and North America (Loney and Stratford, 1999; Picavet and Schouten, 2003). The effect of most treatments (e.g., anti-inflammatory drugs, neuromuscular training and cognitive therapy) is fairly small, and 60-75% of the patients have recurrent symptoms within a year with 10% developing chronic LBP (van den Hoogen et al., 1998). Motor control deficits (e.g., delayed 'reflex' responses, increased antagonistic co-contraction) have been suggested as potential cause and/or effect of LBP and its recurrent behavior (Cholewicki et al., 2000; Radebold et al., 2001; van Dieën et al., 2003b).

Motor control provides an essential contribution to low-back stabilization, since the spine is inherently unstable without active musculature in spite of stiffness and damping provided by passive tissue (Bergmark, 1989a; Crisco and Panjabi, 1991b). The muscular contribution to stabilization of the spine involves muscle viscoelasticity and reflexive feedback. Muscle viscoelasticity comprises the stiffness and damping of the muscles and can be altered by co-contraction and selective muscle activity. Given the limited contribution of passive tissues especially in upright trunk postures and the difficulty to separate these components, properties of passive tissues and muscle viscoelasticity are usually lumped into intrinsic stiffness and damping. Feedback comprises visual, vestibular and proprioceptive contributions, where the latter is based on information of muscle length and muscle lengthening velocity from muscle spindles (MS) and on tendon force from Golgi tendon organs (GTO). Most studies on low-back stabilization have focused either on intrinsic stiffness and damping (e.g., Gardner-Morse and Stokes (2001); Brown and McGill (2009)) or on reflexes (e.g., Radebold et al. (2001)) by experimentally excluding the other component or analytically merging both. This could lead to incorrect estimates, especially because changes in co-contraction could result in changes in proprioceptive reflexes and vice versa (Matthews, 1986; Kirsch et al., 1993). Therefore, combined identification is essential, but only a few studies have pursued this for low-back stabilization.

Moorhouse and Granata (2007a) and Hendershot et al. (2011) identified MS feedback and intrinsic stiffness of the trunk. However, low-back stabilization was not described, since their position-driven, upper-body perturbations stabilized the trunk. (Goodworth and Peterka) identified low-back stabilization focusing mainly on visual (Goodworth and Peterka, 2009a) and vestibular (Goodworth and Peterka, 2010) feedback, while a simplified representation of proprioceptive

reflexes (only stretch velocity MS feedback) and intrinsic contributions (only stiffness) was used. Thus, a detailed analysis of the contribution of proprioceptive reflexes to low-back stabilization is still lacking.

The goal of this study was to simultaneously identify intrinsic and reflexive contributions to low-back stabilization in healthy subjects. This approach could help identify motor control deficits in LBP.

Methods

Subjects
Fifteen healthy adults (age, 23-58 year; mean age, 35 year) participated in this study and gave informed consent according to the guidelines of the ethical committee of VU University Amsterdam. Subjects did not experience LBP in the year prior to the experiments.

Experiments
During the experiments, subjects assumed a kneeling-seated posture, while being restrained at the pelvis (Figure 1). A force perturbation $F_{pert}(t)$ was applied in ventral direction at the T10-level of the spine by a magnetically driven linear actuator (Servotube STB2510S Forcer and Thrustrod TRB25-1380, Copley Controls, USA). For comfort and better force transfer, a thermoplastic patch (4x4 cm) was placed between the actuator and the back of the subject. To reduce the effects of head and arm movement during the measurements, the subjects were instructed to place their hands on their head.

Visual feedback depicting the trunk rotation in sagittal (flexion/extension) and coronal (lateral bending) plane was provided to the subjects. Task instructions were to minimize the flexion/extension excursions (*Resist task*), or to relax as much as possible while limiting flexion/extension to about 15 degrees (*Relax task*). In addition, subjects were instructed in both tasks to minimize lateral flexion. Both tasks were repeated four times with the same perturbation signal.
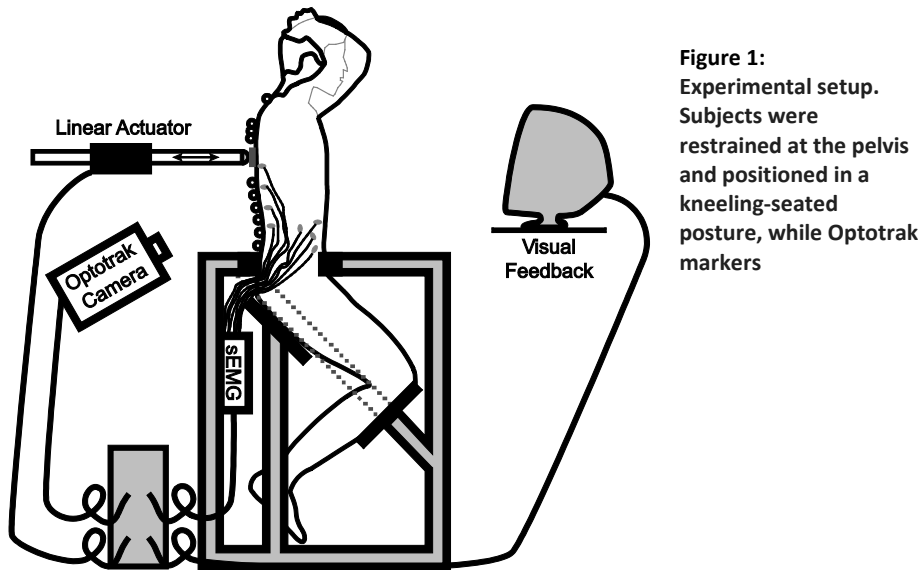
Figure 1:
Experimental setup.
Subjects were
restrained at the pelvis
and positioned in a
kneeling-seated
posture, while Optotrak
markers

The perturbation $F_{pert}(t)$ (Figure 2) consisted of a dynamic disturbance of ±35 N combined with a 60 N baseline preload to maintain contact with the subject, because the actuator was not connected to the subject and therefore only capable of pushing. The dynamic disturbance (Figure 2) was a crested multi-sine signal (Pintelon and Schoukens, 2001) of 20 seconds duration with 18 paired frequencies, which were logarithmically distributed within a bandwidth of 0.2-15 Hz. To reduce adaptive behavior to high frequent perturbation content, the power above 4 Hz was reduced to 40% (Mugge et al., 2007). Because the perturbation was random-appearing, subjects were not expected to react with voluntary activation on the perturbation.

Each run consisted of a ramp force increase to preload level (3 s), a stationary preload (2 s), a start-up period to reduce transient behavior (the last 5 s of the dynamic disturbance), and twice the dynamic disturbance (2 x 20 s), which resulted in 50 s per run.

Figure 2: The force perturbation F_{pert} (black) is projected in frequency domain (TOP) and time domain (MIDDLE). The resulting contact forces $F_C(t)$ (MIDDLE) and actuator displacements $x_A(t)$ (BOTTOM) are shown in time domain during a relax task (blue) and a resist task (red).
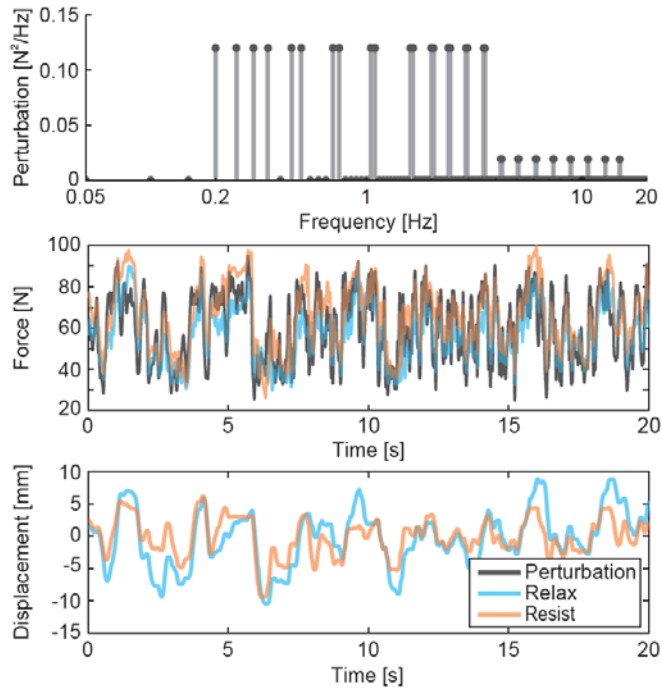
Data Recording and Processing

Kinematics of the lumbar vertebrae (L1 – L5), the thorax (T1, a cluster of markers at T6, T12), and the pelvic restraint were measured using 3D motion tracking at 100 Hz (Optotrak3020, Northern Digital Inc, Canada). The trunk rotation angle (based on markers at T12 and the pelvic restraint) in sagittal and coronal plane was provided as visual feedback to the subjects in real-time. The actuator displacement $x_A(t)$ and contact force $F_c(t)$ between the rod and the subject were measured at 2000 Hz (Servotube position sensor & Force sensor FS6-500, AMTI, USA). Trunk kinematics were described in terms of translation, since kinematic analysis indicated that an effective low-back bending rotation point, necessary to define rotations, was not well defined and inconsistent over subjects and tasks. Activity of sixteen muscles (8 bilateral pairs as listed in Table 1) was measured at 1000 Hz (surface electromyography (sEMG) Porti 17, TMSi, the Netherlands) as described in Willigenburg et al. (2010). The EMG data $e_j(t)$ (with j = #muscle) was digitally filtered (zero-phase, first-order, high-pass) at 250 Hz (Staudenmann et al., 2007b) and then rectified.

All fifteen subjects showed a comparable admittance with an actuator displacement RMS of 2.72±0.49 mm (relax) and 1.78±0.36 mm (resist). Further analysis of local low-back bending patterns (van Drunen et al., 2012) showed substantial low-back bending in eight subjects where at least 32% of the trunk rotations were attributed to bending above L5 (while measurements were not below L5) during both task instructions. In the other seven subjects, at least one task instruction resulted in less than 6% trunk rotation attributed to bending above L5, suggesting that bending below L5 and/or pelvic rotations accounted for much of the observed trunk rotations. Hence, the data collected on these subjects was not suitable for studying lumbar stabilization. Therefore, this paper will consider only the eight subjects demonstrating substantial low-back bending.

System identification

Closed loop system identification techniques (van der Helm et al., 2002; Schouten et al., 2008b) were used to estimate the translational low-back admittance ($\hat{H}_{adm}(f)$) and reflexes ($\hat{H}_{emg}(f)$) as frequency response functions (FRFs). The admittance describes the actuator displacement ($x_A(t)$) as a function of the contact force ($F_c(t)$), representing the inverse of low-back mechanical impedance. The reflexes describe the EMG data ($e_j(t)$) as a function of the actuator displacement ($x_A(t)$). Because the subjects interacted with the actuator, FRFs were estimated using closed loop methods:

$$\hat{H}_{adm}(f) = \frac{\hat{S}_{F_{pert}x_A}(f)}{\hat{S}_{F_{pert}F_c}(f)} \; ; \hat{H}_{emg_j}(f) = \frac{\hat{S}_{F_{pert}e_j}(f)}{\hat{S}_{F_{pert}x_A}(f)} \tag{1}$$

with $\hat{S}_{F_{pert}x_A}(f)$ representing the estimated cross-spectral density between signals F_{pert} and x_A, etc.. The cross-spectral densities were only evaluated at the frequencies containing power in the perturbation signal. For improved estimates and noise reduction, the cross-spectral densities were averaged across the 8 time segments per task (four repetitions each containing two 20 s-segments) and over 2 adjacent frequency points (Jenkins and Watts, 1969). Finally, $\hat{S}_{F_{pert}e_j}(f)$ was averaged over the left and right muscles.

The coherence associated with $\hat{H}_{adm}(f)$ and $\hat{H}_{emg}(f)$ was derived as:

$$\hat{\gamma}^2_{adm}(f) = \frac{\left|\hat{S}_{F_{pert}x_A}(f)\right|^2}{\hat{S}_{F_{pert}F_{pert}}(f)\hat{S}_{x_Ax_A}(f)} \; ; \hat{\gamma}^2_{emg_j}(f) = \frac{\left|\hat{S}_{F_{pert}e_j}(f)\right|^2}{\hat{S}_{F_{pert}F_{pert}}(f)\hat{S}_{e_je_j}(f)} \tag{2}$$

Coherence ranges from zero to one, where one reflects a perfect, noise-free relation between input and output. Since spectral densities were averaged over 16 points, a coherence greater than 0.18 is significant with P<0.05 (Halliday et al., 1995).

Parametric identification

A linear neuromuscular control (NMC) model was constructed to translate the FRFs into physiological elements representing intrinsic and reflexive contributions (Figure 3). The intrinsic contribution consists of the trunk mass (m), and the lumbar stiffness and damping (k, b). The reflexive contribution involves the lumbar muscle spindle (MS) position and velocity feedback gains (k_P, k_V) with a time delay (τ_{REF}). Muscle activation dynamics were implemented as a second order system (Bobet and Norman, 1990) with a cut-off frequency (f_{ACT}) and a dimensionless damping (d_{ACT}). Contact dynamics between the subjects' trunk and the actuator were included as a damper and a spring (b_C, k_C). The activation signal ($A(t)$) in the model was scaled to the EMG data using a scaling parameter (e_{SCALE}). Several other model configurations were explored by removing some elements and/or including Golgi tendon organ (GTO) force feedback (k_F) with its own time delay (τ_{GTO}) or with the same time delay as the muscle spindles (τ_{REF}), vestibular acceleration feedback (k_{VEST}, τ_{VEST}), MS acceleration feedback (k_A), or a second DOF representing a head mass connected to the torso by a spring and damper (m_H, b_H, k_H).

The parameters were identified by fitting the NMC-model on the FRFs of both the low-back admittance and the reflexive muscle activation for all repetitions. The value of the trunk mass (m) was estimated for each individual subject using anthropometric methods (Clauser et al., 1969), resulting in an average of 39.8 kg. The relax and resist task were optimized simultaneously assuming masses, time delays, activation and contact dynamics, and EMG-scaling to be constant over conditions. The criterion function used in the estimation was:

$$err = \sum_{1}^{\#rep} \sum_{k} \frac{\hat{\gamma}_{adm}^2(f_k)^2}{1+f_k} \left| \log\left(\frac{\hat{H}_{adm}(f_k)}{H_{adm}^{mdl}(f_k)} \right) \right|^2 + q \sum_{1}^{\#rep} \sum_{k} \frac{\hat{\gamma}_{emg}^2(f_k)^2}{1+f_k} \left| \log\left(\frac{\hat{H}_{emg}(f_k)}{H_{emg}^{mdl}(f_k)} \right) \right|^2 \quad (3)$$

with f_k as the power containing frequencies, and $H_{adm}^{mdl}(f_k)$ and $H_{emg}^{mdl}(f_k)$ as the transfer functions of the model. The criterion describes the goodness of fit of the complex admittance (left term) and reflexive muscle activity (right) term where the weighting factor q was selected to be 0.25 to provide equal contribution of the admittance and reflexive muscle activity to the criterion function. In some cases the

model became unstable, which was resolved by a penalty function for positive real Eigen values.

Model validation

The accuracy of the parameters was evaluated using the Standard Error of the Mean (*SEM*) (Ljung, 1999):

$$SEM = \frac{1}{N} diag\left[\left(J_p^T J_p\right)^{-1}\right] \sum err^2 \tag{1}$$

where the Jacobian J_p contains the gradient to the optimal parameter vector *p* of the predicted error *err*. The more influence a parameter has on the optimization criterion, the smaller the *SEM* will be.

The validity of the optimized model and its parameters was assessed in the time domain using the variance accounted for (VAF). A *VAF* of 100% reflects a perfect description of the measured signal by the model. The experimental measurements $x_A(t)$ were compared with the estimated model outcomes $\hat{x}_A(t)$:

$$VAF_x = \left[1 - \frac{\sum_1^n (x_A(t_n) - \hat{x}_A(t_n))^2}{\sum_1^n (x_A(t_n))^2}\right] \cdot 100\% \tag{2}$$

where *n* is the number of data points in the time signal. For the EMG, VAF_e was calculated by replacing $x_A(t)$ and $\hat{x}_A(t)$ with $e_j(t)$ and $\hat{e}_j(t)$, respectively. To reduce noise contributions, measured data was reconstructed with only the frequencies that contain power in the perturbation.

Table 1: EMG coherence within the range of 0.2-3.5 Hz for all muscles averaged over all subject (mean (±std)).

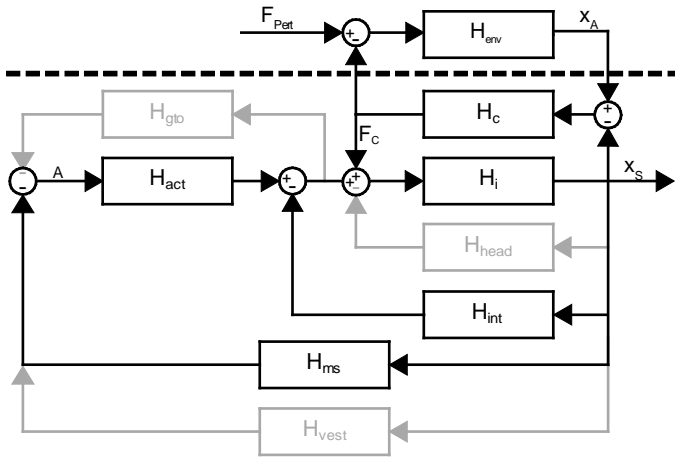| Muscles	Coherence	
	Relax	*Resist*
Abdominal		
Rectus Abdominus	0.06(0.05)	0.17(0.18)
Obliquus Internus	0.07(0.07)	0.14(0.11)
Obliquus Externus (lateral)	0.10(0.10)	0.14(0.10)
Obliquus Externus (anterior)	0.10(0.08)	0.15(0.10)
Back		
Longissimus (thoracic)	0.42(0.13)	0.44(0.13)
Iliocostalis (thoracic)	0.38(0.14)	0.35(0.12)
Iliocostalis (lumbar)	0.42(0.14)	0.47(0.10)
Longissimus (lumbar)	0.57(0.11)	0.68(0.08)

Figure 3:
The model structure. The signals force perturbation ($F_{pert}(t)$), contact force ($F_c(t)$), actuator displacements ($x_A(t)$), the spinal displacement ($x_S(t)$), and muscle activity ($A(t)$) are displayed. Involved are the dynamics of the trunk inertia ($H_I = 1/(ms^2)$) and intrinsic properties ($H_{INT} = b\,s + k$), the head ($H_{HEAD} = m_H\,s^2\,(b_H\,s + k_H) / (m_H\,s^2 + b_H\,s + k_H)$), the contact point ($H_C = b_C\,s + k_C$), the actuator environment ($H_{ENV} = 1 / (m_{ENV}\,s^2 + b_{ENV}\,s + k_{ENV})$), and the muscle activation dynamics ($H_{ACT} = (2\pi f_{ACT})^2 / (s^2 + 4\pi f_{ACT}\,d_{ACT}\,s + (2\pi f_{ACT})^2)$). Reflexive feedback is described by muscle spindles ($H_{MS} = (k_A\,s^2 + k_V\,s + k_P)\,e^{-\tau ref\,s}$) of which the acceleration component k_A is optional, Golgi tendon organs ($H_{GTO} = k_F\,e^{-\tau ref\,s}$) and the vestibular organs ($H_{VEST} = k_{VEST}\,e^{-\tau vest\,s}$). The gray pathways are only implemented during the explorative model search, as well as the division of τ_{REF} into time delays for the MS (τ_{MS}) and GTO (τ_{GTO}).

Statistics

Significance ($p<0.05$) in effects of task instruction on the FRF gains and the model parameters was evaluated with a repeated-measures ANOVA. For the FRF gains only the first five frequency points (e.g., a bandwidth of 0.2-1.1 Hz) were analyzed, because effects of task instruction were negligible at higher frequencies.

Results

Frequency Response Functions (FRFs)

Human low-back stabilizing behavior is described by the FRFs of the admittance and the reflexes (Figure 4), while high coherences indicate good input-output correlation. The coherence of the admittance was above 0.8 for the resist task, and above 0.75 for the relax task up to 3.5 Hz ($\hat{\gamma}^2_{adm} > 0.55$ over the whole frequency range). As shown in Table 1, the coherence levels of the abdominal

muscles were generally insignificant ($\hat{\gamma}^2_{emg}$ < 0.18), resulting in the exclusion of the abdominal muscles from further analysis. Between 0.2 and 3.5 Hz, significant coherences were found for all dorsal muscles (Table 1), of which the lumbar part of the Longissimus muscle was the highest with an average coherence of 0.57. This is considered high given the noisy character of sEMG measurements and the number of muscles involved in trunk stabilization. Therefore, the lumbar part of the Longissimus muscle was used for modelling.
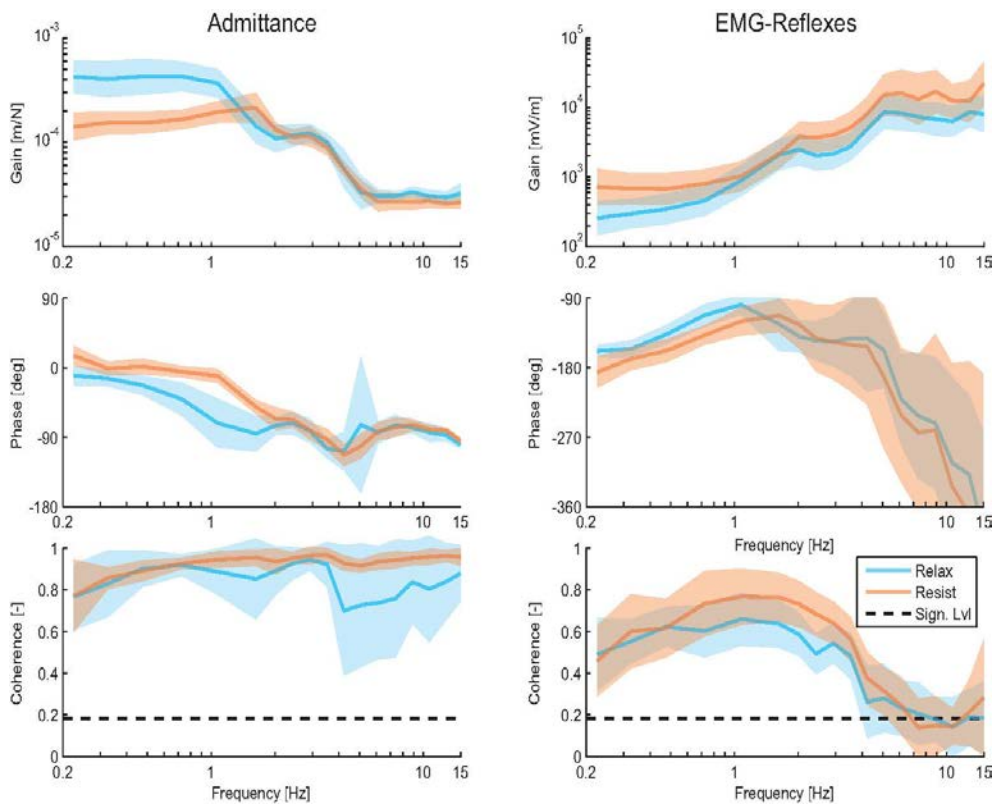
Figure 4:
The FRFs and coherences of the human low-back admittance (left) and EMG reflexes of the Longissimus Muscle (right) averaged over all subjects for the relax task (blue) and resist task (red). Shadings represent the standard deviations.

The low-back admittance FRF resembles a second order system (i.e., a mass-spring-damper system). The high-frequency behavior (>4 Hz) is mainly influenced by trunk mass combined with contact dynamics. The low-frequency response (<1 Hz) reflects intrinsic stiffness and reflexive behavior. The intermediate frequencies are dominated by the intrinsic damping and reflexive responses. The reflexive FRF reflects position feedback (low-frequency flat gain, -180° phase), velocity feedback (first order gain ramp and -90° phase at the intermediate frequencies) and force and/or acceleration feedback (high-frequency second-order ramp-up).

Identification of intrinsic and reflexive parameters

To select the most appropriate model structure, eight explorative model configurations were compared by evaluating their *VAF* and *SEM* values (Table 2). All model configurations included the trunk mass, lumbar stiffness and damping, and contact dynamics. This intrinsic model (1) described the displacements well (VAF_x = 87%), but could not describe the EMG due to the lack of reflexes. Adding MS feedback to the intrinsic model (2) slightly improved the displacement *VAF* (90%) and described the EMG measurements rather well (VAF_e = 36%). To describe the second order reflexive characteristics, a MS acceleration component (3) associated with MS nonlinearity (Schouten et al., 2008b), a vestibular acceleration component (4), or force feedback from the GTO (5) were included.

Table 2:
Results of different model configurations: The variance accounted for (VAF) and percentage Standard Errors of the Mean of the subject-averaged parameter values (%SEM) averaged over all subjects and parameters (mean(±std)). The intrinsic model includes trunk inertia, intrinsic properties and contact dynamics. Feedback from the muscle spindles (MS), the vestibular organ (Vest) and Golgi tendon organ (GTO) has been added as well as a head mass (Head), an acceleration component from the muscle spindles (MSacc), and separate time delays for the MS and GTO (τMS & τGTO).

Model options	VAF_x [%]		VAF_e [%]		SEM
	Relax	*Resist*	*Relax*	*Resist*	[%]
(1) Intrinsic	87.5 (7.3)	85.9 (7.1)	-	-	9
(2) Intrinsic + MS	89.5 (6.9)	90.6 (3.7)	34.9 (14.9)	36.9 (21.1)	40
(3) Intrinsic + MS + MS$_{acc}$	89.3 (7.4)	90.4 (4.2)	36.6 (13.3)	44.8 (08.5)	35
(4) Intrinsic + MS + Vest	89.3 (7.4)	89.9 (4.2)	37.8 (12.6)	45.0 (09.8)	2154
(5) Intrinsic + MS + GTO	89.2 (7.3)	91.3 (3.4)	37.2 (13.9)	39.3 (21.0)	113
(6) Intrinsic + MS + GTO (τ_{MS} & τ_{GTO})	88.9 (7.1)	91.3 (3.5)	38.0 (13.9)	39.1 (20.6)	58
(7) Intrinsic + MS + GTO + Vest	89.4 (7.3)	91.4 (3.7)	41.8 (12.6)	48.9 (07.2)	106
(8) Intrinsic + MS + GTO + Head	89.3 (7.1)	91.2 (3.4)	34.3 (27.1)	44.0 (18.2)	40

These resulted in a comparable VAF_x (90% for all) and a slightly improved VAF_e (41%, 41% and 38%, respectively). Including even more components and parameters in the model by assigning separate time delays for the MS and GTO (6), combining the MS, GTO and vestibular feedback (7) or adding an extra DoF representing the head mass (8) resulted in either comparable VAFs (models 6 & 8) or improved VAFs with poor SEM values (model 7), which indicate over-parameterization resulting in decreased reliability of the estimated parameters for these models. For further analysis the intrinsic model with MS feedback (2) was selected, as it contained the essential intrinsic and reflexive components for which SEM values (average 40% of the subject-averaged parameter values) indicated a reliable estimate of the parameters.

Figures 5 and 6 illustrate the fit of the model predictions to the measured FRFs and time history data, respectively. An accurate fit was obtained up to around 3.5 Hz, with some deviations at higher frequencies which are also apparent in the EMG time history data. After removing the high frequent deviations in the EMG by a 3.5 Hz low-pass filter, a VAF_e of 50% was obtained, indicating a good fit at frequencies with high coherence values. Considering the variation in gender and age of the subject group, parameter estimates (Figure 7) were consistent over subjects.
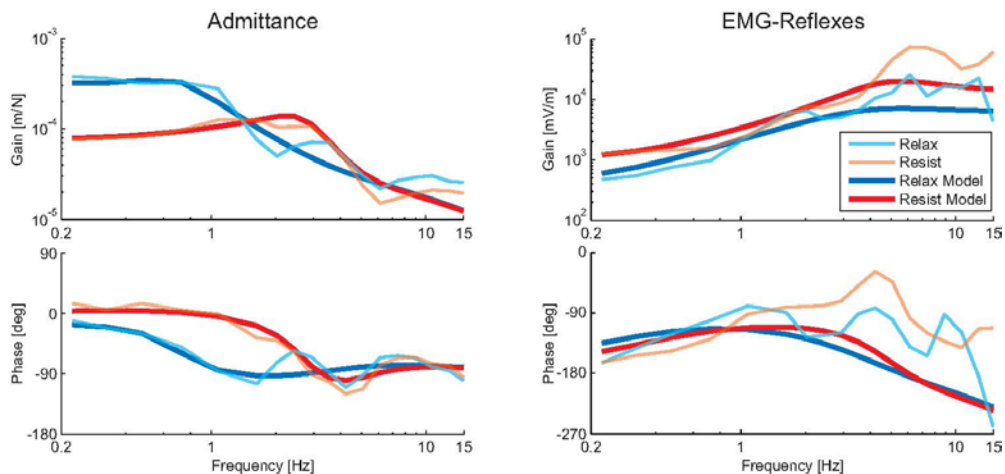
Figure 5:
Model predictions (dark) versus the measured data (light) of the admittance (left) and the EMG reflexes of Longissimus muscle (right) for one typical subject during a relax task (blue) and a resist task (red).
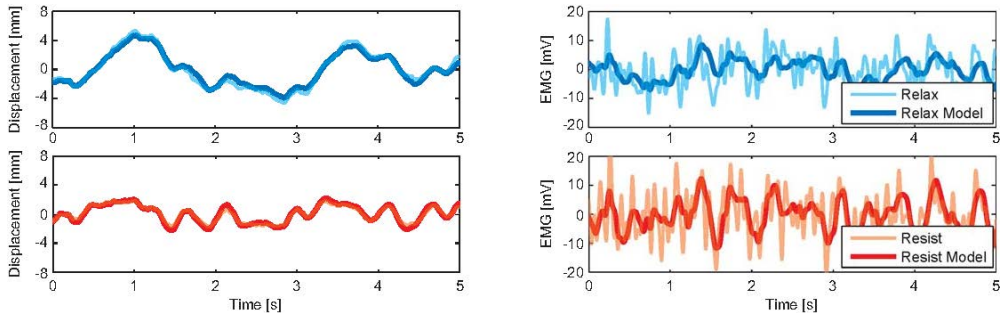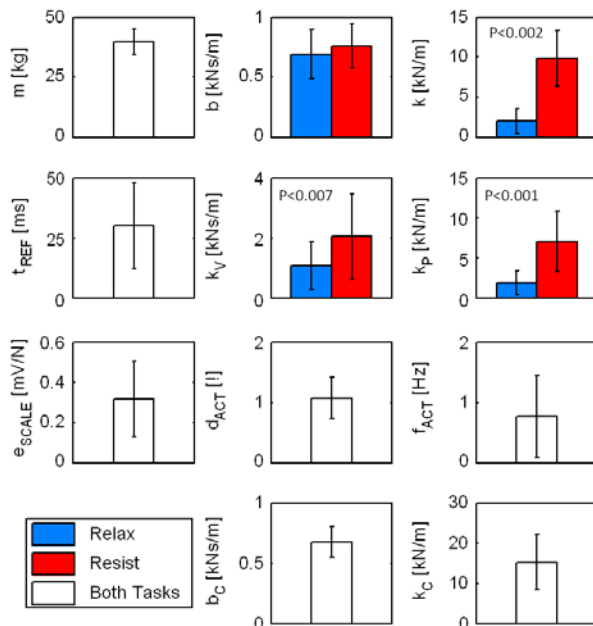
Figure 6
Model predictions (dark) versus the measured data (light) of the displacement (left) and the EMG of Longissimus muscle (right) for one typical subject during a relax task (blue) and a resist task (red).

Task

Subjects modulated low-back stabilization with task instruction, where admittance below 1.1 Hz in the resist task was 61% lower (P<0.02) than in the relax task. At frequencies above 2 Hz, admittance was not affected by task instructions. The reflex FRF-gain was task dependent below 1.1 Hz and increased by 73% (P<0.03) for the resist task. Underlying these differences, the resist task coincided with significantly higher intrinsic stiffness (P<0.002), position feedback (P<0.001) and velocity feedback (P<0.007), while no significant difference was found for the intrinsic damping (p<0.55).

Figure 7:
Subject-averaged estimated parameters. The error bars represent the standard deviations. The parameters modulated due to task instruction have different estimated values for the relax task (red) and the resist task (blue).

Intrinsic and reflexive contributions

The reflexive contribution to low-back stabilization is illustrated simulating the admittance of the complete model (2) and removing (MS) reflexes (Figure 8). Note that parameters of the simplified models were not re-estimated and do not represent the best possible fit. Differences were primarily observed at the lower frequencies, where the MS reflexes reduced the admittance. During the resist task, the reflexive contribution led to a 25% reduced admittance at the lowest tested frequency, indicating that the intrinsic co-contraction was the main contributor to low-back stabilization. During the relax task however, the reflexive contribution was more substantial and led to a 52% reduced admittance.

Discussion

The goal of this study was to simultaneously identify intrinsic and reflexive contributions to low-back stabilization in healthy subjects. Upper-body sway was evoked using continuous force perturbations at the trunk, while subjects performed a resist or relax task. Frequency Response Functions (FRFs) and coherences of the admittance (kinematics) and reflexes (EMG) were obtained. Finally, intrinsic and proprioceptive parameters were captured by a physiological model. This methodology allowed for quantification of the intrinsic and proprioceptive feedback contributions simultaneously.

The FRFs of admittance and reflexes showed a consistent response in all subjects. High coherences were found for the admittance (across tested bandwidth) and the reflexes (up to 3.5 Hz). In comparison with the relax task, the resist task resulted in a 61% decrease in admittance and a 73% increase in reflex gain below 1.1 Hz. In only eight subjects substantial low-back bending was found, resulting in exclusion of the other seven subjects and a limited sample size for statistics.
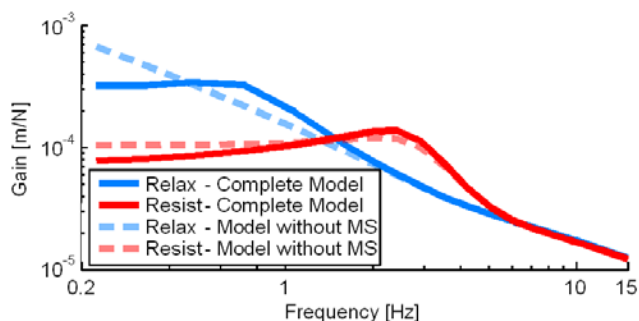

Figure 8:
Effect of MS feedback illustrated using NMC models of a typical subject during a relax (blue) and resist (red) task visualized by the admittance of the complete models including MS feedback (solid) and this model without MS feedback (dashed).

Several model configurations were explored. All configurations were based on physiological elements with the intrinsic system (trunk mass, and lumbar stiffness and damping) as core structure, which predicted the kinematics effectively. Therefore, sEMG measurements were included to identify the reflexive components. A model configuration including the intrinsic system and MS (position and velocity) feedback described an average of 90% of the variance in low-back displacements and 36% of the variance in EMG measurements (VAF_e of 50% up to 3.5 Hz). This is reasonable, given that the low-back contains 5 vertebrae and multiple muscles and was described by a 1-DoF model with only one lumped flexor/extensor muscle where feedback parameters were estimated using the Longissimus muscle disregarding reflexes of deeper muscles. Although vestibular and visual feedback are expected to contribute to low-back stabilization (Goodworth and Peterka, 2009a), our measurements do not contain enough information to separately include their contributions (poor reliability of the estimated parameters). Including extra vestibular (e.g., galvanic vestibular stimulation) and/or visual stimuli could give more information about these feedback systems.

The estimated trunk mass (39.9 kg) and intrinsic stiffness (2.0 kN/m) were comparable with values in Moorhouse and Granata (2005), while the estimated intrinsic damping (692 Ns/m) during the relax task was higher, possibly because the hand-position on the head in the current experimental setup results in higher stabilization demands. The estimated reflex time delay of 30.2 ms is within the expected (short-latency) range (Goodworth and Peterka, 2009a). For the resist task, increased intrinsic stiffness (from 2.0 to 9.9 kN/m) was found similar to Gardner-Morse and Stokes (2001) and Granata and Rogers (2007b), where increased muscle activation led to increased intrinsic stiffness. Also the proprioceptive feedback gains modulated with task instruction. Both position and velocity-referenced information seems to be more important for a resist task, because the model showed a strong increase in MS position and velocity feedback. The model variations in Figure 8, indicate that reflexes increase the overall resistance in both the resist and the relax task. During the resist task, the model attributes a substantial resistance to the intrinsic stiffness and damping and a minor resistance to the MS feedback. During the relax task, the reflexive contribution increases the resistance substantially at the lowest frequency, indicating that the energy-consuming intrinsic co-contraction becomes less dominant during natural posture maintenance.

Finally, this study proposed a method to identify intrinsic and reflexive contributions to low-back stabilization and applied this method on a group of healthy subjects. Future studies should apply this method to LBP patients, to determine whether motor control deficits can be identified.

Acknowledgements

Chapter 3

Chapter 4

Trunk stabilization estimated using pseudorandom force perturbations: a reliability study

M. Griffioen, E. Maaswinkel, W.W.A. Zuurmond, J. H. van Dieën, R.S.G.M. Perez

Abstract

Measurement of the quality of trunk stabilization is of great interest to identify its role in first occurrence, recurrence or persistence of LBP. Our research group has developed and validated a method to quantify intrinsic and reflex contributions to trunk stabilization from the frequency response function (FRF) of thorax movement and trunk extensor EMG to perturbations applied by a linear actuator. However, the reliability of this method is still unknown. Therefore, the purpose of this study was to investigate the between-day reliability of trunk FRFs in healthy subjects and LBP patients. The test-retest ICC's in patients were substantial for both admittance and reflex gains ($ICC_{3,1} > 0.73$ and 0.67). In healthy subjects, the reliability of admittance gain was also substantial ($ICC_{3,1}$ 0.66), but the reliability of the reflexive gain was only moderate ($ICC_{3,1}$ 0.44). Although sample sizes were limited (thirteen healthy subjects and eighteen LBP patients, these results show that trunk stabilization can be measured reliably, and represent a promising step towards using this method in further research in LBP patients.

Introduction

Trunk stabilization is needed to maintain control over trunk posture and movements during daily life activities (MacKinnon and Winter, 1993; van der Burg et al., 2005). Trunk stabilization is dependent on both active (muscular) and passive (osteoligamentous) structures and it has been suggested that low-back pain (LBP) might cause impaired trunk stabilization (Van Dieen et al., 2003; Panjabi 1992), which in turn might contribute to persistence or recurrence of LBP (Hodges and Moseley, 2003; MacDonald et al., 2009). It has also been suggested that poor trunk stabilization could be a predictive factor or even primary cause of LBP (Cholewicki et al., 2005). Therefore, measurement of the quality of trunk stabilization is of great interest to identify its role in the first occurrence, recurrence or persistence of LBP.

Specifically, several studies have indicated longer reflex delays after an external mechanical perturbation of trunk posture in LBP patients than in controls (Magnusson et al., 1996; Radebold et al., 2000). In apparent contrast, higher trunk stiffness, i.e. a higher mechanical resistance to such perturbations, has also been reported (Hodges et al., 2009). In fact, increased trunk intrinsic stiffness could explain the longer delays found, as with increased intrinsic stiffness the same mechanical disturbance will cause a smaller and slower deviation of trunk posture. This could result in a longer apparent reflex delay, caused by the smaller deviations in combination with thresholds of sensors signaling these deviations or even in the method detecting the responses, while the true neural delay could be unaffected.

Protocols to properly identify trunk stabilization (in terms of intrinsic stiffness and reflexive responses) must be well standardized and reliable to determine their clinical relevance and to support their use as clinical outcome measures. Many methods to measure trunk stabilization have been described in the literature, but documentation on the reliability of these methods is sparse (Chapter 2, Maaswinkel et al., submitted for publication). Hendershot et al. (2012) performed a reliability study on a method that used pseudorandom position-controlled perturbations and found high within-day and moderate to fair between-day intraclass correlation coefficients (ICC's) for trunk stiffness (0.90 and 0.67 respectively) and reflex gain (0.85 and 0.37 respectively). A potential problem with the position controlled perturbations and therefore the fixed trunk displacement imposed, is that the subject is unable to exert any influence over the resulting displacement and will therefore not be motivated to resist. It has been observed

in former studies on upper extremity control that subjects reduce their efforts to resist position controlled perturbations after several seconds (de Vlugt et al., 2003a; de Vlugt et al., 2003b).

In contrast, pseudorandom force perturbations do not have this drawback and require the subject to actively resist the perturbation during the entire trial. Our research group has developed and validated a method to assess both the intrinsic and reflexive component of trunk stabilization by applying thorax perturbations with a linear actuator while subjects are restrained at the pelvis in a kneeling-seated position (van Drunen et al., 2013). However, the reliability of this method is still unknown. Reliability might be influenced by LBP because of possible variability over time in motor control impairments in LBP (Granata et al., 2004). Therefore, the purpose of this study was to investigate the between-day reliability of a pseudorandom force perturbation method to measure trunk stability in both healthy subjects and in LBP patients.

Methods

Subjects

Thirteen healthy subjects (5 males, age range 22-28 years, mean mass: 74 kg (± 13 kg)) and eighteen patients with LBP (10 males, age range 29-69 years, mean mass: 89 kg (±23 kg)) participated in this reliability study. All participants met the following inclusion and exclusion criteria; the healthy subjects did not have LBP in the year prior to the experiments. The group of patients suffered from non-specific LBP, or LBP following back surgery, for at least six weeks. Fusions, prostheses or other operations that cause substantial anatomical changes were excluded. Subjects had no radicular pain caused by lumbar nerve root compression or a hernia nuclei pulposi, nor did they have any neurological disorders that might interfere with trunk control (e.g. Cerebro Vasculair Accident, Multiple Sclerosis or Parkinson's disease). All participants read and signed an informed consent form prior to the experiment according to the guidelines of the medical ethical committee of VU Medical Center Amsterdam.

Protocol

To assess the test-retest reliability, two separate measurements were performed following the procedure described below. The time between repeated measurements for healthy subjects was 1-3 days. Patients repeated the protocol

after 1-2 weeks. This was done in order to decrease burden and to prevent influence of possible muscle-soreness after the first measurement.

The experimental setup was similar to previous studies (van Drunen et al., 2013; Maaswinkel et al., 2015b). The participants were positioned in a semi-kneeling-seated posture with their pelvis restrained (Fig. 1). The subjects were blindfolded to prevent visual feedback and were asked to cross their arms during the trials. During trials, a ventral force perturbation was applied at the T10 level of the spinous process by a magnetically driven linear actuator (Servotube STB2510S Forcer and Thrustrod TRB25-1380, Copley Controls, USA). A thermoplastic patch (4x4 cm2) was placed between the device and the subject for comfort and better force transfer. Each subject was instructed to 'sit as still as possible' during the perturbations (resist-task). The patients performed additional trials in which they were asked to 'Relax, but sit upright' (relax-task). Each condition was repeated three times.

Figure 1:
The experimental setup

The same pseudorandom force perturbation signal was used for each participant and for both consecutive assessments and consisted of a pseudorandom dynamic force disturbance of ±35 N combined with a 60 N baseline preload. The dynamic disturbance was a crested multi-sine (sum of sine waves) (Pintelon and Schoukens, 2001) that contained 18 logarithmically distributed paired frequencies within a bandwidth of 0.2-15 Hz (Fig. 2). Lower frequencies would require longer trials to

achieve sufficient reliability of the FRF at these frequencies, which may interfere with the assumption of time-invariance inherent in our analysis techniques. Power above 4 Hz was restricted to 40% to reduce adaptive behavior to high frequency content (Mugge et al., 2007). Because a random perturbation was applied, subjects were not expected to voluntarily react to the disturbance. Each run lasted 50 seconds, consisting of a 3 second ramp force increase to the 60 N load level, a two second stationary load, a start-up period to reduce transient behavior (the last 5 seconds of the dynamic disturbance), and twice a twenty second dynamic disturbance.
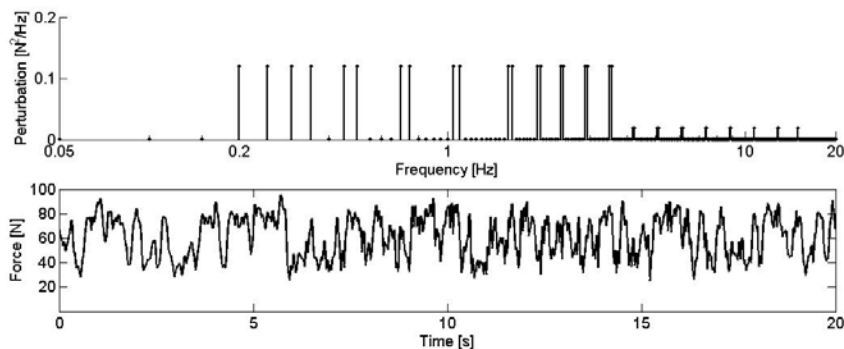
Figure 2:
The power spectrum (above) and time series (below) of the applied force perturbation.

After each trial, patients were asked for their momentary pain using a 10-point numeric pain rating scale (NPRS) (Freyd, 1923). Additionally, patients filled in a 7-days pain diary, using a 10-point NPRS, prior to both measurements. Both momentary pain and pain-diary scores were used for LBP-identification (NPRS-score > 0) and to assess the stability of pain between the two measurements. To correct for possible changes in severity between consecutive assessments of known prognostic factors in patients with low back pain (i.e.. illness beliefs, fear of movement, catastrophizing, depression and anxiety), the Oswestry Low Back Pain Questionnaire (Fairbank et al., 1980), Back beliefs questionnaire (Symonds et al., 1996), Tampa scale for kinesiophobia (Kori et al., 1990), *Hospital Anxiety and Depression Scale* (Zigmond and Snaith, 1983) and Pain catastrophizing scale (Sullivan et al., 1995) were used.

Data recording and processing
The horizontal displacement of the thorax and the contact force between the

pushing device and the thorax were measured at 2000 samples/s (Servotube position sensor & Force sensor FS6-500, AMTI, USA). Activity of the M. Longissimus at the level of L3 and L4 was bilaterally recorded at 2048 samples/s (surface electromyography (sEMG) REFA, TMSi, the Netherlands). The electrodes were placed by the same researcher on both measurement days. The electrode placement area was first shaved and cleansed with rubbing alcohol before applying the electrodes 3 cm lateral to the spinous processes. The M. Longissimus was chosen because of the high coherence between this muscle's activity and thorax displacement (van Drunen et al., 2013). The EMG data were digitally filtered (first-order, zero-phase, high-pass) at 250 Hz (Staudenmann et al., 2007), rectified and normalized to the maximum value during the trial.

System identification

Closed loop system identification techniques (van der Helm et al., 2002; Schouten et al., 2008a; van Drunen et al., 2013; Maaswinkel et al., 2015b) were used to estimate the translational admittance ($H_{adm}(f)$) and reflexes ($H_{emg}(f)$) of the trunk as frequency response functions (FRFs). The admittance describes the actuator displacement ($x_A(t)$) as a function of the contact force ($F_C(t)$). The reflexes describe the EMG data ($e(t)$) as a function of the actuator displacement ($x_A(t)$). Because the subjects interacted with the actuator, FRFs were estimated using closed loop methods:

$$H_{adm}(f) = \frac{S_{F_p X_A}(f)}{S_{F_p F_C}(f)}; \quad H_{emg}(f) = \frac{S_{F_p e}(f)}{S_{F_p X_A}(f)} \tag{1}$$

with $S_{F_{pX_A}}(f)$, $S_{F_{pF_C}}(f)$ and $S_{F_{p}e}(f)$ representing the estimated cross-spectral densities between the actuator displacement ($x_A(f)$) and Fourier transformed force-perturbation ($F_P(f)$), contact force ($F_C(f)$)(interaction with the subject) and EMG ($e(f)$) respectively. The cross-spectral densities were only evaluated at the frequencies containing power in the force perturbation. The cross-spectra were averaged across the 6 time segments per task (three trials each containing two segments of 20 seconds) and over 2 adjacent frequency points to improve estimates and reduce noise (Jenkins and Watts, 1969). Finally, the cross-spectra between EMG and force perturbations were averaged over the left and right muscles. The coherence of the admittance and reflexes associated with (γ^2_{adm}) and (γ^2_{emg}) was derived as:

$$\gamma^2{}_{adm}(f) = \frac{\left|S_{F_pX_A}(f)\right|^2}{S_{F_pF_p}(f)S_{X_AX_A}(f)}; \quad \gamma^2{}_{emg}(f) = \frac{\left|S_{F_pe}(f)\right|^2}{S_{F_pF_P}(f)S_{ee}(f)} \tag{2}$$

Coherence ranges from zero to one, where a coherence of one reflects a perfect, noise-free relation between input and output. Since spectral densities were averaged over 12 points, a coherence greater than 0.24 is significant with $P<0.05$ (Halliday et al., 1995).

Statistics

To test for any significant differences between the questionnaires and pain scores between the two measurements in patients, a paired samples t-test was used. Normality was tested with the Shapiro-Wilk and in case of non-normality, a Wilcoxon signed-rank test was performed. To satisfy the assumption of normality, the gains of admittance and reflexes were log-transformed. Sphericity was checked with Mauchly's test and if the assumption of sphericity was violated, a Greenhouse-Geiser correction was used (Girden, 1992). To investigate whether the admittance or reflexes between the first measurement and the retest significantly differed, a 2 factor (measurement-day [2] x frequency [18]) repeated measures ANOVA was performed on the gain of the admittance and on the gain of the reflexes. Significant main effects were followed up by Bonferroni corrected pair-wise comparisons and significant interaction effects were followed up by one-way repeated measures ANOVA's. Effects with $P < 0.05$ were considered significant.

Because task-related modulation of admittance and reflex gain mainly occurs below the natural frequency of about 1.1Hz (van Drunen et al., 2013), the average of the first five frequency pairs was taken to calculate the reliability of the low-frequency gains of the admittance and reflexive FRFs. To detect any significant differences between measurement-days, a paired samples t-test was performed over these low frequency gains.

To test reliability, the intraclass correlation coefficient (ICC (3,1)) was calculated according to Shrout et al. (1979). The ICC ranges from 0 to 1 where <0.40 indicates a 'poor' to 'fair' agreement, 0.41 to 0.60 represents a 'moderate' agreement, 0.61-0.80 represents a 'substantial' agreement and >0.81 represents an 'almost perfect' agreement (Landis and Koch, 1977). To quantify the absolute reliability, the Standard Error of Measurement (SEM), Minimal Detectable Change (MDC) and the Limits of Agreement (LoA) were calculated. The calculation of the SEM and the

MDC was performed according to Weir (2005), the LoA were calculated according to Bland and Altman (Bland and Altman, 1986). Bland-Altman plots were plotted over all 18 frequency pairs to provide a visual illustration of agreement and to detect any form of bias. All data recording, processing and system identification were done using MATLAB, version R2011a (The Mathworks, Inc., Natick, MA). All statistical analyses were conducted using IBM SPSS statistics 20.

Results

No significant differences were found in momentary pain and other prognostic factors measured with the questionnaires between the measurement-days in the patients. However, there was a significant difference in pain-diary scores (Table 1). The clinical important difference on a 10-point NPRS for average pain scores is 2.5 points (Farrar et al., 2010). Two patients showed a decrease of more than 2.5 points in their pain-diary scores and were therefore excluded from further analysis.

Table 1: Averaged of the questionnaires and pain-scores in patients.

	Mean (±SD) measurement 1	Mean (±SD) measurement 2	df	t	p	Effect size	95% CI
Momentary pain†*	3.5 [1.8, 6.4]	2.8 [1.2, 5.4]	-	-0,653*	0.513	0.15	-
Pain-Diary	5.7 (±1.5)	5.0 (±1.9)	16	2.260	0.038**	0.49	[0.05, 1.46]
ODI	33.5 (±16.1)	30.4 (±18.1)	15	1.205	0.247	0.30	[-2.35, 8.48]
BBQ	27.1 (±7.5)	28.3 (±7.4)	15	-0.434	0.671	0.11	[-6.66, 4,41]
TSK†*	39 [33, 44]	37 [32, 43]	-	-0.945*	0.344	0.24	-
HADS	10.3(±6.7)	9.3 (±6.5)	15	1.331	0.203	0.33	[-0.64, 2.76]
PCS	17.7 (±9.8)	19.6 (±8.3)	14	-0.997	0.336	0.26	[-5.88, 2.15]

†Median (Interquartile range [IQR])
*Z-score calculated with the Wilcoxon rank-sum test
** Significant differences between measurement-days (P<0.05)
ODI= Oswestry Low Back Pain Disability Questionnaire; BBQ= Back Beliefs Questionnaire; TSK= Tampa Scale for Kinesiophobia; HADS= Hospital Anxiety and Depression Scale; PCS= Pain Catastrophizing Scale.

The low-back stability in both healthy subjects and patients is described by the FRF's of admittance and reflexes (Figs. 3, 4 and 5), with high coherence indicating good input-output correlations. The subject-averaged coherence exceeded the 0.05 probability level of 0.24 in both groups and conditions. Therefore, all data were used for further analysis. The admittance FRF resembles a second-order system (i.e. a mass-spring-damper system) combining both intrinsic and reflexive responses (Schouten et al., 2008b; van der Helm et al., 2002; Pintelon and Schoukens, 2001). The lower frequencies (<1.1 Hz) reflect intrinsic stiffness and

reflexes, where the high-frequencies (>2 Hz) are mainly influenced by body mass and contact dynamics. The intermediate frequencies resemble intrinsic damping and reflexive behavior. The reflexive FRF indicates the presence of position feedback (low frequency flat gain), velocity feedback (intermediate frequencies) and acceleration and/or force feedback (high-frequency second order ramp-up).

No significant differences (P>0.05) were found between measurement-day one and measurement-day two in the admittance or reflexive gains (Table 2, Figs. 3a, 3b and 3c). Also no significant differences (P>0.05) were found in the low frequency gains (average of frequency pairs below 1.1 Hz) of the admittance and reflexes (Table 3). The Bland Altman Plots of the admittance and reflexive gains in the resist-task (shown for healthy subjects and patients in figure 4) showed no forms of bias, meaning that differences between the two measurement-days were uniformly distributed over the means.

The test-retest ICC's in patients calculated over the averaged lower frequency gains were substantial for both admittance and reflex gains (ICC$_{3,1}$ 0.73 and 0.67 for resist-task, 0.80 and 0.70 for relax-task). In healthy subjects, the reliability of admittance gain in the resist-task was also substantial (ICC$_{3,1}$ 0.66), but the ICC of the reflexive gain was only moderate (ICC$_{3,1}$ 0.44). The SEM of the reflexive gain, however, showed lower values in healthy subjects (0.35) then in patients (0.48).

When evaluating the reliability for the 18 separate perturbation frequencies, high ICC's were found for admittance gain over the full range of frequencies in both healthy subjects and LBP patients (see Figure 5, upper graph). The same consistency can be seen for the reflex gain during the resist-task in LBP patients. However, there was a decline in ICC's between 1.1-3.5 Hz for the reflex gain in healthy subjects during the resist-task and in patients during the relax-task and again between 13-15 Hz in the resist-task in healthy subjects (see Figure 5, middle graph). Reliability is directly related to inter-subject variability. For example, small intra-subject variability (high agreement) in combination with large inter-subject variability results in low reliability (ICC) (de Vet et al., 2006). Therefore, the standard deviations (SD) of the reflex gain values between subjects were evaluated for all frequencies. The SD's for healthy subjects were lower at almost all frequencies compared to LBP patients and were lowest between 1.1-3.5 Hz (see Figure 5, lower graph), explaining the decrease of ICC's in healthy subjects. The ICC's between 1.1-3.5 Hz during the relax-task in patients could not be explained by inter-subject variability, suggesting that reflex gains between these frequencies,

which most likely reflect velocity feedback, cannot be measured reliably during a relax-task in patients.

Table 2:
Main and interaction effects of the repeated measures ANOVA for measurement-days on the admittance and reflex gains over all 18 paired frequency points.

Healthy subjects	Resist					
	F	df	P			
Admittance						
Measurement-day	0.754	1, 12	0.402			
Measurement-day x frequency*	1.331	3.3, 39.2	0.278			
Reflexes						
Measurement-day	0.000	1, 12	0.984			
Measurement-day x frequency*	1.569	4, 48.2	0.197			
Patients	Resist			Relax		
	F	df	P	F	df	P
Admittance						
Measurement-day	0.252	1, 15	0.623	0.864	1, 15	0.367
Measurement-day x frequency*	1.290	2.5, 37.9	0.291	2.490	3.4, 50.3	0.065
Reflexes						
Measurement-day	1.638	1, 15	0.220	0.214	1, 15	0.650
Measurement-day x frequency*	1.999	4.4, 65.8	0.099	1.006	6.1, 90.9	0.427

Use of Greenhouse-Geiser correction in view of a violation of the assumption of sphericity.
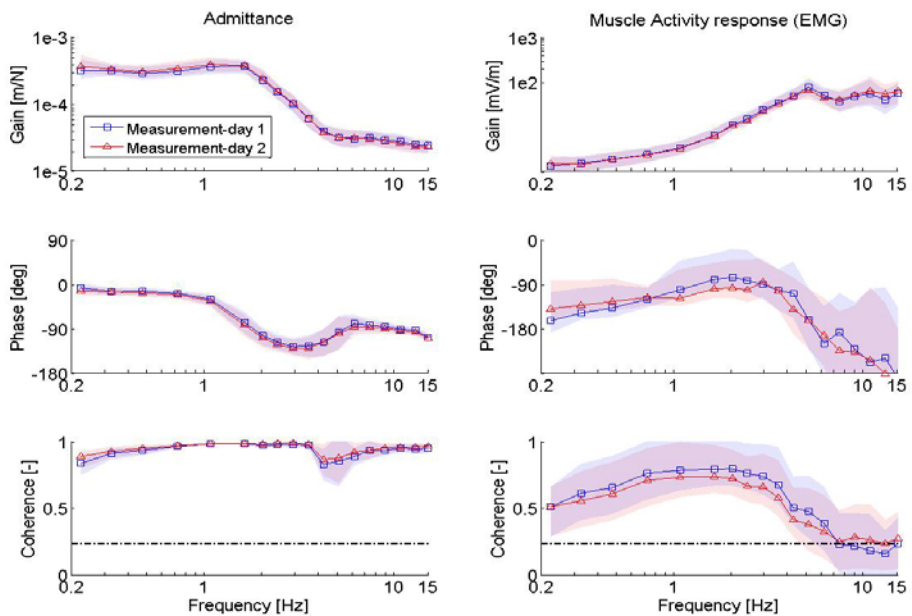

Figure 3A: Frequency response functions of the resist-task condition on measurement-day 1 (□) and measurement-day 2 (Δ) in healthy subjects. Shadings represent one standard deviation. The dashed line in the coherence-plots represents the significance level for coherence.

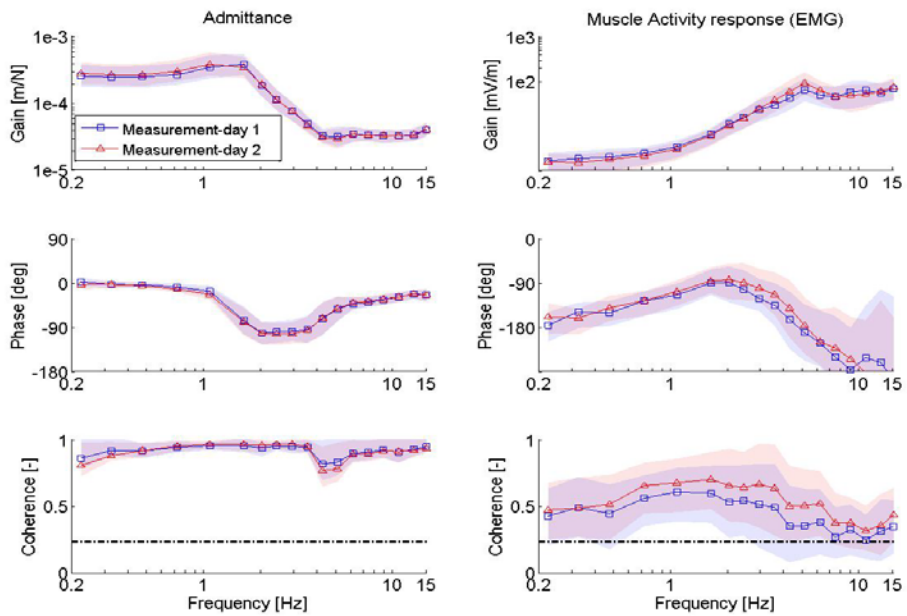**Figure 3B: Frequency response functions of the resist-task condition on measurement-day 1 (□) and measurement-day 2 (Δ) in patients. Shadings represent one standard deviation. The dashed line in the coherence-plots represents the significance level for coherence.**
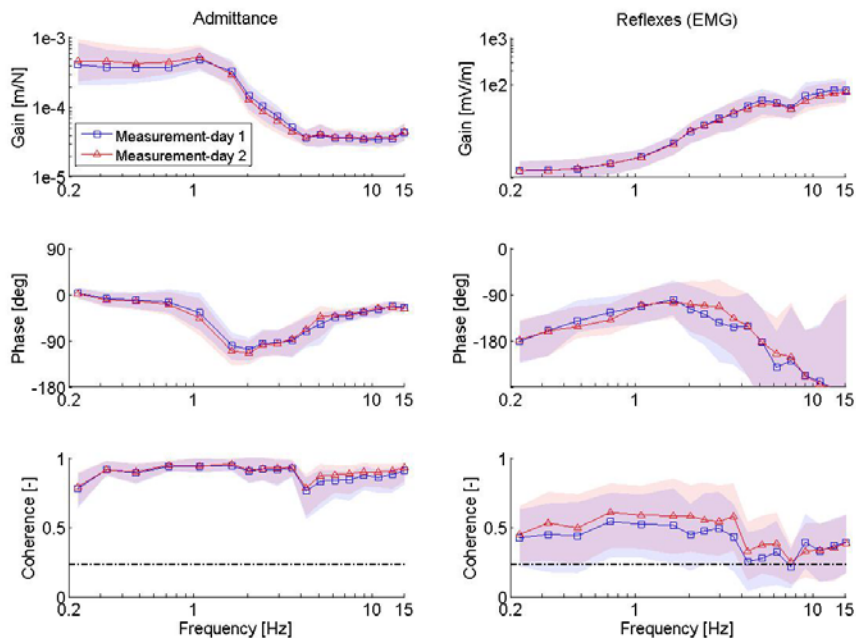

Figure 3C: Frequency response functions of the relax-task condition on measurement-day 1 (□) and measurement-day 2 (Δ) in patients. Shadings represent one standard deviation. The dashed line in the coherence-plots represents the significance level for coherence.

Table 3: Main effects of measurement-day on the averaged low frequency admittance and reflex gains calculated with a paired-samples t-test.

|	Mean (±SD) measurement 1	Mean (±SD) measurement 2	df	t	p	Effect size	95% CI
Resist							
Admittance healthy subjects	-8.11 (±0.23)	-8.02 (±0.25)	12	-1.483	0.164	0.394	[-0.20, 0.04]
Reflexes healthy subjects	0.59 (±0.47)	0.59 (±0.40)	12	-0.010	0.992	0.003	[-0.28, 0.28]
Admittance patients	-8.33 (±0.44)	-8.24 (±0.41)	15	-1.185	0.255	0.210	[-0.26, 0.07]
Reflexes patients	0.46 (±0.83)	0.54 (±0.53)	15	-0.553	0.589	0.096	[-0.39, 0.23]
Relax							
Admittance patients	-8.02 (±0.54)	-7.88 (±0.52)	15	-1,730	0.104	0.257	[-0.31, 0.03]
Reflexes patients	0.23 (±0.88)	0.38 (±0.62)	15	-0.973	0.346	0.164	[-0.46, 0.17]
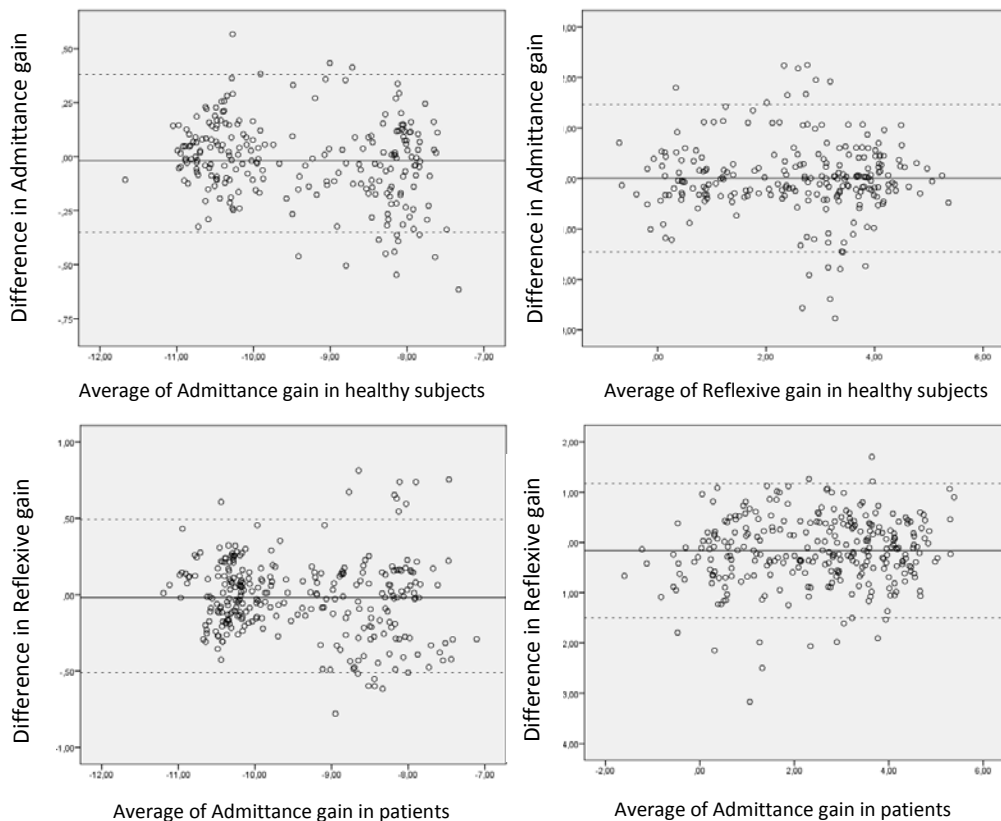
Figure 4: Bland Altman plot of the admittance gain (left) and reflexive gain (right) during the resist-task in healthy subjects (above) and LBP patients (below). The open black circles represent the differences in admittance gain or reflex gain between the two measurement-days in all subjects for all frequency points. The horizontal line represents the mean difference of the admittance and reflex gains, where the dotted lines represent the limits of agreements; in healthy subjects respectively [-0.35, 0.38] for admittance and [-1.47, 1.47] for reflexes and in patients respectively [-0.51, 0.48] for admittance and [-1.50, 1.17] for reflexes.

ICC's per frequency for Admittance (upper) and reflexive gain (middle)
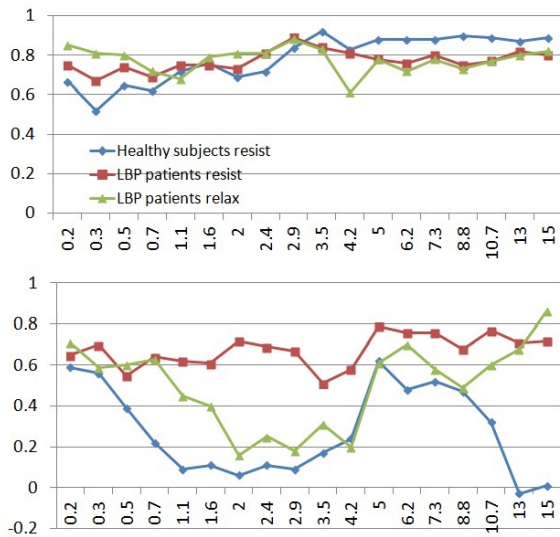

Figure 5: The upper graph represents the calculated ICC"s for the admittance gain (on the y-axis) for all frequencies [Hz] (on the X-axis). The middle graph represents the calculated ICC's for the reflex gains for all frequencies and inter-subject SD's for reflex gains for all frequencies are shown in the lower graph.

Standard Deviations per frequency for reflexive gain

Table 4: Between-day reliability of the low frequency gains.

	$ICC_{3,1}$	p	SEM	LoA
Resist				
Admittance Healthy subjects	0.66 [0.22, 0.88]	0.004*	0.13	[-0.46, 0.30]
Reflexes healthy subjects	0.44 [-0.16, 0.79]	0.066	0.35	[-0.92, 0.92]
Admittance patients	0.73 [0.39, 0.89]	<0.001*	0.23	[-0.71, 0.52]
Reflexes patients	0.67 [0.27, 0.87]	0.002*	0.48	[-1.20, 1.05]
Relax				
Admittance patients	0.80 [0.51, 0.92]	<0.001*	0.24	[-0.77, 0.49]
Reflexes patients	0.70 [0.33, 0.88]	0.001*	0.48	[-1.30, 1.01]

Significant ICC-scores

$ICC_{3,1}$= Intraclass correlation coefficients [95% confidence interval]; SEM= standard error of measurement; LoA= Limits of agreement.

Discussion

The purpose of the present study was to determine the test-retest reliability of a method to measure trunk stability using pseudorandom force perturbations. The reliability showed to be satisfactory for healthy subjects during a resist-task and LBP patients during both a resist-task and relax-task, with the exception of reflex gains in healthy subjects, for which reliability was only moderate. The Bland Altman plots for both groups showed no relationship between the discrepancies of admittance gain and reflex gain between measurement-days and the mean values in both groups. These results show that trunk stabilization can be quantified reliably, and represent a promising step towards using this method in further research in LBP patients. The small SEM's show that within-person measurement error is moderate, which holds promise for detection of (small) differences between assessments.

The admittance gain was consistently more reliable than reflex gain in both groups across conditions, which can be explained by the inherently noisy character of EMG-signals. Also, variability in reflex sensitivity might contribute to a decreased reliability (Granata et al., 2004). To adjust for this variability and possible measurement error, averaging over more repetitions could increase the reliability of measuring reflex gains (Voglar and Sarabon, 2014), but might not be feasible for patients with LBP. Remarkably, the ICC's (which are measures of how well subjects can be distinguished from each other) of both admittance and reflex-gains were higher in patients than in healthy subjects, which might be explained by the relatively low between-subject variability and low SEM in the healthy subjects compared to the patients (Table 3) (Portney and Watkins, 2000). The higher between-subject variability in patients might be due to variability of motor control impairments with LBP, as diverse changes in trunk control have been found in the literature, with evidence of decreased as well as increased trunk stiffness and reflexes (Hodges and Moseley, 2003; van Dieen et al., 2003). On group level, the means in admittance gain for both groups do not differ, confirming these observations. In line with the between-subject variability, the SEM's were also lower in healthy subjects than in patients, which implies a lower minimal detectable change and, therefore, a higher agreement.

The present study is one of the few evaluating the reliability of measuring trunk stability (Maaswinkel et al., submitted for publication). Hendershot et al., (2012) performed a short-term reliability study (between-day interval of 3-14 days

approximately) on a method with position perturbations in healthy subjects. When comparing the present results to those of Hendershot et al., (2012), we see that the between-day reliability in healthy subjects was similar for trunk admittance (ICC=0.66 and ICC=0.67 respectively) and reflex gain (ICC=0.44 and ICC=0.37 respectively). However, the lower limits of the 95% confidence interval of Hendershot et al., (2012) were higher (0.55 and 0.23) than in the present study (0.22 and -0.16). This might be explained by the larger number of participants in their study (n=33) compared to ours (n=13). Larivière et al., (2015) performed a medium-term reliability study (between-day interval of eight weeks) on a similar method as Hendershot et al., (2012). The reliability was comparable to Hendershot et al., (2012) but, when averaging the scores over three (or more) trials, reliability improved to an ICC > 0.70 for most of the parameters (Larivière et al, 2015). A drawback of position perturbations, however, is that subjects might not be motivated enough to maximally resist the perturbation as they would during force perturbations (de Vlugt et al., 2003a; de Vlugt et al., 2003b). In the present study, a distinction was made between a resist-task as a measure of the maximal stabilizing capacity and a relax-task as a more natural stabilizing task. This distinction gives insight in both the capability of a subject to forcefully resist a perturbation, as well as the capability to relax, which provides information that may be relevant to identify neuromuscular control impairments in LBP patients. In an earlier conducted experiment on healthy subjects, task related modulations were shown at the lower frequencies, where admittance in the resist task was 61% lower (P = 0.02) than in the relax task. The reflex gain was 71% higher (P = 0.03) in the resist task than in the relax task (van Drunen et al., 2013). In the current study, task modulations in patients were less prominent, with a 3.7% lower admittance gain in the resist task than in the relax task and a 50% higher reflex gain in the resist task compared to the relax task. These results suggest that patients might be less able to modulated between tasks than healthy subjects.

One reliability study was performed on a method that included pseudorandom force perturbations applied to the pelvis with a robotic platform (Reeves et al., 2014). Ten healthy subjects were instructed to either keep their trunk position upright or their trunk force constant during perturbation. Subjects were measured on two days, separated by a minimum of 24 hours. ICC scores on position stabilizing (ICC = 0.76), flexion force stabilizing (ICC = 0.89) and extension force stabilizing (ICC = 0.83) were all excellent. Three other studies on the reliability of a trunk stabilization measurement used sudden loading techniques of the trunk or upper arm on healthy subjects (Hodges et al., 2009; Voglar and Sarabon, 2014;

Santos et al., 2011). Even though the ICC's were all comparable to those in the present study, a drawback of sudden loading methods is the inability to selectively include power in the perturbation signal, which necessitates a relatively large perturbation force and a large number of repetitions to allow identification of intrinsic and reflexive contributions to stabilization, which both might not be feasible for studying trunk control in LBP patients.

There are some limitations to this study. Firstly, a relatively small number of people (13 healthy subjects and 18 patients) participated in this study. According to the COSMIN checklist (Terwee et al., 2012), a minimum of 50 subjects is needed to consider the quality of the reliability study as 'good'. However, this checklist was initially developed for the scoring of studies on the clinimetric properties of questionnaires, which are more susceptible to psychological influences. Despite the low number of subjects, results showed to be satisfactory indicating that subjects are sufficiently distinguishable from one another in spite of measurement errors. Also, scores showed to be close for repeated measures. Secondly, no relax-task was performed by the healthy subjects. However, in line with the results that we found in the patients, we expect the reliability of the relax-task in healthy subjects to be comparable to the resist-task in healthy subjects. Also, there was a different time-span between the measurement-days for patients (1-2 weeks) and healthy subjects (1-3 days). Although a learning-effect was unlikely due to the unpredictability of the applied perturbation, one could expect reliability scores to increase when time between measurements decreases because within-subject changes that could be of influence on motor control would be less likely to take place. However, such a difference in reliability did not occur, with ICCs not being higher in the group of healthy subjects who had less time between the measurements than the patients. Lastly, two patients were excluded in this study because of a decrease of >2.5 in pain diary-scores between measurement-days. This was done to ensure similarity between both measurements. When including these patients, the ICC scores for the resist-task remained the same for the reflex gain and increased slightly for the admittance gain (from 0.73 to 0.75). However, the ICC scores for the relax-task decreased from 0.80 to 0.79 for the admittance gain and even from 0.70 to 0.66 for the reflex-gain. Although these reductions are limited, they may provide an indication of sensitivity of the measurements to change in disease severity, and therefore of the possibility to monitor disease trajectories over time. The exact relationship between changes in pain and changes in admittance and reflex gains, however, still has to be established for this method. Furthermore, the influence of known confounders such as fear of

movement, illness beliefs or catastrophizing should be established to be able to interpret the relationship between disease severity and motor control.

In short, the results indicate that the test-retest reliability of admittance gain estimated using pseudorandom force perturbations is substantial in both patients and healthy subjects, while the reliability of reflex gains was substantial in patients and moderate in healthy subjects. Further research should provide insight in the impairment of motor control in LBP patients and assess if the method is responsive to changes in severity of LBP.

Chapter 5

Effects of vision and lumbar posture on trunk neuromuscular control

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Abstract

The goal of this study was to determine the effects of vision and lumbar posture on trunk neuromuscular control. Torso perturbations were applied with a pushing device while the subjects were restrained at the pelvis in a kneeling-seated position. Torso kinematics and the muscle activity of the lumbar part of the M. Longissimus were recorded for 14 healthy subjects. Four conditions were included: a flexion, extension and neutral lumbar posture with eyes closed and the neutral posture with eyes open. Frequency response functions of the admittance and reflexes showed that there was no significant difference between the eyes open and eyes closed conditions, thereby confirming that vision does not play a role in the stabilization of the trunk during small-amplitude trunk perturbations. In contrast, manipulating posture did lead to significant differences. In particular, the flexed condition led to a lower admittance and lower reflex contribution compared to the neutral condition. Furthermore, the muscle pre-activation (prior to the onset of the perturbation) was significantly lower in the flexed posture compared to neutral. This confirms that flexing the lumbar spine increases the passive tissue stiffness and decreases the contribution of reflex activity to trunk control.

Introduction

The human trunk is inherently unstable without motor control, as any deviation from the vertical will be aggravated by gravity. Research into how unstable postures are controlled has mainly focused on the control of upright stance, often considering the body as a single inverted pendulum rotating around the ankles (van der Kooij et al., 2001; Welch and Ting, 2008). However, understanding the stabilization of the trunk specifically might be important as impaired trunk control has been observed in patients with such diverse disorders as low back pain (Descarreaux et al., 2005; Willigenburg et al., 2013), Parkinson's disease (van der Burg et al., 2006), stroke (Ryerson et al., 2008) and spinal cord injury (Seelen et al., 1997).

Trunk control is dependent on adequate sensory feedback and muscular control, as the passive stiffness of the spine's ligaments and intervertebral discs alone is insufficient to maintain trunk stability (Bergmark, 1989b; Crisco and Panjabi, 1991a). Previous studies have shown that upright stance control is attained by sensory integration mechanisms that generate corrective torques based on a combination of proprioceptive reflexes with short delays (20-50ms) and corrective responses based on integrated information from proprioceptive, visual and vestibular systems with relatively long feedback delays (150-200ms) (Peterka, 2002; Cenciarini and Peterka, 2006; Maurer et al., 2006). However, very little research has focused on the sensory information used in trunk control.

Vision contributes to trunk control with anticipatory feed-forward information (Krishnan and Aruin, 2011; Mohapatra et al., 2012; de Santiago et al., 2013; Mohapatra and Aruin, 2013) and/or reactive feedback information. Very little work has been done to investigate the influence of visual information on the reactive control of trunk posture. Goodworth and Peterka (2009b) showed small but significant effects on trunk control of a tilting visual field during unpredictable pelvic-tilt perturbations, while the long-latency component (including visual information) of their model generated twice the amount of corrective torque compared to any other feedback component. In contrast, Moorhouse and Granata (2007b) have suggested that trunk control under unpredictable external perturbations is mainly attributable to proprioceptive reflexes. Similarly, van Drunen et al. (2013a) have shown that a model with intrinsic stiffness and damping and proprioceptive reflexes only (no visual and/or vestibular components) was able to describe the dynamic behavior of the trunk during dynamic perturbations. Therefore, trunk control may be different from stance

control and a more detailed analysis of the contribution of sensory modalities with long (e.g. visual) and short (e.g. muscle-spindle) delays to trunk stabilization is needed.

Muscle spindles have an important influence on trunk control, through feedback of position and movement of the trunk. Muscle spindle contributions may depend on the posture of the lumbar spine. For example, sitting with a flexed spine lengthens the lumbar muscles, which affects the information from muscle spindles, and in turn, may affect reflex activity (O'Sullivan et al., 2002; Granata and Rogers, 2007a). Furthermore, the passive stiffness of the trunk increases with flexion, lateral flexion and extension (McGill et al., 1994). Therefore, changing lumbar posture might influence the stability of the trunk and the contribution of intrinsic and reflexive mechanisms.

The goal of this study was to determine the effects of vision and lumbar posture on trunk neuromuscular control. Based on the modelling work of van Drunen et al. (2013a), it was hypothesized that visual information has no effect on trunk control during small-amplitude trunk perturbations. Furthermore, it was hypothesized that posture would affect trunk control and change the relative contributions of intrinsic and reflexive mechanisms.

Methods

Subjects

The study was approved by the ethical committee of the Faculty of Human Movement Sciences of the VU University Amsterdam. Fourteen healthy subjects participated in the experiment (5 males, age range 22-28 years, mean mass: 74kg (±13kg)). All subjects gave their informed consent prior to the experiment. Subjects reported no low back pain in the year prior to the experiment and did not suffer from any visual impairments or neurological disorders that could affect balance control.

Experimental set-up

Subjects were positioned in a kneeling-seated posture, while the pelvis was fixed to reduce pelvic motion (Figure 1). During the trials, subjects were requested to keep their arms crossed in front of their chest. A force perturbation was applied at the level of the spinous process of T10 in ventral direction. For comfort and better force transmission, a thermoplastic patch (5 x 5cm) was placed between the

Figure 1:
The experimental set-up.

pushing rod and the back of the subject. During all trials, subjects were instructed to minimize flexion/extension and lateral flexion excursions and thus resist the force perturbation as good as possible. Each subject performed a total of 4 conditions: neutral posture-eyes open, neutral posture-eyes closed, flexion posture-eyes closed and extension posture-eyes closed. During the flexion and extension posture trials, the pelvis was rotated maximally in the posterior (flexion) or anterior (extension) direction while the trunk was kept upright, resulting in a lumbar flexion of 22.9° (±1.7°) and lumbar extension of 19.5° (±5.7°) compared to neutral posture. Each condition was repeated four times, giving a total of 16 trials per subject.

Force perturbation

As the pushing rod was not attached to the subject, a 60N preload was applied to maintain contact. Superimposed on the preload, a dynamic disturbance with a 35N amplitude was applied (Figure 2, second panel) as described by van Drunen et al. (2013a). The dynamic disturbance (F_p(t)) was a crested multi-sine (Pintelon and Schoukens, 2001) of 20s duration containing 18 logarithmically spaced frequency pairs with a bandwidth ranging from 0.2 to 15Hz (Figure 2, top panel). To reduce adaptive behavior to high frequency content, the power above 4Hz was reduced to 40% (Mugge et al., 2007). Since the perturbation was perceived as random by the subjects, no feed-forward or voluntary activation was expected to occur in relation to the perturbation. Each force perturbation consisted of a 3s ramp force

Figure 2:
The power spectrum (top panel) and time signal (second panel) of the applied force perturbation, a typical example of the measured displacement during an eyes-open and eyes-closed trial (third panel) and a typical example of the measured EMG during an eyes-open trial (bottom panel).
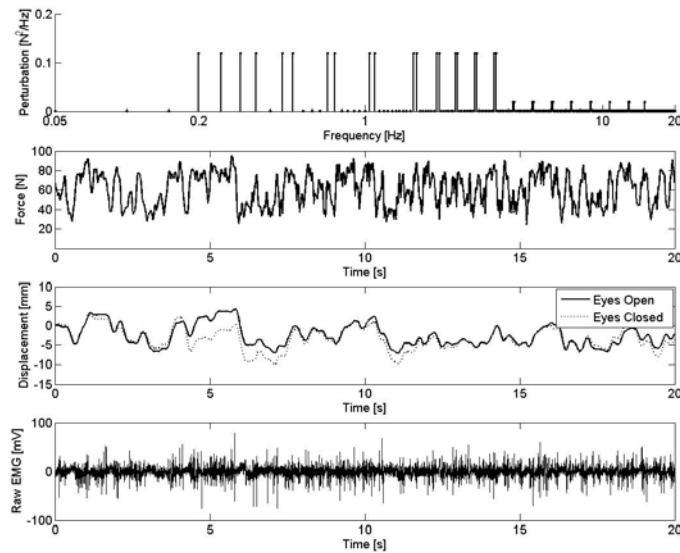
increase to 60N preload, a 2s static preload, the last 5s of the disturbance (as a start-up to reduce transient behavior) and twice the 20s dynamic disturbance giving a total of 50s per run.

Data recording and processing

The kinematics of the lumbar spine (L1-L5), the thorax (cluster of 3 markers at T6) and the pelvis (cluster of 3 markers at the sacrum) were measured using 3D motion tracking at 100Hz (Optotrak3020, Northern Digital Inc, Canada). The actuator displacement (x_A(t)) and contact force (F_c(t)) between the rod and the subject were measured at 2000Hz (Servotube position sensor & Force sensor FS6-500, AMTI, USA). Preliminary kinematic analysis revealed that rotation occurred both at the level of the lumbar spinal column and at the level of the pelvis. This indicated that the pelvic restraint was not able to completely eliminate movement of the pelvis. However, despite movement of the pelvis, all subjects showed substantial movement in the spine and could therefore be included for further analysis. Since the kinematic analysis indicated that an effective low-back bending rotation point, necessary to define rotations, was not well defined and inconsistent over subjects and tasks, trunk kinematics were described in terms of translation of the pushing rod.

Activity of the lumbar part of the M. Longissimus (*e(t)*) was recorded bilaterally at 2048Hz with surface electromyography (sEMG; REFA, TMSi, the Netherlands). The electrodes were placed 3cm lateral to the space between the spinous processes of

L3 and L4. The M. Longissimus was chosen given a high coherence between its activity and trunk displacement (van Drunen et al., 2013a). The EMG signals were digitally high-pass filtered at 250Hz (first order, zero-phase) (Staudenmann et al., 2007a), rectified and scaled to maximal voluntary contraction (MVC) level. The MVC was determined with 2 maximal extension contractions at the end of the experiment. For each contraction, the subject was instructed to build-up to a maximal contraction in 5s and hold the contraction for 3s against manual resistance provided by the experimenter. The EMG during the 3s plateau was averaged and the highest value of both contractions was used as MVC. To test whether differences in reflex activity between the different conditions can be explained by an altered level of muscle pre-activation, the normalized EMG amplitude was calculated over the 2s static preload (60N) preceding the dynamic disturbance. Finally, since the M. Longissimus counteracted the perturbation, the muscle activity during the perturbation was expressed as negative.

System identification

Closed-loop identification (van der Helm et al., 2002; Schouten et al., 2008a; van Drunen et al., 2013a) was used to determine the trunk translational admittance ($H_{adm}(f)$) and reflexes ($H_{emg}(f)$) as frequency response functions (FRFs). The admittance describes the actuator displacement ($x_A(t)$) as a function of contact force ($F_c(t)$), whereas the reflexes describe the EMG ($e(t)$) as a function of actuator displacement ($x_A(t)$). Because the subjects interacted with the actuator, FRFs were estimated using closed loop methods.

$$H_{adm}(f) = \frac{S_{F_p x_A}(f)}{S_{F_p F_c}(f)}; H_{emg}(f) = \frac{S_{F_p e}(f)}{S_{F_p x_A}(f)} \tag{1}$$

with $S_{F_p x_A}(f)$, $S_{F_p F_c}(f)$ and $S_{F_p e}(f)$ representing the estimated cross-spectral densities between the Fourier transformed force-perturbation ($F_p(f)$) and actuator displacement ($x_A(f)$), ,contact force ($F_c(f)$) and EMG ($e(f)$) respectively.

The cross-spectral densities were only calculated at the frequencies that contained power in the force perturbation. To reduce noise and improve the estimate, the cross-spectra were averaged across the 4 trials per condition, the two 20s time segments (dynamic disturbance) and across the 2 adjacent frequency points (Jenkins and Watts, 1969). Finally, the cross-spectra between force perturbation and EMG were averaged across the left and right muscles. The coherence of the admittance (γ^2_{adm}) and reflexes (γ^2_{emg}) was calculated as:

$$\gamma_{adm}^2(f) = \frac{\left|S_{F_p x_A}(f)\right|^2}{S_{F_p F_p}(f) S_{x_A x_A}(f)} \; ; \gamma_{emg}^2(f) = \frac{\left|S_{F_p e}(f)\right|^2}{S_{F_p F_p}(f) S_{ee}(f)} \tag{2}$$

Coherence ranges from zero to one, where one reflects a perfect, noise-free relation between input and output. Since the spectral densities were averaged across 16 points, a coherence larger than 0.18 is considered significant at the $p < 0.05$ level (Halliday et al., 1995a). Therefore, all frequency points with a subject-averaged coherence of 0.18 or larger were included for further analysis.

Statistics

The gains of the admittance and reflexes were log-transformed to satisfy the assumption of normality. Sphericity was checked using Mauchly's test. If the assumption of sphericity was violated, a Greenhouse-Geisser correction was used (Girden, 1992). Partial Eta Squared (η_p^2) was used as a measure of effect size. To investigate whether there was a significant difference in the admittance or reflexes between the eyes open and eyes closed condition, a 2 factor (condition [2] x frequency [18]) repeated measures ANOVA was performed on the gain of the admittance ($H_{adm}(f)$) and also on the gain of the reflexes ($H_{emg}(f)$). Furthermore, to investigate the differences between the neutral, flexion and extension conditions, another 2 factor (condition [3] x frequency [18]) repeated measures ANOVA was performed. Significant interaction effects were followed up by one-way repeated measures ANOVA's and significant main effects were followed up by Bonferroni corrected pair-wise comparisons.

Furthermore, to test if there was a significant difference between the levels of muscle pre-activation, a paired-samples t-test was performed on the EMG amplitude of the eyes-open and eyes-closed condition, and a one-factor repeated measures ANOVA was performed on the EMG amplitude of the neutral, flexed posture and extended posture conditions. A significant main effect was followed up by Bonferroni corrected pair-wise comparisons. Effects were considered significant when the corrected $p < 0.05$.

Results

A typical example of the measured position of one subject during the eyes-open and eyes-closed trials shows that the displacement corresponds with the force imposed (Figure 2).

The trunk stabilizing behavior is described by the FRF's of the admittance and reflexes (Figures 3 & 4), while high coherences indicate good input-output correlations. The subject-averaged coherence always exceeded the 0.05 probability level of 0.18 and therefore all data were used for further analysis. The FRF of the admittance resembles a combination of a second-order system (i.e., a mass-spring-damper system) and reflexive responses (c.f. Schouten et al., 2008). The behavior at high frequencies (> 2Hz) is predominantly determined by the mass of the trunk and contact dynamics. The low-frequency behavior (< 1Hz) is a reflection of the intrinsic stiffness and reflexes. The intermediate frequencies are also mainly determined by the reflexes and intrinsic damping. The FRF of the reflexes indicates the presence of position feedback (flat gain and -180° phase lag at lower frequencies), velocity feedback (+1 gain slope and -90° phase lag at intermediate frequencies) and acceleration and/or force feedback (second-order ramp-up at the high frequencies).

In line with the resemblance of the eyes open and eyes closed conditions in Figure 2, no significant effects of vision were found in the gain of the admittance and reflexes (Table 1, Figure 3). Furthermore, there was no significant difference between the baseline EMG of the eyes-open (23±13% of MVC) and eyes-closed (26±20% of MVC) condition (p = 0.309). Therefore, the hypothesis was confirmed that visual information does not contribute to stabilization of the trunk in the present task

Table 1:
Main and interaction effects of the ANOVA's for vision on the gain of the admittance and reflexes. * denotes a Greenhouse-Geisser correction due to a violation of the assumption of sphericity.

Admittance	F	df	P	Pairwise Comparisons
Condition	0.126	1, 12	0.729	-
Condition x Frequency[*]	1.044	3.7, 44.2	0.392	-
Reflexes				
Condition	0.326	1, 12	0.579	-
Condition x Frequency[*]	2.076	2.7, 33	0.127	-

For the influence of posture, two significant effects were found (Table 2). The flexed posture condition led to a significantly lower admittance gain compared to the neutral posture (p = 0.028, 95% CI [-0.237 -0.013]) (Figure 4, left top panel). The significant interaction indicated that this difference occurred mainly at the low (0.3-1 Hz) and high (7-15 Hz) frequencies. There were no significant differences in the admittance for the extended posture condition. For the reflexes, a lower gain in the flexed posture, compared to neutral, was visible but this failed to reach statistical significance (p =0.053, 95% CI [-1.177 0.008]) (Figure 4, right top panel). The flexed posture condition did lead to a significantly lower reflex gain compared to the extended posture condition (p = 0.013, 95% CI [-1.678 -0.193]). The changes in the reflex gains coincided with changes in muscle pre-activation as the EMG amplitude during the flexion posture (15±12% of MVC) was significantly lower (p = 0.005, 95% CI [-18.2 -3.4]) compared to the neutral condition (26±20% of MVC). Therefore, the second hypothesis was confirmed that posture would influence the intrinsic and reflexive contributions to trunk control.
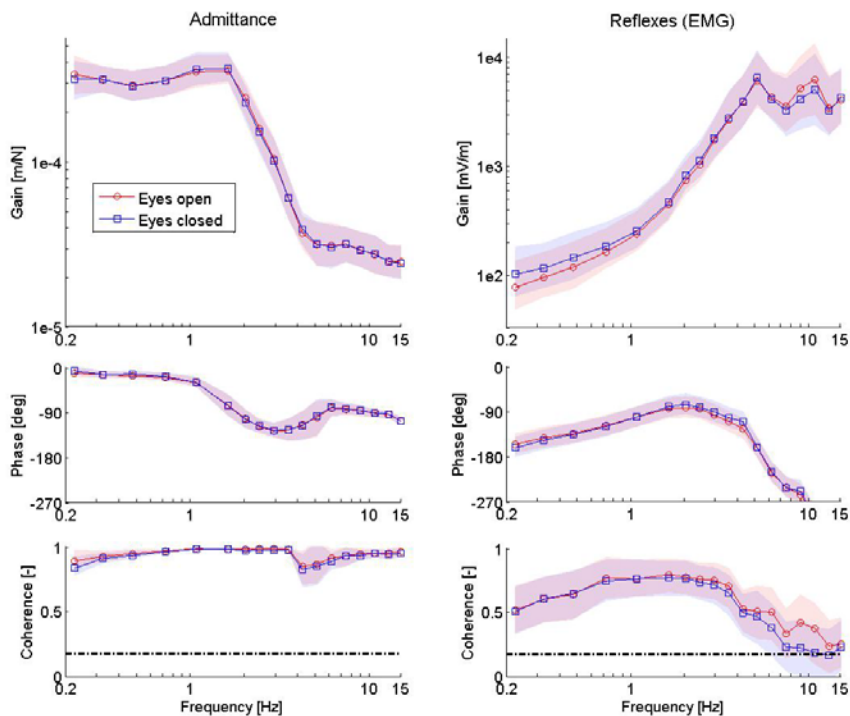

Figure 3:
Frequency response function for the eyes-open (O) and eyes-closed (□) condition averaged across all subjects. The shaded area represents one standard deviation. The dashed line in the lower plots represents the significance level for coherence.
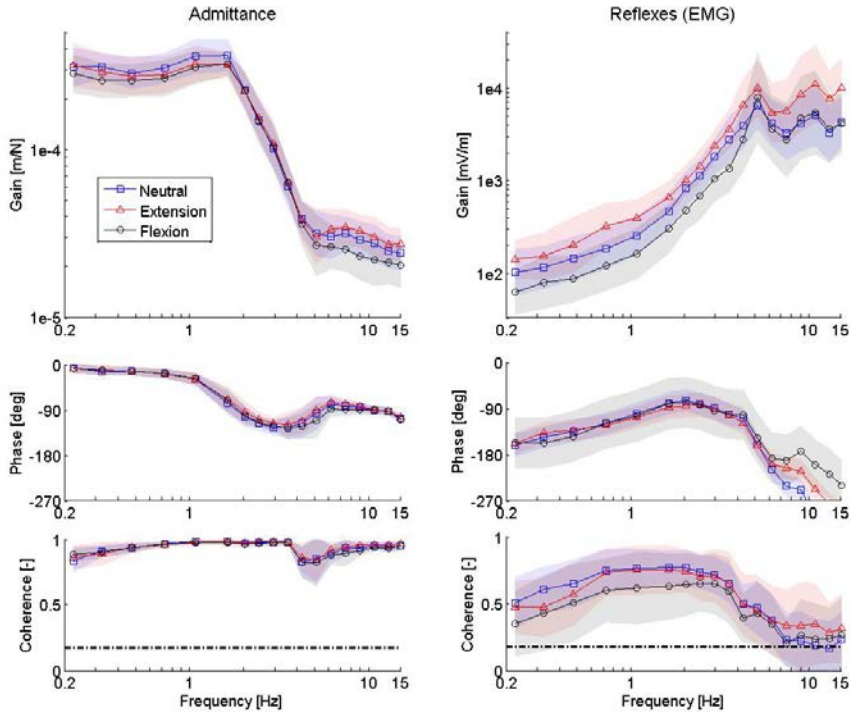
Figure 4:
Frequency response functions of the neutral (□), extended (Δ) and flexed (O) posture conditions averaged across all subjects. The shaded area represents one standard deviation. The dashed line in the lower plots represents the significance level for coherence.

Discussion

The purpose of the present study was to determine the effect of vision and sitting posture on trunk neuromuscular control. The results showed that having the eyes open had no effect on trunk neuromuscular control, thereby confirming that visual information does not contribute to stabilization of the trunk during small-amplitude trunk perturbations. Changing the posture of the lumbar spine did have an effect on the intrinsic and reflexive contributions to trunk control. In particular, flexing the lumbar spine led to a lower admittance and a lower contribution of reflexes.

Table 2:
Main and interaction effects of the ANOVA's for posture on the gain of the admittance and reflexes. * denotes a Greenhouse-Geisser correction due to a violation of the assumption of sphericity.

Admittance	F	df	P	Pairwise Comparisons
Condition*	7.119	1.4, 16.4	0.011	Flexion < Neutral (p=0.028)
Condition x Frequency*	2.853	4.1, 49.3	0.032	Flexion < Neutral @ 0.3, 0.7, 1, 7, 9, 11, 13, 15 Hz
Reflexes				
Condition	9.011	2, 24	0.001	Flexion < Extension (p=0.013); Flexion < Neutral (p=0.053)
Condition x Frequency*	0.884	6.3, 75.9	0.515	-

The absence of an effect of vision on trunk control in the present experiment, is in contrast with the results of Goodworth and Peterka (2009b). They found that manipulating visual information by tilting the visual field, had an effect on the motor control of the spine. There might be several explanations for this disparity: direction of perturbation, perturbation type/experimental set-up, and visual flow amplitudes.

In the present experiment, the perturbation was in the anterior-posterior direction, while Goodworth and Peterka (2009b) perturbed in the medio-lateral direction. The visual flow in the medio-lateral direction may provide more information on trunk orientation and consequently have a stronger effect on trunk control. However, when subjects are perturbed in anterior-posterior direction by sitting on a moving platform, an effect of vision is observed (van Drunen et al., 2015). Therefore, perturbation direction cannot be the only explanation.

More likely, the difference in the results might be explained by the experimental set-up and perturbation type. In the present study, the trunk (and therefore head) position in space could be controlled by the visual feedback, as well as by the proprioceptive feedback, as both feedback mechanisms would counteract a displacement of the trunk/head in space. During the perturbations applied by Goodworth and Peterka (2009b) and van Drunen et al. (submitted), only visual feedback is appropriate to maintain the trunk/head position in space, while proprioceptive trunk feedback minimizes lumbar bending and thus aggravates the trunk/head displacements in space. Therefore, in the present experiment, a trade-off between visual and proprioceptive information can exist whereas in the experiments of Goodworth and Peterka (2009b) and van Drunen et al. (submitted), both sources provide unique information.

Finally, the results of Goodworth and Peterka (2009b) showed that the effect of visual information is dependent on the amplitude of visual flow. The contribution of vision increased with larger amplitudes of visual manipulations. Therefore, in the present experiment, the amplitude of the perturbation might have led to only small displacements of the upper body/head in space and the resulting visual flow might have been too small to excite an effect of visual information on trunk control. However, this still answers a relevant question for many activities of daily life (e.g. standing, sitting, desk work, etc.) in which only small upper body/head motion occurs.

Compared to the neutral posture, flexing the lumbar spine led to a decrease in the gain of the admittance, indicating more resistance to the perturbation. Since a decrease in reflex gain and pre-activation of the M. Longissimus was observed, the higher resistance could not be the result of higher muscle activation or a higher co-contraction level. However, there are indications that flexing the spine puts the muscles in a more optimal range of the force-length relationship (Raschke and Chaffin, 1996). Therefore, the same torque could have been generated with decreased activation. Furthermore, the increased flexion may have led to an increase in passive tissue stiffness (McGill et al., 1994) which also could have compensated for the decreased muscle activation (both reflex activity and co-contraction). The flexion-relaxation phenomenon might explain the decreased muscle baseline and reflex activity (Solomonow et al., 1999; Rogers and Granata, 2006). Finally, the increased passive tissue stiffness itself, may have led to a lower reflex gain.

Several limitations need to be discussed. First, only a limited number of subjects participated in this experiment, which could have limited power to detect differences between conditions. However, the results do not indicate any non-significant trends. Second, there was a lack of complete pelvis fixation which, in combination with movement at the SI-joints, allowed the pelvis to contribute to the motion of the trunk. However, this contribution was consistent for all subjects and all trials and therefore did not influence any differences between conditions.

In conclusion, visual information does not seem to play a role in controlling trunk posture under small-amplitude anterior-posterior torso perturbations. In contrast, posture does affect trunk control, through changes in the intrinsic stiffness and proprioceptive reflex activation.

Chapter 5

Chapter 6

Trunk stabilization with low-back pain:
Identification of intrinsic and reflexive contributions of a heterogeneous patient population

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Abstract

The goal of this study was to assess differences in low-back stabilization between low-back pain (LBP) patients and healthy controls. Upper-body sway was evoked by continuous force perturbations to the trunk, with subjects restrained at the pelvis. Subjects were instructed to 'maximally resist the perturbation' (resists task: RT) or to 'relax but remain upright' (natural balance task: NT) to investigate their maximal ability, natural behavior and their ability to modulate between both tasks. Frequency response functions (FRFs) of the admittance (kinematics) and reflexes (EMG) were obtained and used to estimate intrinsic and reflexive neuromuscular parameters with a physiological model. On group level, LBP patients displayed less reflexive modulation between both tasks and more reliance on intrinsic components during maximal stabilization than healthy controls, suggesting impaired reflexive adaptation with LBP. Individual patients, however, showed either increased or decreased admittance, reflexes and modulation indicative of heterogeneity in the patient group. Four categories of patients were tentatively defined each with a unique pattern of motor control differences relative to healthy controls.

Introduction

Low-back pain (LBP) is a common disorder affecting 40-60% of the adult population in Western society annually (Loney and Stratford, 1999; Picavet and Schouten, 2003). Irrespective of the type of treatment, 60-75% of the patients have recurrent symptoms within a year after treatment and 10% develop chronic LBP (van den Hoogen et al., 1998). In LBP patients, diverse changes in motor control have been found, with evidence of increased as well as decreased excitability of the motor neuron pool of the trunk muscles (Hodges and Moseley, 2003; van Dieën et al., 2003b). Some authors have interpreted these motor control changes as a cause of pain and pain recurrence, due to tonic muscle activity or negative effects on spinal stability (Hodges and Moseley, 2003; MacDonald et al., 2009), while others have interpreted these as adaptations to LBP, protective against pain and re-injury (Lund et al., 1991; van Dieën et al., 2003a). Finally, sub-populations of LBP patients may show different and even opposite changes in motor control, perhaps indicating clinically relevant sub-groups (Dankaerts et al., 2006).

Motor control is essential to low-back stabilization, since the spine without musculature is inherently unstable (Bergmark, 1989a; Crisco and Panjabi, 1991b). The muscular contribution to maintenance of an upright posture comprises reflexive feedback control and the intrinsic mechanical properties of muscles regulated by co-contraction (Moorhouse and Granata, 2007a; Brown and McGill, 2008). While a few studies on healthy subjects have used mechanical perturbations to identify intrinsic and reflexive contributions to low-back stabilization simultaneously (Granata and Rogers, 2007b; Goodworth and Peterka, 2009a; van Drunen et al., 2013b; van Drunen et al., InPress), analysis of neuromuscular control impairments with LBP has mostly focused either on the intrinsic properties (Roland, 1986; van Dieën et al., 2003a; Hodges et al., 2009) or on the reflexes (e.g., Radebold et al. (2001)). This may result in incorrect estimates, because changes in co-contraction can lead to modulation of reflexes (Matthews, 1986).

To be able to operate in altering conditions or perform different tasks, modulation of motor control is of vital importance. In healthy subjects, low-back motor control modulation has been found for changing task instruction, amplitude and frequency range of the perturbation, and availability of feedback such as vision or vestibular information (Buchanan and Horak, 1999; Goodworth and Peterka, 2009a; Goodworth and Peterka, 2010; van Drunen et al., 2013b; van Drunen et al.,

InPress). The present paper studied motor control during natural low-back stabilization (task instruction 'relax but stay upright', henceforth referred to as NT) and maximal stabilizing abilities (task instruction 'maximally resist the perturbation', henceforth referred to as RT), to obtain insight in the maximal stabilizing abilities of subjects and the difference between natural and maximal stabilization (modulation).

The goal of this study was to assess differences in motor control during low-back stabilization between LBP-patients and healthy controls. To identify motor control during low-back stabilization, frequency response functions (FRFs) of the admittance (inverse stiffness resulting from the intrinsic and reflexive muscle contributions) and the reflexive EMG (the reflexive contribution alone) were obtained during natural and maximal stabilization. Based on previous findings of increased co-contraction (van Dieën et al., 2003a) and intrinsic stiffness (Hodges et al., 2009; Miller et al., 2013), we hypothesized that LBP patients would show lower admittance in the NT and, related to that, less modulation between the NT and RT. However, given the inconsistencies between studies on motor control changes in LBP and given that previous studies have shown differences in motor control between sub-populations of LBP patients (Dankaerts et al., 2006), we tentatively defined sub-groups in our patient group based on their outcomes compared to the healthy controls. We anticipated the following sub-groups:

- LBP patients who do not have low-back motor control issues resulting in a similar admittance and modulation as healthy controls (*G1*).
- LBP patients who are unable to produce sufficient muscle force (Lee et al., 1999) resulting in more motion and thus higher admittance in both tasks (*G2*).
- LBP patients attempting to limit muscle forces, causing high admittance in the NT and consequently strong task modulation (*G3*).
- LBP patients attempting to limit movement (Roland, 1986; Hodges et al., 2009), causing low admittance in the NT and limited task-related modulation (*G4*).

Methods

Patients & Controls

Twenty-two subjects suffering from LBP and a control group of fifteen healthy subjects participated in this study. The patients and control group were group-matched on sex, age, height and body mass (Table 1). The LBP patients were included if they suffered from non-specific LBP for at least 6 weeks. They were under treatment with physical therapists (6), pain-specialists (11) and rehabilitation centers (5). During the experiments, patients reported their current low-back pain level with a BS-11 score (Jensen et al., 1989). None of the subjects suffered from radicular pain caused by lumbar nerve root compression or a hernia nuclei pulposi. They did not suffer from any (neurological) disorders that could affect balance control, nor did they use medication that could affect balance control. The healthy controls did not experience LBP in the 12 months prior to the experiments. All subjects gave informed consent according to the guidelines of the medical ethical committee of VU Medical Center.

Table 1:
Information about the patient and control group. Average values are given with their standard deviations (±) or range ([xxx]).

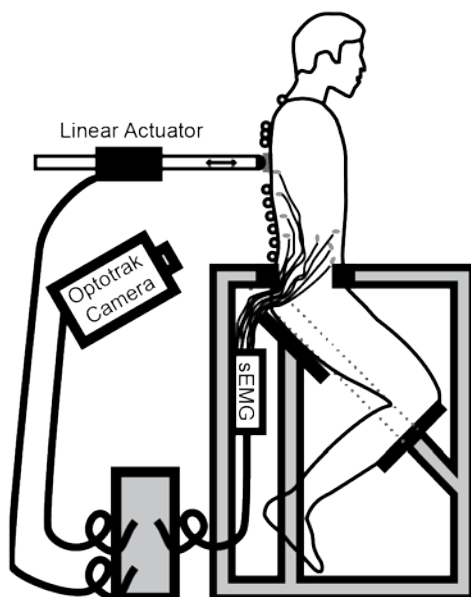|	Patients	Controls
Gender [#Male/#Female]	12/10	9/6
Age [years]	45±11	45±16
Body Length [cm]	175±11	175±09
Body weight [kg]	46±10	42±07
Pain score [-]	3.9 [2-5.6]	-

Figure 1:
Experimental setup. Subjects were restrained at the pelvis and positioned in a kneeling-seated posture, while the linear actuator is perturbing the thorax. Kinematics of the spine (markers (O)) and muscle activity of abdominal and back muscles (EMG electrodes) were measured.

Experiments

In the experimental setup, subjects were seated in a kneeling-seated posture with their pelvis restrained (Figure 1). Force perturbations $F_p(t)$ were applied in ventral direction on the T10 thoracic vertebra by a magnetically driven linear actuator (Servotube STB2510S Forcer and Thrustrod TRB25-1380, Copley Controls, USA), with a thermoplastic patch (4x4cm) placed between the subject and the actuator to increase force transfer and comfort. During the trials, subjects were instructed to keep their eyes closed, arms crossed in front of the chest, and to minimize lateral excursions. Task instructions were to 'maximally resist the perturbation' by minimizing flexion/extension excursions (resist task: RT), or to 'relax but remain sitting upright' (natural balance task: NT).

The force perturbation $F_p(t)$ was a crested multi-sine signal (Pintelon and Schoukens, 2001) with a 35N amplitude superimposed on a 60N baseline preload to maintain contact between the actuator and the subject (Figure 2& van Drunen et al. (2013b)). The multi-sine signal had a duration of 20s and a bandwidth ranging from 0.2 to 15Hz consisting of 18 pairs of adjacent frequencies, which were logarithmically spaced. To reduce motor control modulation due to high-frequency perturbations, the perturbation power above 4Hz was reduced to 40% relative to the lower frequencies (Mugge et al., 2007). Because of the random appearing character of this perturbation, subjects were not expected to react on the perturbations with voluntary activation.
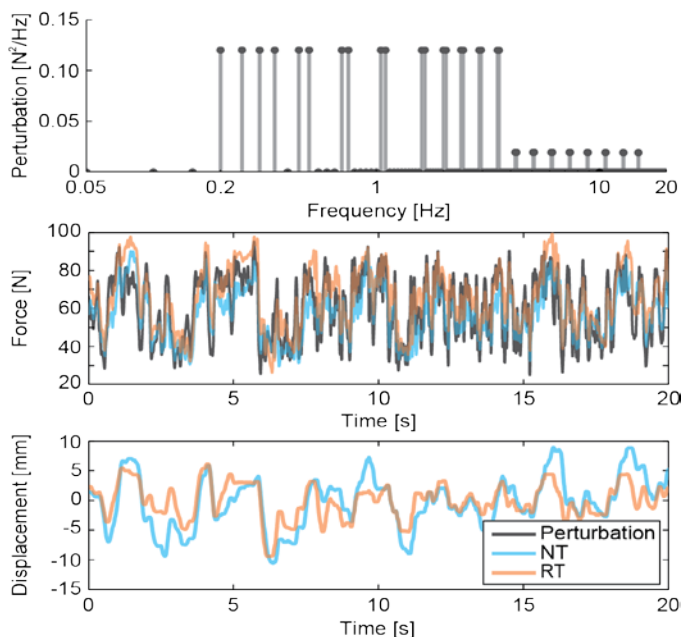

Figure 2:
The force perturbation F_p (black) is projected in frequency domain (TOP) and time domain (MIDDLE). The resulting contact force F_c (MIDDLE) and actuator displacement x_a (BOTTOM) are shown in time domain for both the behave natural (NT: blue) and resist (RT: red) task.

Each trial had a duration of 50s and consisted of a linear increasing force up to the preload level (3s), a steady preload force (2s), a start-up period to reduce transient behavior (the last 5 seconds of $F_p(t)$), and two repetitions of the force perturbations (2x20s). All subjects performed three trials of both tasks in varying order, resulting in a total of 6 trials per subject.

Data Recording and Processing

Kinematics of the thorax (cluster of 3 markers at T6) were measured with 3D motion tracking at 100 samples/s (Optotrak3020, Northern Digital Inc., Canada). The actuator displacement $x_a(t)$ and contact force $F_c(t)$ between the actuator and subject were measured at 400 samples/s (Servotube position sensor & Force sensor FS6-500, AMTI, USA). Lumbar kinematics were described in terms of translations, since kinematic analysis indicated that a low-back bending virtual rotation, necessary for rotational descriptions, was not well defined and inconsistent over subjects. Muscle activity $e(t)$ of the lumbar part of the M. Longissimus was measured bilaterally as described in Willigenburg et al. (2010) at 2048 samples/s (surface electromyography (sEMG), Refa, TMSi, the Netherlands). The EMG recordings were digitally filtered (zero-phase, first-order, high-pass) at 250Hz (Staudenmann et al., 2007b) and then rectified. The muscle activity was transformed into force by scaling the EMG amplitudes (averaged over left and right) to the applied force during the 2s steady preload force during each trial.

System Identification

Closed loop identification techniques (Guitton et al., 1986; Pintelon and Schoukens, 2001; van der Helm et al., 2002) were used to describe the translational low-back admittance ($H_{adm}(f)$) and reflexes ($H_{emg}(f)$) as frequency response functions (FRFs). The admittance describes the actuator displacement ($x_a(t)$) as a function of the contact force ($F_c(t)$), representing the inverse of low-back mechanical impedance. The reflexes describe the scaled EMG amplitude ($e(t)$) of the lumbar part of the M. Longissimus as a function of the actuator displacement ($x_a(t)$). Because the subject interacted with the actuator, FRFs were estimated using closed loop methods:

$$H_{adm}(f) = \frac{S_{F_p x_a}(f)}{S_{F_p F_c}(f)} \; ; H_{emg}(f) = \frac{S_{F_p e}(f)}{S_{F_p x_a}(f)} \qquad (1)$$

with $S_{F_p x_a}(f)$, $S_{F_p F_c}(f)$, and $S_{F_p e}(f)$ representing the estimated cross-spectral density between Fourier transformed force-perturbation ($F_p(f)$) and actuator displacement ($x_a(f)$), contact force ($F_c(f)$), and EMG ($e(f)$), respectively. The cross-spectral densities were only evaluated at the frequencies containing power in the perturbation signal. For improved estimates and noise reduction, the cross-spectral densities were averaged across the 6 time segments per task (three trials containing $F_p(t)$ twice) and over 2 adjacent frequency points (Jenkins and Watts, 1969). Finally, $S_{F_p e}(f)$ was averaged over the left and right muscles.

The coherence associated with $H_{adm}(f)$ and $H_{emg}(f)$ was derived as:

$$\gamma^2_{adm}(f) = \frac{\left|S_{F_p x_a}(f)\right|^2}{S_{F_p F_p}(f) S_{x_a x_a}(f)} \; ; \gamma^2_{emg}(f) = \frac{\left|S_{F_p e}(f)\right|^2}{S_{F_p F_p}(f) S_{ee}(f)} \qquad (2)$$

Coherence ranges from zero to one, where one reflects a perfect, noise-free relation between input and output. Since spectral densities were averaged over 12 points (2 adjacent frequencies and 6 repetitions), a coherence greater than 0.24 is significant with P<0.05 (Halliday et al., 1995b).

Because task-related modulation of the FRFs mainly occurs below the natural frequency around 1.1Hz (van Drunen et al., 2013b), low-frequency gains (*LF*-gains) of the admittance (LF_{adm}) and reflexive (LF_{emg}) FRFs were defined by averaging over the four frequency pairs within the 0.3-1.1Hz range. The lowest frequency pair (0.2Hz) was excluded given low coherence for several subjects. Modulation (*M*) between the two task instructions describes the ratio between the *LF*-gains of both tasks. Since the *RT* resulted in lower admittance and higher EMG with respect to the *NT* (van Drunen et al., 2013b), modulation was defined positive in the expected direction:

$$M_{adm} = \frac{LF_{adm}(NT)}{LF_{adm}(RT)} - 1 \; ; M_{emg} = \left(\frac{LF_{emg}(NT)}{LF_{emg}(RT)}\right)^{-1} - 1 \qquad (3)$$

Parametric identification

A linear neuromuscular control (NMC) model was constructed to translate the FRFs into physiological elements representing intrinsic and reflexive contributions (van der Helm et al., 2002; Schouten et al., 2008c; van Drunen et al., 2013b). The effective mass (*m*) was defined anthropometrically (Clauser et al., 1969). Passive

tissue properties, muscle co-contraction, cross-bridge dynamics and force-length and force-velocity relationship were lumped into two parameters describing the overall intrinsic stiffness and damping (k, b) of the low back. The reflexive contribution was described by a position and a velocity feedback gain (k_p, k_v) with a time delay (τ_{ref}). Muscle activation dynamics were implemented as a second order system (Bobet and Norman, 1990) with a cut-off frequency (f_{act}) and a dimensionless damping (d_{act}), set to of 0.75 Hz and 1.05, respectively, as the average activation dynamics in van Drunen et al. (2013b). Contact dynamics between the subjects' trunk and the actuator were included as a spring and damper (k_c, b_c).

The parameters were estimated by fitting the NMC-model on the FRFs of both the low-back admittance and the reflexive muscle activation for all trials. The natural and resist task were optimized simultaneously assuming time delay and contact dynamics to be constant over conditions. The cost function used in the estimation was:

$$err = \sum_{1}^{\#rep}\sum_{k} \frac{\gamma_{adm}^2(f_k)^2}{1+f_k}\left|\log\left(\frac{H_{adm}(f_k)}{H_{adm}^{mdl}(f_k)}\right)\right|^2 + q\sum_{1}^{\#rep}\sum_{k} \frac{\gamma_{emg}^2(f_k)^2}{1+f_k}\left|\log\left(\frac{H_{emg}(f_k)}{H_{emg}^{mdl}(f_k)}\right)\right|^2$$

(4)

with f_k as the power containing frequencies, and $H_{adm}^{mdl}(f_k)$ and $H_{emg}^{mdl}(f_k)$ as the transfer functions of the model. The procedure optimizes the goodness of fit of the complex admittance (left term) and reflexive muscle activity (right) term, where the weighting factor q was selected to be 0.25 to provide equal contribution of the admittance and reflexive muscle activity to the cost function.

The validity of the optimized model and its parameters was assessed in the time domain using the variance accounted for (*VAF*). A *VAF* of 100% reflects a perfect description of the measured signal by the model. The experimental measurements $x_a(t)$ and $e(t)$ were compared with the estimated model outcomes $\hat{x}_a(t)$ and $\hat{e}(t)$:

$$VAF_x = \left[1 - \frac{\sum_{1}^{n}(x_a(t_n) - \hat{x}_a(t_n))^2}{\sum_{1}^{n}(x_a(t_n))^2}\right]\cdot 100\%$$

(5)

where *n* is the number of data points in the time signal. For the EMG, VAF_e was calculated by replacing $x_a(t)$ and $\hat{x}_a(t)$ with $e(t)$ and $\hat{e}(t)$, respectively. To reduce

noise contributions, the measured data were reconstructed with only the frequencies that contain power in the force perturbation signal.

Statistics

The FRF-gains, *LF*-gains and parameter values were tested for correlation with upper body mass, upper body length (Clauser et al., 1969) and age, and scaled proportionally to correct for correlation. The FRF- and LF-gains were log-transformed to satisfy the assumption of normality. To compare FRF gains between tasks and groups, a 3-way mixed factorial ANOVA (group [2] x task [2] x frequency [18]) was performed. To test our hypotheses, LF gains and the modulation of LF-gains were compared between groups with Mann-Whitney U tests. In addition, estimated model parameters were compared between groups using Mann-Whitney U tests. Results with a p-value smaller than 0.05 were considered significant.

Results

Group level comparison between LBP patients and controls

The trunk stabilization behavior as described by the FRFs of the admittance and EMG response was clearly task dependent ($F(1,35) = 33.42$, $p < 0.001$ for admittance and $F(1,35) = 22.99$, $p < 0.001$ for reflex gains), but not clearly different between the LBP patients and the healthy control group ($F(1,35) = 0.25$, $p = 0.618$ for admittance and $F(1,35) = 0.005$, $p = 0.847$ for reflex gains; Figure 3). High mean coherence levels (average and standard deviation of 0.88±0.12)for the admittance indicates good input-output correlations, while the mean EMG coherence (0.54±0.27) was good considering the noisy character of EMG signals. For the EMG, subjects (4 patients, 1 control) with *LF*-coherences below the significance level were excluded from further analysis (including the parametric identification). The admittance resembled a combination of a second-order system (i.e., mass-spring-damper system) and reflexive responses. At low frequencies (<1.1Hz), task effects due to changes in intrinsic properties and/or reflexive contributions resulted in a 36% decrease in admittance and a 91% increase in reflexes during the RT. Above 1.1Hz, the admittance is mainly dependent on trunk mass and contact dynamics, and consequently FRFs overlap. The reflexive FRFs predominantly indicate presence of position feedback, as evidenced by a flat gain and -180° phase lag at lower frequencies, and of velocity feedback, as evidenced by a slope of the gain of approximately +1 and phase lag of -90° at intermediate frequencies).
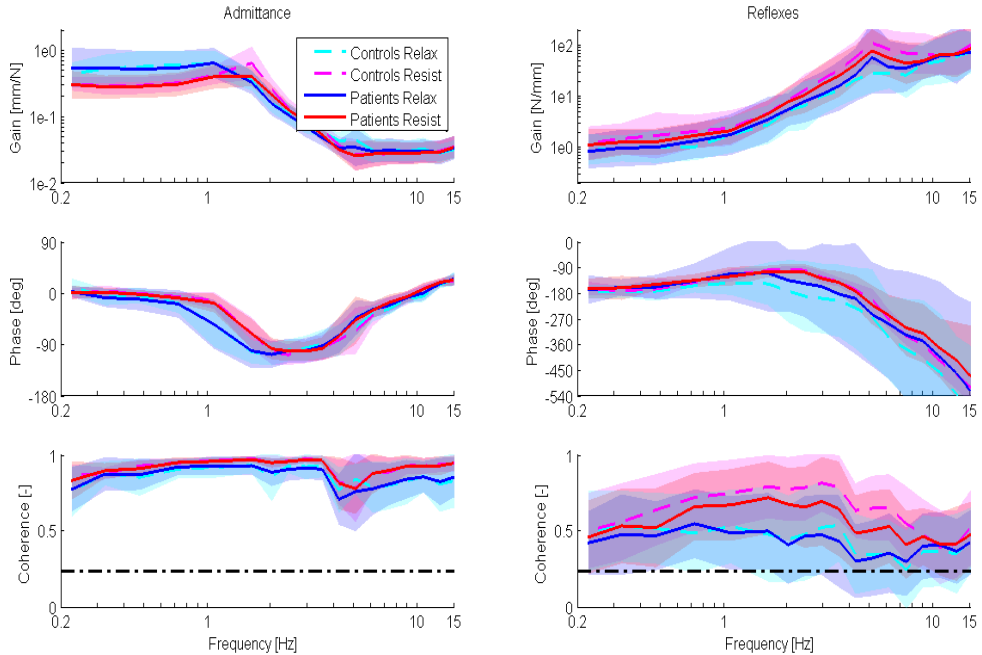
Figure 3:
Group averaged Frequency Response Functions (FRFs) of the admittance (left) and EMG (right). Results for controls (dotted, dark lines) and patients (solid, light lines) during the behave naturally (NT: blue) and resist (RT: red) tasks were averaged over subjects (with shadows as standard deviation). The gain (amplitude difference), phase (time shift) and coherence (correlation) illustrate the transformation of the input signal into the output signal.

In contrast with our hypotheses, low-frequency admittance in the NT and modulation in low-frequency admittance between NT and RT were not lower in the patient group than in the control group (p = 0.725 and p = 0.915, respectively). As expected, admittance in the RT was not different between groups (p = 0.748). Low-frequency reflexive gains were also not different between groups (p = 0.193 and p = 0.145 for NT and RT respectively), but task-dependent modulation in the reflexive gains was lower in patients than in controls (p = 0.010).

In Figure 4, the modeling results are presented with the estimated parameter values and the variance accounted for (VAF). Good displacement and reasonable EMG VAF values for the controls (VAF_x 90%; VAF_e 39%) and patients (VAF_x 92%; VAF_e 26%) represent an adequate fit of the model to the data. In the control group, the effective stiffness (combined intrinsic stiffness and muscle spindle (MS) position feedback) was dominated by the intrinsic stiffness (NT=63%; RT=72%), while the intrinsic damping and velocity feedback contributed similarly to damping during NT (54%) and the reflexive component dominated during RT (67%). Significant effects of task instruction were found with higher intrinsic stiffness

(p<0.001) and velocity feedback gain (p<0.001) during RT. On the group level, patients had a significantly lower velocity feedback gain during RT (p = 0.045) and thus appeared to rely more on intrinsic contributions, as was also suggested by their lower task-related modulation of EMG gains.
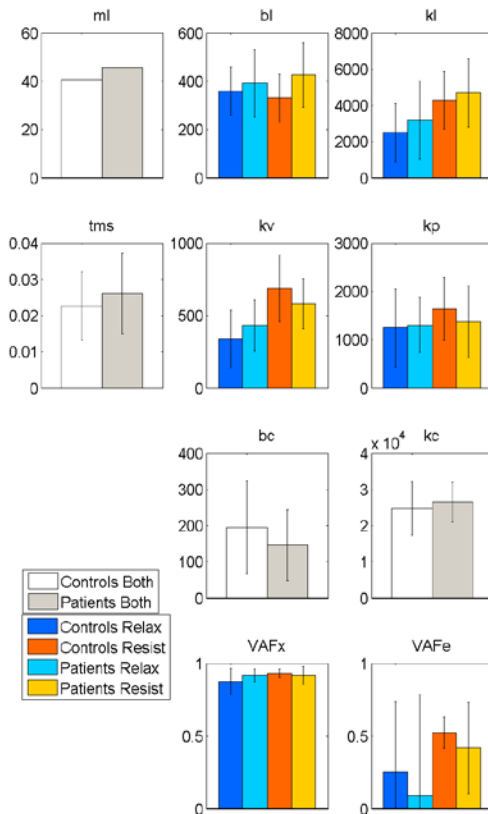

Figure 4:
Subject-averaged estimated parameters of both the controls (solid) and patients (striped). The error bars represent the standard deviations. Parameters that modulated due to task instruction have different values for the behave naturally (NT: blue) and the resist task (RT: red).

Sub-groups

In line with the expected heterogeneity of the LBP population, the patient data showed higher variances of *LF*-gains and modulation in the admittance (+64%) and reflexes (+27%). The heterogeneous character of the LBP patient population manifested itself as a variety of differences in the admittance and reflexive FRFs between individual patients and the control group (Figure 5). Most deviations were present below 1.1Hz, appearing for instance as increased admittance in one task (as found for patient p16), both tasks (p6), or as no modulation between tasks (p13), while some patients displayed comparable FRFs to the control group (p22).
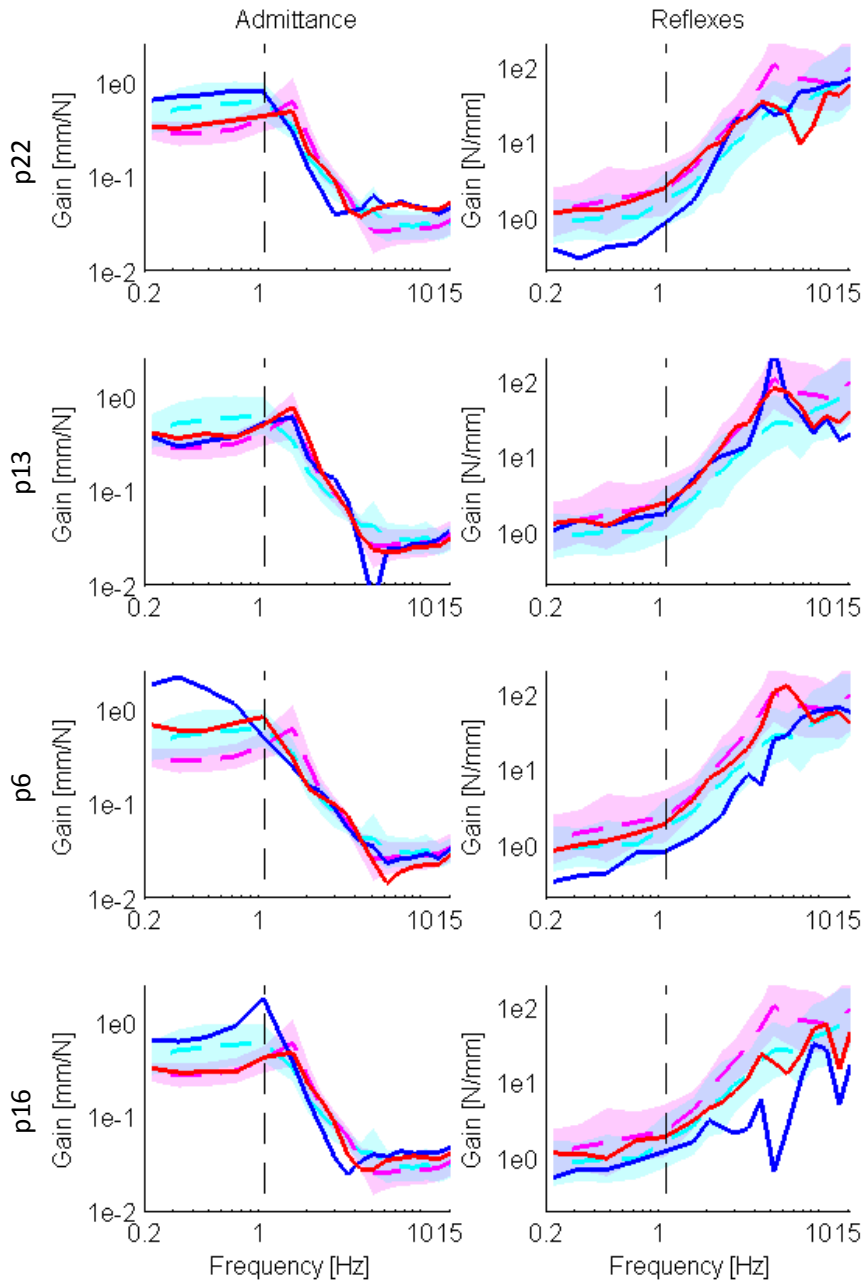
Figure.5:
Individual patients: Gains of the admittance (left) and reflexes (right) during the behave naturally (NT: blue) and the resist (RT: red) task for 4 individual patients (solid lines) and the averaged controls (dotted lines with shades as standard deviations). Differences were present mainly below 1.1Hz (dotted black line), where reflexes and co-contraction can influence balance control.

After correction for the negative correlation between *LF*-gains and body mass (no correlation was found with upper body length and age), the *LF*-gains of the two tasks were plotted against each other (Figure 6). In the scatter plot, an area containing most of the data of the controls was established based on the average ± one standard deviation of the *LF*-gain during both tasks (the gray area in Figure 6). The controls area of the admittance comprised 33% (5/15) of the control group and 50% (11/22) of the patient group. A similar plot was constructed based on the EMG FRFs. In this plot, the controls area contained 57% (8/14) of the controls and 22% (4/18) of the patients. The overall low specificity indicates a large dispersion in the control group, which will be addressed in the discussion.
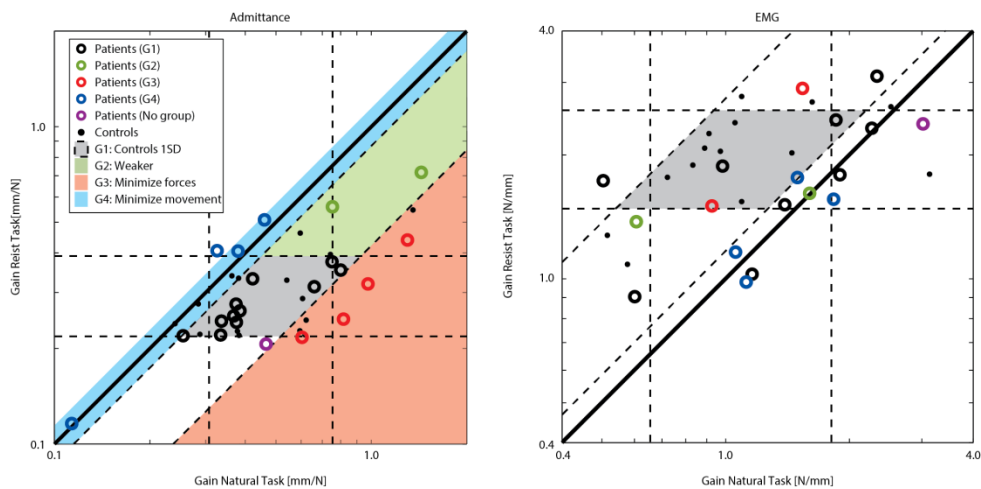

Figure 6:
Clustering results for the admittance (left) and the EMG (right) gains during the behave naturally (NT: horizontal axis) and resist (RT: vertical axis) task within the 0.3Hz to 1.1Hz frequency range. The controls are plotted individually (small black dots) and on group level with standard deviation (black dotted lines) of the relax and resist gain and the modulation level. Patients (colored circles) were separated in the 4 sub-groups within the areas of normal admittance (G1: grey area), muscle weakness (G2: green), limit muscle forces (G3: red), limit movement (G4: blue). One patient (purple) was not within a group.

All but one of the patients could be classified in either the sub-groups *G1* (no control issues; 11 patients), *G2* (muscle weakness; 2 patients), *G3* (limited muscle forces; 4 patients) or *G4* (limited movement; 4 patients). Strikingly, subjects in *G1* ('normal admittance') achieved their normal admittance in a different way than controls, i.e. they had a lower position feedback gain (p = 0.013, Table 2) and a tendency towards reduced EMG gain modulation (p = 0.084). Admittance in group *G2* was significantly lower than in the control group in both tasks, in line with the

classification criterion for this group (p = 0.029 and p = 0.015 for NT and RT respectively). In addition, *G2* had a lower intrinsic stiffness than controls in the RT (p=0.017) and tended towards a lower velocity feedback gain in this task (p = 0.067). *G3* modulated significantly less between tasks than controls did (p = 0.001), again in line with the classification criteria. On top of that, *G3* had a significantly higher admittance in the NT (p = 0.023), which was probably due to lower, albeit non-significantly lower, intrinsic stiffness and damping in the NT. Finally, *G4* only showed a tendency towards lower admittance in the NT, but had a significantly lower task-related modulation of admittance (p = 0.001) as well as EMG gains (p = 0.018). In addition, *G4* had a lower EMG gain in the RT (p = 0.025) and higher velocity feedback in the NT (p = 0.046).

Table 1:
Statistically significant differences (in %) between the control group and the patients (all together and classified in sub-groups). Statistics were applied for the natural balance (*NT*) and maximally resist (*RT*) task instructions and the modulation (*M*) on the low-frequency admittance (*LF_{adm}*) and EMG (*LF_{emg}*), and estimated parameters: intrinsic stiffness (*k*) and damping (*b*), velocity feedback gain (*k_v*), position feedback gain (*k_p*) and the reflexive time delay (*τ_{ref}*). Sub-groups were defined as: normal admittance (*G1*), muscle weakness (*G2*), limit muscle forces (*G3*), limit movement (*G4*). The bold numbers represent the inclusion criterion for classification into the sub-group. The number of patients per sub-group (*#pat*) are given for the LF-gains and parameters.

		Patients				
		All	**G1**	**G2**	**G3**	**G4**
LF-gains	**#pat**	**22**	**11**	**2**	**4**	**4**
LF_adm	NT			+106%*	+73%*	
	RT			+110%*		
	M				+168%**	−112%***
LF_emg	NT					
	RT					−32%*
	M	−58%*				−100%*
Parameters	**#pat**	**18**	**9**	**2**	**2**	**4**
b	NT					
	RT					
k	NT					+53%*
	RT			−63%*		
k_v	NT					
	RT	−23%*				
k_p	NT					
	RT			−42%*		
τ_ref	**Both**					

***p<0.005; **p<0.010; *p<0.05

Discussion

The goal of this study was to assess differences in motor control during low-back stabilization between low-back pain (LBP) patients and healthy controls. On group level, LBP patients displayed less reflexive modulation between both tasks and more reliance on intrinsic components during maximal stabilization, suggesting impaired reflexive adaptation with LBP. On the individual patient level, however, both increased and decreased admittance, reflexes and modulations were found consistent with a heterogeneous patient group. Therefore, patients were separated in four sub-groups based on the admittance and hence different motor control changes with respect to healthy controls.

The healthy control population results were comparable with van Drunen et al. (2013b). However, a slightly higher admittance below 1.1Hz was found resulting in lower intrinsic and reflexive parameter estimates, most likely due to the absence of real-time visual feedback on low-back posture. Modulation due to task instructions was present below 1.1Hz (LF-gains) with during RT lower admittance, higher reflexes, and higher parameter estimates of the intrinsic stiffness and velocity feedback gain. Comparable to van Drunen et al. (2013b), the physiological model described the data adequately, with VAF-values of 92% (kinematics) and 26% (EMG).

LBP-patients were categorized using low-frequency FRF-gains by comparing patients with a healthy control population (average ± one standard deviation). Another option would have been to categorize patients on the basis of the neuromuscular model parameters. FRFs and model parameters both allow for quantification and separation of intrinsic and reflexive contributions, while FRFs do not require a-priori model assumptions. In addition, model parameters have a larger error margin due to the combination of within group variance (the same as in the FRFs) and the estimation error resulting from the optimization. A point of concern of the FRF categorization is the low specificity (the areas defined as normal contained 33% of the controls for the admittance and 57% for the EMG). Obviously, this could be improved by using the controls average ± two standard deviations increasing the specificity of the admittance and EMG to 93% and 86%, respectively, but at the cost of sensitivity. For the tentative sub-grouping presented here, we chose to use a non-conservative estimate of 'normal' motor control. While this study illustrates the potential of the method used to delineate changes in motor control with LBP, clearly a much larger sample is needed to define boundaries of normal control and to define sub-groups of patients.

Our expectation was that LBP-patients could be divided into four sub-groups as motivated in the introduction. A large portion of the patients was contained by the first category (*G1*) describing no motor control impairments. However, patients within *G1* showed significantly higher intrinsic contributions to the effective stiffness and damping during the RT. Presumably, higher co-contraction levels led to higher muscle stiffness and damping, which however requires higher and sustained trunk muscle forces and may cause faster muscle fatigue due to higher energy consumption. This suggests that even in *G1* motor control is impaired during maximal stability tasks. Two patients showed higher admittance than normal in both tasks (*G2*). These patients had a lower than normal intrinsic stiffness in the RT, but did otherwise not differ significantly from controls. This, would be consistent with muscle weakness causing an overall less effective stabilization and affecting the dominant contribution in the RT the most, although other causes cannot be ruled out. Subjects in *G3* had a higher than normal low-back admittance in the NT, but were apparently able to stabilize their trunk as well as control subjects, when instructed to perform maximally (RT). Changes in control underlying the worse performance in the NT could not be established. Patients in *G4* did not show significantly decreased admittance in the NT, in spite of the classification criterion. The higher intrinsic stiffness during the NT is in line with previous literature (Hodges et al., 2009; Miller et al., 2013) and points in the direction of increased co-contraction (van Dieën et al., 2003a). However, the difference in modulation between tasks was much more clearly different from healthy controls. Assessment of control in the NT normalized to maximal performance on the RT, as reflected in the modulation, would be in line with the assumption that LBP patients in this sub-group attempt to stabilize their spine more during sub-maximal tasks, to compensate for impairments that in fact threaten stability and that may limit stabilization in the RT (van Dieën et al., 2003b). Finally, it should be noted that *G2* and *G3* on one hand and *G4* on the other hand may resemble sub-groups defined previously as the flexion pattern group with more passive sitting posture (*G2* and *G3*) and the active extension pattern group with an active sitting postures with high levels of co-contraction (*G4*) (Dankaerts et al., 2006).

In this study, modeling was based on intrinsic properties and proprioceptive reflexes. However, vision and vestibular feedback are involved in low-back stabilization as well (e.g., (Goodworth and Peterka, 2009a; Goodworth and Peterka, 2010; van Drunen et al., InPress). While vision was excluded during the measurements by the instructions to close the eyes, vestibular feedback was still

functional. This could have biased the modeling results, where proprioceptive reflexes in the model actually represent lumped proprioceptive and vestibular feedback. Inclusion of vestibular, visual and Golgi tendon organ feedback in the model was explored in van Drunen et al. (2013b), in which we concluded that data resulting from these experiments did not contain enough information to separate their contributions. Thereby, associations of LBP with visual or vestibular deficits were not found in literature, strengthening the reasoning that modeling differences were due to proprioception.

In conclusion, LBP patients displayed on group level impaired reflexive adaptation with less reflexive modulation and more reliance on intrinsic components during the maximal stabilization task. However, the LBP patient-group was found to be heterogeneous, while on individual patient level both increased and decreased admittance, reflexes and modulation were found. This study categorizes LBP patients on basis of their maximal stabilizing abilities and their modulation towards natural stabilization in 4 groups indicative of different motor control impairments. Potentially, this approach could be used to improve diagnostics in LBP.

Chapter 7

Interactions of touch feedback with muscle vibration and galvanic vestibular stimulation in the control of trunk posture

E. Maaswinkel, H.E.J. Veeger, J.H. Van Dieën

Abstract

This study investigated the effect of touch on trunk sway in a seated position. Two touch conditions were included: touching an object with the index finger of the right hand (hand-touch) and maintaining contact with an object at the level of the spine of T10 on the mid back (back-touch). In both touch conditions, the exerted force stayed below 2 N. Furthermore, the interaction of touch with paraspinal muscle vibration and galvanic vestibular stimulation (GVS) was studied. Thirteen healthy subjects with no history of low-back pain participated in this study. Subjects sat on a stool and trunk sway was measured with a motion capture system tracking a cluster marker on the trunk. Subjects performed a total of 12 trials of 60-seconds duration in a randomized order, combining the experimental conditions of no-touch, hand-touch or back-touch with no sensory perturbation, paraspinal muscle vibration or GVS. The results showed that touch through hand or back decreased trunk sway and decreased the effects of muscle vibration and GVS. GVS led to a large increase in sway whereas the effect of muscle vibration was only observed as an increase of drift and not of sway. In the current experimental set-up, the stabilizing effect of touch was strong enough to mask any effects of perturbations of vestibular and paraspinal muscle spindle afference. In conclusion, tactile information, whenever available, seems to play a dominant role in seated postural sway and therefore has important implications for studying trunk control.

Introduction

Control of trunk movement is crucial for maintaining balance during activities of daily living (MacKinnon and Winter, 1993; Van der Burg et al., 2005). Also, precise hand/arm function is dependent on adequate control of trunk movement (Kaminski et al., 1995; Pigeon et al., 2000) and it has been suggested that impaired trunk control might induce instability of the lumbar spine and consequently cause low back pain (Panjabi 1992a; Panjabi 1992b) or play a role in low back pain recurrence (Willigenburg et al., 2013; Descarreaux et al., 2005). Furthermore, control of trunk movement is affected in neurological disorders such as Parkinson's disease (Van der Burg et al., 2006), stroke (Ryerson et al., 2008) and spinal cord injury (Seelen et al., 1997).

Trunk control is dependent on adequate motor control as the intrinsic stiffness of the trunk is insufficient (Moorhouse et al., 2007). In turn, proper motor control depends on adequate sensory feedback. The influence of different sensory modalities in feedback control is often studied by interfering with these modalities and measuring the resulting changes in motion (Goodworth and Peterka, 2009; Brumagne et al., 1999; Willigenburg et al., 2012). Furthermore, the involuntary/reflexive component of trunk control can be identified by applying external perturbations and measuring the resulting trunk muscle responses (Cholewicki et al., 2000; Van Drunen et al., 2013). These external perturbations require application of time-varying forces to the subject's trunk. This usually involves contact with an external object for the whole or a part of the test duration. However, there is evidence that contact with an external object may, through tactile information, have a profound influence on postural control (Lackner et al., 2001; Jeka and Lackner, 1994; Clapp and Wing, 1999).

The effect of tactile stimuli on postural control has been illuminated specifically in studies of standing postural sway. For example, when subjects stand upright and their calf muscles are vibrated, to interfere with muscle spindle information, a large increase in sway is observed (Lackner et al., 2000). However, when subjects are allowed to keep a very light contact through the hand with an external object, this effect of muscle vibration is strongly reduced. Still, several questions remain unanswered. First, is the effect of touch specific for contact with the hand, or does it

apply to other body areas as well? Second, does the effect of touch interact specifically with muscle vibration, or does it interact also with other sensory modalities? Furthermore, for the purpose of understanding trunk control, measurements of standing postural sway provide limited information, since postural adjustments can be made in several joints (e.g. ankle, knee, hip). Therefore, the measured sway can be attributed to several joints and might not accurately reflect trunk control. In sitting, trunk control can be studied without the influence of responses from the lower extremities.

The purpose of the current experiment was to determine the effect of touch on trunk sway in a seated position. To investigate whether the effect is specific for touch with the hand, a second contact condition, namely contact through the back, was included. Finally, to determine whether the effect of touch interacts specifically with muscle vibration, or also with other sensory modalities, a second sensory perturbation, galvanic vestibular stimulation (GVS), was included. It was hypothesized that touch through both hand and back reduces the effects of muscle vibration and GVS. The results obtained may contribute to a better understanding of the influence of touch on the control of trunk posture.

Methods

Experimental setup

The study was approved by the ethical committee of the faculty of human movement sciences of the VU University Amsterdam. 13 Healthy subjects without history of low-back pain participated (10 males, 3 females; age range: 20-35 years; mean mass: 77 (SD 10) kg; mean height: 182 (SD 8) cm). Subjects sat upright on a height adjustable stool with their feet on the ground at shoulder width apart and their knees bent at a 90° angle (figure 1). Trunk sway was measured with a motion capture system (Optotrak3020, Northern Digital Inc, Canada) tracking, at 100 Hz, a cluster of 3 markers attached to the back at the level of the spine T6.

Subjects performed a total of 12 trials of 60-seconds duration in a randomized order, combining the experimental conditions of no-touch, hand-touch or back-touch, with no sensory perturbation, muscle vibration or GVS.
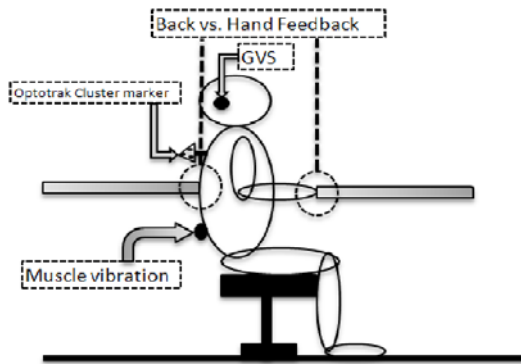
Figure 1:
A schematic drawing of the experimental set-up. Trunk sway was measured with a cluster marker attached on the back at the level of the spine T6. Muscle vibration was applied bilaterally on the lower back at the level of the spine L4. Hand-touch was provided at shoulder height in front of the body while back-touch was provided in the mid-sagittal plane at the level of the spine T10.

Since the eyes were closed for the muscle vibration and GVS to have a stronger effect, an eyes open condition was included to check whether closing the eyes affects trunk sway. During selected trials, subjects were allowed to touch a solid object attached to a force sensor. During all touch conditions, the force exerted on the force sensor was monitored by the experimenter and never exceeded 2 N to assure that the mechanical stabilizing advantage was kept to a minimum. Hand-touch was provided between shoulder and elbow height in the mid-sagittal plane and Back-touch was provided at the level of the spine of T10 in the mid-sagittal plane. During all trials, the subject's arm was held in the same (hand-touch) position to prevent any effects of changing arm posture. During the trials with muscle vibration, a custom made vibrator was attached bilaterally to the lower back at the level of L4, 5 cm lateral of the spine. The vibrator was turned on right before the onset of the trial and the vibration frequency was set to 90 Hz.

For the GVS trials, a direct current was applied to the mastoid processes by a custom-made constant current stimulator (Balance Lab, Maastricht Instruments, The Netherlands). The current was applied as a sinusoid with a frequency of 1 Hz and 1.5 mA amplitude (Pavlik et al., 1999). Subjects were instructed to rotate their head sideways ('look over your shoulder',) to induce illusory movement in the fore-aft direction. Furthermore, to eliminate possible effects of turning the head, subjects were instructed to maintain their head turned sideways during all trials.

Data Analysis

Per trial, the first and last 10 seconds of the signal were discarded to eliminate transient behavior, leaving 40s which were used for further data analysis. The average position of the cluster marker in the sagittal plane was calculated. Preliminary analysis showed that a considerable drift occurred, especially during the vibration trials. Accordingly, the analysis was split into two parts. First, the signals were corrected for drift by applying a linear piecewise detrend and, subsequently, trunk sway in the fore-aft direction (sagittal plane) was quantified by calculating the standard deviation of the detrended signals. Second, to analyze the effects of touch condition on drift, the drift of the raw data was quantified by calculating the difference between the average position during the first and last second of the 40-seconds signal. Quantifying the drift by a 3- or 5-second window led to similar results.

Statistical Analysis

To investigate whether closing the eyes affected trunk postural sway, a repeated measures ANOVA with 2 factors (touch condition, eyes open vs. closed) was performed. To determine whether trunk sway was affected by touch and/or perturbation conditions, a 2 factor (touch condition, perturbation condition) repeated measures ANOVA was performed. Furthermore, a similar ANOVA was performed on the calculated drift. Significant main effects were followed up by Bonferroni corrected pair-wise comparisons. Effects were considered significant when the corrected $p < 0.05$. The assumption of normality was checked by visual inspection of the q-q plots and box plots of the residuals. A Shapiro-Wilk test was also performed on the residuals. There was no violation of the assumption of normality. Sphericity was checked using Mauchly's test. If the assumption of sphericity was violated, a Greenhouse-Geisser correction was used (Girden, 1992).

Results

A typical example of the measured position of the trunk in fore-aft direction for a reference (eyes closed) and muscle vibration trial is presented in figure 2.
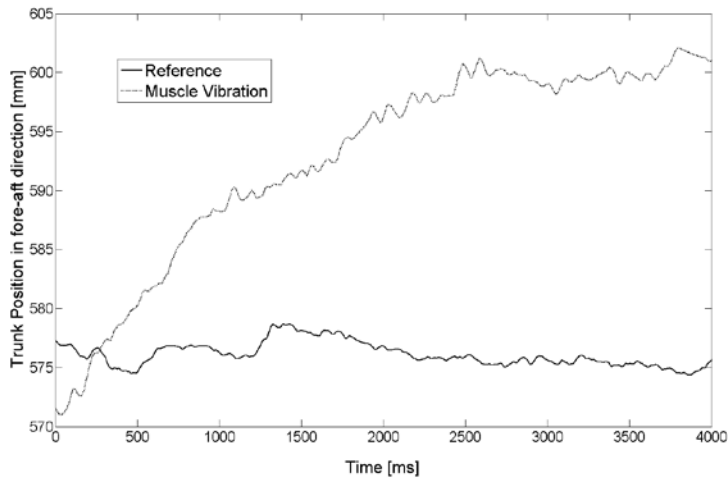
Chapter 7

Figure 2:
A typical example of the position of the trunk in fore-aft direction for a reference (eyes closed) trial and a trial with muscle vibration, showing considerable drift.

The ANOVA results are presented in table 1. Closing the eyes did not significantly affect trunk sway (p = 0.6) (figure 3, top panel). Trunk postural sway was significantly reduced in the hand-touch (p = 0.01, 95% CI [-0.371 -0.050]) as well as in the back-touch condition (p = 0.016, 95% CI [-0.425 - 0.042]) (figure 3, top panel). For the perturbation conditions, only GVS led to a significant increase in sway (p = 0.015, 95% CI [0.036 0.337]). A trend for an increase in trunk sway could be observed for the muscle vibration condition (figure 3, top panel), but failed to reach statistical significance (95% CI [-0.062 0.193]). There was no significant interaction of perturbation and touch condition.

Table 1:
Main and interaction effects of both ANOVAs for sway and for drift. * denotes Greenhouse-Geisser correction due to a violation of the assumption of sphericity.

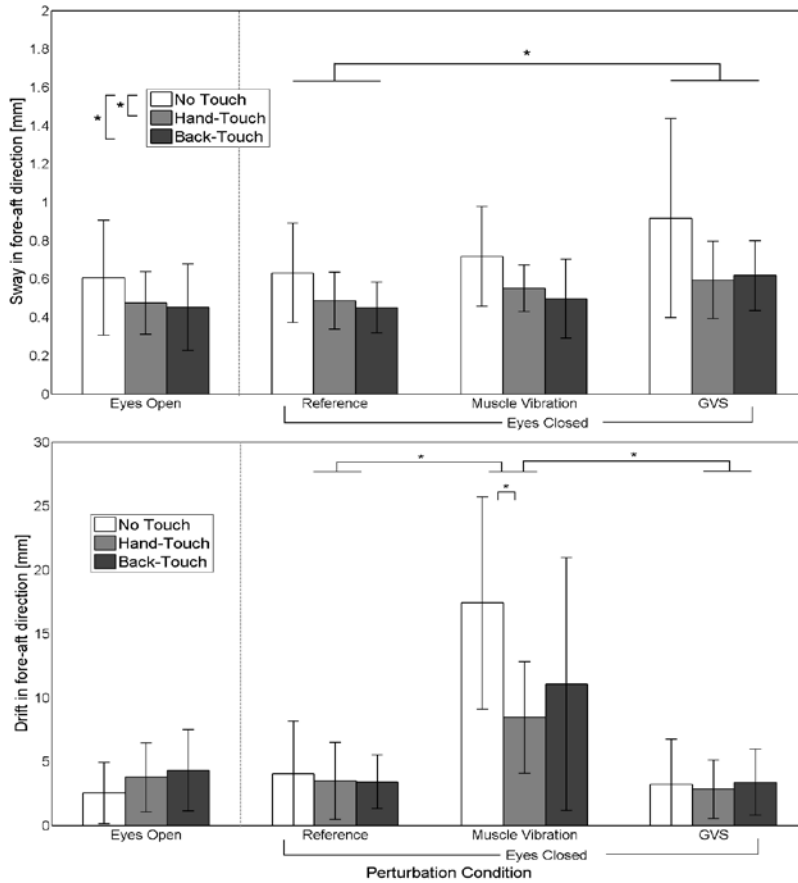| Sway				
	F	df	p	Pairwise Comparisons
Touch Condition (*)	10.724	1.4 – 16.7	0.002	No touch > Hand touch No touch > Back touch
Perturbation Condition	5.631	2 – 24	0.010	GVS > Reference
Touch x Perturbation	0.684	4 – 48	0.606	-
Drift				
Touch Condition	3.116	2 – 24	0.063	-
Perturbation Condition (*)	32.082	1.5 – 17.6	< 0.001	Vibration > Reference Vibration > GVS
Touch x Perturbation (*)	3.313	3.0 – 36.5	0.030	Vibration/No touch > Vibration Hand touch

Figure 3:
Mean sway (top panel) and drift (lower panel) in fore-aft direction. Error bars represent one standard deviation. * denotes significance at the p < 0.05 level. In the top panel, a significant main effect for both touch and perturbation condition was found. In the lower panel, a significant main effect for perturbation was found. Furthermore, a significant interaction was present indicating the significant difference between vibration hand-touch and vibration no-touch.

Significantly more drift was observed for the muscle vibration condition compared to the reference (p < 0.001, 95% CI [3.920 13.413]) and GVS conditions (p < 0.001, 95% CI [4.973 13.359]) (figure 3, lower panel). Furthermore, a significant interaction was present, indicating that for the vibration condition, hand-touch was effective in decreasing the drift compared to the no-touch condition (p = 0.019, 95% CI [-3.978 -0.348]). Back-touch also decreased the drift in the vibration condition but this failed to reach statistical significance on post-hoc tests (figure 3, lower panel).

Discussion

The purpose of the present experiment was to determine the effect of touching an external object on trunk postural sway in a seated position. Furthermore, the possible interaction of touch with paraspinal muscle vibration and GVS was studied. The results showed that touch through hand or back was effective in decreasing trunk sway and in decreasing the effects of muscle vibration and GVS. GVS led to a large increase in sway whereas closing the eyes did not significantly affect sway. The effect of muscle vibration was only observed as an increase of drift and not of sway.

he results demonstrated an important factor in studying trunk control: the possible interference of touch with other sensory modalities. In the current experimental set-up, the stabilizing effect of touch was strong enough to mask any effects of manipulation in the vestibular and paraspinal muscle spindle afference. These results are consistent with findings from standing postural sway: for example, Lackner et al. showed that in standing postural sway, allowing the subjects to touch a laterally positioned surface strongly decreased the observed (lateral) sway, even in the presence of vibration to the m. peroneus longus and brevis tendons (Lackner et al., 2000).

Several studies have shown that vestibular information plays an important role in postural control (Goodworth and Peterka, 2009; Bent et al., 2000). The present results support these findings as perturbing the vestibular organ with GVS resulted in a large increase in sway. Muscle vibration led to a strong increase in drift and a trend for an increase in sway could also be observed. These results are consistent with other experiments (Claeys et al., 2011; Brumagne et al., 2004).

Several mechanisms for the stabilizing effect of touch have been proposed. In standing postural sway, the exerted touch force was well below the force that one might expect to result from the movement due to sway. Therefore, touching an external object can be expected to have a non-significant mechanical stabilizing effect in this case. In a seated position, the observed sway is considerably smaller; hence, the mechanical stabilizing effect of a light (< 2 N) touch may be relatively large compared to standing. However, Jeka & Lackner showed that, in standing, allowing the subjects to assert higher touch-forces did not lead to an additional

stabilizing effect (Jeka and Lackner, 1994). Therefore, it is likely that sensory mechanisms largely determined the stabilizing effect of touch.

A second possible contribution to the stabilizing effect of touch might be of proprioceptive nature. When the subject touches an external object, for example with the hand, a change in trunk posture will lead to changes in all joints connecting the trunk to the external object (shoulder, elbow, wrist). This may provide the subject with additional information about trunk sway. However, the results from Rabin et al. do not support the contribution of proprioceptive information from the arm to be the only stabilizing factor (Jeka et al., 1998). In the study of Rabin et al., subjects were instructed to stand in a heel-to-toe stance, making them more unstable in the lateral direction. Furthermore, the heel-to-toe standing subjects were allowed to touch in front of the body (stable sway direction) or to the side (unstable sway direction). The results showed that when subjects were allowed to touch in the unstable sway direction (e.g. to the side for heel-to-toe stance), the reduction in sway was larger compared to touch in the stable direction (Rabin et al., 1999). Since the amount of rotation in the arm joints was independent of touch direction, it is unlikely that proprioceptive information from the arm joints was the only contributor to the stabilizing effect.

Finally, the results from Rabin et al. suggest that tactile feedback may contribute to the stabilizing effect. The pressure receptors in contact with the external object provide the subject with additional information of his/her sway. Two factors may influence the contribution of the sensory information. First, the amount of available pressure receptors might affect the amount of available information. In this case, one would expect a larger effect of hand-touch as the hand has a larger density of pressure receptors compared to the back (Wing et al., 2011). Secondly, if the contact point is used as a passive pressure probe, one would expect a larger effect of back-touch as the contact point on the back is more directly coupled to the trunk and therefore better suited as a "pressure gauge" for deviations of the trunk. However, the current findings indicate that hand- and back-touch are equally effective in reducing sway suggesting that both aforementioned factors contribute similarly.

The present findings have important implications for studying trunk control. Many methods for studying trunk control apply external

perturbations, which implies that the body is in contact with an external object. The present findings indicate that irrespective of the body part in contact with the external object, the tactile information has a strong influence on postural control. For example, the contribution of other sensory modalities to postural control becomes difficult to investigate because the dominant effect of touch will mask any effects of perturbations to these sensory modalities. Even when the touch-surface is not stable but when moving rhythmically, as is often the case with external perturbations, the influence of touch is dominant as the body sway is strongly coupled to the moving touch-surface (Jeka et al., 1997; Jeka et al., 1998; Wing et al., 2011). For future research, it would be interesting to combine a moving touch-surface with interference of other sensory modalities, for example GVS and/or muscle vibration, to see whether the interference can still be observed in the postural sway.

The current study has several limitations. First, since the available information was limited, an a-priori power analysis was not performed. Therefore, a post-hoc Monte Carlo power analysis was performed to check whether the obtained power was sufficient. This power analysis indicated that sufficient power was obtained for all effects except for the sway interaction effect. Given the limited power, the absence of an interaction should be interpreted with care and our results suggest that effects of other sensory inputs may be difficult to detect when tactile information is available.

A second limitation was the age of the sample population, which consisted of healthy young adults. The present results might not be representative of older adults and/or patients as it has been shown that proprioceptive reweighting might change with age (Wing et al., 2011) and low-back pain (Brumagne et al., 2004).

In conclusion, tactile information, whenever available, seems to play a dominant role in the control of trunk posture in young healthy adults.

Chapter 7

Chapter 8

Effects of support surface stability on feedback control of trunk posture

G. Andreopoulou, E. Maaswinkel, L.E. Cofré Lizama, J.H. Van Dieën

ABSTRACT

This study aimed to examine the interactions of visual, vestibular, proprioceptive and tactile sensory manipulations and sitting on either a stable or an unstable surface on mediolateral (ML) trunk sway. Fifteen individuals were measured. In each trial, subjects sat as quiet as possible, on a stable or unstable surface, with or without each of four sensory manipulations: visual (eyes open/ closed), vestibular (left and right galvanic vestibular stimulation alternating at 0.25 Hz), proprioceptive (left and right paraspinal muscle vibration alternating at 0.25 Hz) and tactile (minimal finger contact with object moving in the frontal plane at 0.25 Hz). The root mean square (RMS) and the power at 0.25 Hz (P25) of the ML trunk acceleration were the dependent variables. The latter was analyzed only for the rhythmic sensory manipulations and the reference condition. RMS was always significantly larger on the unstable than the stable surface. Closing the eyes caused a significant increase in RMS, more so on the unstable surface. Vestibular stimulation significantly increased RMS and P25 and increased more on the unstable surface. Main effects of the proprioceptive manipulation were significant, but the interactions with surface condition were not. Finally, also tactile manipulation increased RMS and P25, but did not interact with surface condition. Sensory information in feedback control of trunk posture appears to be reweighted depending on stability of the environment. The absolute effect of visual and vestibular manipulations increases on an unstable surface, suggesting a relative decrease in the weights of proprioceptive and tactile information.

INTRODUCTION

The human ligamentous spine, devoid of muscular control is incapable of carrying the weight of the upper body, as the smallest perturbation will cause it to buckle (Crisco & Panjabi, 1992). Therefore, in addition to passive structures such as the intervertebral discs and the ligaments, back and abdominal muscles contribute to stabilization of the trunk against perturbations (Panjabi, 1992) through modulation of co-activation and the resultant muscle stiffness and damping (Cholewicki et al. 1997; van Dieen et al, 2003) and under feedback control based on the sensory information provided by visual, vestibular, proprioceptive and tactile afferents (Goodworth & Peterka, 2009; Maaswinkel et al, 2014).

The postural control system appears to use multiple sources of sensory information on trunk movement for feedback control. The vestibular and visual systems provide indirect information on motion and spatial orientation of the trunk (Mergner & Rosemeier 1998). The somatosensory system likewise provides indirect information through sensing of shear or pressure induced by motion between body and support area (Lestienne & Gurfinkel 1988; Massion 1992). Also, in studies of whole body control (Lackner et al. 2000) and of trunk control (Maaswinkel et al. 2014) it was shown that tactile information contributes. Proprioceptive information appears to be a more direct source of information on trunk movement and probably the only source of information on spinal curvature. Muscle spindles are thought to be the main source of this information (Brumagne et al. 2008), although joint receptors may also be involved (Solomonow et al. 2004).

It has been suggested that the central nervous system (CNS) weighs information from different sensory sources, relative to one another, to generate appropriate feedback commands (Peterka et al. 2002; van der Kooij et al. 2005). Information from multiple systems appears combined also in control of the trunk (Brumagne et al. 2004; Carver et al. 2006; Goodworth and Peterka 2009). An advantage of this reweighting may be that the CNS can adjust gains of sensory inputs from other locations, when the quality of the input from one location decreases due to for example aging or injury (Brumagne et al. 2004).

Sensory weighting in feedback control also appears to be affected by environmental conditions. Studies have shown that effects of triceps surae muscle vibration were less when standing on an unstable than on a stable surface, indicating that proprioceptive information from triceps surae muscles was used

less in postural control on an unstable support than on a stable support (Ivanenko et al. 1999; Kiers et al. 2012). This effect has been explained by an altered relation between muscle strain and the body's orientation in the gravitational field on the unstable support (Ivanenko et al. 1999; Kiers et al. 2012). When standing on a rigid surface, foot orientation is fixed, hence shank angle determines the length of the lower leg muscles and bears a direct relation with the orientation of the body with respect to gravity. This is not the case when standing on a tiltable or compliant surface. Somewhat simplified: the state of the two degrees of freedom (shank angle and foot/surface angle) present on an unstable surface can not be sensed by one degree of freedom (ankle angle) proprioceptive information. In addition, standing on an unstable support would reduce the input into the somatosensory system arising from the contact with the support surface (Pasma et al. 2012). Finally on an unstable surface movement amplitudes will increase, which, for control of standing postures, has been indicated to cause upweighting of vestibular information (Maurer et al. 2006; van der Kooij and Peterka, 2011) and visual information (Fransson et al. 2007; Polastri et al. 2012; Assländer and Peterka 2014) relative to proprioceptive information.

The goal of the present study was to examine the effects of surface conditions on the importance of different sources of sensory information, as reflected in the effects of sensory manipulations on mediolateral postural trunk control. We hypothesized interaction effects between surface conditions and the sensory manipulations, reflecting larger effects of visual and vestibular information on an unstable surface than on a stable surface and a reduced effect of proprioceptive manipulation. We also tested for an interaction between surface conditions and tactile manipulations, but we had no a priori expectation on the direction of this interaction, if any.

METHODS

Subjects

Fifteen subjects participated in this study (9 females and 6 males, age: 26.1 SD 2.8 yrs, height: 173.5 SD 11.9 cm; body mass: 65.5 SD 13.9 kg). The exclusion criteria for this study were current low-back pain, any neurological disorder that could affect balance and also, presence of any musculoskeletal problem in the lumbar area. Subjects were asked to sign informed consent, after being briefed and instructed about the research protocol. The protocol was approved by the ethics

committee of the Faculty of Human Movement Sciences of the VU University Amsterdam.

Experimental protocol

The experiment took place in a single visit to the laboratory, during which subjects performed a total of 10 trials, each lasting 65s. Trunk postural sway was measured while subjects were seated in two surface conditions; sitting on a rigid surface and on a surface that was unstable in the frontal plane. Four different sensory manipulations were applied: visual, vestibular, proprioceptive and tactile. The order of the trials was randomized.

For the stable surface condition, subjects sat on a rigid flat surface. For the unstable surface condition, subjects sat on an adjustable chair, keeping the hips and knees 90° flexed and the feet supported. This seat with foot support was mounted on a rocking support (see-saw) with one degree of freedom in the frontal plane. The height of the seat was 185 mm and the radius of curvature of the support was 240 mm. A metal bar was placed around the subject for safety reasons. If the subjects touched the bar during the trial, the trial was discarded and repeated. In every trial, subjects had to cross their arms, except for the trial with the tactile manipulation, where one hand was touching a sphere at the end of a robot arm while the other was still crossed (figure 1).
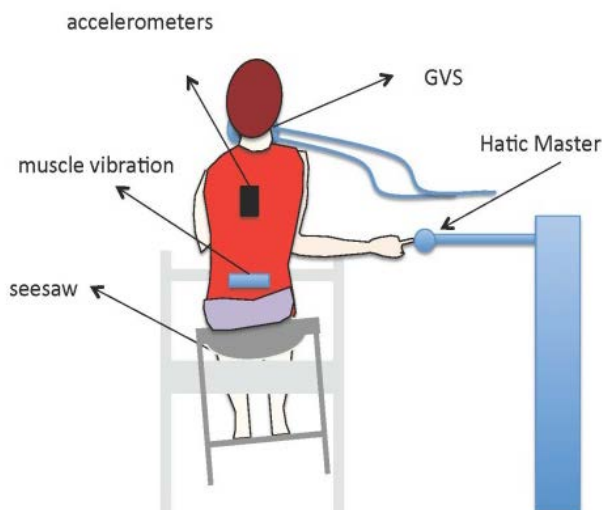

Figure 1:
Schematic illustration of the experimental set-up (in the unstable surface condition).

The visual manipulation consisted of subjects closing the eyes. During all other trials their eyes were open. Except for the manipulation of visual information, all sensory manipulations were applied at a fixed frequency of 0.25 Hz, to facilitate the comparison between the different conditions.

For manipulation of vestibular information, galvanic vestibular stimulation (GVS) was used. A sinusoidal, mean zero, amplitude 1.5 mA, current was applied, through electrodes placed over the mastoid processes, by a linear isolated stimulator (Stmisola, Biopac systems, Inc., Goleta CA, USA). GVS activates afferent fibers of the vestibular nerve and excites a wide range of vestibular neurons including the otolith system and the semicircular canals, causing an illusion that the body leans towards the cathodal side (Cohen et al. 2012), which with this stimulation protocol occurred in an alternating fashion from left to right at the stimulus frequency.

For the proprioceptive manipulation, muscle-tendon vibration (MTV) was applied over the muscle bellies of the paraspinal muscles in the mid-lumbar area. Vibration alternated between left and right paraspinal muscles, as a square wave at a fixed frequency of 0.25 Hz, applied by a custom-made stimulator consisting of two electromotors (Graphite Brushes S2326.946, Maxon, Sachseln, Switzerland) driven in a velocity-loop at 100 Hz (4-Q-DC Servo Control LSC 30/2, Maxon, Sachseln, Switzerland). Muscle vibration activates mainly Ia-afferents, which causes illusions of lengthening and reflex responses to counteract the perceived movement (Goodwin et al. 1972; Roll et al. 1989).

For the tactile perturbation, subjects were asked to touch, as lightly as possible, the head of the arm of a haptic master (Moog-FCS, Nieuw-Vennep, The Netherlands), which was to their right side, outside their field of vision and which was moving at a frequency of 0.25 Hz over a range of 5 cm. Subjects were instructed to look straight ahead and not at their arm. Touching a stationary surface reduces trunk sway (Maaswinkel et al. 2014), and it has been shown that whole body sway is coupled to the rhythm of moving surfaces when these are touched (Jeka et al. 1998; Wing et al. 2011).

Measurements and data analysis

Postural sway was measured by a hybrid inertial sensor at a sample frequency of 100 Hz (Dynaport, McRoberts, the Hague, Netherlands), placed at the back over the 10th thoracic vertebrae. The sensor recorded accelerations and angular velocities in three planes. All data analysis was performed using custom-made

software in Matlab R2014a (Mathworks, Natick MA, USA). For analysis we used acceleration data to represent trunk movement, as it is more sensitive becuase higher frequency components are reflected more strongly in the signal than in velocity or the position signals. Inertial sensors allow relatively noise-free measurement of acceleration, in contrast with optical methods, which measure position and obtain acceleration through double differentiation, thereby introducing considerable noise. Data recording was started after the subject had adopted an upright posture and sensory manipulations had been started. Moreover, the first 5 s of every trial were discarded, in order to eliminate transient behavior. Data were bi-directionally, low-pass filtered, with a 2nd order 6 Hz Butterworth filter and subsequently the root mean square (RMS) of the mediolateral (ML) acceleration and the power spectral density of the ML acceleration at 0.25 Hz (P25; the frequency used for the rhythmic perturbations) were calculated. The latter was determined using the Welch estimation method, using a Hamming window size of 10 s, with 5 s overlap and a 10000-point DFT, yielding a spectral resolution of 0.01 Hz. For illustrations, the spectra were normalized to total power.

Statistics analysis

Statistical analyses were performed with SPSS 20. (IBM Software, Armonk NY, USA). Normality of the data was confirmed by visual inspection of the q-q plots and box plots of the residuals and the Shapiro-Wilk test. To test the hypotheses that surface conditions (stable and unstable) and the four sensory manipulations had interaction effects on RMS trunk acceleration, we performed 3-way factorial ANOVA's, with subject as a random factor and surface condition (stable/unstable) and sensory manipulation (yes/no) as fixed factors. In case of a significant interaction effect, the effect of the sensory manipulation was tested with a paired t-test with Bonferroni correction. The effects of each of sensory manipulations were tested separately as the intensities of the perturbations applied cannot be compared between sensory modalities.

Interactions in which the effect of the sensory manipulation indicating a larger increase of sway on the unstable surface could arise from the unstable support itself amplifying the effect of any perturbation and hence do not necessarily imply reweighting of sensory information. To circumvent this interpretation problem, two additional analyses were performed. When main effects of the sensory manipulation were present, the relative change in RMS due to the sensory manipulation was compared between surface conditions with paired t-tests, thus

correcting for effects of changes in the dynamics of the controlled system. In addition, for the rhythmic perturbations, factorial ANOVA's were performed on the P25 values. As for the RMS, significant interaction effects were followed up by t-tests with Bonferroni correction for sensory manipulation within each surface condition. For all tests, results were considered significant at $p < 0.05$.

RESULTS

Due to technical problems one subject did not perform one trial with VTS. In addition, we excluded data from another subject for the eyes closed on stable support surface condition, in view of exceptionally high acceleration values of which the origin was unclear.
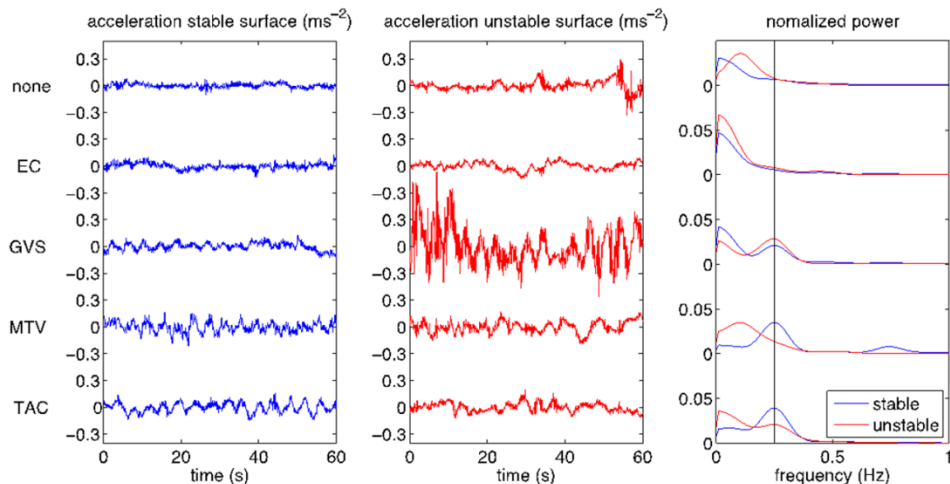

Figure 2:

Example of trunk acceleration data of a single subject in each of the conditions. A) Time series of acceleration on the stable surface, B) Time series of acceleration on the unstable surface, C) Normalized power spectra of the accelerations on both surfaces. None = no sensory manipulation, EC = eyes closed or visual manipulation, MTV = muscle-tendon-vibration or proprioceptive manipulation, GVS = galvanic vestibular stimulation or vestibular manipulation, TAC = tactile manipulation.

As the acceleration data in Figure 2 show, trunk sway was generally more pronounced on the unstable support. Moreover, it can be seen that the sensory manipulations tended to increase sway differently between the support surface conditions, with clear rhythmic responses in trunk sway identifiable in the time series (Figures 2A and B) as well as in the normalized power spectra (Figure 2C). Note also that the signals in the unperturbed and eyes closed conditions contain very little power at 0.25 Hz. In general, the unstable support condition caused a

higher RMS acceleration (Table 1), while P25 showed this main effect only in the ANOVA for the GVS (Table 2).

Condition	Manipulation		Surface		Manipulation x Surface	
	F	p	F	p	F	p
Eyes closed	**16.985**	**.001**	**31.830**	**.000**	**27.439**	**.000**
Vestibular	**31.010**	**.000**	**26.430**	**.000**	**20.993**	**.001**
Proprioceptive	**10.617**	**.006**	**11.105**	**.005**	.022	.884
Tactile	**12.400**	**.004**	**15.008**	**.002**	2.364	.148

Table 1:
Results of four separate factorial ANOVA's on the RMS trunk accelerations, with subject as random factor and sensory manipulation and surface as fixed factors. Significant effects are highlighted in bold.

Closing the eyes caused a significant increase in trunk acceleration, while an interaction with support surface was also found (Table 1; Figure 3A). The increase in RMS was significant only in the unstable support condition (p < 0.001) and the relative increase of the RMS was significantly larger in the unstable condition than in the stable condition (p = 0.008; Figure 3B).
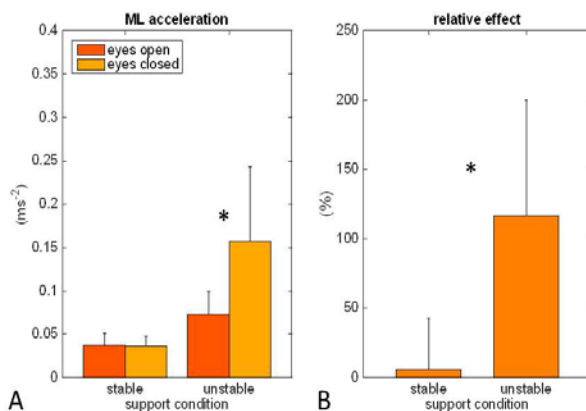

Figure 3:
Mean values of the RMS of mediolateral trunk acceleration (A) for the eyes open and eyes closed conditions at both support surfaces, as well as the relative effects on RMS of the eyes closed compared to eyes open condition on both support surfaces (B). Error bars indicate one standard deviation and asterisks indicate significant effects paired t-tests.

GVS caused a significant increase in RMS, and interacted with the surface conditions (Table 1). The increase in RMS was clearly larger on the unstable than on the stable support (Figure 4A), but still it was significant in the stable (p = 0.032) and unstable condition (p < 0.001; Figure 4). The relative effect of GVS on the RMS was significantly larger on the unstable than the stable condition (p = 0.009; Figure 4B). A similar pattern of effects as for the RMS was observed for the power spectral density at 0.25 Hz specifically (Table 2, Figure 4C).

Condition	Manipulation		Surface		Manipulation*Surface	
	F	p	F	p	F	p
Vestibular	**7.527**	**.017**	**6.590**	**.023**	**6.033**	**.029**
Proprioceptive	**19.249**	**.001**	2.414	.144	2.861	.115
Tactile	**10.903**	**.006**	1.501	.242	2.056	.175

Table 2:
Results of three separate factorial ANOVA's on power spectral density of trunk acceleration at 0.25 Hz, with subject as random factor and sensory manipulation and surface as fixed factors. Significant effects are highlighted in bold.

While the proprioceptive manipulation significantly increased the RMS and P25 values, there were no interactions with the surface condition (Tables 1 and 2), even though the effect on RMS and P25 appeared more pronounced at the stable support surface (Figure 5C). In line with this, the relative effect of MTV on the RMS acceleration was not different between support conditions (p = 0.257, Figure 5B).
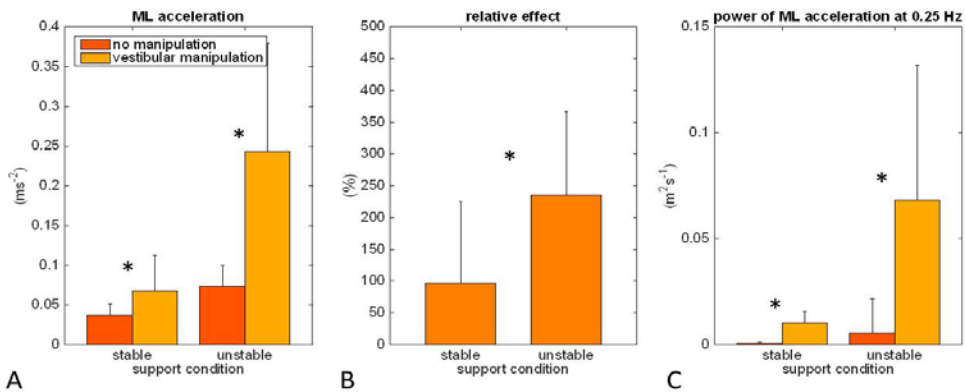

Figure 4:
Mean values of the RMS of mediolateral trunk acceleration (A) for the conditions with and without GVS at both support surfaces and the relative effects on RMS of the GVS compared to no GVS condition on both support surfaces (B), as well as mean values of power spectral density of mediolateral trunk acceleration at 0.25Hz (C). Error bars indicate one standard deviation and asterisks indicate significant effects paired t-tests.

Touching the moving arm of the haptic master increased RMS and P25 acceleration. Although for both variables a tendency was observed towards smaller effects of touching the haptic master on the unstable support, there were no significant interactions between the tactile manipulation and the support conditions (Tables 2 and 3; Figures 6A and C). Similarly for the relative effects on the RMS, only a trend toward a larger relative effect on the stable support was found (p = 0.062; Figure 6B).
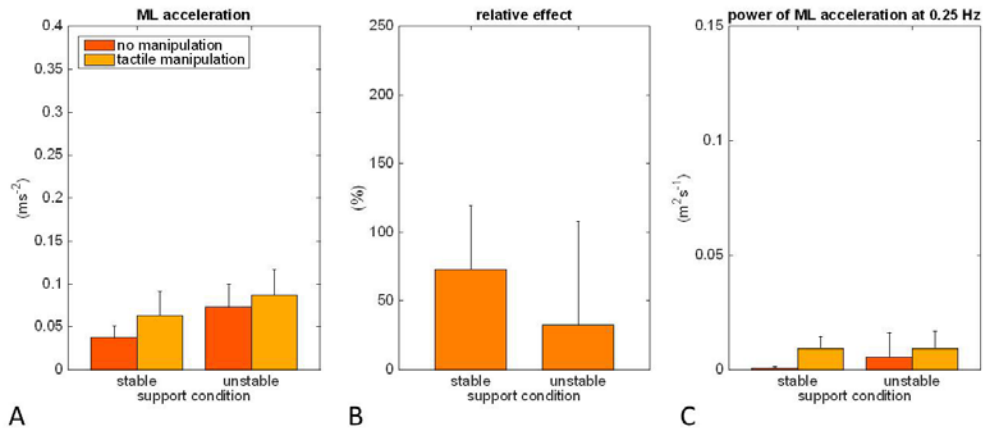
Figure 5:
Mean values of the RMS of mediolateral trunk acceleration (A) for the conditions with and without MTV at both support surfaces and the relative effects on RMS of the MTV compared to no MTV condition on both support surfaces (B), as well as mean values of power spectral density of mediolateral trunk acceleration at 0.25Hz (C). Error bars indicate one standard deviation.

DISCUSSION

The purpose of the present study was to examine the effect of sensory manipulations on trunk control during stable and unstable sitting. We hypothesized interaction effects between surface conditions and the sensory manipulations, reflecting larger effects of visual and vestibular manipulations on an unstable surface than on a stable surface and a reduced effect of proprioceptive manipulation. We also tested for an interaction between surface conditions and tactile manipulations. The results showed the expected interactions for the visual and vestibular manipulations with the surface conditions, but not for the proprioceptive and tactile manipulations.

When comparing the surface conditions, the unstable condition led to an increase in postural sway. Increased sway due to surface instability is not surprising and has previously been reported (Cholewicki et al. 2000; Radebold et al. 2001; Silfies et al. 2003; Reeves et al. 2006; Slota et al. 2008). The current study adds to this that changes in stability of the surface interact with manipulations of visual and vestibular information, suggesting reweighting of these sensory modalities in control of trunk posture. Such re-weighting of sensory systems should be considered in research and clinical practice when aiming to assess or train trunk

control and for example raises questions regarding the use of unstable surfaces for so-called proprioceptive training (c.f. Kiers et al. 2012).

When vision was occluded in the stable condition, mediolateral trunk acceleration did not significantly increase. Similarly, Maaswinkel et al. (2014) did not find an effect of closing the eyes on anteroposterior trunk sway in stable sitting. These findings contrast with effects of closing the eyes on postural sway observed in many previous studies (for an overview see Mazaheri et al. 2013). Possibly, this is attributable to the smaller effect of sway angle on head movement in sitting compared to standing. In the present study, mediolateral sway did increase with closing the eyes in the unstable condition. In line with this, Silfies et al. (2003) showed that chair movement in unstable sitting increased faster with seat instability when visual input was lacking. However, this effect was significant only for anteroposterior sway and total path length and not for mediolateral sway. Goodworth & Peterka (2009) did not find a significant effect of closing the eyes in mediolateral sway in standing on an actively tilting platform. On the other hand, tilting the visual environment did increase sway. Combined, these data may suggest that the use of visual information in control of trunk sway is dependent on the amplitude of the visual stimulus and hence of trunk sway, which would also explain the interaction effect with surface condition found in the present study.

As expected, there was an interaction between vestibular manipulation and surface condition; relative effects and P25 were higher on the unstable surface than on the stable one. These results are in line with Fitzpatrick et al. (1994) who applied GVS while standing and found a larger EMG response in the lower-leg muscles while standing on an unstable, compared to a stable surface. As for visual manipulation, the increased effect of vestibular manipulation could be due to increased reliance on vestibular inputs with increased movement amplitudes. This is in line with upweighting of vestibular information with increasing movement amplitudes, as predicted by models of sensory weighting (Maurer et al. 2006; van der Kooij and Peterka 2011) and empirically supported by data on mediolateral trunk sway (Goodworth and Peterka, 2009).

A significant increase in sway was observed also with muscle vibration on both surfaces, but absolute and relative effects on acceleration were not different between support conditions. We had hypothesized a smaller effect of the proprioceptive manipulation on the unstable surface than on the stable surface, in line with reduced effects of calf muscle vibration on unstable surfaces (Ivanenko et al. 1999; Kiers et al. 2012). On the unstable surface, proprioceptive information is

ambiguously related to trunk orientation in space, which makes this input less pertinent and could even lead to responses that further offset balance. However, although some models of sensory reweighting assume that weighting of a specific input is dependent on discrepancies with a veridical signal (Mahboobin et al. 2009), other models suggest that it is based on the signal's variability (van der Kooij and Peterka 2011) or on its amplitude in relation to a sensory threshold (Maurer et al. 2006). While such weighting processes could account for upweighting of sensory channels in an absolute sense at increasing amplitudes without downweighting of 'competing' channels, these models assume a reciprocal weighting to avoid changes in the overall feedback gain. The present data suggest that the relative but not the absolute weight of proprioceptive information decreased on the unstable surface, since the effects of visual and vestibular input increased, while that of proprioceptive input remained constant. While this is in line with a shift toward reliance on vestibular and visual information as movement amplitudes increase (Goodworth and Peterka, 2009; Polastri et al. 2012; Assländer and Peterka 2014), it does not support the reciprocal nature of sensory reweighting. Polastri et al. (2012) likewise reported an asymmetric change in weighting of visual and proprioceptive information, which was however not supported by data presented by Assländer and Peterka (2014). It should be noted here that other sensory modalities may play a role. Sensing the ground reaction force through pressure sensors in the skin can potentially contribute to trunk control in the present task (c.f. Maurer et al. 2006). This source of information is greatly attenuated on the unstable surface and since it is not known whether and how its weighting changes, the reciprocal nature of weighting of all relevant sensory modalities cannot be excluded.

The tactile manipulation also caused an increase in sway in all the trials and did not interact with surface condition, although a tendency towards smaller effects was found in the unstable condition. Several studies have shown that light touch can reduce postural sway in the mediolateral direction in standing whether the eyes are open or closed (Jeka & Lackner 1994; Holden et al. 1994). Also light finger touch with a moving object leads to entrainment of the whole body to the movement frequency of the object (Jeka et al. 1997; Jeka et al. 1998). While it has previously been shown that tactile information has a strong influence on trunk sway, irrespective of the body part that is in contact with an external object (Chapter 7, Maaswinkel et al, 2014), this study adds that also the effect of touching a moving object generalizes to control of trunk posture in sitting.

Some limitations of the current study need to be addressed. Most importantly, the strength of the different manipulations applied was not scaled, rendering direct comparisons of the effects of these sensory manipulations impossible. Secondly, with the change in surface conditions, the dynamics of the controlled system changed. Hence increased responses to sensory manipulations cannot directly be attributed to upweighting of sensory information. Therefore, we also compared relative effects within surface conditions. Consistent increases in both relative and absolute effects are suggestive though no definitive proof of upweighting of the sensory information manipulated. Finally, the subjects that participated in this study consisted of young healthy individuals; consequently, the results cannot be generalized to clinical populations in which trunk control is affected such as low back pain (e.g. Radebold et al. 2001) or Parkinson's Disease (van der Burg et al. 2006). Further study in patient populations could reveal differences in the use of sensory information in such tasks compared to healthy controls (c.f. Claeys et al. 2011; Willigenburg et al. 2013).

CONCLUSION

The aim of the present study was to investigate the effect of sensory manipulations on trunk control on stable and unstable sitting. Interactions between surface condition and the manipulation of visual and vestibular information were found, with stronger effects of these manipulations on the unstable surface. The effects of muscle vibration to manipulate proprioceptive information and of touching a slowly moving object were constant between the two surface conditions. These findings suggest a relative upweighting of visual and vestibular information compared to proprioceptive and tactile information in trunk control on an unstable surface.

Chapter 9

Unpredictable torso perturbations interact with the effect of lumbar muscle vibration in the control of upright trunk posture

E. Maaswinkel, R.S.A. Hendriksen, A.S. Ouwerkerk, J.H. Van Dieën

Abstract

The purpose of this study was to investigate the interaction between pseudorandom torso perturbations and proprioceptive feedback by lumbar muscle spindles in trunk control. 19 healthy subjects were positioned in a semi-kneeling position with the pelvis restrained. Each subject performed a total of 6 trials, combining the experimental conditions of no vibration, alternating agonist-antagonist muscle vibration at 0.2 Hz over dorsal and ventral trunk muscles and over left and right trunk extensor muscles with or without a mechanical pseudorandom trunk perturbation. Trunk sway was measured by a motion capture system and the normalized power of the sway at 0.2 Hz was calculated. Also, the actuator displacement and contact force between actuator and subject were measured and subsequently used for non-parametric system identification. The results showed that the effect of a perturbation on vibration was similar for both vibration conditions. Vibration led to a significant increase in sway at 0.2 Hz, whereas the torso perturbations led to a significant decrease. Furthermore, a significant interaction indicated that the increase in sway with vibration was significantly reduced in the presence of the perturbation. Finally, alternating muscle vibration had no significant effect on the admittance of the trunk at other frequencies. The presence of tactile information from the pseudorandom perturbation appears to provide a source of information for the stabilization of the trunk and seems to result in sensory reweighting as indicated by the attenuated effect of muscle vibration.

Introduction

Controlling trunk movement is essential for maintaining balance during activities of daily life (MacKinnon and Winter, 1993; van der Burg et al., 2005). Accurate function of the hand/arm is also dependent on adequate control of trunk movement (Kaminski et al., 1995; Pigeon et al., 2000). Furthermore, control of trunk movement is affected in patients with low back pain (Panjabi, 1992a, b) and different neurological disorders (e.g.: stroke (Ryerson et al., 2008), Parkinson's disease (van der Burg et al., 2006) and spinal cord injury (Seelen et al., 1997)).

Without muscular control, one would be incapable of controlling trunk motion, as the smallest perturbation will cause the spine to buckle (Crisco and Panjabi, 1992). Therefore, in addition to passive structures, an active muscular contribution in the form of co-activation and feedback control is required to stabilize the trunk against gravity.

For trunk stabilization, proprioceptive information from muscle spindles (Brumagne et al., 2008) and possibly joint receptors (Solomonow, 2004) is a direct source of information on trunk movement and likely the only information source on spinal curvature. The contribution of proprioceptive information to feedback control of trunk motion is often studied by interfering with the muscle spindle information by attaching a vibrator over the muscle belly and measuring the resulting change in posture (Brumagne et al., 1999; Claeys et al., 2011). In addition to proprioceptive information, tactile information, from contact with an external object, seems to have a stabilizing effect (Lackner et al., 2001). Maaswinkel et al. (2014) showed that the availability of a stationary source of tactile information can lead to sensory reweighting, as indicated by the profound influence of touching an external object on the magnitude of the effect of muscle vibration. Furthermore, Andreopoulou et al. (2015) showed that the motion of the upper body becomes entrained to a source of tactile information which is moving in a predictable way (a sinusoid). However, whether contact with an external object which is moving in an unpredictable way provides a useful source of tactile information for the subject and hence results in sensory reweighting remains an open question.

The involuntary/reflexive components of trunk control can be identified by applying mechanical external perturbations and measuring the resulting trunk motion and muscle response (Cholewicki et al., 2000; van Drunen et al., 2013). This approach has been used to estimate the contribution of sensory modalities to trunk stabilization (Maaswinkel et al., 2015). Applying mechanical perturbations,

however, usually involves contact with an external object (i.e. the perturbation device), which provides the subject with an unpredictably moving source of tactile information (i.e. a pseudorandom contact force). Furthermore, some methods (e.g. van Drunen et al., 2013; Maaswinkel et al., 2015) apply a static preload, which may lead to an increase in the subjects' trunk stiffness . This increased stiffness may limit the role of feedback and thus proprioceptive information in trunk control (Stokes et al., 2000). Therefore, the question arises as to whether an external perturbation with preload (i.e. a pseudorandom contact force) might interfere with the estimation of the contribution of other sensory modalities.

Accordingly, the purpose of the present experiment was to investigate the interaction between the presence of a pseudorandom contact force and the manipulation of lumbar muscle spindle information by means of muscle vibration, alternating between agonist and antagonist muscles. It was hypothesized that alternating muscle vibration would lead to an increase in motion at the alternating frequency and that the presence of an external perturbation would reduce this effect, i.e. lead to a smaller increase in motion at the alternating frequency as compared to without perturbation. Furthermore, it was hypothesized that alternating muscle vibration has no influence on trunk responses at other frequencies as represented by the admittance of the trunk.

Methods

Subjects
The study was approved by the ethics committee of the Faculty of Human Movement Sciences of the VU University Amsterdam. 19 healthy subjects participated (9 males, 9 females; age range: 20-27 years; mean mass 69 (SD 11) kg; mean height 178 (SD 9) cm). The subjects had no current and history of low-back pain, no neurological disorder that could affect trunk control and also no musculoskeletal problems in the lumbar area. Prior to the experiment, all subjects gave their informed consent.

Experimental setup
Subjects sat blindfolded and upright in a height adjustable chair, in a semi-kneeling position (Figure 1). To reduce the effect of pelvic motion, the pelvis was restrained. Furthermore, to reduce the effect of movement of the arms, the subjects were instructed to sit with their arms crossed.
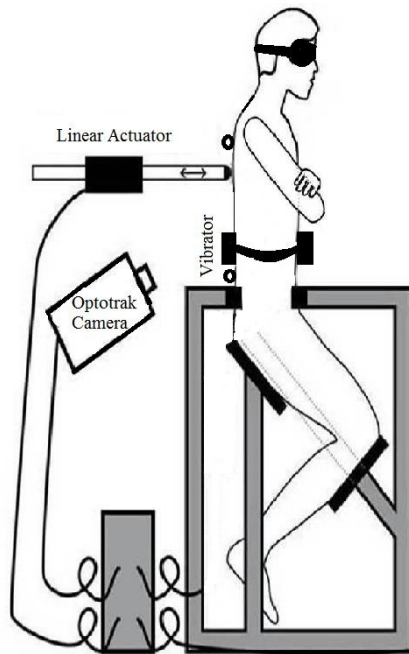
Figure 1:
The experimental set-up. Subjects sat blindfolded, with the arms crossed and pelvis restrained. A linear actuator applied unpredictable continuous perturbations to the trunk.

Muscle vibration

Vibration was applied by two custom build vibrators (dimensions 8x4x3,5 cm) consisting of two electro motors ((Graphite Brushes S2326.946, Maxon, Sachseln, Switzerland) driven in a velocity-loop at 80 Hz (4-Q-DC Servo Control LSC 30/2, Maxon, Sachseln, Switzerland). The vibrators were either attached bilaterally, 3 cm lateral of the spine at the level of L3 (m. erector spinae) or one vibrator was attached to the back, on a support that made contact bilaterally 2 cm lateral of the level of the spine L3 (m. erector spinae) and one was attached over the M. Rectus Abdominus. During both vibration conditions, the vibrators alternated with a frequency of 0.2 Hz resulting in a periodic motion of the trunk in the medio-lateral direction or anterior-poterior direction respectively.

Force perturbation

During the contact conditions, a force perturbation was applied in ventral direction at the level of the spinous process T7 by a linear actuator (Servotube STB2410S Forcer and Thrustrod TRB25-1380, Copley Controls, USA). A thermoplastic patch (4x4 cm) was placed between the pushing rod and the back of

the subject for better force transmission and comfort. During all trials, subjects were instructed to minimize lateral and flexion/extension excursions and to remain sitting as still as possible (i.e. resist the perturbation as much as possible).

Each subject performed a total of 6 trials of 50s duration in a randomized order, combining the experimental conditions of no vibration (NV), anterior-posterior vibration (APV) and medio-lateral vibration (MLV) with no force perturbation and a force perturbation with the instruction to resist the perturbation as much as possible (i.e. remain still).

As the subjects were not attached to the pushing rod, a 60N preload was applied to maintain contact. Superimposed, a dynamic disturbance with an amplitude of 35N was applied (Figure 2), as described by van Drunen et al. (2013). The dynamic disturbance was a crested multi-sine of 20s duration containing 17 logarithmically spaced frequency pairs covering a bandwidth of 0.3-15 Hz. The power at 0.2 Hz, present in the original signal used by van Drunen et al. (2013), was removed to enable frequency domain separation of the effects of the perturbation and muscle vibration. Power above 4 Hz was reduced to 40% to reduce adaptive behavior to high frequency content (Mugge et al. 2007). As the subjects perceived the perturbation as random, no voluntary activation and or feed-forward activation in relation to the perturbation was expected to occur. Each force perturbation consisted of a 3s ramp force increase to 60N, a 2s static 60N preload, the last 5s of the dynamic disturbance (to reduce transients) and twice the 20s dynamic disturbance giving a total of 50s per run.
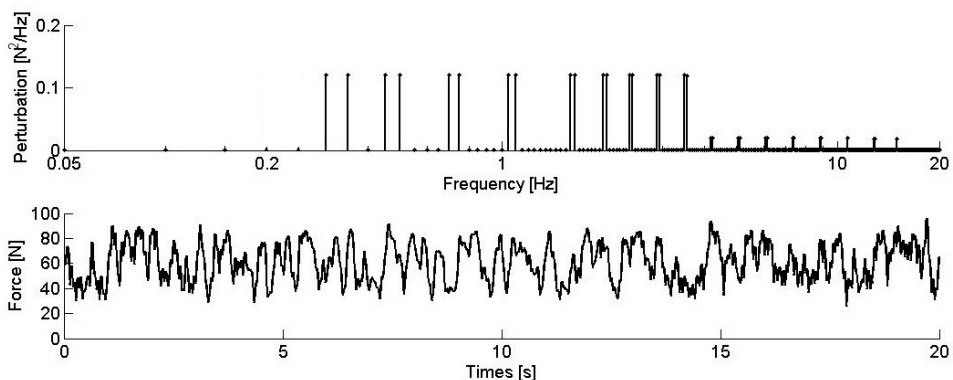

Figure 2:
The dynamic disturbance presented in both the frequency domain (top panel) and time domain (lower panel).

Data recording and processing

Actuator displacement and contact force between the rod and subject were measured at 2000 Hz (Servotube position sensor & Force sensor FS6-500, AMTI, USA) and were used for system identification (see below). Furthermore, trunk sway (a cluster of 3 markers at the level of the spine T6) was measured by a motion capture system at 100 Hz (Optotrak 3020, Northern Digital Inc., Canada). From this, the normalized power of the sway at 0.2 Hz was calculated in the sagittal plane for the APV conditions and in the coronal plane for the MLV conditions.

System Identification

Closed-loop identification (Schouten et al., 2008; van der Helm et al., 2002; van Drunen et al., 2013) was used to determine the trunk translational admittance ($H_{adm}(f)$) as frequency response function (FRF). The admittance describes the actuator displacement ($x_A(t)$) as a function of contact force ($F_c(t)$). Because the subject interacts with the actuator, the FRF was estimated using closed loop methods.

$$H_{adm}(f) = \frac{S_{F_p x_A}(f)}{S_{F_p F_c}(f)} \quad ; \quad \quad (1)$$

with $S_{F_p x_A}(f)$ and $S_{F_p F_c}(f)$ representing the estimated cross-spectral density between the Fourier transformed force-perturbation ($F_p(f)$), actuator displacement ($x_A(f)$) and contact force ($F_c(t)$) respectively.

The cross-spectral densities were only calculated at the frequencies that contained power in the force perturbation. To reduce noise and improve the estimate, the cross-spectra were averaged across the two 20s time segments (dynamic disturbance) and across the 2 adjacent frequency points (Jenkins and Watts, 1969). The coherence of the admittance (γ_{adm}^2) was calculated as:

$$\gamma_{adm}^2(f) = \frac{|S_{F_p x_A}(f)|^2}{S_{F_p F_p}(f) S_{x_A x_A}(f)} ; \quad \quad (2)$$

Coherence ranges from zero to one, where one reflects a perfect, noise-free relation between input and output. Since the spectral densities were averaged across 4 points, a coherence larger than 0.63 is considered significant at the $p < 0.05$ level (Halliday et al., 1995). Therefore, all frequency points with a subject-averaged coherence of 0.63 or larger were included for further analysis.

Statistics

To satisfy the assumption of normality, the gain of the admittance was log-transformed. Sphericity was checked using Mauchly's test. A Greenhouse-Geisser correction was used whenever the assumption of sphericity was violated (Girden, 1992).

To investigate the effect of the mechanical perturbation on the vibration conditions, a 2-factor (mechanical perturbation [2] x vibration [2]) repeated measures ANOVA was performed for both the APV and MLV conditions. Significant interaction effects were followed up by Bonferroni corrected pair-wise comparisons. Furthermore, to test for significant differences in the gain of the admittance between the different vibration conditions, a 2-factor (vibration condition [3] x frequency [17]) repeated measures ANOVA was performed. Effects were considered significant when the corrected $p < 0.05$.

Results

A typical example of the normalized power of the trunk sway for one subject for all trials is presented in Figure 3, clearly showing peaks at the frequency at which the muscle vibration alternated between agonist-antagonist muscles (0.2 Hz) in all conditions.

Table 1:
Main and interaction effects of the ANOVA's for the (mechanical) perturbation and vibration for both the anterior-posterior and medio-lateral vibration conditions.

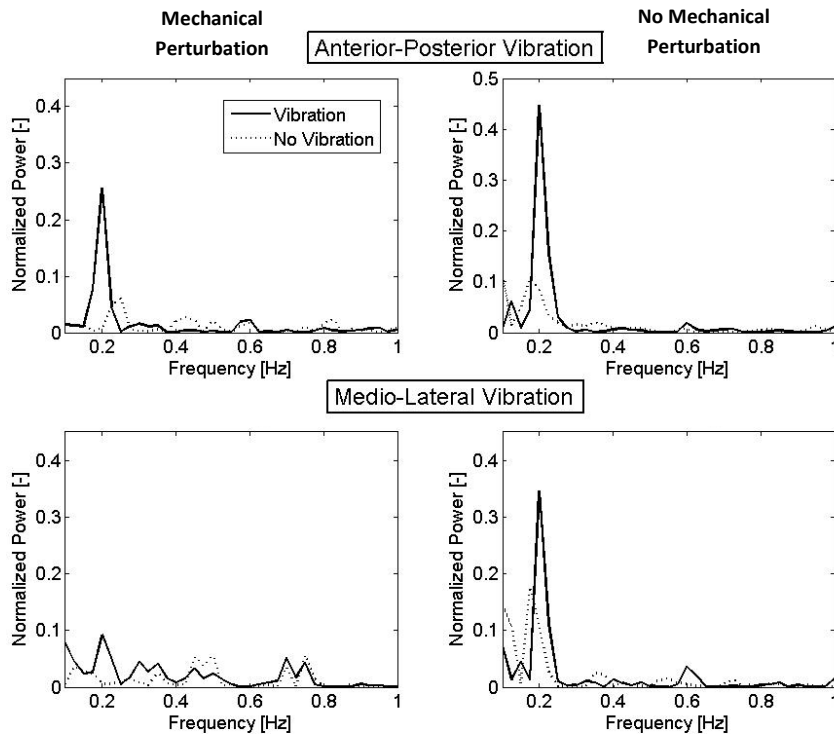| Anterior-Posterior Vibration (APV)			
	F	**df**	**P**	
Vibration	156.03	1, 18	< 0.001	Vibration > no vibration
Perturbation	15.95	1, 18	0.001	Perturbation < no perturbation
Vibration x Perturbation	5.84	1, 18	0.027	Vibration → larger increase without perturbation
Medio-Lateral Vibration (MLV)			
Vibration	66.22	1, 18	< 0.001	Vibration > no vibration
Perturbation	78.06	1, 18	< 0.001	Perturbation < no perturbation
Vibration x Perturbation	63.25	1, 18	< 0.001	Vibration → larger increase without perturbation

Figure 3:
A typical example of the normalized power of the sway for one subject for the Anterior-Posterior Vibration trials (top panels, sway in sagittal plane) and the Medio-Lateral Vibration trials (lower panels, sway in coronal plane). It can be clearly seen that vibration leads to an increase in power at 0.2 Hz (solid compared to dashed lines) while the magnitude of the effect is smaller in the trials with mechanical perturbation (left panels).

The effect of the mechanical perturbation and muscle vibration were similar for the APV and MLV conditions (Table 1). Vibration led to a significant increase in power at 0.2 Hz for the APV (95% CI [0.325 0.457], Figure 4) and MLV (95% CI [0.128 0.216], Figure 5) conditions respectively, whereas the mechanical perturbation led to a significant reduction in power at 0.2 Hz for both conditions (APV 95% CI [0.030 0.093] and MLV 95% CI [0.132 0.214]). Furthermore, for both conditions a significant interaction effect was found. The increase in power at 0.2 Hz with vibration was significantly reduced by the presence of the mechanical perturbation in both the APV (95% CI [-0.151 -0.012]) and MLV (95% CI [-0.371 -0.216] conditions.
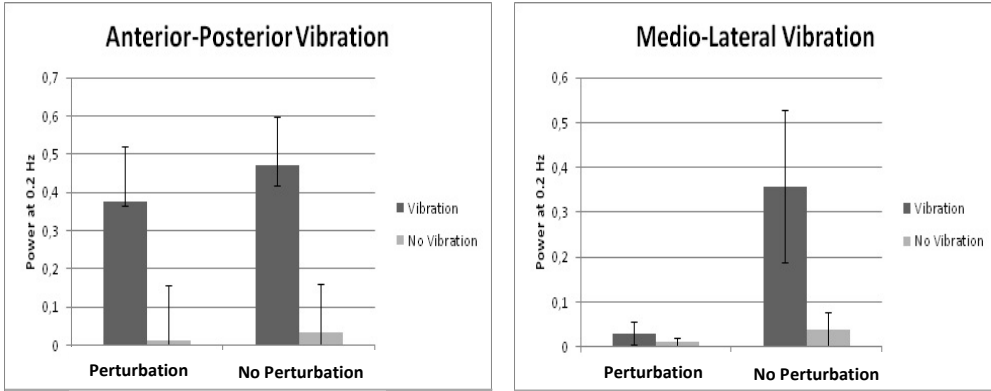
Figure 4:
The power at 0.2 Hz in the anterior-posterior direction with and without anterior-posterior vibration (left figure) or medio-lateral vibration (right figure) and mechanical perturbation. Vibration led to a significant increase in power whereas the mechanical perturbation led to a significant decrease in power at 0.2 Hz. Furthermore, the increase in power at 0.2 Hz with vibration is significantly smaller with the mechanical perturbation compared to without.

The trunk stabilizing behavior is described by the FRF of the admittance (Figure 5), while high coherences indicate good input-output correlations. The subject-averaged coherence exceeded the 0.05 probability level of 0.63 for all but one frequency point which was excluded accordingly from further analysis. In the admittance, no significant main effect of vibration was found ($p = 0.266$) and there was also no significant interaction with vibration($p = 0.270$) indicating that alternating vibration at 0.2 Hz (either in the coronal or sagittal plane) did not influence the trunk stabilizing behavior at any of the other frequencies (0.3-17 Hz) (Figure 5).
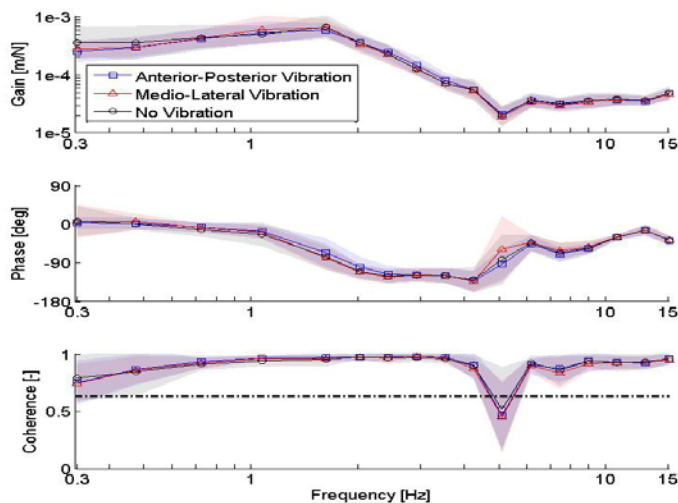

Figure 5:
Frequency response function for the APV (□), MLV (Δ) and no vibration (O) conditions averaged across all subjects. The shaded area represents one standard deviation. The dashed line in the lower plot represents the significance level for coherence.

Discussion

The purpose of the present experiment was to investigate the interaction between the presence of a mechanical perturbation (i.e. a pseudorandom contact force with the thorax) and the manipulation of lumbar muscle spindle information by means of alternating agonist-antagonist muscle vibration. The results showed that alternating muscle vibration led to a significant increase in motion at the alternating frequency (power at 0.2 Hz) whereas the presence of a mechanical perturbation led to a decrease in motion at 0.2 Hz. Furthermore, the increase in power at 0.2 Hz during the vibration trials was significantly reduced during the application of the unpredictable mechanical perturbation. Finally, alternating muscle vibration at 0.2 Hz did not lead to significant differences in motion at other frequencies as represented by the admittance of the trunk (Figure 5).

The present results confirm the importance of proprioceptive information for the stabilization of the trunk, also during mechanical external perturbations and confirm that mechanical perturbation as applied here can be used to obtain information on proprioceptive control. The results also show that the effect of muscle vibration, as a proprioceptive manipulation, is reduced by the presence of the external perturbation. This observation can be explained in two ways. First, previous research (Lackner et al., 2000; Maaswinkel et al., 2014) indicated that a tactile stimulus provides useful sensory information for trunk control and hence may result in sensory reweighting, as indicated by a smaller effect of manipulation of proprioceptive information (i.e. muscle vibration) in the presence of an external contact. The present results would expand upon previous literature (Jeka and Lackner, 1994; Jeka et al., 1997; Lackner et al., 2001) by showing that the tactile stimulus does not have to be stationary but may in fact be moving in an unpredictable way. Furthermore, the attenuating effect of the perturbation might also be explained in mechanical terms, as the preload of the perturbation will lead to an increase of trunk muscle activation, which will cause an increased trunk stiffness. On the other hand, higher muscle activation may result in a larger effect of muscle vibration (Goodwin et al., 1972). If the increase in stiffness is relatively large, a net decrease in motion might result.

All in all, our results show that even though the mechanical perturbation leads to a smaller effect of muscle vibration, the effect is still present, indicating continued use of proprioceptive information. Although the same effects were observed both in the sagittal and in the coronal plane (during APV and MLV respectively), the magnitude of the effects were different. A pronounced difference was the strong

attenuation of the increase in power at 0.2 Hz during MLV caused by the mechanical perturbation (Figure 4). One possible explanation might be that shear, due to the vibration induced motion perpendicular to the pushing rod (MLV condition), provides a stronger tactile stimulus compared to the unpredictably varying compressive stress in the direction of the pushing rod (APV condition) and hence the tactile information was able to compensate more effectively leading to a smaller effect of proprioceptive manipulation.

Finally, the absence of an effect of alternating muscle vibration on the admittance of the trunk at other frequencies is consistent with linear system control models and therefore supports the use of a linear system identification approach as used in previous studies (Goodworth and Peterka, 2009; Maaswinkel et al., 2015; van Drunen et al., 2013).

In conclusion, an external mechanical perturbation decreases, but does not nullify the effect of muscle vibration in the control of upright trunk posture. Furthermore, it is likely that the tactile stimulus provided by the perturbation is a reliable source of sensory information for the stabilization of the trunk even when the source of the tactile information is moving in an unpredictable way and may result in sensory reweighting as indicated by the attenuated effect of proprioceptive manipulation (i.e. muscle vibration).

Chapter 10

Epilogue

Conclusions

The main goals of this thesis were to advance our understanding of the neuromuscular control in low-back stabilization and to gain insight into the interaction between low-back stabilization and low-back pain. To achieve these goals, a method to investigate the intrinsic and reflexive contributions to low-back stabilization was developed. Compared to healthy controls, stabilization in twenty-two low-back pain (LBP) patients showed less reflexive modulation due to task instruction and more reliance on intrinsic components during maximal stabilization, suggestive of a disturbed reflex adaptation with LBP. However, individual patients showed either increased or decreased admittance, reflexes and modulation, indicative of heterogeneity within the patient group. Four categories of patients were tentatively defined, each with a unique pattern of motor control differences relative to healthy controls.

In the second part of this thesis, the interaction of tactile information with sensory feedback from other sources was investigated. In three consecutive studies it was shown that the availability of tactile information leads to sensory reweighting and provides a useful source of feedback on trunk orientation in space even when the source of the tactile information is moving in an unpredictable way. Therefore, when studying trunk control and the contribution of different sensory sources, tactile information, whenever available, should be considered a dominant contributor of sensory feedback leading to smaller contributions of feedback from other sources.

General Discussion

A major objective of low-back stabilization is to keep the trunk upright by counteracting the downward pull of gravity. As was shown in chapter 2, many methods exist to assess trunk stabilization but not all measure the contributions of co-contraction and reflexes simultaneously, which may pose a threat to the validity of the results and might lead to misinterpretations. In chapters 3 and 4, we set out to develop a method that is able to separate intrinsic from reflexive contributions to low-back stabilization and determined its test-retest reliability. Furthermore, in chapter 3, we demonstrated the ability of subjects to actively modulate low-back stabilization by instructing them to perform specific tasks. The instruction to resist the perturbation as much as possible led to increased low-back resistance and reduced lumbar flexion/extension excursions.

In chapter 5, it was shown that closing the eyes did not significantly affect low-back stabilization. In the specific experimental set-up, the trunk (and head) position in space could be controlled by visual feedback, as well as proprioceptive feedback, as both feedback mechanisms would counteract a displacement of the trunk/head in space. Therefore, a trade-off between visual and proprioceptive information might exist.

The posture of the lumbar spine was found to influence neuromuscular control, as reflected by increased low-back resistance with increased lumbar flexion (Chapter 5). In contrast, lumbar extension did not significantly affect low-back stabilization. The higher resistance with increased flexion may have been the result of increased passive tissue stiffness, as both the reflexive contributions and co-contraction were reduced, which might be explained by the flexion-relaxation phenomenon. However, there are indications that flexing the spine puts the extensor muscles in a more optimal range of the force-length relationship where the same torque could have been generated with decreased activation levels.

In chapter 6, the low-back stabilization of twenty-two LBP patients was identified and compared to a group of healthy controls. On a group level, patients displayed less reflexive modulation between task instructions and relied more on intrinsic components during maximal stabilization, which suggests a disturbed reflex adaptation with LBP. However, on an individual level, patients showed either increased or decreased admittance, reflexes and modulation which indicates the heterogeneity within the LBP patient group. This suggests that sub-populations of

LBP patients show different and even opposite changes in motor control which might indicate clinically relevant sub-groups.

Tentatively, a new categorization was proposed in chapter 6, based on the maximal low-back stabilizing ability (task instruction to maximally resist the perturbation) and the modulation towards more natural low-back stabilization (task instruction to relax but stay upright) during trunk perturbations. Four sub-groups were defined, each with a unique pattern of motor control differences relative to healthy controls.

> **G1**: The large group of patients (n = 11) belonging to this category showed no differences in admittance and modulation compared to healthy controls. However, these patients showed significantly higher intrinsic contributions (co-contraction) leading to higher muscle stiffness and damping during maximal stabilization, suggesting impaired motor control during this task.

> **G2**: Two patients showed higher admittance than normal during both tasks and had lower intrinsic stiffness during maximal stabilization. This would be consistent with muscle weakness, causing overall less effective stabilization and would affect maximal stabilization the most.

> **G3:** Four patients showed higher admittance during the natural stabilization task which may indicate that these patients, when given the chance, attempt to minimize muscle forces.

> **G4:** Four patients showed significantly reduced task modulation and a tendency towards a lower admittance during natural stabilization. This suggests that these patients attempted to limit low-back movement.

Classification of the patients was performed on the basis of the frequency response functions (FRFs) of the admittance. Including the reflexes and/or neuromuscular modeling parameters could improve the classification, but may decrease the reliability because the model parameters had a rather large variance compared to the FRFs, suggesting that focusing on the FRFs would be preferable.

In the second part of this thesis, the influence of tactile information on trunk control was investigated. First, in chapter 7, it was shown that tactile information through hand and back interacted with the contribution of other sensory modalities (vestibular and proprioceptive). In chapter 8, it was shown that the

source of tactile information does not have to be stationary and that the sway of the upper body becomes entrained to the motion of the tactile source. Finally, in chapter 9, it was shown that the interaction effect between tactile information and other sensory modalities still holds when the source of tactile information is moving in an unpredictable way. Therefore, when applying external perturbations, the tactile information provided by contact with the perturbation apparatus should be considered a significant contributor to sensory feedback. In this thesis, a continuous perturbation was used which provides tactile feedback to the subject during the full duration of the measurement. Therefore, applying transient perturbations (e.g. an impulse) might have added value in identifying the contribution of different sensory sources to low-back stabilization.

Limitations

The system identification techniques applied throughout this thesis are appropriate for linear and time-invariant systems. However, the human neuromuscular system is intrinsically non-linear and time-variant. Therefore, the applied perturbations were designed to only lead to small changes in position around a fixed working point, to minimize the contribution of non-linear behavior; and a relatively short measurement period was used, to minimize changes in neuromuscular control due to fatigue and other time-variant behavior.

A downside of the applied trunk perturbations was the necessity of a preload in frontal direction to assure that contact was maintained between the pushing rod and the subject. As a result of this preload, abdominal muscle activity was diminished substantially and the relax-task was somewhat un-intuitive, since the preload had to be counteracted at all times. Furthermore, perturbations in multiple directions might contribute to our understanding of trunk stabilization by identifying direction specific reflex activation.

In this thesis, all muscle activity was assessed by surface EMG of four superficial back and abdominal muscles. The M. Longissimus at the lumbar level was found to be most coherent with the perturbation signal and was therefore subsequently used for analysis and modeling throughout most of the chapters. Muscles that are anatomically located closer to the spine (deep muscles) may also be relevant, as impairments of those muscles have been related to LBP (Danneels et al., 2002; Hodges et al., 2003; MacDonald et al., 2009). However, these muscles can only be accurately assessed using intramuscular EMG which was not considered in this thesis.

The parametric model applied in chapters 3 and 6 describes low-back stabilization as a one-pivot inverted pendulum, which is clearly a simplified representation of reality. Preliminary work (van Drunen et al., 2012) identified different spinal bending patterns in different subjects, indicating that introducing additional pivot points might provide necessary detail to improve our ability to model and understand low-back stabilization.

Future Directions

To further our understanding of low-back stabilization, an exploration of the contribution of deeper muscles and different spinal bending strategies (see van Drunen et al., 2012) seems warranted. Furthermore, perturbing specific sensory modalities directly (as applied in the second part of this thesis) could contribute to modeling and understanding their contribution to low-back stabilization.

The neuromuscular control deviations found in LBP patients and the proposed classification in chapter 6, are a first step in improving diagnostics. While this thesis illustrates the potential of this approach, a much larger group of patients and controls needs to be measured, to be able to define clear boundaries of normal controls and sub-groups of patients. A further exploration of different sub-groups also seems warranted.

After clear sub-groups of patients have been identified, longitudinal studies could look into treatment effects in combination with neuromuscular control deficits. Patients categorized in G2 (muscle weakness) could benefit from strength training while patients in G4 (limit low-back movement) could benefit from therapy focused on muscle relaxation (e.g. massage or trigger point therapy). Furthermore, a longitudinal study could be conducted to investigate whether the identified differences in motor control are causally related to the recurrence or chronicity of LBP.

Finally, to investigate the clinical feasibility, a minimum set of requirements in terms of hardware, software and test protocol needed to identify the different sub-groups of patients needs to be determined.

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Summary

Chronic non-specific low-back pain (LBP) is a common health problem in Western society, affecting a large majority of the population. Many patients recover fairly quickly without specific treatment, but relapses are common and for a large minority, LBP develops into a chronic problem. Many risk factors have been identified, but the evidence for the causal relationship between these factors and LBP is weak. Common treatments often focus on one or several prognostic factors (neuromuscular control, pain sensitization and pain-related fear) and there is some evidence that exercise therapy targeting neuromuscular control is effective. However, a large number of patients does not respond to treatment and this limited success is often attributed to a lack of adequate diagnostics. The changes in neuromuscular control with LBP are diverse and complex with evidence of both increased and decreased excitability. These changes may cause pain and pain recurrence, due to e.g. tonic muscle activity, but may also be protective against pain and re-injury by stabilizing the spine. Gaining further insight in the neuromuscular control of the low back seems essential for a breakthrough in the current treatment methods of chronic LBP.

Low-back stabilization involves a complex biomechanical system that counteracts the downward pull of gravity on the large mass of the upper body while it balances on top of the lumbar vertebrae which, in turn, balance on the sacrum. The human spine is not structurally stable and the musculature is essential to prevent the spine from buckling. Spinal stiffness can be provided by intrinsic components (passive tissues and agonist-antagonist muscle co-contraction) and reflexive components (muscle activation initiated by feedback from sensory organs). How these components interact and contribute to low-back stabilization is still unknown.

The goal of this thesis was to advance the understanding of the neuromuscular control in low-back stabilization and to gain insight into the interaction between low-back stabilization and low-back pain. To achieve this goal, three main research questions were formulated:
1. Can the intrinsic and reflexive contributions to low-back stabilization be determined reliably?
2. How does low-back stabilization modulate between different conditions and task instructions?

3. How does low-back stabilization differ between healthy subjects and LBP patients?

Since the experimental methods applied throughout this thesis imply that the subjects is in contact with an external object (the pushing-rod applying the external perturbation), the second part of this thesis deals with the following additional research questions:

1. Does tactile information on the back interact with sensory feedback from other sources (i.e. does it lead to sensory reweighting)?
2. Does sensory reweighting occur with a moving source of tactile information?
3. Does tactile information interact with sensory feedback even when the source of tactile information is moving in an unpredictable manner?

To answer these questions, new experimental protocols had to be developed.

Developing the method

In chapter 2, a systematic review into methods used to assess trunk stabilization showed that many different methods exist but that not all measure the contributions of co-contraction and reflexes simultaneously, which may pose a threat to the validity of the results and might lead to misinterpretations. Therefore, in chapters 3 and 4, we set out to develop a method that can distinguish between intrinsic and reflexive contributions to low-back stabilization and demonstrated good test-retest reliability.

Modulation of low-back stabilization

Substantial modulation of low-back stabilization was found due to task instruction (chapter 3) and posture (chapter 5). Compared to a natural low-back stabilization task, the instruction to maximally resist the perturbation led to decreased lumbar movement. This was achieved by increased co-contraction and velocity feedback. While an extended lumbar posture did not significantly change low-back stabilization, lumbar flexion resulted in higher low-back resistance, reduced reflexive contributions and lower co-contraction levels. The flexion-relaxation phenomenon, i.e. reduced muscle activity in a maximally flexed posture due to increased passive tissue stiffness, may explain this result.

Low-back stabilization with low-back pain

Low-back stabilization was compared between healthy controls and LBP patients during trunk perturbations, while either maximally resisting the perturbation or stabilizing the low-back in a natural way (chapter 6). Compared to the control group, the patients displayed less reflexive modulation due to task instruction and higher intrinsic contributions during maximal stabilization, suggesting impaired reflexive adaptation in LBP. In line with literature, this thesis describes diverse changes in motor control with LBP, where individual patients showed either an increase or decrease in admittance, reflexes and/or modulation, indicative of heterogeneity within the LBP patient group. This suggests that sub-populations of LBP patients may show different and even opposite changes in motor control, indicating clinically relevant sub-groups.

A new categorization of LBP patients was proposed based on the maximal low-back stabilizing ability (task instruction to resist the perturbation) and the modulation towards natural low-back stabilization. Tentatively, four sub-groups of patients were defined, each with an unique pattern of motor control differences relative to healthy controls: no low-back motor control impairment (1), low-back muscle weakness (2), limiting low-back muscle forces (3) and limiting low-back movements (4).

Tactile information in low-back stabilization

In the second part of this thesis, the influence of tactile information on trunk control was investigated. First, in chapter 7, it was shown that tactile information through hand and back interacts with the contribution of other sensory modalities (vestibular and proprioceptive). In chapter 8, it was shown that the source of tactile information does not have to be stationary and that the sway of the upper body becomes entrained to the motion of the tactile source. Finally, in chapter 9, it was shown that the interaction effect between tactile information and other sensory modalities still holds when the source of tactile information is moving in an unpredictable way. Therefore, when applying external perturbations, the tactile information provided by contact with the perturbation apparatus should be considered a significant contributor to sensory feedback.

Samenvatting

Chronische aspecifieke onderrugpijn is een veel voorkomend gezondheidsprobleem in de Westerse samenleving die een groot deel van de bevolking treft. Veel patiënten herstellen redelijk snel zonder specifieke behandeling, maar een terugval komt vaak voor en bij een grote minderheid ontwikkelt de onderrugpijn zich tot een chronisch probleem. Vele risicofactoren zijn geïdentificeerd, maar de oorzakelijke relatie tussen deze factoren en onderrugpijn is zwak. Veel voorkomende behandelingen richten zich vaak op één of meerdere prognostische factoren (neuromusculaire aansturing, pijn sensitisatie en pijn-gerelateerde angst) en er zijn indicaties dat oefentherapie gericht op de neuromusculaire aansturing effectief is. Echter, een groot deel van de patiënten reageert niet op de behandeling en dit beperkte succes wordt vaak toegeschreven aan een gebrek aan adequate diagnostiek. De veranderingen in de neuromusculaire aansturing bij onderrugpijn zijn divers en complex, met bewijs voor zowel toegenomen als afgenomen spierprikkelbaarheid. Deze veranderingen kunnen bijdragen aan pijn en de terugkeer van pijn, door bijv. tonische spieractiviteit, maar kunnen ook beschermen tegen pijn en nieuwe beschadiging door het verhogen van de stabiliteit van de wervelkolom. Het verkrijgen van meer inzicht in de neuromusculaire aansturing van de onderrug lijkt essentieel voor een doorbraak in de huidige behandelingsmethoden voor onderrugpijn.

Onderrugstabilisatie betreft een complex biomechanisch systeem dat er voor zorgt dat de neerwaarts gerichte zwaartekracht, die werkt op de grote massa van het bovenlichaam, wordt tegengewerkt terwijl deze massa balanceert op de lumbale wervels, die op hun beurt weer balanceren op het sacrum. De menselijke wervelkolom is niet structureel stabiel en de musculatuur is essentieel om te voorkomen dat de wervelkolom bezwijkt. De stijfheid van de wervelkolom kan worden beïnvloed door intrinsieke componenten (passief weefsel en agonist-antagonist spier co-contractie) en reflexieve componenten (spier activatie op basis van feedback van sensorische organen). Hoe deze componenten interacteren en bijdragen aan onderrugstabilisatie is tot op heden onbekend.

Het doel van dit proefschrift was om bij te dragen aan de kennis op het gebied van de neuromusculaire aansturing tijdens het stabiliseren van de onderrug en om verder inzicht te verkrijgen in de interactie tussen onderrugstabilisatie en

onderrugpijn. Om dit doel te bereiken werden de volgende 3 hoofdonderzoeksvragen geformuleerd:

1. Kunnen de intrinsieke en reflexieve bijdragen aan onderrugstabilisatie betrouwbaar worden bepaald?
2. Hoe moduleert onderrugstabilisatie tussen verschillende condities en taakinstructies?
3. Hoe verschilt onderrugstabilisatie tussen gezonde proefpersonen en patiënten met onderrugpijn?

Aangezien de experimentele methoden die in dit proefschrift worden gebruikt impliceren dat de proefpersonen in contact staan met een extern object (de duw-kop die de externe perturbatie aanbrengt), behandelt het tweede gedeelte van dit proefschrift de volgende aanvullende onderzoeksvragen:

1. Interacteert tactiele informatie op de rug met sensorische feedback van andere bronnen (oftewel, leidt het tot sensorische herweging)?
2. Treedt er sensorische herweging op wanneer de bron van de tactiele informatie beweegt?
3. Interacteert tactiele informatie met sensorische feedback zelfs wanneer de bron van de tactiele informatie beweegt op een onvoorspelbare manier?

Om al deze vragen te beantwoorden moesten er nieuwe experimentele methoden ontwikkeld worden.

Het ontwikkelen van de methode

In hoofdstuk 2 wordt in een systematische review naar methoden voor het beoordelen van romp stabilisatie beschreven hoe er veel verschillende methoden bestaan, maar dat deze niet allemaal de bijdragen van co-contractie en reflexen tegelijk meten. Dit kan een bedreiging vormen voor de validiteit van de resultaten en kan leiden tot misinterpretatie. Om deze reden hebben we in hoofdstuk 3 en 4 een methode ontwikkeld die onderscheid kan maken tussen de intrinsieke en reflexieve componenten van onderrugstabilisatie en een goede test-hertest betrouwbaarheid gedemonstreerd.

Modulatie van onderrugstabilisatie

Substantiële modulatie van onderrugstabilisatie werd gevonden ten gevolge van taakinstructie (hoofdstuk 3) en houding (hoofdstuk 5). Vergeleken met een

natuurlijke onderrugstabilisatietaak leidde de instructie om maximaal verzet te bieden tegen de perturbatie tot verminderde lumbale beweging. Dit werd bereikt door toegenomen co-contractie en snelheidsfeedback. Een houding van de onderrug in extensie leidde niet tot significante veranderingen in onderrugstabilisatie. Daarentegen resulteerde flexie van de onderrug in hogere bewegingsweerstand in de onderrug terwijl er minder reflexieve bijdragen en lagere con-contractie niveaus werden gevonden. Het flexie-relaxatie fenomeen, oftewel een verlaagde spieractiviteit tijdens maximale onderrugflexie ten gevolge van passieve weefselstijfheid, kan dit resultaat verklaren.

Onderrugstabilisatie met onderrugpijn

Onderrugstabilisatie werd vergeleken tussen gezonde proefpersonen en patiënten met onderrugpijn tijdens rompperturbaties met de taakinstructie om maximaal verzet te bieden tegen de perturbatie of te stabiliseren op een natuurlijke manier (hoofdstuk 6). Vergeleken met de gezonde proefpersonen lieten patiënten minder reflexmodulatie zien ten gevolge van taakinstructie en hogere intrinsieke bijdragen tijdens maximale stabilisatie wat een aangedane reflex adaptatie bij onderrugpijn suggereert. In lijn met de literatuur beschrijft dit proefschrift diverse veranderingen in de motorische aansturing bij onderrugpijn waar individuele patiënten een toename of afname van admittantie, reflexen en/of modulatie laten zien wat indicatief is voor heterogeniteit binnen de patiëntengroep. Dit suggereert dat subpopulaties van patiënten met onderrugpijn verschillende en zelfs tegenstrijdige veranderingen in de motorische aansturing laten zien wat indicatief is voor klinisch relevante subgroepen.

Een nieuwe categorisatie van patiënten met onderrugpijn werd voorgesteld op basis van de maximale onderrugstabilisatie (taakinstructie om maximaal verzet te bieden tegen de perturbatie) en de modulatie ten opzichte van de natuurlijke onderrugstabilisatie. Verkennend werden er vier subgroepen van patiënten gedefinieerd elk met een uniek patroon van afwijkingen in de motorische aansturing vergeleken met gezonde proefpersonen: geen aangedane motorische onderrugaansturing (1), onderrugspier zwakte (2), beperken van spierkrachten in de onderrug (3) en beperken van beweging in de onderrug (4).

Tactiele informatie in onderrugstabilisatie

In het tweede deel van dit proefschrift werd de invloed van tactiele informatie op rompaansturing onderzocht. Als eerste, in hoofdstuk 7, werd gedemonstreerd dat tactiele informatie via de hand en de rug interacteert met de bijdragen van andere

sensorische modaliteiten (vestibulair en proprioceptief). In hoofdstuk 8 werd laten zien dat de bron van de tactiele informatie niet stationair hoeft te zijn en dat de zwaai van het bovenlichaam gekoppeld raakt aan de beweging van de tactiele bron. Tot slot werd in hoofdstuk 9 gedemonstreerd dat het interactie-effect tussen tactiele informatie en andere sensorische modaliteiten stand houd zelfs wanneer de bron van de tactiele informatie beweegt op een onvoorspelbare manier. Als er externe perturbaties worden toegepast, is het daarom belangrijk om de tactiele informatie ten gevolge van het perturbatieapparaat te beschouwen als een significante bijdrager van sensorische feedback.

List of Publications

Papers in international peer reviewed journals

Maaswinkel E, Griffioen M, Perez RSGM, van Dieën JH. Submitted. *Methods for assessment of trunk stabilization: a systematic review.* (Chapter 2)

Van Drunen P, Maaswinkel E, van der Helm FCT, van Dieën JH, Happee R (2013). *Identifying intrinsic and reflexive contributions to low-back stabilization.* Journal of Biomechanics 46: 1440-1446. (Chapter 3)

Griffioen M, Maaswinkel E, Zuurmond WWA, van Dieën JH, Perez RSGM. Submitted. *Trunk stabilization estimated using pseudorandom force perturbations: a reliability study.* (Chapter 4)

Maaswinkel E, van Drunen P, Veeger HEJ, van Dieën JH (2015). *Effects of vision and lumbar posture on trunk neuromuscular control.* Journal of Biomechanics 48: 298-303. (Chapter 5)

Maaswinkel E, Veeger HEJ, van Dieën JH (2014). *Interactions of touch feedback with muscle vibration and galvanic vestibular stimulation in the control of trunk posture.* Gait & Posture 39: 745-749. (Chapter 7)

Andreopoulou G, Maaswinkel E, Cofré Lizama LE, van Dieën JH (2015). *Effects of support surface stability on feedback control of trunk posture.* Experimental Brain Research 233(4): 1079-1087. (Chapter 8)

Maaswinkel E, Hendriksen RSA, Ouwerkerk AS, van Dieën JH. Submitted. *Tactile information from an unpredictable contact force interacts with the effect of lumbar muscle vibration in the control of upright posture.* (Chapter 9)

Conference proceedings

Van Drunen P, Maaswinkel E, Veeger HEJ, van Dieën JH, Happee R (2012). *Spinal bending patterns in sagittal plane perturbations.* The 19th Congress of the International Society of Electrophysiology and Kinesiology (ISEK), Brisbane, Australia.

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quantifying intrinsic properties and proprioceptive feedback. Neuroscience, New Orleans, USA.

Maaswinkel E, Veeger HEJ, van Dieën JH (2012). *Interactions of touch feedback with muscle vibration and galvanic vestibular stimulation in the control of trunk posture.* Neuroscience, New Orleans, USA.

Maaswinkel E, Veeger HEJ, van Dieën JH (2013). *Interactions of touch feedback with muscle vibration and galvanic vestibular stimulation in the control of trunk posture.* The 4th Dutch Conference on Bio-medical Engineering, Egmond aan Zee, The Netherlands.