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# Measuring Spinal Mobility and Sagittal and Frontal Plane Pattern in EDS Patients Compared to Healthy Individuals, Using a Spinal Mouse.

**Thesis to attain the title:**

**MSc of Science**

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## I. Abstract[1]

Background

Ehlers-Danlos syndrome (EDS) is a group of heritable disorders that effects the fascia and collagen structure in the body which is characterized by elastic skin, hypermobile joints and fragile arteries. There could be a lot of benefits for osteopaths, and other manual therapists, to know how the mobility and the posture pattern in the spine are in EDS patients, in order to apply the right treatment or refer to a medical doctor. The aim of study is to investigate if there are any differences in spinal mobility and posture patterns in EDS patients compared to healthy subjects

Methods

In this clinical control study (CCS) a spinal mouse was used as a device to measure the spine in full flexion, extension and lateral flexion, in the sagittal and frontal plane to compare the mobility and the pattern in EDS patients with healthy individuals. The statistical analysis was made with a SPSS 22.0 program. The study included 31 subjects diagnosed with EDS and 31 subjects of healthy people as a control group. A modified fingertip-to-floor test (MFTF) test and palpation were also used. Palpation was used to decide, with a 3-graded scale, if the vertebras were in lateral flexion (left +1, neutral 0, right -1) flexion (+1) or extension (-1). A

Results

The EDS group showed an increased range of movement (ROM) of the spine, measured in degrees, in all parameters (flexion, extension, right lateral flexion and left lateral flexion) compared to healthy individuals. The mean difference between the EDS group and the control group (CTR) was in flexion (-12,61), extension (6,81), right lateral flexion (11,03) and left lateral flexion (-11,58), $p>0,05$.

Conclusion

The data collected in this study show that there was a statistically significant increased ROM in the spine, $p>0,05$, in inclination of flexion, inclination of extension, right lateral flexion and left lateral flexion between EDS patients and healthy patients. The palpation showed no significant results regarding spinal pattern.



Keywords

Ehlers-Danlos syndrome, spinal mobility, measured angle of the spine.

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## V. List of abbreviations

BLT – balanced ligamentous technique

CCS – case-control study

CM-1 – chiary malformation type 1

CTR – control group

ES – effect size

FTF – finger-to-floor test

GJH – gereralized joint hypermobility

HTDC – hereditary disorder of connective tissue

HVLAT – high velocity low amplitude technique

HVT – high velocity technique

ICC – intraclass correlation coefficient

JHM – joint hypermobility

JHS – joint hypermobility syndrome

LBP – low back pain

M - mean

MDC – minimal detectable change

NSAID – non steroidal antiinflammatory drugs

RMDQ – Roland Morris disability questionnaire

ROM – range of movement

SEM – standardized errors of measurement

SLR – straight leg raising test

SRM – standardized responsive mean

# 1 Introduction[1]

EDS is a group of heritable disorders that effects the fascia and collagen structure in the body which is characterized by elastic skin, hypermobile joints and fragile arteries. EDS are divided into six subtypes and current diagnostic criterions and subtypes are seen in Villefranche Nosology, 1998 (Rand-Hendriksen et al, 2006). To diagnose EDS there is often used a Beighton scale to measure joint hypermobility in the elbow, hip, knee and finger joints but there is no measurement of the vertebral column (Beighton et al, 1998).

In a case report made on three teenaged boys diagnosed with EDS, a flattening of the lumbar spine, and normal appearance of the rest of the spine, was seen in a radiological investigation (Kozolowski et al, 1991). In Beighton and Horans study, (1969) included 100 EDS patients, 18 of them had some degree of scoliosis and three patients had a marked kyphosis at the thoraco-lumbar junction with a slight slip of the first lumbar vertebra. Rozen et al, (2006) found that hypermobility in the cervical spine could be a predisposing factor for new daily persistent headache. In a study comparing patients with benign joint hypermobility (JHM) to a control group with healthy subjects the JHM group had more low back pain (LBP), disability and limited physical motion than the control group (Kim et al, 2013).

Because a lack of knowledge of EDS, a group of patients are underdiagnosed from the medical profession (Hakim and Grahame, 2003), and they could often end up in the osteopathic clinic to seek help. There could be a lot of benefits for osteopaths, and other manual therapists, to know how the mobility and the posture pattern in the spine are in EDS patients, in order to apply the right treatment or refer to a medical doctor. The aim of this CCS is to investigate if there are any differences in spinal mobility and posture patterns in the sagittal and frontal plane, in EDS patients compared to healthy subjects. The aim is also to look if there are any similarities in EDS patients spinal mobility and posture patterns.

# 2 Background[1,2]

## 2.1 EDS (ICD-10: DQ 79.6)[2]:

EDS is a group of heritable disorders that effects the fascia and collagen structure. EDS is characterised by stretchy and soft skin, hypermobile joints and fragile arteries. They also have delayed wound healing, formation of atrophic scars and easy bruising (Malfait et al, 2010). It is caused by a genetic defect of the collagen structure, mainly the collagen type I and V, which effects the structure of ligaments and fascia (Bird, 2007) (Callewart et al, 2008).

There are mainly six EDS types classified by Villefranche Nosology, 1998:

*Classical type (Former type I and II):* This EDS type is characterised by skin hyperextensibility, wide artophic scars and joint hypermobility. General fatigue is also common.

*Hypermobility type (former type III):* This EDS type is mainly characterised by hypermobile joints but also skin hyperextensibility.

*Vascular type (former type IV):* This EDS type is characterised by thin and translucent skin, arterial, intestinal and uterine fragility or rupture, extensive bruising, characteristic facial appearance, Acrogeria, hypermobility of small joints, tendon and muscle rupture, clubfoot, arteriovenous and caratiod-cavernous sinus fistula, pneumo and hemopeumothorax and gingival recession. This type of patients also often has a history of sudden death of family members or relatives.

*Kyphoscoliosis type (former type VI):* This EDS types is characterised by general joint laxity, severe muscle hypotonia and scoliosis at birth, scleral fragility and rupture of the ocular globe, tissue fragility and skin scaring, easy bruising, arterial rupture, marfanoid habitus, microcornea and osteopenia.

*Arthrochalasia type (former type VIIA and VIIB):* This EDS type is characterised by severe general joint hypermobility and subluxations, congenital hip dislocation, skin hyperextesibility, fragile tissue and scaring, easy bruising, muscle hypotonia, kyphoscoliosis and mild osteopenia.

*Dermatosparaxis type (former type VIIC):* This EDS type is characterisedsby severe skin fragility, sagging and redundant skin, soft and doughy skin texture, easy bruising, premature rupture of fetal membranes and large hernias.

There is also some other small and rare types of EDS; type V, VIII, IX, X and XI. Some of these types is very rare and has only been described in one family.

(Beighton et al. 1998)

### 2.2 Etiology and pathogenesis of EDS[2]

EDS is caused by a genetic defect in the collagen structure, in mainly collagen I and V, and leads to an abnormality in the collagen structure (Bird, 2007) (Callewart et al, 2008) (Malfait et al, 2010) (Mao and Bristow, 2001). This abnormality in the collagen structure will affect the ligaments and fascia and make them more fragile and weakened and therefore more prone to injury and tissue trauma (Hakim and Grahame, 2003). Ligament is a tissue type that consists of 90% type I collagen and 10 % type III collagen. (Nordin and Frankel, 2001). The collagen V is not as common and is mainly distributed in skin, tendon, bone, cornea, placenta and fetal membranes (Malfait et al, 2010). According to Mallik et al, (1994) there is also a decreased joint proprioception in patients with hypermobility syndrome.

The genetic abnormality of the collagen structure effects the fibrous proteins in the extracellular matrix. The fibrous proteins get distorted and the fine balance between normal tissue tension and elasticity becomes tilted. The distorted collagen fibres result in tissue fragility and laxity as the tissue loses its tensile properties (Hakim and Grahame, 2003) (Beighton et al, 2012). According to Mao and Bristow (2001) the cause of the genes affecting the collagen is not sufficient to explain the whole disease in patients with EDS and research is now expanding beyond the collagen-modifying genes and the collagen.

In the EDS classic type there is a mutation of the *COL5A1* and *COL5A2* genes, which effects the type V collagen (Malfait et al 2010), (Mao and Bristow, 2001). Type

V collagen is not the most frequent collagen type in the human body but is widely distributed in several tissues as skin, tendon, bone, cornea, placenta and fetal membranes (Malfait et al, 2010). Type V collagen coassembles with type I collagen to form a type of fibrils. Type V collagen is believed to control fibril assembly in several tissues (Malfait et al, 2010).

In the EDS hypermobility type there is no known causative gene and this type of EDS is the most common type (Malfait et al, 2006) (Mao and Bristow, 2001). Although, the TNXB gene has been associated with EDS hypermobility typJHe (Zweers et al, 2003), (Zweers et al, 2005), (Mao and Bristow, 2001). This type of EDS is also believed by some doctors to be the same as the joint hypermobility syndrome, (JHS) and is being discussed if the two diagnoses are one and the same, as there in many similarities but the exact genetic basis has not been established yet (Hakim and Grahame 2003).

### 2.3 Symptoms and clinical features of EDS classic and hypermobile type[2]

In diagnosis like EDS and hypermobility syndrome there is, except joint instability and pain, also other symptoms and increased risk of herniation, prolapse of intervertebral discs, stretchy skin, scars, varicose veins, uterine / rectal prolapse, subluxations and dysplasi of joints, osteoarthritis, fibromyalgia, muscle and ligament tear and inflammation (Keer and Grahame, 2003).

In EDS classical type there is except hypermobility of joints, especially cutaneous hyperextensibility. Wounds take longer time to heal and wide “cigarette paper”-like scars are also a characteristic feature of this EDS type (Malfait et al, 2010). They can also suffer from molluscoid pseudotumors, subcutaneous spheroids and piezogenic adipose. They also often suffer from repetitive hernias such as inguinal, hiatal, umbilical and incisional hernias. The musculoskeletal manifestations are often joint hypermobility and joint subluxations and dislocations. The most effected joints are the shoulders, patella, digits, hip, radius and clavicles (Malfait et al, 2010). There are also other features as clubfoot, pes planus, tempomandibuar joint dysfunction

and osteoarthritis related to the joint hypermobility. Primary muscular hypotonia, delayed motor development and mild motor disturbance may occur. Fatigue and muscle cramp is quite common. In several types of EDS, as the kyphposcolios type (type VI), scoliosis can be common but as there is no or little measuring of the spinal mobility. One study from Stanitski et al, (2000) as many as 51,7% of the examined EDS patients (type, I,II and III) showed radiographic signs of scoliosis. In the same study as many as 83% of the subjects had back and neck pain.

There is also a tendency of prolonged bleeding because of the poor support of the cutaneous blood vessels, which easily ruptures (Malfait et al, 2010). Easy bruising is also common. Aortic root dilation may occur as also mitral or tricuspidal valve prolapse but is very uncommon. Otherwise aneurysms, rupture of large arteries and arteriovenous fistulae is more associated with the vascular type of EDS (Malfait et al, 2010). The prevalence of EDS classical type is estimated to be 1:20 000 (Malfait et al, 2010).

In the hypermobility type of EDS, hypermobility of the joints is the most common characteristic. The skin is often soft or velvet and can be hyperextensible. Easy bruising can also occur. Subluxations and dislocations are also common in this EDS-type. Chronic pain is a very common complaint, which can be very physically and psychologically disturbing. Degenerative joint disease is also a common feature related to the joint hyper mobility (Malfait et al, 2010).

The most differentiating symptom of these two EDS-types is the scarformation in the classic type.

During pregnancy and delivery there can be an increased risk of complications in patients with EDS (Shirley et al, 2012), (Malfait et al, 2010). Prematurity is more frequent in cases where the fetus is affected because of premature rupture of the membranes (Malfait et al, 2010). Breech presentation is also more frequent as well as dislocations of hips and shoulders of the baby during delivery. For the pregnant

women there is an increased risk of complications with episiotomy incisions, tearing of the perineal skin and uterine prolapse (Malfait et al, 2010).

### 2.4 Diagnostic criteria[2]

The diagnostic criteria for EDS are the presence of one or more major criteria of the Brighton criteria (see below) and one or more minor criteria contribute to the diagnosis. In the absence of major criteria the minor criteria is not sufficient for a diagnosis.

The examination should consist of a history and especially family history of joint hypermobility and cardiovascular disorders and symptoms of joint dislocations, subluxations, easy bruising, easy bleeding and poor wound healing (Shirley et al, 2012). The physical examination should include joint mobility, scoliosis, pes planus and examination of the skin (softness, laxity, scars and striae) (Shirley et al, 2012). Blue sclera may also be present. The Beighton scale can be used to examine the joint hypermobility. Cardiovascular examination should be performed to evaluate vessel or valve abnormalities. A genetic consultation can also be performed, especially in children with recurrent dislocations and a positive family history, but the EDS diagnosis is mainly a clinical diagnosis (Shirley et al, 2012).

EDS and hypermobility is a group of patients that is considered to be underdiagnosed from the medical profession (Hakim and Grahame, 2003), (Grahame and Hakim, 2008), (Shirley et al, 2012), as there is often a lack of knowledge of both hypermobility and EDS in the medical profession.

The Brighton criteria are often used to diagnose Hypermobility syndrome (Beighton et al, 2012). It consists of 2 major criteria and 4 minor criteria. The major criterion has a high diagnostic specific because it is very uncommon in the general population. One or more major criterion is needed for a clinical diagnosis or is highly indicative (Beighton et al, 1998). A minor criterion has a less diagnostic specificy and one or more criteria contribute to the diagnosis of a specific EDS-type (Beighton et al, 1998). Only the minor criteria are not sufficient to diagnose EDS.

The Brighton criteria consist of:

Major criteria:

- A Beighton score of 4/9 or greater.
- Arthralgia for longer than 3 months in 4 or more joints.

Minor criteria:

- A beighton c´score of 1,2 or 3/9. If age 50+ 0,1 or 3 is needed.
- Arthralgia >3 months in one to 3 joints or back pain in >3 months, spondylosis, spondylolysis or spondylolisthesis.
- Dislocation or subluxation in more than one joint, or in one joint in more than one occasion.
- Soft tissue rheumatism >3 lesions (epicondylitis, tenosynovitis, bursitis)
- Marfanoind habitus
- Abnormal skin (Striae, hyperextensibility, thin skin, papyraceous scaring).
- Eye signs (dropping eyelids or myopia or antimongoloid slant).
- Varicose veins or hernia or uterine, rectal prolapse.

(Beighton et al. 2012)

To diagnose the type of EDS there are major and minor criteria for each type:

In the classic type of EDS the major criteria is:

- Skin hyperextensibility
- Widened atrophic scars (tissue fragility)
- Joint hypermobility

Minor criteria:

- Smooth velvety skin
- Molluscoid tumors
- Subcutaneous spheroids
- Complications of joint hypermobility (sprains, dislocations, pesplanus)
- Muscle hypotonia
- Easy bruising

- Tissue extensibility (hiatal hernia, anal prolaps, cervical insufficiency)
- Surgical complaints (postoperative hernias)
- Positive family history

The major criteria in EDS hypermobility type is:

- Hyperextensibility of the skin or smooth and velvety skin
- Generalized joint hypermobility

Minor criteria:

- Recurrent joint dislocations
- Chronic joint or limb pain
- Positive family history

The Beighton scale is often used as a diagnostic tool to measure the joint hypermobility in patients with EDS or hypermobility syndrome (Keer and Grahame, 2003). The Beighton scale is included in the Brighton criteria and is a 0-9 graded scale. It measures the joints of the extremities (elbow, hip, knee and finger joints, see table 1) but there is no measure of the vertebral column. The joints are graded in both left and right side.

Table 1: The Beighton scale

| Findings | Score |
|---|---|
| Passively dorsiflex the fifth metacarpophalangeal joint > 90° | 2 |
| Oppose the thumb to the volar aspect of the ipsilateral forearm | 2 |
| Hyperextend the elbow to > 10° | 2 |
| Hyperextend the knee to > 10° | 2 |
| Place hand flat on the floor without bending the knees. | 1 |

The Contompasis score is a modification of the Beighton scale, which is more descriptive of the degree of hypermobility. This score adds one more test, eversion of the foot and allows a degree between 2 and 6, depending on the degree of mobility, for each Beigthon score and can give a total possible score between 2 and 54 points (Keer and Graham, 2003) This test is more descriptive but is more time consuming.

Another 10-graded test is the 10-point Hospital del Mar (Barcelona) criteria. This scale tests a wider range of joints and includes mobility test of the shoulder, hip, patella, ankle foot and toes (Keer and Grahame, 2003). This test can be useful to investigate other joints than the Beighton score and it also distinguish between men and women. A positive score for hypermobility for men is 4 or greater and for women 5 or greater (Bulbena et al. 2014).

## 2.5 Conventional treatment[2]

There is no cure to EDS and symptoms are individually managed. The treatment offered except Non-Steroidal Anti-inflammatory Drugs (NSAID) and painkillers is physiotherapy focusing on joint and muscle strength, prophylactic braces and surgery (Shirley et al, 2012).

The aim for treatment is to restore joint stability to reduce the stress and avoid further damage or dislocation of the joints. In some cases pain relief or pain management is the only treatment (Keer and Grahame, 2003) (Shirley et al, 2012). If painful or damage joints may be untreated patients may further stress or injure the joint and pain may also become chronic as their muscles easily get fatigue (Beigthon et al. 2012). It is also of great importance to educate the patient about their disease so the patient can avoid any harmful body positions and avoid any improper sport acidity etc (Beigthon et al. 2012) (Shirley et al, 2012) (Keer and Grahame, 2003) .

Regarding physical activity, low-impact and pool activities are recommended and to avoid high-impact sport that could increase joint stress and damage (Shirley et al, 2012). Non-operative treatment should aim to enhance joint stability and strength and also to enhance joint proprioception and neuromuscular coordination (Shirley et al. 2012). Multidisciplinary treatment is required and mental health support of these patients is needed (Keer and Grahame, 2003).

In a study from Rombaut et al, (2011) the effectiveness of medication, surgery and physiotherapy were studied in a group of 79 patients diagnosed with EDS hypermobility type. In this study 79 patients (92,4%) used a variety of analgesics drugs (paracetamol, NSAID and opiates). Fifty-six patients (70,9%) underwent surgery in lower or upper extremities and 41 patients (51,9%) were enrolled in a physical therapy programme. Of the 56 patients that underwent surgery only 33,9% reported a positive effect of the surgical intervention and of the 41 patients that received physiotherapy 63,4% reported a positive effect. These results of the study suggest that there is little effective treatment for patients with EDS hypermobility type and that

further studies for effective and evidence-based treatment for this patient group is needed.

### 2.6 Alternative treatment[1]

According to Simpson, (2006), osteopathic manipulative treatment along with proper exercise-therapy may be beneficial for patients with benign joint hypermobility to reduce pain and restore joint proprioception.

Colloca and Polkinghorn, (2003) wrote a report of two cases where the subjects had EDS and got chiropractic treatment. Both patients had neck and back pain, extremity pain and headache. They had both abnormal spinal curvatures like kyphosis and scoliosis. One patient had postsurgical thoracolumbar spinal fusion for scoliosis and osteoporosis. Spinal adjustments were delivered to spinal segments and extremities utilizing an Activator II Adjusting Instrument and Activator Methods Chiropractic Technique. The patients were also given postural advice and exercises and stabilization exercises. Both patients reduced anti-inflammatory and pain medication usage when they had chiropractic treatment and a significant improvement in pain and disability measured by a visual analogue scale. Objective improvements in physical examination and spinal alignment were observed after chiropractic treatment.

It seems that repetitive muscle vibration can have an improvement in balance and proprioception in JHS and EDS hypermobility type patients (Celletti et al, 2011). Vibratory stimulation was applied on a 15 year-old girls quadriceps in her both legs for 30 minutes, and for every 10 minutes the vibration was interrupted so she could rest for one minute. The treatment was performed three days in a row. Rombergs test showed marked instability with an evident to fall in the pretreatment session but after treatment there was increased stability, no data was shown. The Berg Balance Scale showed marked improvement of proprioception with an improvement of 26% (Celletti et al, 2011)

## 2.7 Measuring device and techniques[1]

*Spinal Mouse*

A Spinal Mouse® is a hand-held computer-aided electromechanical device. It measures the spinal curvature and mobility from C7 to S3. It has two rolling wheels that follow the spinous processes of the spine. An operator needs to palpate and mark the spinous processes from C7 till S3 and data is sampled every 1.3mm as the device is rolled along the spine. The sampled data is handled by a computer-software (Ripani et al. 2008). The spinal mouse is a safe and non-invasive measuring device for the patient.

*FTF test*

FTF is a test for measuring flexion of the trunk. The procedure of the test is that the patient stands in an erect position with the feet together. The patient bends forward, and with straight legs and extended arms, trying to reach the floor with the fingertips. The distance between the middle finger and the floor is measured in centimeters using a tape measure (Jam, 2015). A MFTF-test could be favorably to use when the subjects expects to reach the floor in a FTF test, like in EDS patients. The procedure of a MFTF test differs from a FTF test in that the subject is standing on a stool when bending forward (Gauvin et al, 1990).

*Beighton score[2]*

Beighton score is a 0-9 graded scale and it measures the joints in the extremities, (elbow, hip, knee and finger joints, see table 1) in bith left and right side. The patient is passively dorsiflexing the fifth metacarpophalangeal joint (<90°, 2 points), opposing the thumb to the volar aspect of the ipsilateral forearm (2 points), hyperextending the elbow (<10°, 2 points), hyperextending the knee (<10°, 2 points) and placing a flat hand to the floor without bending the knees (1point). A total grade < 4 points is considering a positive result (general hypermobility). (Beighton and Horan, 1969)

*Palpation*

Motion palpation is of great importance, for manual therapists, in the diagnosis of muscular and articular derangements (Wiles, 1980). Motion palpation is used by schools of osteopathy, chiropractic and occasional medicine. It is defined as palpation of the human spine in the finding of articular mechanical, discal or muscular changes (Alley, 1983). Different techniques are used to palpate the articulations in the human spine, the chiropractic profession has developed original methods to assess the functional mobility of the articulations, in particular Gillet and Liekens method which are often used (Wiles, 1980). British osteopaths advocates the pads over two vertebraes and dispose for two boney points to be covered by one finger. The separation is thereby easily felt (Alley, 1983).

The direction in which a vertebra moves is named by the direction in which the vertebral body moves (Parson, 2006). In the present study the vertebraes in the spine are palpated to decide if they are in lateralflexion, flexion or extension. Palpation is to get insight of the spinal pattern in the subjects.

In a systematic review, about palpation, made by Seffinger et al, (2014) they concluded that pain provocation tests are the most reliable test and regional ROM tests are more reliable than segmental ROM tests. Further conclusion is that intraexaminer reliably is better than interexaminer reliability.

## 2.8 Link to osteopathy[1]

EDS patients come to the osteopathic clinic for seeking help for their problems, especially with joint pain, and it seems that manual treatment methods could be beneficial for these patients. (Michael and Simpson, 2006).

The aim of this thesis is to investigate if there are any differences in spinal mobility and posture patterns in the sagittal and frontal plane, in EDS patients compared to healthy subjects. The aim is also to look if there are any similarities in EDS patients spinal mobility and posture patterns. This study might show if there are any specific segment which is more prone to hypermobility. It could be important for

osteopaths to know about the mobility of the spine in EDS patients to choose proper techniques when treating those patients. For example, not use a high velocity technique (HVT) in a hypermobile spinal segment, Aspinall (1990), because of the risk to stress the segment which could lead to both neurological damages and injuries in the connective tissue.

If it is shown that subjects diagnosed with EDS have a different pattern in spine mobility and posture, and it shows that those subjects have the similar pattern, it could be helpful when diagnosing EDS. In an article by Beigthon and Horan (1969) they found some degree of scoliosis in 33 of 100 patients with EDS, examined with x-ray. In 3 of these patients they also found a kyphosis with an posterior slip of the L1 vertebra and anterior wedging at several vertebras in the spine. In the clinic the osteopaths use their hands to palpate when examining the patient therefore in the present study palpation is used as a tool to look at the spinal pattern both in the group where the subjects are diagnosed with EDS and in the control group.

EDS is an underdiagnosed condition in the medical profession because of lack of knowledge (Hakim and Grahame, 2003). With this study the knowledge of EDS and the spinal mobility could be raised which is of value not only for osteopaths but also for the person who seek help. The patient will be met by a knowledgeable clinician which is safe and gives security.

# 3 Hypotheses[1,2]

Nullhypothesis($H_0$): EDS patients have the same angle of the spine in full flexion, extension and lateral flexion than normal healthy individuals.

Alternative Hypothesis($H_A$): EDS patients have a significantly increased angle, $p>0,05$, of the spine in full flexion, extension and lateral flexion compared to normal healthy individuals.

Additional questions:
Is there a correlation between the findings of the MFTF-test and the flexion inclination measured by the Spinal mouse?
Are there any differences between the EDS patients and healthy individuals?
Is there a correlation between the findings of the palpation of the spine and the findings of the Spinal mouse and is there a difference between EDS patients and healthy individuals regarding the palpation findings?
Are there any differences in the spinal pattern in probands with EDS and healthy people, using palpation and spinal mouse as tools?

# 4 Methodology[1,2]

## 4.1 Type of study[2]

The present study is a CCS.

## 4.2 Subjects[2]

### 4.2.1 Inclusion and exclusion criteria

Inclusion criteria EDS group:

- Subjects with EDS diagnose, classical type or hypermobility type.
- Age of 18-65 years.

Exclusion criteria EDS group:

- Pregnant women.
- Subjects who have had a spinal surgery.

Inclusion criteria control group:

- Age 18-65 years.

Exclusion criteria control group:

- Subjects with EDS or JHM diagnose.
- Subjects with a Beighton score of 4 or greater.
- Pregnant women.
- Subjects who have had a spinal surgery.

### 4.2.2 Subjects acquisition[2]

Subjects for both groups to this study were enrolled thru ads on social media on the Internet. The Sweden's national Ehlers-Danlos Syndrome association also helped to enrol subjects for the EDS-group**.**

### 4.2.3 Number of subjects[2]

The total number of enrolled subject for this study are 67 subjects (7 men and 60 females). Of these 67 subjects 4 were excluded from the control-group according to the inclusion and exclusion criteria. In the EDS-group 1 subject were unable to participate due to severe low-back pain and were unable to perform the flexion, extension and lateral flexion motions preformed during the Spinal mouse measurement procedure and the Finger-to-floor test procedure. Of these 62 remaining subjects, 31 subjects participated in each group and each group consisted of 3 men and 28 females.

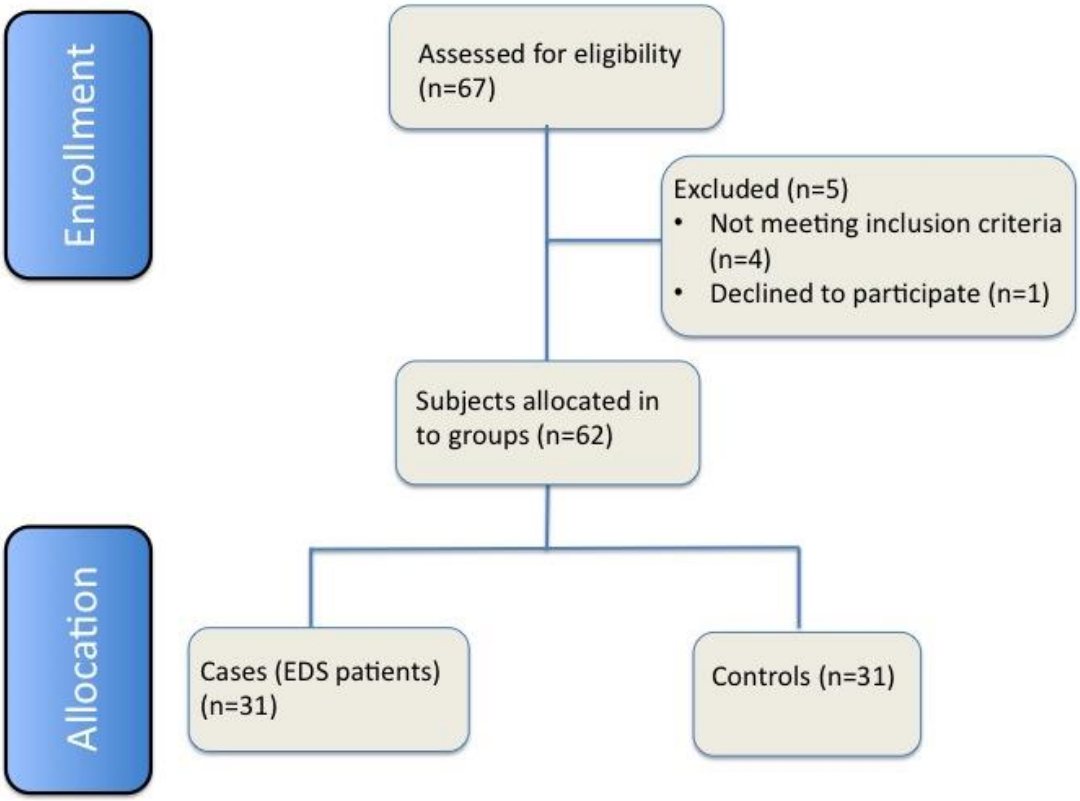



Figure 1. Flow chart for allocation into two groups.

## 4.3 Target parameters[2]

### 4.3.1 Primary target parameter

The Primary target parameter is the ROM in the thoracic and lumbar spine in flexion, extension and lateral flexion, measured by a Spinal Mouse.

### 4.3.2 Secondary target parameter

The secondary target parameter is a MFTF test measuring the distance from the fingertip to the floor in cm.

## 4.4 Measuring instruments[1]

### 4.4.1 Spinal Mouse[1]

A Spinal Mouse® is a hand-held computer-aided electromechanical device. It measures the spinal curvature and mobility from C7 to S3. It has two rolling wheels that follow the spinous processes of the spine. An operator needs to palpate and mark the spinous processes from C7 till S3 and data is sampled every 1.3mm as the device is rolled along the spine. The sampled data is handled by a computer-software (Ripani et al. 2008). The spinal mouse is a safe and non-invasive measuring device for the patient.

### 4.4.2 Fingertip-to-floor test (FTF)[1]

FTF is a test for measuring flexion of the trunk. The procedure of the test is that the patient stands in an erect position with the feet together. The patient bends forward, and with straight legs and extended arms, trying to reach the floor with the fingertips. The distance between the middle finger and the floor is measured in centimeters using a tape measure (Jam, 2015). A MFTF test, which is used in this study, is the same procedure but the subjects stand on a stool when bending forward (Gauvin et al, 1990).

### 4.4.3 Beighton Score[2]

Beighton score is a 0-9 graded scale and it measures the joints in the extremities, (elbow, hip, knee and finger joints, see table 1) in both left and right side. The patient

is passively dorsiflexing the fifth metacarpophalangeal joint (<90°, 2 points), opposing the thumb to the volar aspect of the ipsilateral forearm (2 points), hyperextending the elbow (<10°, 2 points), hyperextending the knee (<10°, 2 points) and placing a flat hand to the floor without bending the knees (1point). A total grade < 4 points is considering a positive result (general hypermobility). (Beighton and Horan, 1969)

### 4.4.4 Palpation[1]

Palpation of the vertebras decided if the vertebra is in flexion, neutral or extension or lateralflexion: left, neutral or right. A 3-graded scale was used: -1 = extension, 0= neutral and +1 = flexion in the sagittal plane and in the frontal plane -1= left lateral flexion, 0 = neutral and +1 = right lateral flexion.

## 4.5 Interventions[2]

All subjects in the control-group were first tested with the Beighton scale and excluded from the study if they reached a score of < 4 points. All subjects in both groups were then measured with the MFTF test, standing on a 20cm high wooden box. After the MFTF test a palpation of the spine was made for all subjects in a standing upright position and mobility tested for flexion, extension, left and right lateral flexion. A 3-graded scale was used to present the findings of the palpation where -1 = extension, 0= neutral and +1 = flexion in the sagittal plane and in the frontal plane -1= left lateral flexion, 0 = neutral and +1 = right lateral flexion.

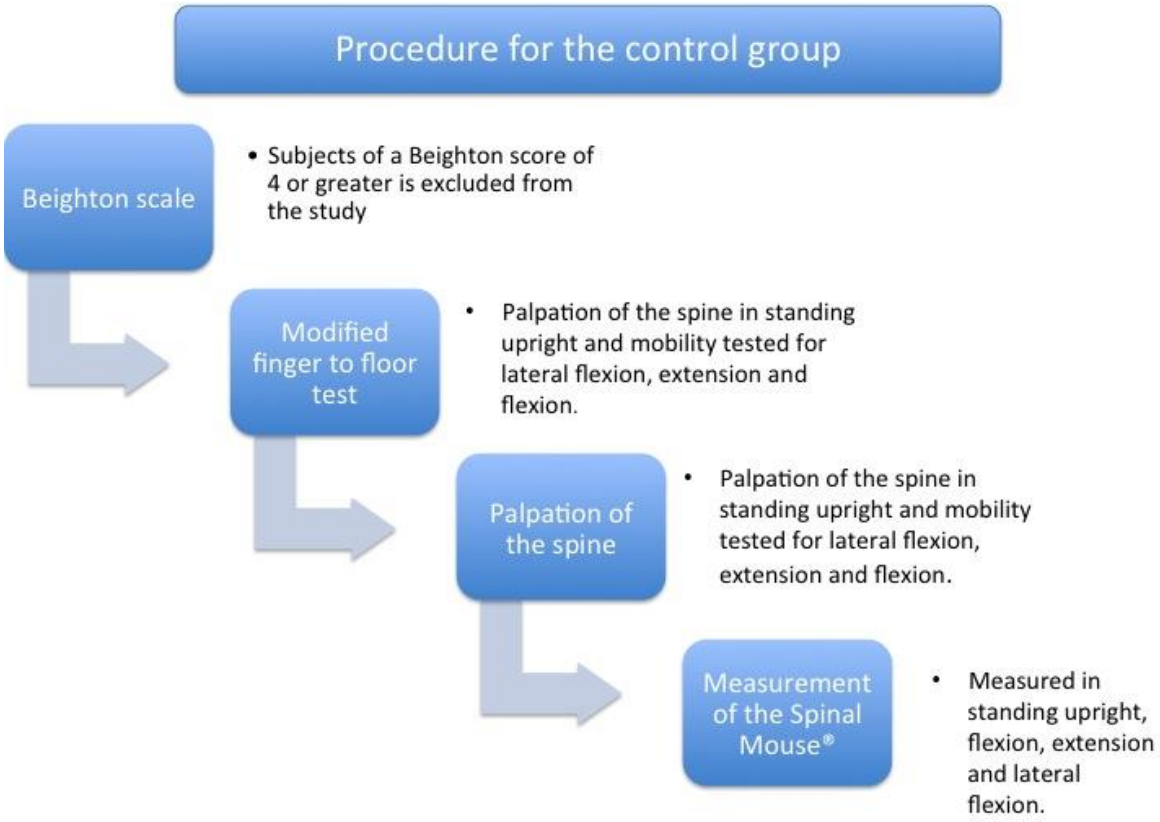



Figure 2. Procedure for the control group.

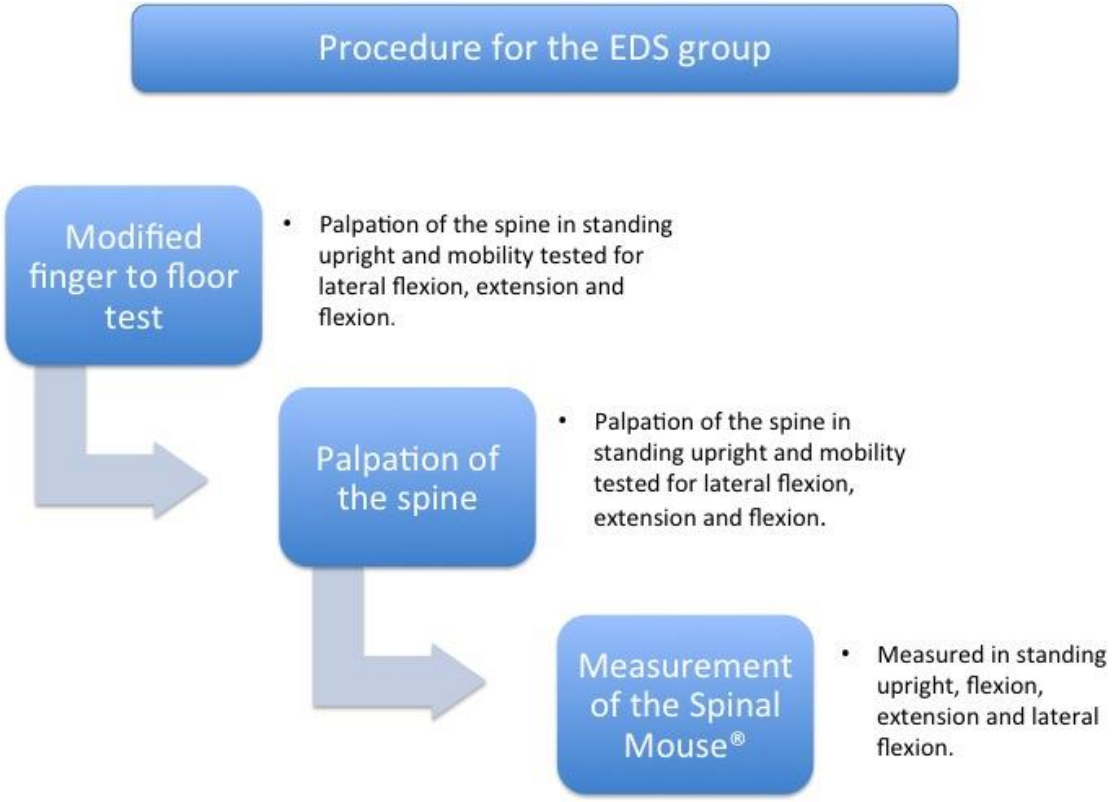



Figure 3. Procedure for the subjects diagnosed with EDS.

Last the measurement of the spinal mouse was done where the subjects were measured in 6 different positions:

- Standing upright position looking straight ahead (Figure 4).
- In a flexed position with fingers towards the floor and knees straight (Figure 5).
- In an extended position with head and eyes looking straight forward and arms crossed over the chest (Figure 6).
- In a lateral flexed position to both right and left.


Figure 4. Measuring with a spinal mouse in standing position

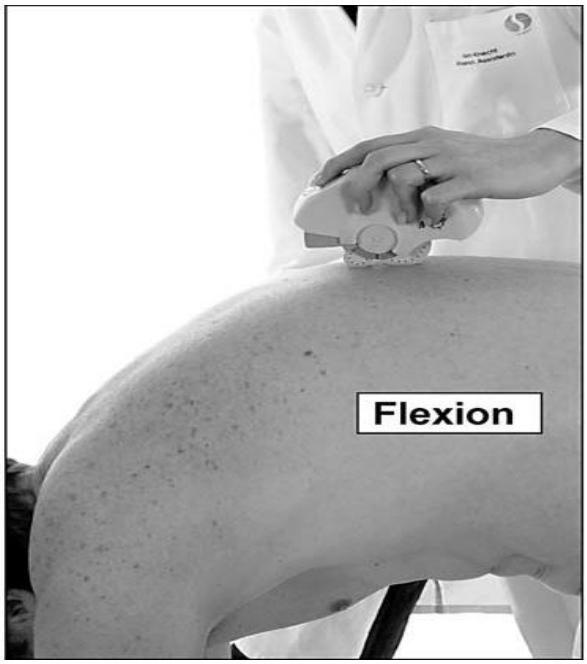



Figure 5. Measuring with a spinal mouse in flexion

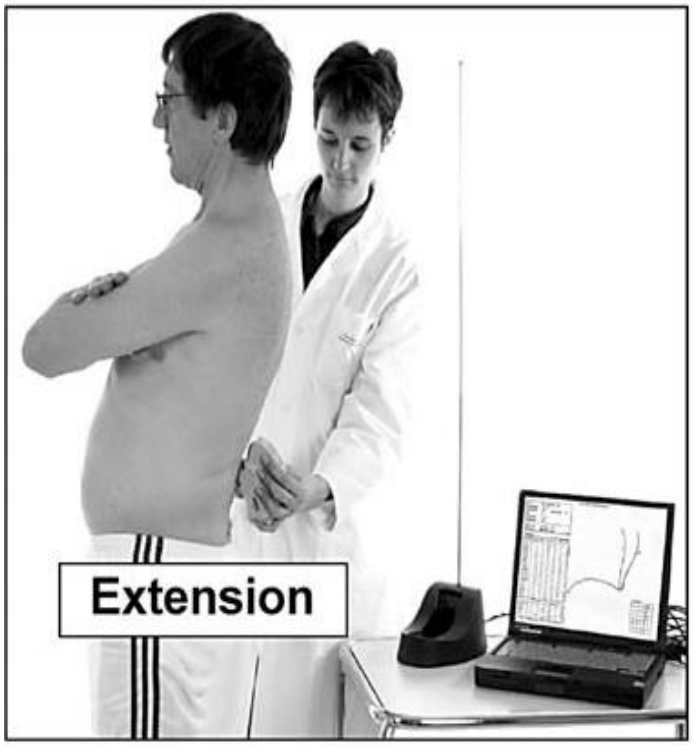



Figure 6. Measuring with a spinal mouse in extension.

### 4.6 Statistics[1,2]

The statistical analysis was made with SPSS 22.0. Normal distribution was checked with a Kolmogorov-Smirnov test. Differences between groups were calculated with a t-test or a Mann-Whitney test. For correlation Pearson correlation coefficient is calculated. The statistical analysis was calculated by medistat GmbH, Kiel.

# 5 Results[1,2]

## 5.1 Subjects characteristics[2]

A total of 62 subjects participated in the study, 56 (90.3%) females and 6 (9.7%) males. There were 31 subjects (28 females and 3 males) participating in each group (EDS and CTR).

Table 2. Patient charcteristics.

| | Num-ber | Age at date of assesment (years) | | | | |
|---|---|---|---|---|---|---|
| | | Min | Max | Mean | Std deviation | Median |
| EDS_group | | | | | | |
| Female | 28 | 19 | 65 | 38,89 | 11,229 | 37,50 |
| Male | 3 | 30 | 52 | 44,00 | 12,166 | 50,00 |
| Total | 31 | 19 | 65 | 39,39 | 11,212 | 38,00 |
| Control group | | | | | | |
| Female | 28 | 20 | 62 | 40,14 | 12,355 | 40,00 |
| Male | 3 | 34 | 46 | 39,00 | 6,245 | 37,00 |
| Total | 31 | 20 | 62 | 40,03 | 11,836 | 39,00 |

The age in the EDS group varied from 19-65 years (mean 39.39, SD= 11.21) and 20-62 (mean 40.03, SD=11.84) in the CTR- group, and no significant difference was found regarding the age between the two groups, p=0.826. (Figure 7)

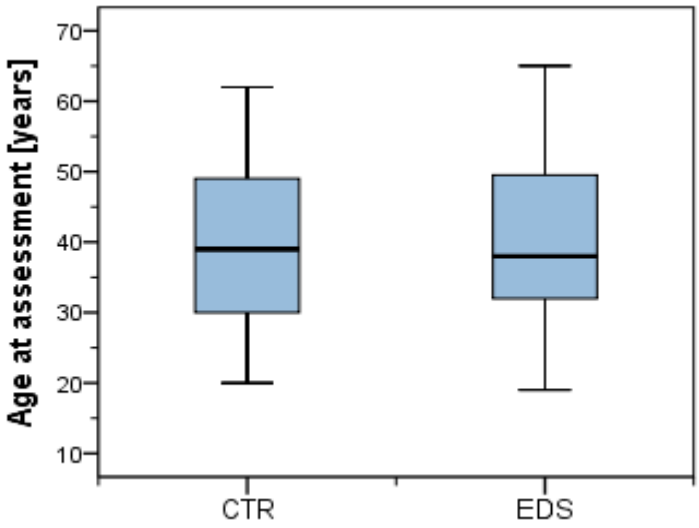



Figure 7. Age of participants in control group and subjects diagnosed with EDS.

*Result of the hypothesis*[1,2]

The Kolmogorov-Smirnov test, with a significance of p>0,05, was used for normal distribution, which showed no significant deviations so parametric methods could be used for further statistics.

A t-test was performed to compare the subjects diagnosed with EDS and a control group of healthy individuals to see if there was a significant difference in the mobility of the spine. The collected data showed a significantly increased inclination in the spine in EDS diagnosed subjects opposed to the CTR group, in flexion inclination, extension inclination, and right lateral flexion and left lateral flexion.

In flexion inclination the EDS-group showed higher inclination, Mean (M)=104,29°, SD=16,58) than the CTR-group (M=91,68°, SD=18,01) t(60)= -2.87, p=0.000.

In extension the EDS-group showed higher inclination (M-30,58, SD=14.20) than the CTR-group (M=-23.77°, SD=7.26), t(44.67)=2.38, p=0.022.

In the right lateral flexion the EDS-group showed a higher inclination (M=-25.29°, SD=10.42) than the CTR-group (M=-14.26°, SD=8.04) t (60)= 4.67, p=0.000.

In the left lateral flexion the EDS-group showed a higher inclination (M=26.39°, SD=9.57) than the CTR-group (M=14.81°, SD=5.51) t (47.91)= -5.84, p=0.000.

Table 3. Descriptive statistics of the parameters: left and right lateral flexion inclination, flexion and extension inclination.

| | | | | | | | Percentiles | | |
|---|---|---|---|---|---|---|---|---|---|
| Group | | N | Mean | Std. Deviation | Minimum | Maximum | 25th | 50th (Median) | 75th |
| CTR | Left lateral flexion Inclination | 31 | 14,806 | 5,5101 | 5,0 | 26,0 | 10,000 | 14,000 | 19,000 |
| | Right lateral flexion Inclination | 31 | -14,258 | 8,0414 | -40,0 | -3,0 | -19,000 | -15,000 | -8,000 |
| | Flexion inclination | 31 | 91,677 | 18,0137 | 59,0 | 132,0 | 75,000 | 91,000 | 104,000 |
| | Extension inclination | 31 | -23,774 | 7,2558 | -38,0 | -13,0 | -30,000 | -22,000 | -18,000 |
| EDS | Left lateral flexion Inclination | 31 | 26,387 | 9,5731 | 9,0 | 47,0 | 21,000 | 27,000 | 33,000 |
| | Right lateral flexion Inclination | 31 | -25,290 | 10,4186 | -47,0 | -7,0 | -31,000 | -25,000 | -20,000 |
| | Flexion inclination | 31 | 104,290 | 16,5795 | 62,0 | 129,0 | 92,000 | 106,000 | 117,000 |
| | Extension inclination | 31 | -30,581 | 14,1957 | -63,0 | -3,0 | -39,000 | -32,000 | -18,000 |

*Correlation with age*[2]

For analyzing the correlation with age in flexion, extension, right lateral flexion and left lateral flexion, Pearson correlation coefficient was used. Significant correlation was found in extension inclination in the EDS group (R=0.529, p=0.002) analyzed with Pearson correlation coefficient. No correlation with age was found for the CTR group. (See fig 8)

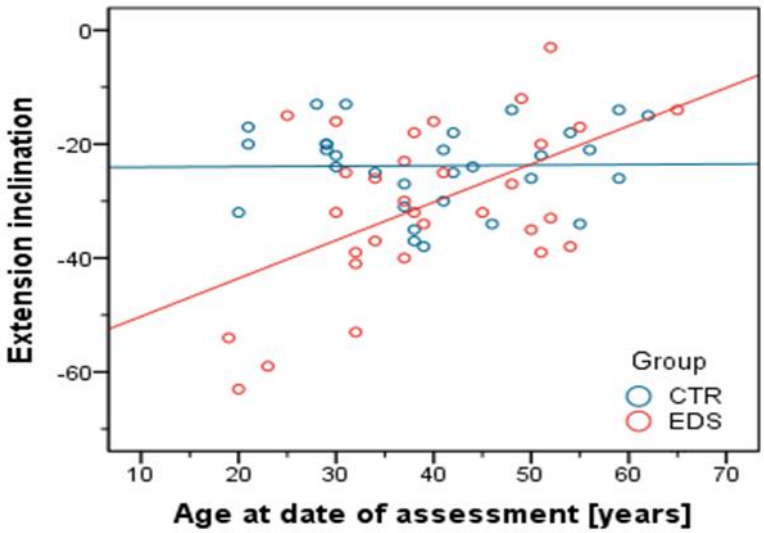



Figure 8. Extension inclination and age correlation in both groups

*Correlation between the EDS-group and the control group for the different age groups*[2]

For the comparison between the two groups (EDS and CTR) in the different age groups (18-35, 36-55 and 56-65) a Kolmogorov-Smirnov test showed no significant deviations from normal distribution, therefore a parametric t-test could be used for analyzing the statistics. However, the age group 56-65 could not be calculated because of too few subjects (EDS n=1, CTR n=4).

Between the other two age groups a significant difference was found (p=<0.05) in extension inclination, left lateral flexion and right lateral flexion in the age group 18-35 and in left and right lateral flexion in the age group 36-55.

In the age group 18-35, the EDS-group (n=12) showed an extension inclination of -38.33° (SD=16.29) and the 18-35 CTR (n=11) showed an extension inclination of -20.64° (SD 5,41), (p=0.003).

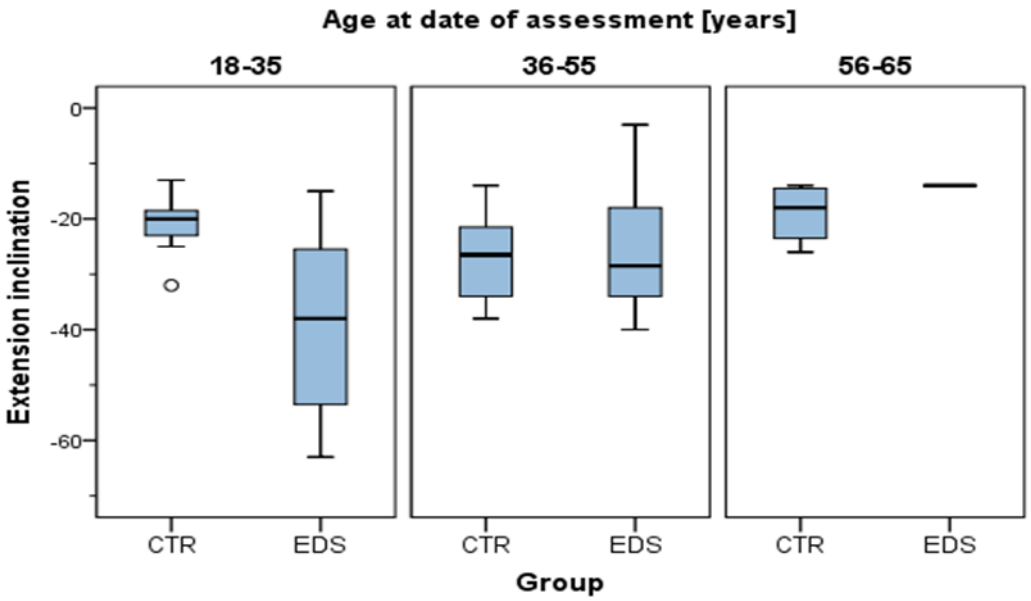



Figure 9. Correlation of the extension inclination between probands in EDS and control group, in different age groups.

In the left lateral flexion the EDS-group (18-35) showed an inclination of 28.82° (SD 5.62) compared to CTR group with 15.73° (SD=6.28), (p=0.000).

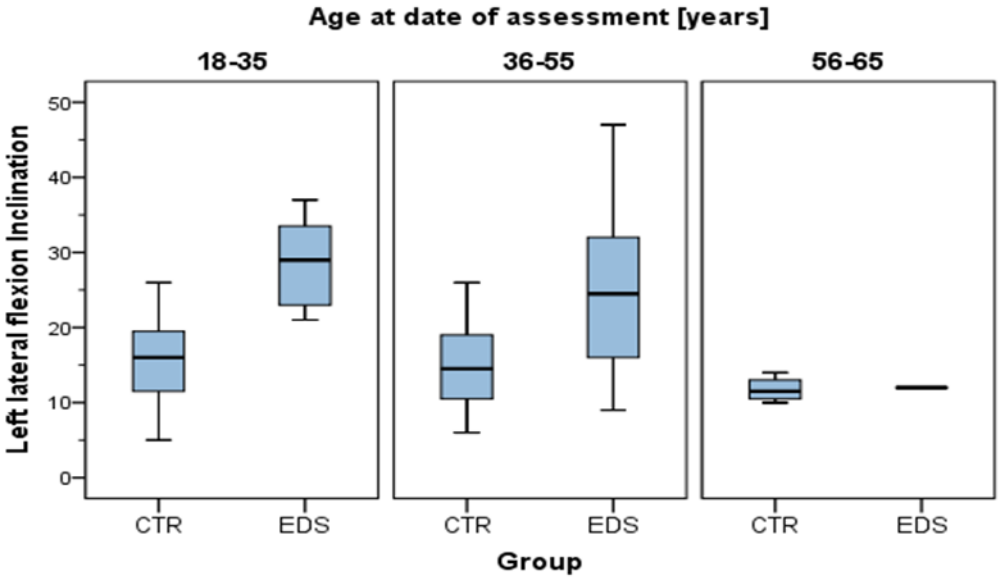



Figure 10. Left lateral inclination correlation between probands in EDS and control groups, in different age groups.

In the right lateral flexion of the age group 18-35 the EDS-group showed higher inclination of -27.58° (SD=6.30) compared to the CTR which showed an inclination of -14.18°, (SD=7.21), (p=0.000).

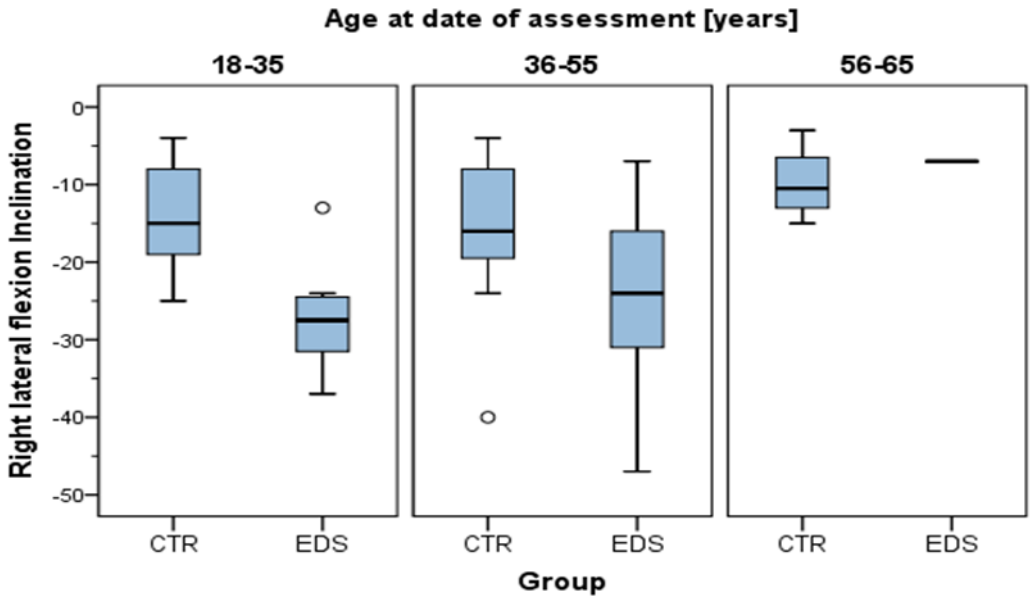



Figure 11. Right lateral inclination correlation between probands in EDS and control groups, in different age groups.

In the age group 36-55 the EDS-group (n=18) showed higher right lateral inclination of -24.78° (SD=11.92) than the CTR (n=16) which showed -15.44° (SD=9.10), (p=0.016). In left lateral flexion the EDS-group showed higher inclination of 25.56° (SD=11.14) than the CTR which showed 14.94° (SD=5.54), (p=0.001). No significant difference was showed in the age group 36-55 between the EDS-group and CTR in flexion and extension inclination (p=0,155), (p=0,801).

No significant difference was shown in the age group 18-35 between the EDS-group and CTR in flexion inclination (p=0,052).

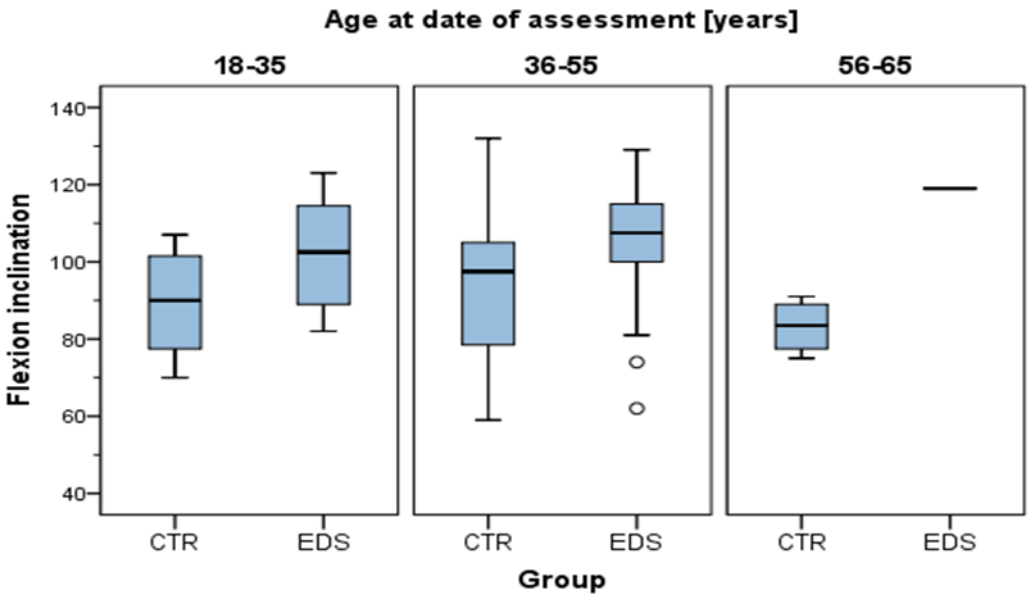



Figure 12. Flexion inclination correlation between probands in EDS and control groups, in different age groups.

*Differences in inclination from upright to flexion, extension and lateral flexion of the spine from C7-S3, thoracic spine, lumbar spine and sacrum and hip joint between subjects diagnosed with EDS and the control group*[2]

In the differences between the EDS and control group in the inclination from:

- Upright to left inclination from C7-S3
- Upright to right inclination from C7-S3
- Upright to flexion inclination from C7-S3
- Upright to extension inclination from C7-S3

- Upright to left inclination at sacrum / hip joint
- Upright to left inclination in the thoracic spine
- Upright to left inclination in the lumbar spine

- Upright to right inclination at sacrum / hip joint
- Upright to right inclination in the thoracic spine

- Upright to right inclination in the lumbar spine

- Upright to flexion inclination at sacrum / hip joint
- Upright to flexion inclination in the thoracic spine
- Upright to flexion inclination in the lumbar spine

- Upright to extension inclination at sacrum / hip joint
- Upright to extension inclination in the thoracic spine
- Upright to extension inclination in the lumbar spine

The Kolmogorov-Smirnov test was used for normal distribution regarding the comparison between the two groups in these parameters, which showed a significant deviation regarding the comparison between the EDS-group and the control group in the ROM from: upright to left lateral flexion of sacrum and hip joint, upright to left lateral flexion at the thoracic spine, upright to left lateral flexion of the lumbar spine and from upright to right lateral flexion at the sacrum and hip joint. These parameters were therefore analyzed with a non-parametric method, a Mann-Whitney U-test. All other parameters were analyzed using a t-test.

Table 4. Differences in inclination between subjects diagnosed with EDS and CTR group.

| Group | | N | Mean | Std. Deviation | Minimum | Maximum | Percentiles 25th | 50th (Median) | 75th |
|---|---|---|---|---|---|---|---|---|---|
| CTR | Upright to left lateral flexion Inclination | 31 | -16,806 | 5,4980 | -27,0 | -6,0 | -20,000 | -16,000 | -13,000 |
| | Upright to right lateral flexion Inclination | 31 | 12,323 | 8,0762 | 1,0 | 38,0 | 6,000 | 11,000 | 17,000 |
| | Left to Right Inclination | 31 | 28,968 | 12,1009 | 12,0 | 54,0 | 18,000 | 26,000 | 41,000 |
| | Upright to flexion Inclination | 31 | 89,194 | 18,8616 | 54,0 | 134,0 | 72,000 | 89,000 | 100,000 |
| | Upright to extension Inclination. | 31 | -26,355 | 6,8971 | -42,0 | -14,0 | -30,000 | -26,000 | -22,000 |
| | Flexion to extension Inclination | 31 | ###### | 20,1938 | 88,0 | 166,0 | 96,000 | 116,000 | 127,000 |
| | Left laterlaflexion of Sacrum / Hip Joint | 31 | 5,258 | 5,5556 | -11,0 | 15,0 | 2,000 | 6,000 | 8,000 |
| | Left lateral flexion Thoracic spine | 31 | 26,355 | 6,4268 | 12,0 | 41,0 | 23,000 | 26,000 | 30,000 |
| | Left lateralflexion Lumbar spine | 31 | 17,903 | 6,4050 | 6,0 | 29,0 | 11,000 | 20,000 | 23,000 |
| | Right lateral flexion Sacrum/Hip Joint | 31 | -5,419 | 4,3495 | -13,0 | 9,0 | -8,000 | -6,000 | -3,000 |
| | Right lateral flexion Thoracic spine | 31 | -25,968 | 7,7437 | -39,0 | -8,0 | -32,000 | -26,000 | -21,000 |
| | Right lateral flexion Lumbar spine | 31 | -17,935 | 7,4159 | -42,0 | -2,0 | -23,000 | -19,000 | -12,000 |
| | Flexion Sacrum/Hip Joint | 31 | 60,548 | 17,8042 | 33,0 | 104,0 | 46,000 | 58,000 | 67,000 |
| | Flexion Thoracic spine | 31 | 60,097 | 8,4038 | 43,0 | 78,0 | 52,000 | 61,000 | 64,000 |
| | Flexion Lumbar spine | 31 | 19,742 | 11,6504 | -3,0 | 38,0 | 8,000 | 21,000 | 28,000 |
| | Extension Sacrum/Hip Joint | 31 | 9,774 | 11,0957 | -9,0 | 39,0 | 2,000 | 9,000 | 16,000 |
| | Extension Thoracic spine | 31 | 36,290 | 14,0835 | 9,0 | 60,0 | 25,000 | 36,000 | 48,000 |

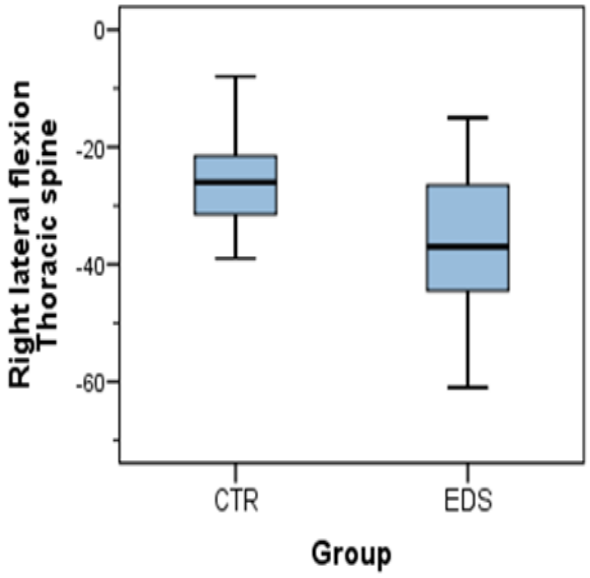
| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Extension Lumbar spine | 31 | -47,742 | 8,7139 | -67,0 | -25,0 | -53,000 | -48,000 | -41,000 |
| EDS | Upright to left lateral flexion Inclination | 31 | -27,839 | 9,8560 | -51,0 | -11,0 | -35,000 | -27,000 | -21,000 |
| | Upright to right lateral flexion Inclination | 31 | 23,581 | 10,4460 | 3,0 | 46,0 | 17,000 | 23,000 | 30,000 |
| | Left to Right Inclination | 31 | 51,484 | 19,3268 | 16,0 | 91,0 | 38,000 | 50,000 | 64,000 |
| | Upright to flexion Inclination | 31 | ###### | 17,6101 | 53,0 | 132,0 | 84,000 | 102,000 | 114,000 |
| | Upright to extension Inclination. | 31 | -33,774 | 14,2822 | -69,0 | -12,0 | -40,000 | -33,000 | -23,000 |
| | Flexion to extension Inclination | 31 | ###### | 25,4516 | 65,0 | 175,0 | 117,000 | 138,000 | 153,000 |
| | Left laterlaflexion of Sacrum / Hip Joint | 31 | ,194 | 5,7875 | -17,0 | 8,0 | -3,000 | 1,000 | 4,000 |
| | Left lateral flexion Thoracic spine | 31 | 33,935 | 14,0141 | 7,0 | 58,0 | 22,000 | 34,000 | 46,000 |
| | Left lateralflexion Lumbar spine | 31 | 24,419 | 8,3577 | 7,0 | 41,0 | 19,000 | 26,000 | 31,000 |
| | Right lateral flexion Sacrum/Hip Joint | 31 | -1,000 | 6,7725 | -13,0 | 16,0 | -6,000 | -1,000 | 4,000 |
| | Right lateral flexion Thoracic spine | 31 | -35,871 | 12,2685 | -61,0 | -15,0 | -46,000 | -37,000 | -25,000 |
| | Right lateral flexion Lumbar spine | 31 | -23,419 | 8,0074 | -35,0 | -9,0 | -30,000 | -24,000 | -17,000 |
| | Flexion Sacrum/Hip Joint | 31 | 71,581 | 18,0735 | 36,0 | 104,0 | 60,000 | 72,000 | 87,000 |
| | Flexion Thoracic spine | 31 | 62,452 | 10,9357 | 37,0 | 84,0 | 55,000 | 63,000 | 72,000 |
| | Flexion Lumbar spine | 31 | 20,258 | 11,3195 | -5,0 | 44,0 | 14,000 | 17,000 | 29,000 |
| | Extension Sacrum/Hip Joint | 31 | 3,290 | 13,1661 | -26,0 | 25,0 | -6,000 | 4,000 | 13,000 |
| | Extension Thoracic spine | 31 | 39,935 | 16,8660 | 1,0 | 69,0 | 27,000 | 40,000 | 54,000 |
| | Extension Lumbar spine | 31 | -50,452 | 13,8175 | -76,0 | -27,0 | -60,000 | -50,000 | -40,000 |

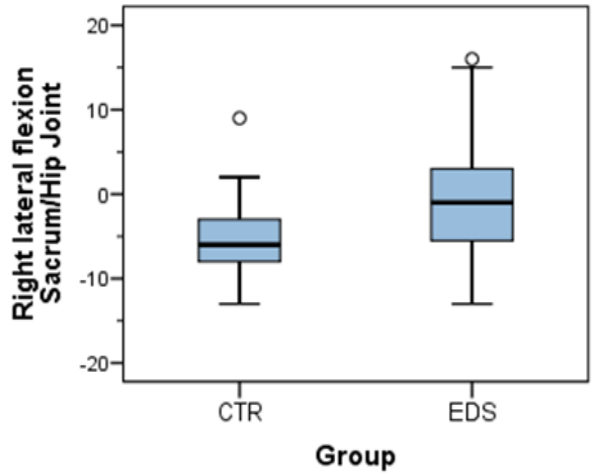
The EDS-group showed a significantly higher difference in the ROM between both upright to left inclination and upright to right inclination of the spine from C7-S3. The EDS-group showed a difference of the inclination of -27,84° (SD=9,86) opposed to CTR with -16,81° (SD=5,50), (p=0.000) in upright to left inclination and in upright to right lateral flexion inclination the EDS-group showed a difference inclination of 23,58° (SD=10,45) opposed to CTR which showed a difference of 12,32° (SD=8,08), (p=0.000) analyzed with a t-test.

In the ROM from upright to flexion inclination of the spine from C7-S3 the EDS-group showed a significantly higher inclination of 101,13° (SD=17,61) than the CTR group which showed a difference of 89,19° (SD=18,86), (p=0.012) analyzed with a t-test.

In the ROM from upright to extension inclination the EDS-group showed a significantly higher difference of 33,77° (SD=14,28) and the CTR group showed 26,36° (SD=6,90), (p=0.013).

In the ROM from upright to the right lateral flexion inclination of the thoracic spine the EDS-group showed a significantly higher difference of inclination of -35,87° (SD=12,27) opposed to the CTR group -25,97° (SD=7,74), (p=0.000). Also in the ROM from upright to right lateral flexion inclination of the lumbar spine the EDS group showed a higher difference of inclination: -23,42° (SD=8,01), compared to the CTR group of -17,94° (SD=7,42), (p=0.007) analyzed with a t-test. Regarding the ROM from upright to right lateral flexion inclination of the sacrum and hip joint the CTR group showed a higher difference of inclination of -5,4° (SD=4,35) compared to the EDS-group of -1,00° (SD=6,78) (p=0.003) analysed with a Mann-Whitney U-test (fig. 13).



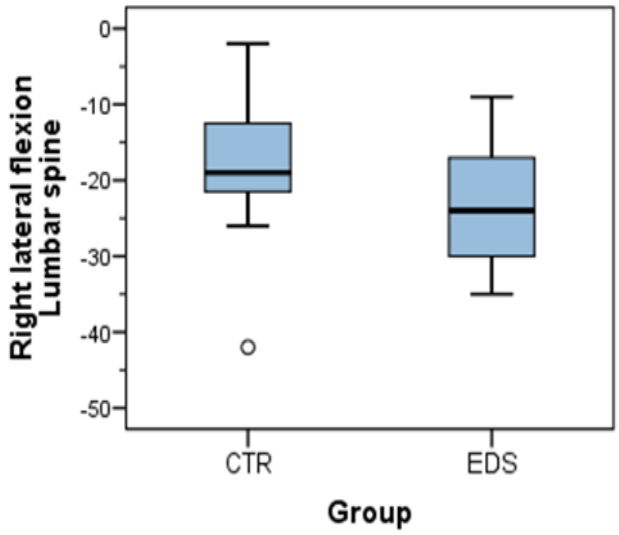




Figure 13. Box plots for the difference in ROM measured in degrees between pro-bands in EDS-group and control group in upright to right lateral flexion inclination at the sacrum and hip joint, thoracic spine and lumbar spine.

In the ROM from upright to flexion inclination of the thoracic spine the EDS-group showed a higher difference in the mean degree of flexion inclination of 62,45° (SD=10,90) and the CTR group: 60,10° (SD=17,80) but it was not significant (p=0,200) analyzed with a t-test.

In the ROM from upright to flexion of the lumbar spine the EDS group also showed a higher difference: 20,26° (SD=11,32) than the CTR group: 19,74° (SD=11,65) but was also not significant (p=0,860).

In the ROM from upright to flexion inclination of the sacrum and hip joint the EDS group showed a significantly higher inclination difference of 71,58° (SD=18,07) than the CTR group: 60,55° (SD=17,80), (p=0.019) analyzed with a t-test. (Fig 13).

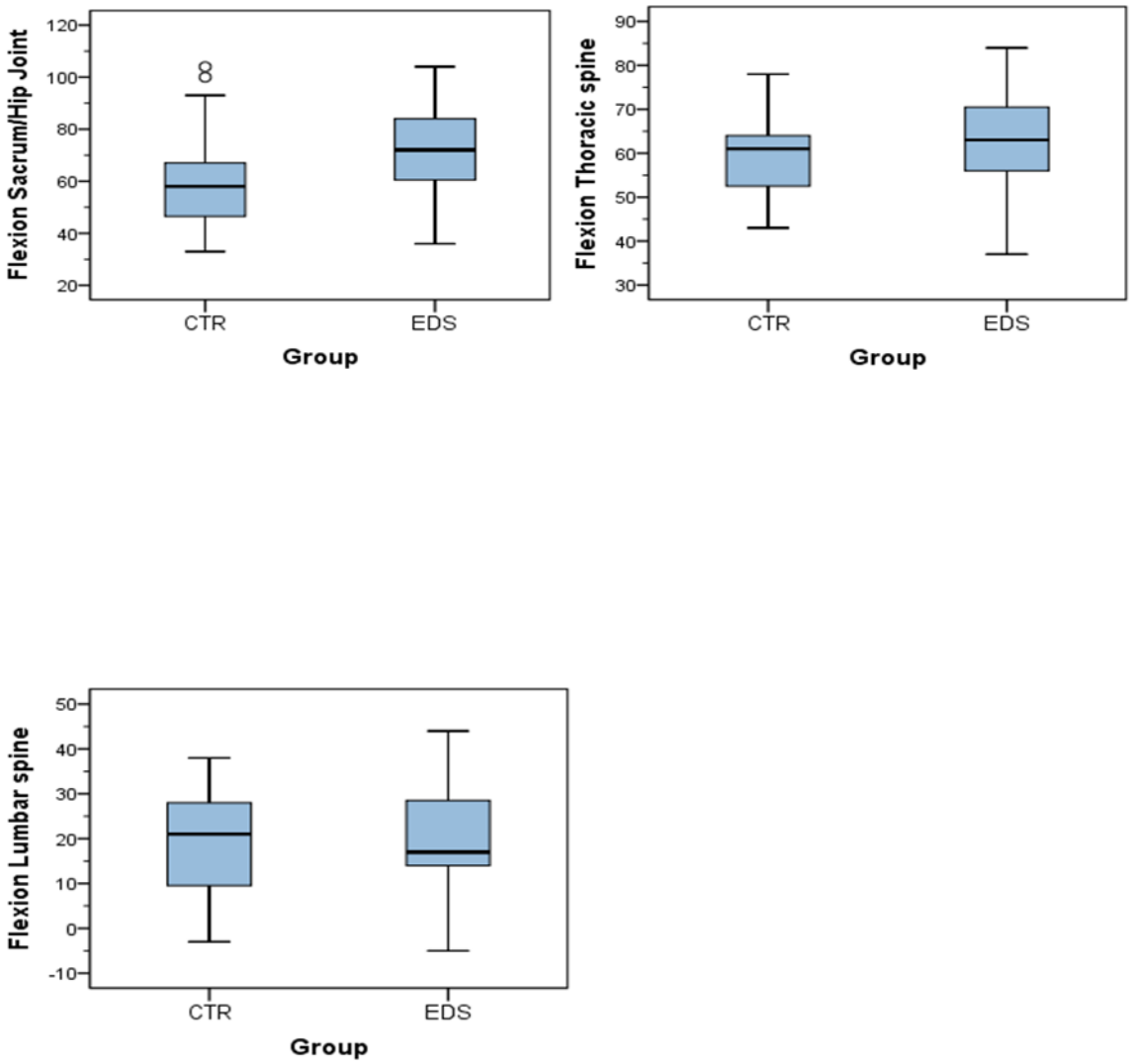



Figure 14. Difference in ROM measured in degrees between probands in EDS-group and control group in upright to flexion inclination at the sacrum and hip joint, thoracic spine and lumbar spine.

In the difference in inclination from upright to extension in the thoracic spine the CTR group had 36,29° (SD=14,08) compared to the EDS-group which showed a higher difference in inclination, 39,94° (SD=16,87) but not significant (p=0,359) analyzed with a t-test.

In the difference in inclination from upright to extension in the lumbar spine the EDS-group showed a higher inclination, -50,45° (SD=13,82) compared to the CTR group: -47,74° (SD=8,71) but also not significant (p=0,360).

In the ROM from upright to extension inclination at the sacrum and hip joint the EDS-group showed significantly higher inclination of 3,29° (SD=13,17) compared to the CTR group of 9,77°, (SD=11,10), (p=0.040) analyzed with a t-test (Fig. 15).

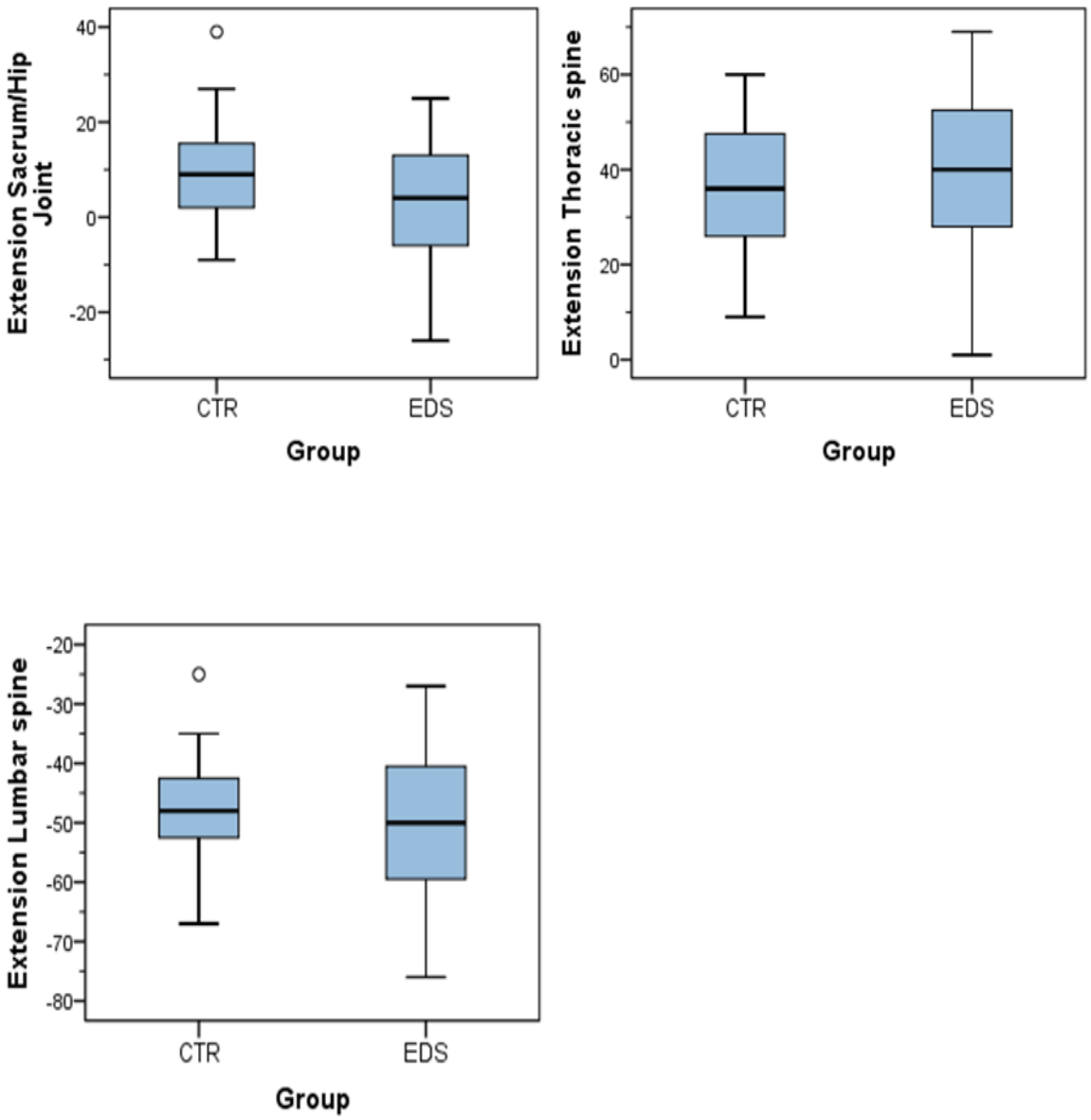



Figure 15. Box plots fort the difference in ROM measured in degrees between the probands in EDS-group and control group in upright to extension inclination at the sacrum and hip joint, thoracic spine and lumbar spine.

In the ROM from upright to left lateral flexion of the thoracic spine the EDS-group showed a significantly higher inclination of 33,94° (SD=14,01) compared to the CTR group of 26,36° (SD=6,43), (p=0.023).

In the ROM from upright to left lateral flexion inclination of the lumbar spine the EDS-group also showed a significantly higher inclination of 24,42° (SD=8,36) compared to the CTR group: 17,90° (SD=6,41), (p=0.00).

Regarding the ROM from upright to left lateral flexion at the sacrum and hip joint the CTR group showed a significantly higher inclination of 5,26° (SD=5,56) compared to the EDS-group: 0,19° (SD=5,79), (p=0.001), analyzed with a Mann-Whitney U-test (Table 5 and fig. 16).

Table 5. Mann-Whitney test for left lateral flexion of sacrum/hip joint, left lateral flexion n thoracic spine, left lateral flexion of the lumbar spine and right lateral flexion of the sacrum and hip joint.

| | Left laterlaflexion of Sacrum / Hip Joint | Left lateral flexion Thoracic spine | Left lateralflexion Lumbar spine | Right lateral flexion Sacrum/Hip Joint |
|---|---|---|---|---|
| Mann-Whitney U | 236,500 | 319,000 | 254,500 | 273,500 |
| Wilcoxon W | 732,500 | 815,000 | 750,500 | 769,500 |
| Z | -3,444 | -2,276 | -3,186 | -2,922 |
| Asymp. Sig. (2-tailed) | ,001 | ,023 | ,001 | ,003 |

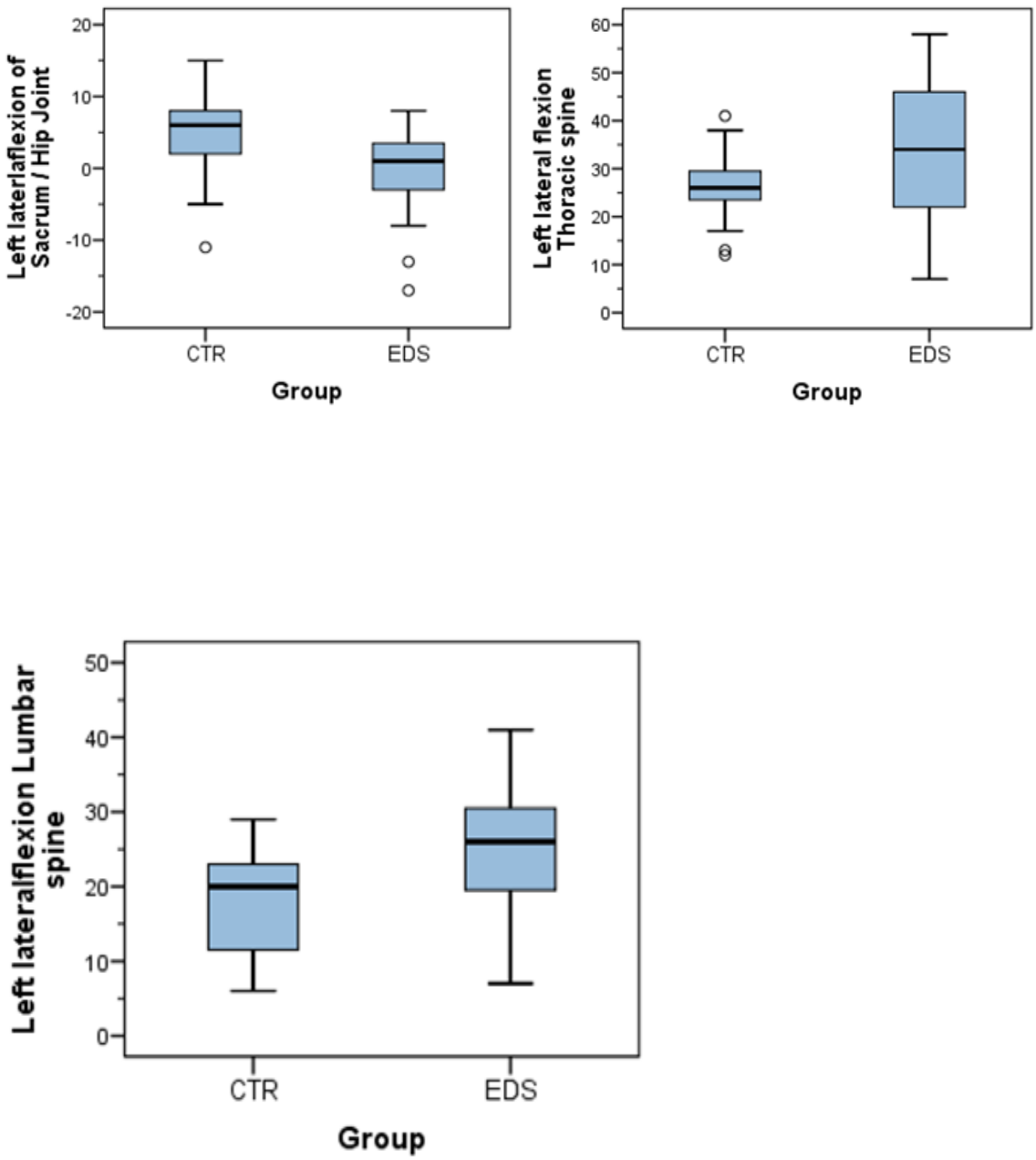



Figure 16. Box plots for the difference in ROM measured in degrees between the probands in EDS and control group in upright to left lateral flexion inclination at the sacrum and hip joint, thoracic spine and lumbar spine.

*Correlations between MFTF test and flexion inclination of spinal mouse*[1]

The collected data showed significant differences in the MFTF test measured in cm. The mean difference in subjects diagnosed with EDS compared to CTR was 6,47cm. The collected data showed significant differences in flexion inclination measured in degrees. The mean difference between subjects diagnosed with EDS and the CTR group was 12,61.

MFTF test: EDS (M=16,61 cm SD=12,41), CTR (M=23,08 cm SD=11,62), p=0,038 and Flexion inclination of spinal mouse: EDS (M=104,29° SD=16,58), CTR (M=91,68° SD=18,01), p=0,006.

Table 6. Sample test for MFTF test and flexion inclination.

| | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 95% Confidence Interval of the Difference | |
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| FTF-test CM | Equal variances assumed | ,064 | ,801 | 2,118 | 60 | ,038 | 6,4677 | 3,0536 | ,3596 | 12,5759 |
| | Equal variances not assumed | | | 2,118 | 59,746 | ,038 | 6,4677 | 3,0536 | ,3590 | 12,5764 |
| Flexion inclination | Equal variances assumed | ,260 | ,612 | -2,868 | 60 | ,006 | -12,6129 | 4,3971 | -21,4084 | -3,8174 |
| | Equal variances not assumed | | | -2,868 | 59,592 | ,006 | -12,6129 | 4,3971 | -21,4097 | -3,8161 |

Using the Kolmogorov-Smirnov test with a significance of p>0,05 there were found to be no significant deviation from normal distribution so parametric methods could be used for further statistics.

Pearson correlation coefficient showed that there was a strong negative correlation between MFTF test and flexion inclination of spinal mouse, r=-0,669, N=62, p=0,001.

In the EDS group: r=-0,660, N=31, p=0,001 and in CTR group: r=-0,662, N=31, p=0,001.

*Description of spinal palpation*[1,2]

[2]Regarding the palpation of the spine there were too few subjects palpated with the status -1 or +1, so therefore a correlation between the findings of palpation and the findings of the spinal mouse at each segment of the spine could not be statistically calculated.

Regarding the palpation of the spine in the sagittal plane the only segment where a majority of the participants showed a deviation from normal status was at T1/2. At the T1/2 segment 20 of 31 subjects in the EDS-group showed a deviation from normal to flexion status (+1) and the control group had 12 of 31 subjects with a flexion deviation according to the palpation findings. The mean flexion of these subjects, measured by the spinal mouse, also showed an increased flexion for the EDS-group (8,05°) opposed to the CTR group (6,83°) at this segment. For the 19 participants in the CTR group, which were palpated as neutral (0) the mean flexion were higher (8,32°) than the 9 participants palpated as neutral in the EDS-group (5,56°) measured by the spinal mouse.

Table 7. Palpation findings in the sagittal plane. Mean value is for the spinal mouse in the level of T1/2

| Group | Palpation sagittal Th1/2 | | N | Mean | Std. Deviation | Minimum | Maximum | Percentiles 25th | 50th (Median) | 75th |
|---|---|---|---|---|---|---|---|---|---|---|
| CTR | 0 | Flexion Th1/2 | 19 | 8,316 | 5,6278 | -2,0 | 23,0 | 4,000 | 7,000 | 12,000 |
| | | Extension Th1/2 | 19 | 6,421 | 2,7349 | 1,0 | 11,0 | 5,000 | 6,000 | 9,000 |
| | 1 | Flexion Th1/2 | 12 | 6,833 | 2,2496 | 2,0 | 9,0 | 5,250 | 7,000 | 9,000 |
| | | Extension Th1/2 | 12 | 7,167 | 3,6390 | 0,0 | 13,0 | 5,250 | 7,500 | 9,750 |
| EDS | -1 | Flexion Th1/2 | 2 | 4,500 | 3,5355 | 2,0 | 7,0 | 1,500 | 4,500 | 6,500 |
| | | Extension Th1/2 | 2 | -1,500 | ,7071 | -2,0 | -1,0 | -1,500 | -1,500 | ,500 |
| | 0 | Flexion Th1/2 | 9 | 5,556 | 3,0459 | 2,0 | 11,0 | 2,500 | 6,000 | 7,500 |
| | | Extension Th1/2 | 9 | ,889 | 4,3716 | -6,0 | 6,0 | -3,000 | 3,000 | 4,500 |
| | 1 | Flexion Th1/2 | 20 | 8,050 | 4,2609 | -1,0 | 16,0 | 4,500 | 7,500 | 12,000 |
| | | Extension Th1/2 | 20 | 8,650 | 3,2811 | 1,0 | 14,0 | 7,000 | 9,000 | 10,000 |

[1]Palpation in the frontal plane showed that in all segments, except in the segment of L3/4, there were more than 50% of the subjects that had the status of neutral (0).

In the segment of L3/4 there were more than 50% of the subjects that deviated from neutral. In the group where the subjects were diagnosed with EDS nine subjects had the palpation status of right lateral flexion (-1) and eight subjects had the palpation status of left lateral flexion (+1). The mean value of the spinal mouse was in right lateral flexion -5,78° and in left lateral flexion 6,63°. There were seven subjects in the CTR that had the palpation status of right lateral flexion and the mean value of the spinal mouse was -4,00°. Two subjects in the CTR had the palpation status left lateral flexion and the mean value of the spinal mouse in those subjects were 4,00°.

In the segment of L3/4 there were 14 subjects that were palpated as neutral in the group where subjects were diagnosed with EDS. They had an increased mean value of the spinal mouse in left lateral flexion of 5,86°. In the CTR group there were 22

subjects that were palpated as neutral and they had an increased mean value of the spinal mouse in right lateral flexion of -3,86°.

Table 8. Palpation findings in the frontal plane. The mean value is for the spinal mouse in the level of L3/4.

| Group | Palpation frontal L3/4 | | N | Mean | Std. Deviation | Minimum | Maximum | Percentiles 25th | Percentiles 50th (Median) | Percentiles 75th |
|---|---|---|---|---|---|---|---|---|---|---|
| CTR | -1 | Left lateral flexion L3/4 | 7 | 5,29 | 3,352 | 2 | 12 | 3,00 | 4,00 | 7,00 |
| | | Right lateral flexion L3/4 | 7 | -4,00 | 3,317 | -10 | 0 | -6,00 | -4,00 | -1,00 |
| | 0 | Left lateral flexion L3/4 | 22 | 3,82 | 2,239 | 0 | 8 | 2,00 | 4,00 | 5,25 |
| | | Right lateral flexion L3/4 | 22 | -3,86 | 1,935 | -8 | 0 | -5,00 | -4,00 | -2,75 |
| | 1 | Left lateral flexion L3/4 | 2 | 4,00 | 1,414 | 3 | 5 | 2,25 | 4,00 | 2,25 |
| | | Right lateral flexion L3/4 | 2 | -4,50 | 2,121 | -6 | -3 | -4,50 | -4,50 | -3,75 |
| EDS | -1 | Left lateral flexion L3/4 | 9 | 6,00 | 3,464 | 1 | 12 | 3,50 | 6,00 | 8,50 |
| | | Right lateral flexion L3/4 | 9 | -5,78 | 3,528 | -12 | -2 | -8,50 | -5,00 | -2,00 |
| | 0 | Left lateral flexion L3/4 | 14 | 5,86 | 3,035 | 2 | 12 | 3,75 | 5,00 | 8,25 |
| | | Right lateral flexion L3/4 | 14 | -5,14 | 3,697 | -13 | 0 | -7,00 | -4,00 | -3,00 |
| | 1 | Left lateral flexion L3/4 | 8 | 6,63 | 2,722 | 4 | 11 | 4,25 | 5,50 | 9,50 |
| | | Right lateral flexion L3/4 | 8 | -4,88 | 3,441 | -11 | -1 | -8,00 | -4,00 | -2,25 |

*Comparison of subjects diagnosed with EDS and CTR group regarding spinal pattern in the sagittal and frontal plane[1]*

To see if there was a difference between the subjects diagnosed with EDS and the CTR group, in the spinal pattern, all subjects were measured with the spinal mouse in an upright position in a frontal and a sagittal plane. The parameters were frontal/sagittal to upright sacrum/hip joint, frontal/sagittal to upright thoracic spine, frontal/sagittal to upright lumbar spine and frontal/sagittal to upright inclination.

Collected data showed significant results for frontal to upright in the thoracic spine. EDS (M=-8,74°, SD=5,33) CTR (M=-6,26°, SD=3,67), p=0,037.

Table 9. Comparison of the two groups regarding spinal pattern in sagittal and frontal plane.

| Group | | N | Mean | Std. Deviation | Minimum | Maximum | Percentiles 25th | 50th (Median) | 75th |
|---|---|---|---|---|---|---|---|---|---|
| CTR | Frontal upright Sacrumk /Hip Joint | 31 | 6,484 | 4,2651 | -4,0 | 15,0 | 5,000 | 7,000 | 9,000 |
| | Frontal upright Thoracic spine | 31 | -6,258 | 3,6694 | -16,0 | 2,0 | -9,000 | -6,000 | -4,000 |
| | Frontal upright Lumbar spine | 31 | 6,516 | 4,2259 | -8,0 | 13,0 | 5,000 | 7,000 | 9,000 |
| | Frontal upright Inclination | 31 | -1,968 | 1,2776 | -5,0 | 1,0 | -3,000 | -2,000 | -1,000 |
| EDS | Frontal upright Sacrumk /Hip Joint | 31 | 5,613 | 3,3434 | -1,0 | 12,0 | 3,000 | 6,000 | 8,000 |
| | Frontal upright Thoracic spine | 31 | -8,742 | 5,3290 | -21,0 | -1,0 | -11,000 | -7,000 | -5,000 |
| | Frontal upright Lumbar spine | 31 | 6,323 | 3,7183 | 0,0 | 16,0 | 4,000 | 6,000 | 8,000 |
| | Frontal upright Inclination | 31 | -1,581 | 1,7469 | -5,0 | 2,0 | -3,000 | -2,000 | 0,000 |

Using Kolmogorov-Smirnov test for normal distribution, frontal upright lumbar spine and frontal upright inclination showed significant deviation, so they were analyzed with the Mann-Whitney test. No significant difference was found between the two groups regarding the spinal pattern in sagittal and frontal plane.

# 6 Discussion

## 6.1 Discussion of methodology[1,2]

[2]A CCS is a study that compares people with a specific disease (cases) with people from the same population without that disease (controls). The study seeks to find associations between the outcome and prior exposure to particular risk factors. CCS is mainly useful where the outcome is rare and past exposure can be reliable measured. Usually CCS is retrospective, but not always (The Cochrane Collaboration, 2014)

The method used in this study is a CCS to investigate if patients suffering from EDS have an increased inclination of the spine, as they do in other joints of the body, compared to normal healthy individuals. This type of method is often easy, quick and cost effective to use (Grisso, 1993) (Lewallen and Courtright, 1998). Recording information and the assessment of exposure could be difficult in this type of study to exclude any information bias (Grisso, 1993). The selection of controls is also important and should be chosen to be as similar to the control as possible regarding age, sex etc. as well as collection of data that should be collected in the same way for both groups (Lewallen and Courtright, 1998) (Grisso, 1993).

In this study there is several limitations. The cervical spine were not measured and included in the measure of the spine in the subjects, as the spinal mouse is not able to measure the cervical spine. Also the rotation movement vector was also not measured, as the spinal mouse is also not able to measure the rotation movement vector (Ripani et al, 2008).

For the purpose to investigate if patients with EDS have an increased inclination and mobility of the spine, it could have been of great interest to know if the inclination also were higher or increased in the cervical spine. As many osteopathic treatment techniques include rotation of the spine it could also be of interest to know if there could have been an increased mobility in the rotational plane of the spine.

The reliability of this study could have been influenced by several factors. A selection bias has occurred during the recruitment of the subjects to this study, as there was no randomization,(Jűni et al, 2001), (Pannucci and Wilkins, 2010). The recruitment was made through ads on social media and also through the webpage of the Swedish national Ehlers-Danlos Syndrome association.

The examiner did not record for each subjects if they regularly received any manual treatment or not. If some subjects have received regular manual treatment it may have affected the mobility of the spine.

Subjects in this study were also selected according to the inclusion and exclusion criteria: Inclusion criteria for the EDS group were subjects diagnosed with EDS, classical type or hypermobility type and age 18-65. And the exclusion criteria were pregnant subjects and subjects who have had spinal surgery. The inclusion criteria for the control group were the age 18-65 and excluded if they had a EDS or JHM diagnose, were pregnant, have had any spinal surgery and also if they had a Beighton score of 4 or greater tested with the Beighton scale. To avoid any risk of having any EDS patients in the control group all subjects with a Beighton score of 4 or greater were excluded, as there is suggested by Hakim and Grahame, (2003), (2008), Shirley et al. (2012) and Gasik and Styczynski, (2009) that EDS is very underdiagnosed and maybe missed in a part of the population.

The age of the participants of this study could have been a potential confounder of the study (Consonni, et al. 1997). The inclusion criteria for age 18-65 in both groups could also have been a to large age span as there were too few subjects (N=5) in the age group 56-65 to be able to calculate statistically on this age group.

However, in the present study a correlation were made between different age groups (18-35 and 36-55). Extension inclination, left and right lateral flexion were higher in 18-35 EDS group compared to the 18-35 and 36-55 control group (EDS 18-35 in extension inclination: -38.33° (SD=16.29) vs. CTR: -20.64° (SD 5,41), (p=0.003), EDS 18-35 in left lateral flexion inclination: 28.82° (SD 5.62) vs. CTR:

15.73° (SD=6.28), (p=0.000), EDS 18-35 right lateral flexion inclination: -27.58° (SD=6.30) vs. CTR: -14.18°, (SD=7.21), (p=0.000). In the age group 36-55 right and left lateral inclination were higher in the EDS group compared to the control group (EDS 36-55 in right lateral flexion inclination: -24.78° (SD=11.92) vs. CTR: -15.44° (SD=9.10), (p=0.016), EDS 36-55 in left lateral flexion inclination: 25.56° (SD=11.14) vs. CTR: -14.94° (SD=5.54), (p=0.001).

The subjects may also have affected the outcome if they are less mobile with age (Seow et al, 1999), the age-span included were however the same in both cases and controls.

There was only one examiner preforming the measure procedure and the procedure was performed in the same way in each subject, which could be a strength to the study as there is important to collect data in the same way from both groups (Lewallen and Courtright, 1998) (Grisso, 1993).

There were blinding of the researcher no 1 and also to the personnel calculating all statistics. According to Karanicolas et al. (2010) blinding is however more common in randomized clinical trials. Also according to Kopec and Esdaile, (1990) blinding of the examiners are preferable. Data collectors and data analyzers were not completely blinded as researcher 2 preformed the data collection and analysis, this may have affected the analysis as this may have subconsciously effected the un-blinded researcher to see just positive results (Karanicolas et al. 2010).

The subjects of this study were also not measured at the same time of the day, which could have had an effect on the outcome of the measure if some subjects are more mobile in the afternoon than in the morning, which could be a confounding factor (Russel et al, 1992).

The manually segmental mobility testing procedure and recording in the Lundberg and Gerdle´s (1999) study, they used a 5-graded scale, which would perhaps to be

preferred to measure the mobility of the spine by palpation. A 5-graded scale makes a more fine degree scale of the mobility in each segment from hypomobility (-2) to hypermobility (+2) in each movement vectors. In the present study a 3-graded scale was used which made a more gross scale of mobility in each segment and did also not account for how mobile a movement vector were, just that a segment more easily could move in to flexion, extension, right or left lateral flexion. The aim of the palpation of the spine in the present study was to correlate the pattern of the palpation findings with the findings of the spinal mouse. This was however statistically impossible due to the too few subjects palpated with the -1, 0 and +1 status.

*Measuring device and tecniques*[1,2]

[2]A spinal mouse was used as measure equipment in this study to measure the inclination of the spine in the sagittal and frontal plane. The device is practical, easy to use and is safe and non-invasive for the patient (Livanelioglu et al. 2015).

A limitation of this measure equipment for this purpose is the possibility of measuring the distance of the spine as the spinal mouse only measures the spine from C7-S3 and does not account for the cervical spine. Also the spinal mouse does not also measure all movement vectors of the vertebral joints, as it does only measures flexion, extension and lateral flexion and not rotation, which could have been an interesting movement vector as rotation often is used in several treatment techniques of the spine by osteopaths. (Gibbons and Tehan, 2001) (Gibbons and Tehan, 2010) (Lenehan et al. 2003)

The body position during the measurement procedure of the spinal mouse in flexion, extension, right lateral flexion an left lateral flexion could also have been a potential risk of injury as the EDS subjects are hypermobile and should not over stretch their joints (Keer and Grahame, 2003), and could have strained their backs during this manoeuvres.

[1]A limitation could also be the difficulty to determine spinous processes due to large muscles or soft tissue. The spinous processes can also be deformed which could lead to an inaccurate measurement result (Livanelioglu et al, 2014) In the present study it was the same therapist pointing out the spinous processes and doing the measurement with the spinal mouse so therefor it could not be shown any interrater correlation (Kellis et al, 2008).

Mannion et al, (2004) examined the validity and reliability of the Spinal Mouse on 20 healthy subjects. On two days with two different examiners, the spinal curvature was measured in, standing position, flexion and extension, and paired T-test, intraclass correlation coefficient (ICC) and standard errors of measurement (SEM) was used to characterise between-day and interexaminer reliability. Between-day average the ICC range for examiner 1 was 0,82 and 0,83 for exam-iner 2. The criteria used in this study is taken from Currier (Currier, 1990) where the level for good reliability is between 0,80-0,89. For the lumbar flexion the SEM was approximately 3 degrees. Mannion et al, (2004) suggests that the Spinal Mouse can be used with confidence in clinical research for measuring spinal mobility.

In recent studies examining the reliability for the Spinal Mouse showed fair to high interrater and intrarater reliability (Kellis et al, 2008). In their study 81 children were used to measure their spine in full flexion and full extension. Three raters did the procedure at two occasions. ICC and SEM were used to examine the between-day and interrater reliability. The intrarater ICC ranged from 0,61 to 0,96 and the inter-rater ICC ranged from 0,70 to 0,93. SEM ranged from 0,61 degrees to 13,18 de-grees.

A systemic review revealed that the Spinal Mouse had the strongest level of relia-bility, together with Debrunner´s kyphiometer and Flexicurve index, comparing with Acrometer, Flexicurve angle, Manual inclinometer, Digital inclinometer, 3D ultra-sound, Raserstereography, Stereovideography, Goniometer, Electrogoniometer, Spinal wheel, Pantograph and Photgrammetry. For the validity the conclusion was that more research are needed (Barrett et al, 2014)

Livanelioglu et al (2015) did a study on 51 patients diagnosed with adolescent idiopathic scoliosis and the aim was to investigate the validity and the reliability of Cobb angle and measurement with the spinal mouse. Spinal mouse measurements were performed by two physiotherapists and the radiological measurements were performed by two orthopedics. The intraobserver and interobserver agreement of Cobb angle and spinal mouse measurements was excellent (ICC=0,872-0,962). They concluded that the spinal mouse was a reliable tool in research.

[2]A MFTF were used in this study to be able to measure the distance between the middle finger and the floor in subjects that is hypermobile as they often easily can reach the floor with extended knees. The height of the box used in this study were 19 cm and as two subjects were able to reach the floor in spite of the extended box maybe a higher box were to be preferred (Gauvin et al 1990).

[1]However, the strength of using MFTF test in this study is that EDS patients often reach the floor in the FTF test and the risk of that is too many measurement values of zero. Biering-Sorenson, (1984) made a study of 479 females and 449 males comparing FTF test with measurement of lumbar flexion obtained by the skin-distraction method. He could not see a strong relationship between the two methods which might depend on too many values of zero because the subjects could reach the floor.

In Ekedahls et als, (2012) study there were 65 subjects with LBP, acute or subacute, and 58% of them had radicular pain as determined by the slump test. Responsiveness and imprecision were assessed by using effect size (ES) and minimal detectable change (MDC). The change in FTF results significantly correlated to the 1 month change in RMDQ both in the entire sample, r = .63, and in the radicular pain group, r = .66. FTF showed adequate responsiveness, ES = 0,8-0,9, in contrast to SLR, ES = 0,2-0,5. The MDC for FTF was 4,5 cm and for SLR 5,7 degrees. The change in FTF results over 1 month was independently more strongly associated with the 12 month change in RMDQ, R2 = .27-.31, than any of the other variables.

The conclusion of their study was that the FTF test has good validity in patients with LBP and even better validity in patient with radicular pain.

A MFTF-test could be favorable to use when the subjects expects to reach the floor in a FTF test, like in EDS patients. The procedure of a MFTF test differs from a FTF test in that the subject is standing on a stool when bending forward (Gauvin et al, 1990).

Gauvin et al, (1990) made a study to examine the intertherapist and the intratherapist reliability of measurement using the MFTF test. The study contained 73 subjects with LBP. For inter- and intratherapist reliability the ICC were calculated. The ICC for intertherapist reliability was .95 and for intratherapist reliability .98, the authors concluded that using MFTF test in patient with LBP was highly reliable (Gauvin et al, 1990).

Using MFTF to measure mobility in the spine could be misleading because motion in the hips and the extremities can affect the measurement of the spine (Gauvin et al 1990). In the present study the MFTF test was made only once on every subject which also could be a misleading factor, repeating the measurements on different days would improve the reliability (Frost et al, 1982).

### 6.2 Discussion of results[1,2]

Lundberg and Gerdle, (1999) made a similar study to the present study on 607 Swedish homecare personnel. They could positively correlate segmental spinal mobility, passive manually tested and spinal mobility, measured by a Debrunner´s kyphometer and general joint mobility, measured by the Beigthon scale. They could also conclude that hyperlordosis were associated with greater lumbar mobility.

*Discussion of the result of the hypothesis[2]*

In the alternative-hypothesis: EDS patients have an increased angle of the spine in full flexion, extension and lateral flexion compared to normal healthy individuals, all four parameters: flexion (104,29° vs. 91,68°, p=0.000), extension (-30,58° vs. -23,77°, p=0.022), right lateral flexion (-25,29° vs. -14,26°, p=0.000) and left lateral flexion (26,39° vs. 14,81°, p=0.000), were significantly higher in the EDS-groups inclination of the spine compared to the control group.

In the article by Lundberg and Gerdle, (1999) they could correlate the Beighton score with segmental mobility of the spine, especially in the 2 lowest segments (L4-S1). They also found a significantly greater total thoracic and lumbar sagittal mobility in the group with pronounced mobility (a Beighton score of <5) measured by a Debrunner´s kyphometer.

Fritz et al. (2005) found lumbar instability, measured by radiographic images of the lumbar spine, in 28 (57%) of 49 patients with low back pain. They also found greater ligamentous laxity measured by the Beighton scale (1,9p for the 28 patients with lumbar instability and 0.90p for the group with no lumbar instability, p= 0.048) in 49 patients with low back pain.

In two articles there was found a positive relationship between general joint hyper mobility, and mobility of the cervical and lumbar spine (Rozen et al, 2006), (Kim et al, 2013). In the article by Rozen et al. (2006) a Beighton score of more than 3 were found in 10 of 12 subjects with daily persistent headache and in 11 of these 12 subjects hypermobility were also found in the cervical spine. In the article by Kim et al. (2013) 32 males with JHS (a Beighton score of 4 or greater) and back pain, they detected significantly increased lumbar spine mobility for the JHM-group compared to the control group (82,66° vs. 54,45°p=0.001), measured by radiographs in flexion and extension. No articles have been found in relation to EDS and mobility of the spine.

The greatest mean difference between the EDS-group and the control group were in the flexion inclination (-12.61°).

From an osteopathic point of view these findings of an increased inclination and mobility in the sagittal and frontal plane in the spine from C7-S3 could be of value in terms of choice of treatment techniques and exercises for patients diagnosed with EDS and may also be beneficial for patients diagnosed, or suspected to have, JHS as the hypermobility type of EDS and JHS may be the same diagnose (Hakim and Grahame, 2003).

In one case report of two cases by Colloca and Polkinghorn, (2003) two patients diagnosed with EDS were successfully treated in terms of decreased medication and pain relief with low force chiropractic treatment (short level adjusting procedures, Activator II Adjusting Instrument and exercises). In this article they also highlight the importance of treating patients with EDS with minimal force and trying to avoid treatment techniques as High-velocity, low-amplitude (HVLA) or deep trigger point work, as these patients are at greater risk of tissue injury, fractures and rupture or injury of blood vessels (Malfait et al, 2010).

*Correlation with age*[2]

Regarding the correlations with age and flexion, extension and lateral flexion inclination of the spine, only the EDS group showed a significant correlation between age and decreased inclination in extension (R=0.529 p=0.002).

In the Lundberg and Gerdle, (1999) article they found a significant correlation between decreased sagittal movements with increasing age especially of the lumbar and thoraco-lumbar movement. In an article by Moll and Wright, (1971), 237 subjects (119 males and 118 females) were measured for spinal mobility in flexion, extension and lateral flexion. In this study they found differences in both sexes regarding spinal mobility and age in all 3 planes of movement. They found an increase in mobility from age group 15-24 to 25-34 and thereafter a decrease of mobility from

35 to 75+. In another article a correlation were found between increased age and decreased mobility in the lumbar spine of 80 subjects (40 males and 40 females) in all planes of movement (Hindle et al. 1990). And in one article made on 109 healthy females age 20-84 a decreased mobility were found in relation to increased age in flexion, extension and lateral flexion from C7-S1 (Einkauf et al. 1987). Also in a recent study from Ramiro et al. (2015) on 393 subjects from age 20-69 measured with 11 spinal mobility measurements also an increased age could be correlated with decreased mobility.

All these studies were made on normal healthy subjects and compared to the result of the present study´s control group, in increase or decrease of mobility of the spine in relation to age, the result was not in line with the other literature.

*Correlation between different age groups[2]*

Regarding correlation between the two groups (EDS and control) in each age group (18-35 and 35-55). A significant difference could be found with increased inclination of the EDS-group in the age group 18-35 in extension inclination (EDS: -38.33° (SD=16.29) vs. CTR: -20.64° (SD 5,41), (p=0.003), right lateral flexion (EDS: -27.58° (SD=6.30) vs. CTR: -14.18°, (SD=7.21), (p=0.000) and left lateral flexion (EDS: 28.82° (SD 5.62) vs. CTR: 15.73° (SD=6.28), (p=0.000).

In the age group 36-55 the EDS group also showed significantly increased inclination in left lateral flexion (EDS: 25.56° (SD=11.14) vs. controls: -14.94° (SD=5.54), (p=0.001) and right lateral flexion (EDS: -24.78° (SD=11.92) vs. controls: -15.44° (SD=9.10), (p=0.016), but not in flexion or extension inclination. In the age group 36-55 the control group showed increased inclination in extension but it was not significant (CTR mean= -27.13° and EDS mean= -26.33°). However the EDS group showed a decrease in extension inclination in relation to increased age and the control group did not show any difference with age in any parameter.

*Differences in inclination from upright to flexion, extension and lateral flexion of the spine from C7-S3, thoracic spine, lumbar spine and sacrum and hip joint between subjects diagnosed with EDS and the control group*[2]

Regarding the mobility in upright to full flexion, extension, right lateral flexion and left lateral flexion of the spine the EDS group had significantly greater degrees of inclination than the control group.

Regarding the inclination of flexion in the thoracic spine, lumbar spine and sacrum / hip joint only flexion of the sacrum and hip joint were significantly (p=>0.05) greater for the EDS-group than the control group. Flexion of the thoracic and lumbar spine was greater than the control group, but not significantly. This information may demonstrate that most of the mobility difference in flexion of the spine may be at the sacrum and hip joint rather than the spine.

Regarding the inclination of extension in the thoracic spine, lumbar spine and sacrum / hip joint only extension at the sacrum and hip joint were significantly greater inclination for the EDS-group than the control group. Extension in the lumbar spine was also greater for the EDS-group, but not significantly. Extension in the thoracic spine was however smaller for the EDS-group compared to the control group but it was not significant. This information may also suggest that there is greater mobility difference between the two groups at the sacrum and hip joint rather than in the thoracic and lumbar spine as in flexion.

In one article by Kim et al. (2013) they studied 32 young males diagnosed with JHS and found an increased disk height in the lumbar spine as well as increased segmental motion in flexion and extension. This was also associated with low back pain, disability and limited activities.

Regarding these findings of the greatest mobility difference in flexion and extension at the sacrum and hip joint it could perhaps be of relevance in terms of treatment of the EDS-group to focus on stabilizing hips and pelvis for increased stability.

Regarding the inclination of lateral flexion in the thoracic spine, lumbar spine and sacrum / hip joint the EDS-group had significantly greater inclination in the right lateral flexion in the thoracic and lumbar spine. But in the right lateral flexion at the sacrum and hip joint the control group had significantly greater inclination. In the left lateral flexion the EDS-group had a significantly greater inclination in the thoracic and lumbar spine but not at the sacrum / hip joint where the control group had significantly greater inclination.

*Correlations between MFTF test and flexion inclination of spinal mouse*[1]

The purpose with this study was to see if EDS patients had an increased angle of the spine in full flexion, extension and lateral flexion using a spinal mouse. In the clinic, it is common that osteopaths use the FTF test or, like in this study the MFTF test, to examine the flexion mobility in the spine. Therefore it was interesting to see if the MFTF test and the measuring with the spinal mouse correlates. The results showed a significant group difference in both parameters. In the MFTF test EDS group had a median value (16,61 cm) which was less than the CTR group (23,08 cm). The result of measuring using the spinal mouse showed that the EDS group had a higher median value (104,29°) than the CTR group (91,68°). This result show that EDS patients seems to be more mobile in the spine in full flexion than healthy people. The correlation between the MFTF test and the flexion inclination of spinal mouse, in this study, was strong (Pearson correlation >0,6 p<0,01). However, according to Gauvin et al (1990) MFTF test could be misleading because the movement in the hips and extremities could influence the measurements and also in the present study the results of inclination showed that EDS patients have increased mobility in the sac/hip joint, in flexion, compared to healthy individuals.

There are a lot of studies made on the reliability of the spinal mouse (Kellis et al, 2008), (Barret et al, 2013), (Topalidou et al, 2014) and (Livanlelioglu et al, 2015) and the reliability of the MFTF test (Gauvin et al, 1990) and the FT F test (Perret et al, 2001) and (Ekedahl et al, 2012) but there is not seen any studies to see the correlation between measurement of the spinal mouse and the FTF or MFTF test.

*Discussion of the description of spinal palpation*[1,2]

[2]Due to the too small sample size palpated with the status -1 or +1, a correlation between the findings of palpation and the findings of the spinal mouse could not be statistically calculated. Any conclusions of this subject are therefore impossible to draw.

At the T1/2 segment the majority of the participants showed a deviation from normal status. Twenty of 31 subjects in the EDS-group showed a deviation from normal to flexion (+1) at T1/2 and in the T1/2 segment 20 of 31 subjects in the EDS-group showed a deviation from normal to flexion (+1) and in the control group 12 of 31 subjects had a flexion (+1) deviation. This may indicate that EDS patients have a tendency of increased flexion at this segment. This information could be of use as EDS patients often tend to suffer from neck pain (Stanitski et al, 2000) and headaches (De Peape and Malfait, 2012) and a flexion in this area may give rise to a poor posture for the cervical spine which could potentially lead to a tension type headache. Osteopathically it may also be of importance if this flexed area may enhance the blood or nerve supply to the upper extremity if it effects the position of the first rib or effects the posture of the cervical vertebraes (Watson and Pizzari, 2010).

[1]In the palpation in the frontal plane there was also a too small sample size palpated with the status of right lateral flexion (-1) or left lateral flexion (+1) so a correlation between palpation findings and findings of the spinal mouse could not be statistically calculated for the frontal plane either.

In the segment of L3/4 in the group where the subjects were diagnosed with EDS there were more than half the group, 17 of 31, that deviated from neutral status (0) in the palpation in the frontal plane. There were 9 subjects that were palpated in right lateral flexion (-1) and there were 8 subjects palpated in left lateral flexion (+1). In the CTR group there were 9 of 31 that deviated from neutral status (0) in palpation in the frontal plane. There were 7 subjects palpated in right lateral flexion (-1) and 2

subjects palpated in left lateral flexion (+1). In the group where subjects were diagnosed with EDS the measuring from the spinal mouse showed an increased angle in right lateral flexion (-5,78°) and in left lateral flexion (6,63°) compared to the angle in healthy subjects, right lateral flexion (-4,00°) and left lateral flexion (4,00°).

To refer back to the question about differences in the spinal pattern, in the present study it seems that subjects diagnosed with EDS are more prone to deviate from normal status (0) in the L3/4 segment than healthy subjects but due to the small sample size it is not right to believe that it is a more common pattern in EDS patients. Therefore in the current situation this study cannot be very helpful when diagnosing EDS, more studies similar to this must be done.

The deviation from normal status (0), palpated in the segment of L3/4, could effect the pattern in the spine because there are often offsets further up in the spine (Parsons, 2006). In the present study it was, for example, shown a deviation from normal (0) in the segment of T1/2.

Osteopathically there are things to consider regarding the segment of L3/4, the crurae from the diaphragm and the psoas muscle create a focus of movement on L3 when they pull in opposite directions. Because L4 and L5 are tight related to the pelvis via the iliolumbar ligaments and move with it, the movement get focused on L3 (Stone, 1999).

*Comparison of subjects diagnosed with EDS and CTR group regarding spinal pattern in the sagittal and frontal plane*[1]

In the present study the spinal pattern in a sagittal and a frontal plane was looked at to see if there was any differences between the EDS group and the CTR group. That because the authors wanted to see if spinal pattern could be any help when diagnosing EDS.

The only significant result was the differences in the frontal plane in the thoracic spine. EDS (M=-8,74°, SD=5,33) CTR (M=-6,26°, SD=3,67) t(60)=2,14, p=0,037. That spinal pattern may go in line with previous studies of scoliosis pattern in EDS patients. Beighton and Horan (1969) did a study on 100 EDS patients and 18 of them had scoliosis pattern. The type of EDS was not mentioned. In another study five patients diagnosed with EDS classical type developed severe spinal deformity. Three patients had double scoliosis in the thoracic and lumbar regions, two had single scoliosis in the thoracic spine and one had a thoracic kyphosis (McMaster, 1994). In Czaprowski´s (2014) study, the aim was to see the frequency of GJH in girls with idiopathic scoliosis among girls aged 9-18 years. The study revealed that 155 girls with idiopathic scoliosis of which 23,2% had GJH compared to 201 healthy girls of which 13,4% had GJH.

In a study by Stanitski et al (2000), they found in 58 EDS type I-IV patients that 51,7% had clinical and radiographic scoliosis. Of these 58 participants, type I had the greatest percentages of scoliosis (61,5%) and type III there were 56,7% that had scoliosis. In 10% of the EDS patients with scoliosis had radiographic signs of grade I spondylolisthesis or retrolisthesis and of these EDS patients with scoliosis, 82% had back or neck pain that limited their activities and in the other group with no scoliosis 71% had limiting back and neck pain.

Czapowski et als, (2011) CCS included 70 subjects in the age of 9-18 years where 34 subjects had single curvature scoliosis and 36 subjects had double curvature scoliosis and 58 subjects, with the same age, in the control group. The study showed that JHM was diagnosed in 51,4% of the subjects in the scoliosis group and 19% of the subjects in the control group. JHM prevalence was found to be higher in children with single curvature scoliosis than double curvature scoliosis.

In this study there was no significant differences neither in the frontal plane nor in the sagittal plane, in the lumbar spine. Kozlowski et al (1991) made a study on three teenaged boys diagnosed with EDS which had a flattening lumbar spine. No conclusion was made on the small number of subjects. Kim et al (2013) did a study on

32 males diagnosed with JHS and a control group of 32 age-matched males without JHS and the objective was to see the intervertebral mobility in JHS patients compared to non-JHS patients. Comparing the Cobbs angle in the lumbar spine in flexion and extension they could see that the JHS group had a significant larger ROM and a higher intervertebral disc height than the control group.

Czaprowski and Pawlowska, (2013) did a study on 37 boys and 38 girls diagnosed with GJH where the profile of the sagittal spine was measured with a digital Saunders inclinometer. No significant differences was seen in the sagittal plane compared with the control group of 197 girls and 150 boys.

The cause and pathogenesis of EDS are a genetic defect in the collagen structure which leads to an abnormality in the collagen structure. This make the ligaments and fascia more fragile and prone to injury and tissue damage (Hakim and Grahame, 2003). This is important for manual therapists like osteopaths to consider when they meet an EDS patient in the clinic. It is essential to use safe and effective techniques when treating these patients and give them advice in training and exercise's. For example exercises to strengthen the muscles with open and closed kinetic chain exercise, and stretching the muscles in a way where the muscle are isolated and not give an impact on the joint (Simpson, 2001). Pool activity could be a good alternative to avoid high impact on the joints (Shirley et al, 2001). Due to this study it seems that EDS patients have an increased mobility in the sacrum/hip joint compared to healthy individuals, therefore when treating this area, HVT would not be preferable (Simpson, 2001) but more functional osteopathic treatment methods like cranial work and balanced ligamentous techniques (BLT) or suggested by Simpson (2001) counterstrain or positional release techniques.

[2]In a search on PubMed and Science direct of the keywords: ehlers-danlos syndrome and combined with spinal mobility, spine and vertebral column and also spinal mobility and connective tissue disorders and spine and hypermobility, three articles were found in the subject ehlers-danlos syndrome in relation to the spine. No article was found in the subject on ehlers-danlos syndrome and spinal mobility.

In one of the articles Kozolowski et al, (1991) found flattening of the lumbar vertebrae's (platyspodyly) in three teenaged boys diagnosed with EDS. They suggest that this sign may be a sign of EDS but further research is needed and no conclusion could be drawn of these three patients.

In an article by Milhorat et al, (2007), 357 (12,7%) of 2813 patients were diagnosed with chiari malformation type I (CM-I) had a hereditary disorder of connective tissue (HDCT). Of these 357 patients 149 had the EDS hypermobility type and 96 patients had the EDS classical type. In this study they found an association of CM-I and HDCT and that patient with the combined disorder of HDCT and CM-I has varying degrees of occipitoatlantoaxial hypermobility which results in cranial settling, caudal displacement of the cerebellar tonsils and retroodontiod pannus formation.

In a study of 100 EDS patients (which type of EDS were not mentioned) 18 of the patients had some degree of scoliosis and 3 patients had a marked kyphosis at the thoraco-lumbar junction with a slight posterior slip of the 1$^{st}$ lumbar vertebrae. Two patients had a remarkably straight thoracic spine and absence of spinal curves. In several patients there were also an anterior wedging of the kyphotic part of the spine (Beighton and Horan, 1969)

Rozen et al, (2006) found generalized hypermobility (Beighton score 3-9) in 10 of 12 patients with new daily persistent headache. And in 11 of these 12 patients, hypermobility in the cervical spine were detected by evaluation of the ROM and palpation of the cervical spine by two physical therapists. The conclusion of this study was that hypermobility in the cervical spine may be a predisposing factor to new daily persistent headache.

In an article by Kim et al, (2013) an association of benign JHM and hypermobility in the lumbar spine and increased back pain, disability and limited physical motion in 32 young males (20-25 years) compared to 32 healthy non-JHM controls was made. Radiographs measured the lumbar spine mobility and they also found that the JHM group had increased lumbar intervertebral heights compared to the control group.

In another article by Czaprowski, (2014) 23,2% of 155 girls from age 9-18 years with idiopathic scoliosis was diagnosed with generalized joint hypermobility (GJH) compared to the control group 13,4% were diagnosed with GJH and was significantly higher in the group with idiopathic scoliosis. The study did not show any correlation between frequency of GJH and the angle of scoliosis but showed a slight difference in GJH frequency in girls with shorter curvature scoliosis (25%) compared to girls with longer scoliosis (10%). But the difference was not significant (P=0.25). No other relations were observed between joint hypermobility prevalence and curve size, curve pattern or number of vertebrae's within a curvature.

In a study of 37 boys and 38 girls aged 10-13 years diagnosed with GJH, the sagittal profile of the spine were measured with a digital Saunders inclinometer. In the study they found no significant differences in the children diagnosed with GJH compared to the control group with 197 girls and 150 boys in the sagittal profile (spinal curvatures) (Czaprowski and Pawlowska, 2013).

# 7 Conclusion[1,2]

The alternative hypothesis that EDS patients have a significant increased angle of the spine in full flexion, extension and lateral flexion compared to normal healthy individuals could be confirmed in this study. The greatest mobility difference in the sagittal plane seemed to be located at the sacrum and hip joint rather than the thoracic or lumbar spine. In right lateral flexion the EDS- group had significantly greater mobility in all parts of the spine from C7-S3. In left lateral flexion the EDS-group had significantly greater mobility in the thoracic and lumbar spine but in the left lateral flexion of the sacrum and hip joint the control group were significantly more mobile.

Regarding the spinal posture pattern in upright posture there were no significant differences between the two groups except in the frontal plane where the thoracic spine of the EDS-group showed a significantly greater lateral flexion curve than the control group.

In the FTF-test the EDS-group also showed a significantly greater mobility than the control group and could also be correlated with the findings of the Spinal mouse©.

Regarding a correlation between the palpation and the findings of the spinal mouse no correlation could be drawn because of too few subjects in the palpation with deviations from normal status.

Conclusion drawn from this study is that the alternative hypothesis, EDS patients have a significantly increased angle of the spine in full flexion, extension and lateral flexion compared to normal healthy individuals, is true. More clinical studies similar to the present study must be done to ensure the results.

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# 9. Appendix

## 9.1 Tables

Group statistics of the results of the hypothesis

| Group | | N | Mean | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| Left lateral flexion Inclination | CTR | 31 | 14,806 | 5,5101 | ,9896 |
| | EDS | 31 | 26,387 | 9,5731 | 1,7194 |
| Right lateral flexion Inclination | CTR | 31 | -14,258 | 8,0414 | 1,4443 |
| | EDS | 31 | -25,290 | 10,4186 | 1,8712 |
| Flexion inclination | CTR | 31 | 91,677 | 18,0137 | 3,2354 |
| | EDS | 31 | 104,290 | 16,5795 | 2,9778 |
| Extension inclination | CTR | 31 | -23,774 | 7,2558 | 1,3032 |
| | EDS | 31 | -30,581 | 14,1957 | 2,5496 |

T-test of the results from the hypothesis

| | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 95% Confidence Interval of the Difference | |
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| Left lateral flexion Inclination | Equal variances assumed | 7,861 | ,007 | -5,837 | 60 | ,000 | -11,5806 | 1,9839 | -15,5490 | -7,6123 |
| | Equal variances not assumed | | | -5,837 | 47,912 | ,000 | -11,5806 | 1,9839 | -15,5696 | -7,5916 |
| Right lateral flexion Inclination | Equal variances assumed | ,822 | ,368 | 4,667 | 60 | ,000 | 11,0323 | 2,3638 | 6,3040 | 15,7605 |
| | Equal variances not assumed | | | 4,667 | 56,381 | ,000 | 11,0323 | 2,3638 | 6,2977 | 15,7668 |
| Flexion inclination | Equal variances assumed | ,260 | ,612 | -2,868 | 60 | ,006 | -12,6129 | 4,3971 | -21,4084 | -3,8174 |
| | Equal variances not assumed | | | -2,868 | 59,592 | ,006 | -12,6129 | 4,3971 | -21,4097 | -3,8161 |
| Extension inclination | Equal variances assumed | 9,105 | ,004 | 2,377 | 60 | ,021 | 6,8065 | 2,8634 | 1,0789 | 12,5340 |
| | Equal variances not assumed | | | 2,377 | 44,674 | ,022 | 6,8065 | 2,8634 | 1,0382 | 12,5747 |

Sample test for different age groups

| Age at date of assessment [years] | | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 95% Confidence Interval of the Difference | |
| | | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| 18-35 | Left lateral flexion Inclination | Equal variances assumed | ,000 | ,994 | -5,283 | 21 | ,000 | -13,1061 | 2,4810 | -18,2656 | -7,9466 |
| | | Equal variances not assumed | | | -5,256 | 20,188 | ,000 | -13,1061 | 2,4935 | -18,3042 | -7,9079 |
| | Right lateral flexion Inclination | Equal variances assumed | ,902 | ,353 | 4,757 | 21 | ,000 | 13,4015 | 2,8172 | 7,5428 | 19,2603 |
| | | Equal variances not assumed | | | 4,728 | 19,998 | ,000 | 13,4015 | 2,8344 | 7,4890 | 19,3141 |
| | Flexion inclination | Equal variances assumed | ,091 | ,765 | -2,060 | 21 | ,052 | -12,0379 | 5,8423 | -24,1875 | ,1118 |
| | | Equal variances not assumed | | | -2,066 | 20,981 | ,051 | -12,0379 | 5,8261 | -24,1547 | ,0789 |
| | Extension inclination | Equal variances assumed | ### | ,003 | 3,428 | 21 | ,003 | 17,6970 | 5,1618 | 6,9624 | 28,4315 |
| | | Equal variances not assumed | | | 3,556 | 13,589 | ,003 | 17,6970 | 4,9770 | 6,9920 | 28,4020 |
| 36-55 | Left lateral flexion Inclination | Equal variances assumed | ### | ,018 | -3,447 | 32 | ,002 | -10,6181 | 3,0800 | -16,8918 | -4,3443 |
| | | Equal variances not assumed | | | -3,576 | 25,542 | ,001 | -10,6181 | 2,9694 | -16,7271 | -4,5090 |
| | Right lateral flexion Inclination | Equal variances assumed | ,918 | ,345 | 2,542 | 32 | ,016 | 9,3403 | 3,6741 | 1,8564 | 16,8242 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Equal variances not assumed | | | 2,583 | 31,331 | ,015 | 9,3403 | 3,6158 | 1,9690 | 16,7115 |
| Flexion inclination | Equal variances assumed | ,723 | ,401 | -1,456 | 32 | ,155 | -10,0278 | 6,8865 | -24,0551 | 3,9995 |
| | Equal variances not assumed | | | -1,440 | 29,324 | ,160 | -10,0278 | 6,9633 | -24,2624 | 4,2069 |
| Extension inclination | Equal variances assumed | ### | ,152 | -,255 | 32 | ,801 | -,7917 | 3,1088 | -7,1242 | 5,5408 |
| | Equal variances not assumed | | | -,260 | 30,671 | ,797 | -,7917 | 3,0484 | -7,0116 | 5,4282 |

T-test of results of differences in inclination between EDS and CTR group.

| | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 95% Confidence Interval of the Difference | |
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| Upright to left lateral flexion Inclination | Equal variances assumed | 8,495 | ,005 | 5,443 | 60 | ,000 | 11,0323 | 2,0270 | 6,9777 | 15,0868 |
| | Equal variances not assumed | | | 5,443 | 47,022 | ,000 | 11,0323 | 2,0270 | 6,9546 | 15,1100 |
| Upright to right lateral flexion Inclination | Equal variances assumed | ,622 | ,433 | -4,747 | 60 | ,000 | -11,2581 | 2,3715 | -16,0018 | -6,5144 |
| | Equal variances not assumed | | | -4,747 | 56,424 | ,000 | -11,2581 | 2,3715 | -16,0080 | -6,5082 |
| Left to Right Inclination | Equal variances assumed | 3,753 | ,057 | -5,498 | 60 | ,000 | -22,5161 | 4,0955 | -30,7083 | -14,3240 |
| | Equal variances not assumed | | | -5,498 | 50,388 | ,000 | -22,5161 | 4,0955 | -30,7405 | -14,2917 |
| Upright to flexion Inclination | Equal variances assumed | ,098 | ,755 | -2,575 | 60 | ,012 | -11,9355 | 4,6346 | -21,2062 | -2,6648 |
| | Equal variances not assumed | | | -2,575 | 59,719 | ,013 | -11,9355 | 4,6346 | -21,2070 | -2,6639 |
| Upright to extension Inclination. | Equal variances assumed | 8,719 | ,004 | 2,605 | 60 | ,012 | 7,4194 | 2,8486 | 1,7213 | 13,1174 |
| | Equal variances not assumed | | | 2,605 | 43,271 | ,013 | 7,4194 | 2,8486 | 1,6756 | 13,1631 |
| Flexion to extension Inclination | Equal variances assumed | 1,255 | ,267 | -3,328 | 60 | ,001 | -19,4194 | 5,8353 | -31,0917 | -7,7470 |
| | Equal variances not assumed | | | -3,328 | 57,051 | ,002 | -19,4194 | 5,8353 | -31,1041 | -7,7346 |
| Right lateral flexion Thoracic spine | Equal variances assumed | 8,524 | ,005 | 3,801 | 60 | ,000 | 9,9032 | 2,6057 | 4,6910 | 15,1154 |
| | Equal variances not assumed | | | 3,801 | 50,630 | ,000 | 9,9032 | 2,6057 | 4,6711 | 15,1353 |
| Right lateral flexion Lumbar spine | Equal variances assumed | 1,255 | ,267 | 2,798 | 60 | ,007 | 5,4839 | 1,9602 | 1,5629 | 9,4049 |
| | Equal variances not assumed | | | 2,798 | 59,650 | ,007 | 5,4839 | 1,9602 | 1,5624 | 9,4053 |
| Flexion Sacrum/Hip Joint | Equal variances assumed | ,004 | ,953 | -2,421 | 60 | ,019 | -11,0323 | 4,5566 | -20,1468 | -1,9177 |
| | Equal variances not assumed | | | -2,421 | 59,986 | ,019 | -11,0323 | 4,5566 | -20,1469 | -1,9177 |
| Flexion Thoracic spine | Equal variances assumed | 2,431 | ,124 | -,951 | 60 | ,346 | -2,3548 | 2,4771 | -7,3097 | 2,6000 |
| | Equal variances not assumed | | | -,951 | 56,271 | ,346 | -2,3548 | 2,4771 | -7,3165 | 2,6068 |
| Flexion Lumbar spine | Equal variances assumed | ,049 | ,826 | -,177 | 60 | ,860 | -,5161 | 2,9175 | -6,3520 | 5,3197 |
| | Equal variances not assumed | | | -,177 | 59,950 | ,860 | -,5161 | 2,9175 | -6,3521 | 5,3198 |
| Extension Sacrum/Hip Joint | Equal variances assumed | 1,409 | ,240 | 2,097 | 60 | ,040 | 6,4839 | 3,0924 | ,2981 | 12,6697 |
| | Equal variances not assumed | | | 2,097 | 58,325 | ,040 | 6,4839 | 3,0924 | ,2944 | 12,6733 |
| Extension Thoracic spine | Equal variances assumed | ,688 | ,410 | -,924 | 60 | ,359 | -3,6452 | 3,9465 | -11,5392 | 4,2489 |
| | Equal variances not assumed | | | -,924 | 58,150 | ,359 | -3,6452 | 3,9465 | -11,5444 | 4,2541 |
| | Equal variances assumed | 7,938 | ,007 | ,924 | 60 | ,359 | 2,7097 | 2,9340 | -3,1591 | 8,5785 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Extension Lumbar spine | Equal variances not assumed | ,924 | 50,604 | ,360 | 2,7097 | 2,9340 | -3,1816 | 8,6010 |

## 10. Declaration of Conformity

I hereby declare on oath, that I have written this thesis independently and that I have only used the sources and aids above mentioned. I have neither submitted this nor any other work elsewhere. Moreover, there is no conflict of interest between this work and other people and/or institutions.

Signature