Changes in motor-flexibility following anterior cruciate ligament reconstruction as measured by means of a leg-amplitude differentiation task with haptic and visual feedback

Eefje G.J. Roelofsen a, b, *, Robert van Cingel c, d, J. Bart Staal a, d, Maria W. G. Nijhuis-van der Sanden d, Ruud G.J. Meulenbroek b

a HAN University of Applied Sciences, Musculoskeletal Rehabilitation Research Group, P.O. Box 6960, 6503 GL Nijmegen, the Netherlands
b Donders Institute for Brain, Cognition and Behaviour, Centre for Cognition, Radboud University Nijmegen, P.O. Box 9104, 6500 HB Nijmegen, the Netherlands
c Sport Medical Center Papendal, Papendalslaan 7, 6816 VB Arnhem, the Netherlands
d Radboud University Medical Center, Scientific Institute for Quality of Healthcare, P.O. Box 9101, 6500 HB Nijmegen, the Netherlands

* Corresponding author at: HAN University of Applied Sciences, P.O. Box 6960, 6503 GL, Nijmegen, the Netherlands.
E-mail address: Eefje.Roelofsen@han.nl (E.G.J. Roelofsen).

https://doi.org/10.1016/j.clinbiomech.2020.105186
Received 2 December 2019; Accepted 28 September 2020
Available online 1 October 2020
0268-0033/© 2020 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

ARTICLE INFO

Keywords:
Adaptive movement behavior
Motor flexibility
Anterior cruciate ligament reconstruction
Visual feedback
Haptic feedback
Fear of harm

ABSTRACT

Background: In the current study changes in lower-limb motor flexibility of patients undergoing Anterior Cruciate Ligament Reconstruction were evaluated in relation to fear of harm.

Methods: Fourteen patients were measured pre- and post-surgery, and data were compared to those of a single measurement in fifteen controls. Lower-limb motor-flexibility was assessed in treadmill-walking and a cyclic leg-amplitude differentiation task augmented with haptic or visual feedback. Flexibility was captured by determining the between-leg coordination-variability (SD of relative phase) and each leg’s temporal variability (sample entropy). Patients were post hoc divided into a higher-fear-group (pre-surgery: n = 6, post-surgery: n = 7) and a lower-fear-group (pre-surgery: n = 6, post-surgery: n = 7) by means of a median split of their scores on a self-reported fear of harm scale. Differences in flexibility-measures between the higher-fear-group and the lower-fear-group were also assessed.

Findings: No pre- and post-surgery differences, nor differences with the control group, were found in motor-flexibility during treadmill-walking but the post-surgery higher-fear-group did show lower values of SD relative phase. In the leg-amplitude differentiation task the SD of the relative phase decreased but sample entropy increased post-surgery towards levels of the control-group. The pre-surgery higher-fear-group showed lower values of sample entropy in visual conditions.

Interpretation: While gait kinematics may not show motor-flexibility changes following anterior cruciate ligament reconstruction, a leg-amplitude differentiation task does show such changes. Differentiating patients on a fear-of-harm scale revealed subtle differences in motor-flexibility. Challenging patients with non-preferred movements such as amplitude differentiation may be a promising tool to evaluate motor-flexibility following ACLR.

1. Introduction

A common sport-related injury among young physically-active individuals is a rupture of the Anterior Cruciate Ligament (ACL) of the knee (Wiggins et al., 2016). When individuals are not able to cope with the ACL-deficiency or want to return to their high-demanding sports, an ACL-Reconstruction (ACLR) may be indicated. After one year, only half of the individuals undergoing ACLR manage to return to their pre-injury sport-level and for the athletes that return to sports, the odds of suffering a second tear are significantly increased (Ardern et al., 2014; Dekker et al., 2017; Paterno et al., 2015; Webster and Hewett, 2019; Wiggins et al., 2016). An ACLR can restore mechanical stability of the knee but the loss of mechanoreceptors and altered neuromuscular control can cause functional instability through decreased arthrokinematic-reflexes (Kim et al., 2017; Young et al., 2016).

Some individuals cope with the loss of proprioceptive information by optimizing muscle-stiffness regulation strategies to contribute to functional joint-stability (Swanik et al., 1997). However, increased muscle stiffness reduces motor-flexibility and leads to a more careful and rigid walking pattern. In this study, motor-flexibility refers to the capability of...
the human motor-system to quickly adapt to changes in individual, task and environment while maintaining motor-performance at an adequate level. Studies into stride-to-stride variability indeed found decreased variability in ACL-deficient individuals compared to the intact contralateral knee and to healthy control knees (Decker et al., 2011; Moraiti et al., 2007). However, some studies have found more variability in ACLR-participants compared to healthy controls (Davis et al., 2019; Leporace et al., 2013; Moraiti et al., 2009; Moraiti et al., 2010). Presumably, the individual feels secure to add extra motion after ACLR even though the proprioceptive channels are not yet restored.

According to optimal variability-theory (Stergiou et al., 2006) healthy movement behavior contains a certain amount of variability, needed to flexibly adapt to changes in the environment. Reduced movement-variability limits the ability to adapt to perturbations, while too much variability has been associated to limited motor control. Limiting the degrees of freedom might be a logical movement-strategy to cope with functional instability in gait. While this strategy might be adequate in low demanding activities, the risk for recurrent trauma will be considerable when returning to sport-specific situations in which one needs to respond to perturbations in complex, changing environments and under stringent time constraints.

Motor adaptations following ACL-injury and ACLR, leading to flexibility-reductions, can be related to higher attentional demands and more controlled motor planning. Electroencephalographic (EEG) studies and neuroimaging studies showed increased activity of cortical areas responsible for motor planning, sensory processing and visuo-motor control in ACLR-individuals compared with healthy controls (Baumeister et al., 2008; Baumeister et al., 2011; Grooms et al., 2015; Kapreli et al., 2009). Such increased attention and planning might be functional to cope with instability after ACLR-injury and during early stages of ACLR-recovery to facilitate connective tissue repair and to prevent potential damage. However, continuation of this cognitive-induced flexibility-reduction is maladaptive, because it limits the adaptability to a changing environment. In addition mechanical load facilitates connective tissue recovery crucial for the functional use of the knee. It is therefore important to gain more insight in factors involved in flexibility-changes after ACLR-injury and ACLR-recovery.

Fear of harm (FoH) may contribute to such cognitive-induced flexibility-reduction. FoH, such fear of re-injury, prompts excessive cognitive control and thus induces a more careful movement pattern. The prediction of harm causes the body to protect the knee in an effort to reduce the risk for re-injury (Vlaeyen and Linton, 2000). Despite growing evidence reporting an association between higher FoH and lower rate of return-to-play (Paterno et al., 2018; Tjong et al., 2014), increased risk for second ACL-injury (Paterno et al., 2018), asymmetric hop performance (Norte et al., 2019), lower peak knee, hip and trunk flexion during jump landing (Trigsted et al., 2018), and asymmetric quadriceps- (Lenz et al., 2015) and hamstring strength (Norte et al., 2019), to our knowledge, there is no evidence of the relation between FoH and lower-limb motor-flexibility in ACLR-patients.

Therefore, the present study aims: 1) to evaluate the lower-limb motor-flexibility of patients before and after ACLR during a treadmill-based walking task and a Leg-Amplitude Differentiation task (LAD-task (EGJ et al., 2016; Roelofsen et al., 2018; Roelofsen et al., 2020); see Appendix), and 2) to investigate to which extent FoH was associated with altered motor-flexibility. Outcome measures were between-leg stability (SD of relative phase between the legs), and temporal variability (sample entropy). We hypothesized that: 1) movement flexibility would be lower pre-ACLR compared to post-ACLR and compared to healthy controls, and 2) higher-FoH would be accompanied by decreased movement flexibility and a more controlled movement pattern.

2. Methods

2.1. Participants

ACLR-participants were recruited from Canisius Wilhelmina Hospital and Sint Maartens Kliniek, Nijmegen, the Netherlands and by online advertisement. Participants were recruited on the following criteria (van Melick et al., 2016): scheduled for ACLR-surgery, aged between 18 and 40, minimal 6–8 weeks after trauma, all types of grafts, no cognitive disorders; no neurological- or muscular diseases or co-morbidities which affect pain and function of the lower-limbs. In addition, the patients’ activity level before ACL-insufficiency was equal to seven or higher on the Tegner-score (engaging in sports minimal 2–5 times a week) (Tegner and Lysholm, 1985). Patients who fulfilled the criteria received an information letter. They had to contact the researcher by e-mail to indicate their willingness to participate in the study, after which potential candidates were assessed by means of a telephone interview. Age and gender-matched control-participants were recruited at Radboud University, Nijmegen, the Netherlands and met the following criteria: no cognitive disorders; no neurological disorders, no pain or complaints that could affect the function of the lower-limbs and Tegner-score ≥ 7. Prior to testing, an informed consent was provided. This study was conducted in accordance with the Helsinki Declaration and the regional medical ethical committee Arnhem and Nijmegen provided approval for the study (2014-1227).

2.2. Procedure

Participants were tested at the Radboud University, Nijmegen, the Netherlands. The ACLR-participants were tested prior to surgery (pre-ACLR) and again 18–20 weeks after surgery (post-ACLR). After 18–20 weeks sport-specific training can be intensified (van Melick et al., 2016) because the biological fixation of the graft has occurred (Pauzenberger et al., 2013). Healthy control participants were tested once. Participants started with the LAD-task after which their gait was analyzed.

2.3. Measures

2.3.1. Treadmill-walking task

Participants wore comfortable shoes and shorts and walked on a treadmill (ERGO-FIT 4000 vitality system, ERGO-FIT GmbH & Co. KG, Pirmasens, Germany) in three conditions: (1) self-indicated comfortable pace (2 min), (2) comfortable pace plus 20% (2 min), and (3) comfortable pace minus 20% (2 min). Two accelerometers (Kinetisense, Cleveland Medical Devices Inc., Ohio, 2011) were positioned to the upper- and lower-leg with 6 cm above- and 6 cm below the patella-center. The x-, y- and z-acceleration coordinates were recorded with a sample-frequency of 128 Hz.

Gait outcome-measures included preferred walking speed in m/s (as indicated on the treadmill-display), stride time (s) (ST), standard deviation of relative phase (SD φ) between the legs and sample entropy (SampEn). Relative phase gives an indication of the between-leg coordination pattern, which for gait centers around 180 degrees phase-difference. The SD φ reflects coordination-variability between the legs: lower SD φ-values reflect a greater stability and higher SD φ reflects more between-leg coordination-variability.

Sample entropy is a measure for temporal variability of the movements of the legs separately. Values close to 0 reflect a perfectly predictable time series and a SampEn converging towards infinity indicates a random time series, so lower SampEn-values indicate less flexibility of the leg-movements (Richman and Moorman, 2000).

Matlab (MATLAB 2012a, The MathWorks Inc., Natick, MA, 2000) was used to analyze the raw accelerometer-data. The raw data were filtered using a fourth-order, low-pass Butterworth filter with a cut-off frequency of 3 Hz. The filtered accelerometer-data were divided in three intervals corresponding to the speed of the treadmill. The middle
6,000 samples of each interval were included in the analysis to avoid variability due to the speed-condition changes. To calculate ST, the y-coordinates of the accelerometer-data of the upper-legs were used, representing the up-down movements of the upper legs in the sagittal plane. High-impact positive peaks, indicating the heel strikes of a stride-cycle, were determined by means of a peak detection procedure and time (in seconds) in between two high-impact positive peaks was calculated. Peak-detection was checked per participant and if necessary the threshold-value for peak-detection was manually adjusted (Lee and Lee, 2002).

Calculation of SD $\varphi$ and SampEn was done on the x-coordinates (forward-backward movements) of the data.

The SD $\varphi$ of the acceleration-signals between the legs was calculated by means of Batschelet's procedures (Batschelet, 1981; Meulenbroek et al., 1998). The SampEn was determined for each interval using the unfiltered acceleration-signals of the upper legs (in x-direction). SampEn $(m, r, N)$ is the negative natural logarithm of the conditional probability that two sequences that are similar for $m$ points remain similar at the next point $(m + 1)$. The number of data points $(N)$ in this study was 6000 samples. We adjusted the value for $m$ at 2 and $r = 0.2$, as recommended by studies regarding the regularity of cyclical human movement behavior (Richman and Moorman, 2000; Yentes et al., 2013).

### 2.3.2. Leg-amplitude differentiation-task

The LAD-task was exploited in earlier studies in healthy participants (Roelofsen et al., 2016), dancers (high-level of motor-skills) (Roelofsen et al., 2018) and in patients receiving Total Knee Replacement (Roelofsen et al., n.d.). In the LAD-task, participants were seated and instructed to make in-phase rhythmic movements of the left and right foot along the sagittal plane. Throughout the task participants generated a fixed amplitude of 150 mm with the reference-foot, and with the experimental-foot (the ACL-deficient or ACL-reconstructed leg in ACLR-participants) either the same amplitude (150 mm), or 30 mm less (120 mm) or 60 mm less (90 mm). Four feedback-conditions were tested in a random order: haptic passive (HP), haptic tracking (HT), visual-derical (VV) and visual-enhanced (VE). In the two haptic-conditions movements were guided by two human-drivers while in the visual-conditions the participants needed to move as accurately and quickly by their-selves. The experimental set-up of the task is shown in Fig. 1 and explained in detail in the Appendix.

The movements of the feet in the LAD-task were recorded by two infrared-emitting diodes (IREDS) placed on the lateral malleoli of the participants’ ankles. Translations of the IREDS were recorded with a 3D motion tracking system OPTOTRAK 3020, Northern Digital Inc., Waterloo, Canada at 100 Hz and a spatial accuracy of 0.2 mm. The outcome-measures of the LAD-task were amplitude-differentiation of the feet-movements (in mm), SD $\varphi$ and SampEn of the feet-movements reflecting coordination-variability between the feet-movements and temporal variability of the feet-movements.

The position-time data in the x-dimension (backward-forward movements) were interpolated and filtered with a second-order, dual-pass Butterworth, low-pass filter with a cut-off frequency of 5 Hz (EGJ et al., 2016). Based on a zero-crossing search algorithm, successive cycles were extracted. The first and last cycle of the trial were excluded from analysis. For each obtained movement-cycle the amplitude (mm) of the in-out dimension was calculated to determine the mean amplitude per 30-s trial. The amplitude-differentiation of the feet per trial was calculated by subtracting the amplitude of the experimental-foot from the amplitude of the reference-foot. The SD $\varphi$ and the SampEn-values were also calculated per trial.

### 2.3.3. Fear of harm

Pre- and post-ACLR, participants filled out the Photographic Sports Activity-Anterior Cruciate Ligament Reconstruction (PHOSA-ACLR). The PHOSA-ACLR is a valid and reliable instrument for the assessment of perceived harmfulness of different physical activities after ACLR (Van Lankveld et al., 2017). The instrument consists of 12 photographs depicting sports-related movements that may invoke FoH after ACLR. Participants were asked to score each activity that was depicted from 0 to 10, where 0 is ‘not harmful at all’ and 10 is ‘extremely harmful’. The average score was calculated by dividing the total score by 12.

### 2.4. Statistical analysis

Normally of outcome measures was assessed by evaluation of Q-Q plots and Kolmogorov-Smirnov test and statistical difference was accepted with $P < 0.05$.

#### 2.4.1. Gait-measures

To evaluate differences between pre-ACLR and post-ACLR of the normally distributed gait-measures (ST, and log-transformed SampEn-values) paired t-tests were used. For the non-normally distributed SD $\varphi$ a Wilcoxon Signed Ranks test was performed. To test for differences between ACLR and controls, the pre-ACLR and post-ACLR outcomes were compared with outcomes of the control-group with two independent t-tests. For SD $\varphi$, two Mann-Whitney tests were performed.

#### 2.4.2. Leg amplitude differentiation-task measures

The amplitude differentiation, SD $\varphi$ between the feet and the log-transformed SampEn of both feet were submitted to separate repeated measures analysis of variance (ANOVA) with feedback-condition (HP, HT, VV, VE), amplitude difference (0 mm, 30 mm, and 60 mm) and ACLR (pre-ACLR and post-ACLR) as within-subject factors. Comparisons with the control-group was done by means of two repeated-measures ANOVA’s (pre-ACLR vs control, and post-ACLR vs control) with feedback-condition and amplitude difference as within subject factors and group (pre-ACLR versus control, and post-ACLR versus control) as between-subjects factor. Analysis focused on pre- and post-surgery-differences and group-differences. Post-hoc contrasts were conducted with paired-t-test or independent-t-test for within- or between-group effects, respectively.

#### 2.4.3. Fear of harm

To test to which extent FoH was associated with altered motor-flexibility measures, ACLR-participants were divided into two groups: 1) the lower-fear-group and 2) the higher-fear-group by means of a median split based on their total average PHOSA-ACLR-score. The median-split procedure was done pre-ACLR (median: 5.92) and again post-ACLR (median: 4.58). Differences between the lower-fear- and higher-fear-group in SD $\varphi$ and SampEn-values of the treadmill-walking-task and the LAD-task were tested pre-ACLR and post-ACLR with a Mann-Whitney-U test.

### 3. Results

Sixteen ACLR-participants were included pre-ACLR, from which one participant was excluded because gait-data were lost, and one participant was excluded because of poor visibility of IRED-data during the LAD-task. Mean time (SD) between surgery and post-ACLR measurement was 20.74 (3.79) weeks. Fifteen gender- and age-matched controls were included. There were no differences between demographics of both groups (see Table 1).

#### 3.1. Gait measures

In Table 2, gait measures are presented. Preferred walking speed of the ACLR-participants did not differ from controls ($P > 0.05$). In addition, no differences were found in ST, SD $\varphi$ and log-transformed SampEn between pre-ACLR and post-ACLR and there was also no difference between the ACLR-group and the control-group.
Fig. 1. Experimental set up. A. Side view of the experimental setup in the haptic conditions. The drivers were separated from each other and from the participant by hardboard partitions. On the left the driver of the left foot is visible and on the right the participant seated in the chair with his feet on the sliding foot supports. The drivers moved the handles in time with the high and low tones of the auditory pacing signal which they heard over headphones. B. Close up of the feet on the sliding foot supports. C. Rear view of the participant in the visual veridical condition. On the screen, the participant received visual information that required the left foot to make a small movement and the right foot to make a large movement. D. Visual feedback in the visual-veridical condition. The green cursors moved up and down congruent with the in and out motions of the feet. The left cursor corresponded to the left foot, while the right cursor corresponded to the right foot. The different amplitudes of the bars are a direct reflection of the required amplitudes of the feet: the right foot (the experimental foot) had to make an amplitude of 120 mm and the left foot (the reference foot) had to produce an amplitude of 150 mm. E. Visual feedback in the visual-enhanced (VE) condition. Equal bars were shown in every amplitude-condition, no matter which amplitude difference was required. F. Condition, feedback-type and instruction that was given to the participants. For further details of the experimental setup and the LAD-task, see Appendix. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

| Condition               | Feedback type       | Instruction                                                                 |
|-------------------------|---------------------|------------------------------------------------------------------------------|
| Haptic passive (HP)     | Haptic feedback     | Let the feet be dragged by the sliders, moved by the drivers. (Passive motion) |
| (panel A and B)         |                     |                                                                               |
| Haptic tracking (HT)    | Haptic feedback     | Move along with movements of the sliders, moved by the drivers. (Guided motion) |
| (panel A and B)         |                     |                                                                               |
| Visual-veridical (VV)   | Augmented visual feedback | Move the feet to move the green cursors between the two dark-blue targets at the ends of the rectangular bars. |
| (panel B, C and D)      |                     |                                                                               |
| Visual-enhanced (VE)    | Augmented manipulated visual feedback | Move the feet to move the green cursors between the two dark-blue targets at the ends of the rectangular bars. |
| (panel B, C and E)      |                     |                                                                               |
values are displayed with three decimals hence the minimal differences between values. There was no effect for ACLR and no effect for group.

### 3.2. Leg amplitude differentiation-task

#### 3.2.1. Amplitude differentiation

Target amplitudes were reached with high accuracy in HP, HT and VV. In VE the distance between target amplitudes and realized amplitudes was largest. There was no effect for ACLR and no effect for group nor an interaction with group.

#### 3.2.2. SD of relative phase

As seen in Fig. 2, SD φ between the feet was higher in the visual conditions compared to haptic conditions and showed a gradual increment with required amplitude difference between the feet.

Pre-ACLR - post-ACLR SD φ was higher pre-ACLR compared to post-ACLR (see Fig. 2). This effect was even more pronounced in visual conditions. The RM-ANOVA confirmed this with a main effect for ACLR: F (1, 12) = 18.03, P = 0.001 and an interaction between feedback-condition and ACLR: F (3, 36) = 9.12, P = 0.002. Post-hoc, paired t-tests between pre-ACLR and post-ACLR showed significant differences in VV, VE and HP, P < 0.05.

ACLR - control. The RM-ANOVA showed no effect for group (pre-ACLR-control), indicating that SD φ pre-ACLR was comparable to SD φ of controls (see Fig. 2). The RM-ANOVA (post-ACLR-control) revealed a significant effect of group (F (1, 25) = 5.95, P = 0.022, the post-ACLR SD φ was lower compared to controls. This effect was more pronounced in the visual conditions. Post hoc independent t-tests showed significant differences between post-ACLR and controls in VV, VE and HP (P < 0.05).

#### 3.2.3. Sample entropy

Sample Entropy-values of the experimental-foot (E) and the reference-foot (R) were lower in visual conditions (excluding post-ACLR) compared to haptic conditions (see Fig. 3).

Pre-ACLR - post-ACLR. In visual conditions SampEn-values were higher post-ACLR compared to pre-ACLR. SampEn-values in haptic conditions were comparable (see Fig. 3). The RM-ANOVA (post-ACLR-control) showed no significant effect for group (pre-ACLR - post-ACLR). The RM-ANOVA (post-ACLR-control) revealed a significant interaction between feedback-condition and group (see Fig. 3). However, the RM-ANOVA (post-ACLR-control) showed no significant effect and no significant interaction between condition and group (see Fig. 3). In visual conditions the post-ACLR SampEn-values were higher compared to controls with P < 0.05. In haptic conditions, values were comparable, except in the experimental-foot; SampEn-values were lower post-ACLR compared to control (P < 0.05).

#### 3.3. Higher-fear vs lower-fear

As can be seen in the upper part of Table 3, the average PHOSA-ACLR score of the higher-fear was significantly higher compared to the lower-fear-group; post-ACLR (P = 0.005) and pre-ACLR (P = 0.003). Based on the median-split procedure, three participants switched from the higher-fear-group pre-ACLR to the lower-fear-group post-ACLR, and two participants switched from the lower-fear-group pre-ACLR to the higher-fear-group post-ACLR. In addition, the pre-ACLR data of the PHOSA-ACLR score was missing. In the middle part of Table 3, flexibility-measures of the higher-fear and the lower-fear-group during treadmill-walking are displayed. Flexibility-measures of the gait task did not differ between the higher-fear and lower-fear-group during treadmill-walking. Flexibility-measures of the gait task did not differ between the higher-fear and lower-fear-group during treadmill-walking. Flexibility-measures of the gait task did not differ between the higher-fear and lower-fear-group during treadmill-walking. Flexibility-measures of the gait task did not differ between the higher-fear and lower-fear-group during treadmill-walking. Flexibility-measures of the gait task did not differ between the higher-fear and lower-fear-group during treadmill-walking.

### Table 1

Demographics.

|                      | Anterior Cruciate Ligament-Reconstruction (n = 14) | Control (n = 15) | p-value |
|----------------------|---------------------------------------------------|------------------|---------|
| Age years (SD)       | 23.2 (4.8)                                        | 23.1 (3.4)       | 0.964   |
| Sex (n male/ female) | 11/3                                              | 10/5             | 0.403   |
| Operated leg (n left/right) | 5/9                                                 |                  |         |
| Graft∗ (Synt/ Ham/ Don) | (111/1)                                             |                  |         |
| Footedness (n left/right/both) | 5/8/1                                               |                  |         |

∗ = Type of graft used in ACLR-surgery; Synt = Synthetic donor material; Ham = Hamstrings tendon; Don = Human donor material.

### Table 2

Gait measures.

|                      | ACLR Pre-ACLR Mean (SD) | Post-ACLR Mean (SD) | Control Mean (SD) |
|----------------------|-------------------------|---------------------|------------------|
| Preferred walking speed (m/s) | 3.55 (1.08)              | 3.29 (1.10)         |                  |
| Stride Time PREF (s) | 1.257 (0.214)            | 1.260 (0.213)       | 1.247 (0.179)    |
|                      | (unaffected)             | (unaffected)        | (unaffected)     |
| Stride Time PREF + 20% (s) | 1.182 (0.204)            | 1.205 (0.311)       | 1.183 (0.163)    |
|                      | (unaffected)             | (unaffected)        | (unaffected)     |
| Stride Time PREF-20% (s) | 1.406 (0.262)            | 1.360 (0.211)       | 1.414 (0.209)    |
|                      | (unaffected)             | (unaffected)        | (unaffected)     |
| SD φ PREF | 63.46 (13.47)             | 64.06 (10.47)       | 67.69 (8.16)     |
| SD φ PREF + 20% | 61.60 (12.84)             | 60.35 (15.02)       | 64.88 (8.90)     |
| SD φ PREF-20% | 65.23 (14.79)             | 68.26 (7.56)        | 64.88 (10.56)    |
| SampEn PREF | 0.56 (0.09)              | 0.53 (0.07)         | 0.55 (0.16)      |
|                      | (affected)               | (unaffected)        | (unaffected)     |
| SampEn PREF + 20%   | 0.55 (0.09)              | 0.57 (0.08)         | 0.54 (0.13)      |
|                      | (affected)               | (unaffected)        | (unaffected)     |
| SampEn PREF-20%     | 0.57 (0.08)              | 0.53 (0.06)         | 0.58 (0.06)      |
|                      | (affected)               | (unaffected)        | (unaffected)     |
| SampEn PREF-20%     | 0.55 (0.10)              | 0.57 (0.06)         | 0.57 (0.05)      |
|                      | (affected)               | (unaffected)        | (unaffected)     |
| SampEn PREF-20%     | 0.58 (0.10)              | 0.48 (0.03)         | 0.53 (0.07)      |
|                      | (affected)               | (unaffected)        | (unaffected)     |
| SampEn PREF-20%     | 0.53 (0.10)              | 0.51 (0.08)         | 0.53 (0.06)      |

SD = Standard deviation; PREF = preferred walking speed; PREF+20% = preferred walking speed +20% of preferred walking speed; PREF-20% = preferred walking speed - 20% of preferred walking speed. Note: stride time-values are displayed with three decimals hence the minimal differences between values.

### 4. Discussion

When comparing lower-limb motor-flexibility in a treadmill-walking task of patients before and after Anterior Cruciate Ligament Reconstruction (ACLR) no flexibility-changes due to ACLR were found.
However, when confronted with the LAD-task ACLR-participants showed decreased between-leg variability and increased temporal variability post-ACLR in the visual feedback-conditions. Moreover, subtle reductions in motor-flexibility in participants with higher FoH-scores confirmed our hypothesis that Fear of Harm (FoH) would be associated with altered motor-flexibility.

Contrary to our hypothesis, no differences were found in motor-flexibility due to ACLR in treadmill-walking. In addition, the gait-flexibility of the ACLR-group was comparable to that of the control-group. The results differ from a previous study showing a significant increase in coordination-variability (SD $\phi$) in a ACLR-group compared to a healthy control-group (Armitano et al., 2018). However, the latter study focused on over-ground walking, while the current study focused on treadmill-walking. The use of a motorized treadmill has been found to reduce stride-to-stride variability across multiple gait-parameters, potentially by exerting a time-constraint on the participants’ gait (Dingwell et al., 2001; Hollman et al., 2016). Secondly, the current study used the SD of the continuous $\phi$ instead of the discrete $\phi$, because in walking, the phase-plane motion does not approximate a circle and this becomes even more apparent if asymmetries exist between the legs (Donker, 2002; Donker et al., 2001).

The current study found no effect of ACLR on motor-flexibility during treadmill-walking when comparing all ACLR-participants. However, dividing the participants in a higher-fear-group and a lower-fear-group resulted in a significantly lower between-leg variability in the higher-fear-group. This confirmed our second hypothesis. The reason why ACLR did not affect motor-flexibility in gait, but ACLR combined with FoH did, may be found in the fact that steady-state walking eliminates the need for increased attention and contributions from higher cortical brain-areas (Koenraadt et al., 2014; Takakusaki, 2013). Therefore, during treadmill-walking the focus of attention of the individual does not necessarily need to change and can remain to be directed to the environment. This allows for optimal motor-flexibility needed to flexibly...
react to sudden changes in environment or task-constraints. In other words, the constraints that may still exist 20 weeks after ACLR no longer hamper motor-flexibility in treadmill-walking. However, FoH possibly results in higher attention and an internal focus, which lead to a subtle decrease in motor-flexibility (smaller SD ɸ). Diminishing motor-flexibility might be a strategy to protect the knee for potential damage. This initial protective response is potentially harmful because it diminishes flexibility, by interfering with automated motor control, and prevents the athlete to react adequately and fast in high-demanding sport-situations (Giesche et al., 2018; Swainik, 2015). This might increase the risk of poor sports-performance and re-injury.

A recent study into the relation between kinesiophobia and gait-characteristics in physically active individuals with ACLR failed to find significant correlations between gait-parameters and kinesiophobia (Luc-Harkey et al., 2018). However, the kinematic gait-parameters in that study (self-selected gait-speed, peak ground-reaction forces and knee-flexion excursion of the ACLR-limb) were not focused on measures of motor-flexibility, whereas our study was. Therefore, both studies measured different constructs.

In line with the cognitive rationale, we presumed that motor-flexibility changes due to mechanical or persistent functional instability following ACLR become apparent when challenging ACLR-individuals with attention-demanding tasks, for example, by increasing task-difficulty. Therefore, we developed the LAD-task that required participants to make cyclic in-phase forward-backward movements of different amplitudes with the feet. Our LAD-task was challenging given the regular anti-phase and amplitude-symmetric character of locomotion. In contrary to the gait-measures, the results of the LAD-task showed a clear effect of ACLR on motor-flexibility in the visual conditions: pre-ACLR between-leg variability and temporal variability of each foot were comparable to healthy controls. However, post-ACLR the between-leg variability clearly decreased while temporal variability increased. An explanation for this result might be that pre-ACLR participants are used to cope with their ACL-insufficiency in such a way that reduction of motor-flexibility is prevented and their attention is focused on environment. The mean time (SD) in months between ACL-trauma and reconstructive surgery in this study was eleven (11) months. All participants in this study have first attempted a conservative treatment consisting of strengthening the quadriceps muscles to cope with the mechanical instability due to ACL-deficiency. This gives ACL-insufficient individuals a considerable amount of time to adapt to the instability they may experience. ACLR-surgery might be associated with a decreased neuromuscular control and a longer period of limited motor-flexibility. Limiting motor-flexibility by increasing between-leg stability might be a functional protective response after ACLR to cope with decreased neuromuscular control and to protect the vulnerable ACL-graft from damage. Since we found reduced post-ACLR between-leg variability in gait associated with higher FoH, we suggest that this protective response is associated with increased attention.

While between-leg variability decreased after surgery, temporal variability increased. Presumably, adding more between-leg stability might be a compensation-strategy to cope with an excessive amount of temporal variability. The results concerning temporal variability were in line with our hypothesis and with recent literature in gait revealing that ACLR-individuals show more temporal variability compared to healthy controls (11–14); possibly, the individual feels more secure to add extra motion, however the proprioceptive channels are not (yet) restored resulting in more temporal variability compared to healthy controls. Although, temporal variability overall increased post-ACLR, we found that participants in the higher-fear-group showed reduced temporal variability compared to the lower-fear-group in the visual conditions of the LAD-task. Again, this was in line with our cognitive hypothesis.

In contrast to the visual conditions, in the haptic conditions there was no effect of ACLR. ACLR-participants performed the LAD-task with haptic feedback with equal accuracy and motor-flexibility as healthy age-matched controls. This finding suggests that ACLR-insufficiency and ACLR do not limit the ability to follow movements that were haptically-imposed. As discussed in earlier work (Roelofsen et al., 2016), due to a direct perception-action coupling, haptic feedback presumably bypasses cognitive control by eliminating the need to plan movements. Therefore, haptic feedback might be a relevant tool in obviating high-level planning of movements in patients that persist in limited motor-flexibility and/or cope with FoH, i.e. a state of increased cognitive control. The present study confirmed this for ACLR-participants.

The current work had some limitations. A limitation of the study is that due to loss to follow up in the ACLR-group, ACLR-participants and age- and gender-matched controls could not serve as participant-pairs in statistical analyses.

Secondly, for further research it is recommended to include more

### Table 3

Higher-fear vs lower-fear.

| Source                  | Higher-fear Mean (SD) | Lower-fear Mean (SD) | P-value |
|-------------------------|-----------------------|----------------------|---------|
| Pre-ACLR (Post-ACLR)    | 6.86 (1.09)           | 3.93 (1.38)          | 0.005 * |
| Post-ACLR (Post-ACLR)   | 5.66 (1.12)           | 3.04 (0.72)          | 0.003 * |

Note that ACLR-participants were divided into the higher-fear and lower-fear group based on a median-split procedure of the PHOSA-ACLR score (pre-ACLR, median: 5.92, post-ACLR median: 4.58), as a result three subjects switched from the higher-fear-group pre-ACLR to the lower-fear-group post-ACLR and two subjects switched from lower-fear-group pre-ACLR to the higher-fear-group post-ACLR. In addition, the PHOSA-ACLR data of two pre-ACLR and two subjects switched from lower-fear-group pre-ACLR to the higher-fear-group based on a median-split procedure of the PHOSA-ACLR score (pre-ACLR median: 5.92, post-ACLR median: 4.58), as a result three subjects switched from lower-fear-group pre-ACLR to the higher-fear-group post-ACLR, median: 5.92, post-ACLR median: 4.58, 0.046 *.

While between-leg variability decreased after surgery, temporal variability increased. Presumably, adding more between-leg stability might be a compensation-strategy to cope with an excessive amount of temporal variability. The results concerning temporal variability were in line with our hypothesis and with recent literature in gait revealing that ACLR-individuals show more temporal variability compared to healthy controls (11–14); possibly, the individual feels more secure to add extra motion, however the proprioceptive channels are not (yet) restored resulting in more temporal variability compared to healthy controls. Although, temporal variability overall increased post-ACLR, we found that participants in the higher-fear-group showed reduced temporal variability compared to the lower-fear-group in the visual conditions of the LAD-task. Again, this was in line with our cognitive hypothesis.

In contrast to the visual conditions, in the haptic conditions there was no effect of ACLR. ACLR-participants performed the LAD-task with haptic feedback with equal accuracy and motor-flexibility as healthy age-matched controls. This finding suggests that ACLR-insufficiency and ACLR do not limit the ability to follow movements that were haptically-imposed. As discussed in earlier work (Roelofsen et al., 2016), due to a direct perception-action coupling, haptic feedback presumably bypasses cognitive control by eliminating the need to plan movements. Therefore, haptic feedback might be a relevant tool in obviating high-level planning of movements in patients that persist in limited motor-flexibility and/or cope with FoH, i.e. a state of increased cognitive control. The present study confirmed this for ACLR-participants.

The current work had some limitations. A limitation of the study is that due to loss to follow up in the ACLR-group, ACLR-participants and age- and gender-matched controls could not serve as participant-pairs in statistical analyses.

Secondly, for further research it is recommended to include more
participants to increase the power of the study. The post-hoc subdivision in a higher-fear, lower-fear-group power was too low to formulate a reliable statement about the association between FoH and motor-flexibility. However, despite the small group-sizes, significant effects were found.

Thirdly, our follow up period was limited to 20 weeks after ACLR. This is on the verge of the start of more demanding training such as agility training and sport-specific training (van Melick et al., 2016). It might be interesting to monitor motor-flexibility also in early stages post-ACLR, when challenging sport-specific tests are not yet safe to exploit.

Despite these limitations, the current study showed that challenging ACLR-participants with an unusual task can detect motor-flexibility changes due to more cognitive control related to FoH. The current task and motor-flexibility measurements can be safe and unloaded additions to the early stages of rehabilitation protocols in which sport-specific testing is not yet possible. Further research is required to explore the evaluative qualities of the LAD-manipulation and feedback-strategies to monitor motor control-changes in ACLR-individuals.

5. Conclusion

Anterior Cruciate Ligament-Reconstruction is not accompanied by changes in motor-flexibility during treadmill-walking, but challenging patients with a leg-amplitude differentiation task does show such changes. Differentiating patients on a fear-of-harm scale revealed subtle reductions in motor-flexibility.

Author statement

Eefje Roelofsen: Conceptualization, methodology, software, data curation, formal analysis, writing –original draft, writing- revised manuscript and point-by-point reply, visualization.

Robert van Cingel: Conceptualization, resources, writing-review and editing.

Bart Staal: Conceptualization, writing-review and editing.

Maria Nijhuis- van der Sanden: Conceptualization, supervision, writing- review and editing.

Ruud Meulenbroek: Conceptualization, methodology, validation, supervision, writing- review and editing.

Declaration of Competing Interest

This research did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements

The authors wish to acknowledge Mark van de Hei, Gerard van Oijen and Hubert Voogd for their technical support, Canisius Wilhelmina Hospital and Sint Maartens Kliniek and their patients for their participation in the study, and Pascal Rehr for his assistance with data acquisition. This research did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix A. The leg-amplitude differentiation task (LAD-task)

Paradigm

The LAD-task is developed as a tool to assess if high-level planning is preventing individuals from exploiting their movement options. Our hypothesis was that presenting individuals with multi-sensory feedback will help to automatically select and guide appropriate motor actions via bottom-up controlled pathways. Due to a direct perception-action coupling, haptic feedback obviates cognitive control and therefore complex movements, which normally require high-level planning, become more fluent, accurate and effortless. Enhanced visual feedback is presumed to have a similar effect: presenting a task visually as a simple task results in less involvement of attentional control and thus to better task performance. In previous studies the LAD-task was developed and tested in healthy participants, dancers, and participants before and after Total Knee Replacement.

Set up

Participants were seated on a desk chair in front of a table (both height adjustable) facing a computer screen that provided instructions and on-line visual feedback about task performance. The participants knee angle was 90° and the table top prevented participants from seeing their legs and feet (see Fig. 1 A and C). Participants wore shorts and placed their bare feet on a marked center on two parallel aluminum foot sliders mounted on linear guides that allowed for motion in the sagittal plane. The sliders could be moved back-and-forth by the participant’s foot displacements, but were also mechanically coupled with driver handles that could be displaced by two trained confederates (the “drivers”; Fig. 1 A). The participant was separated from the two drivers with hardboard partition separated them, and the drivers were also separated from each other with a hardboard division. The drivers were informed about the amplitude of the movements they were supposed to produce by colored lines on a ruler next to the guiding system on the floor: the amplitude of 120 mm was indicated by two red lines, the amplitude of 90 mm was indicated by two blue lines, and the amplitude of 60 mm was indicated by two green lines. Prior to each trial, the drivers were informed about the colour of the guidelines between which they had to move. The direction (backwards or forwards) and the frequency of the movements was imposed to the drivers via headphones. The movement frequency was indicated by a computer-generated auditory pacing signal of 1.36 Hz. A forward push was instructed by a low tone, whereas a high tone instructed the driver to pull the handle back, resulting in the generation of 20 motion-cycles in 30 s (0.67 Hz). Human drivers were used in the experimental set up instead of an electro-mechanical steering device, because this best represent a therapeutic situation in which the therapist and patient move together in a joint action.

Task conditions

Participants were instructed to make in-phase rhythmic movements of the left and right foot along the sagittal plane. Throughout the task, participants generated a fixed amplitude of 150 mm with the reference-foot, and with the experimental-foot either the same amplitude as the reference-foot (150 mm), or 30 mm less (120 mm) or 60 mm less (90 mm). In the ACLR-subjects, the foot that served as experimental-foot was similar to the operated side (i.e. left or right) (see Table 1). The foot that served as experimental-foot was matched within a participant-pair (ACLR-control).

Four different feedback-conditions were tested in a random order. In the two haptic conditions movements were guided by two drivers (see Fig. 1 A) while in the visual conditions the participants needed to move as accurately and quickly by their selves (see Fig. 1. C, D and E).

Haptic passive (HP) condition: the subjects were asked to let their feet be dragged by the sliders on which their feet rested. Subjects focused on the computer screen in front of them to maintain a fixed trunk position and to prevent them from seeing their legs to be moved. The drivers moved the foot supports on the rhythm of the auditory pacing sound.

Haptic tracking (HT) condition: the conditions were the same as described above, however the subjects were instructed to move along with the movements of the sliders, which were moved by the same two drivers.

Visual-veridical (VV) condition: no drivers were involved and the participants had to produce the requested foot movements themselves.
relying on visual feedback presented on the computer screen in front of them. Two rectangular bars represented the amplitude of the left and right foot movements, and two green cursors corresponded with the position of the left and right foot. The green cursors moved between the dark-blue ends of the two bars by moving the feet back and forth. The participants had to move their feet back and forth to move the green cursor between the two dark-blue targets at the ends of a rectangular bars. As shown in Fig. 1 D, the feedback on the screen corresponded directly to the required slider motions.

Visual-enhanced (VE) condition: the participants had to produce the left and right foot movements on the basis of the same visual feedback as in the VV-condition, however the visual feedback was manipulated. The left and right bars on the screen were of the same length as shown in Fig. 1 E and the visual feedback in the VE condition was presented as if equal amplitudes were required. However, in two out of the three amplitude-conditions an amplitude difference was required because the motion of the foot supports to the depicted target motion was adjusted with a factor 1.25 (120 to 150 mm) and 1.67 (90 to 150 mm).

Each condition consisted of a block of 10 trials and each trial had a length of 30 s, resulting in 120 trials that were performed in approximately 1.5 h. Between conditions, a short break of approximately 5 min was introduced.

References

Ardern, C., Taylor, N., Feller, J., Webster, K.E., 2014. Fifty-five per cent return to competitive sport following anterior cruciate ligament reconstruction surgery: an updated systematic review and meta-analysis including aspects of physical functioning and contextual factors. Br J Sports Med. 48 (21).

Armitano, C.N., Morrison, S., Russell, D.M., 2018. Coordination stability between the legs is reduced after anterior cruciate ligament reconstruction. Clin Biomech [internet] 58 (April 2019). https://doi.org/10.1016/j.clinbiomech.2018.07.003, 28-35. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC445594.

Batschelet, E.B., 1981. Circular Statistics in Biology. Academic Press, London.

Baumeister, J., Reinecke, K., Weis, M., 2008. Changed cortical activity after anterior cruciate ligament reconstruction in a joint position paradigm: an EEG study. Scand J Med Sci Sport. 18 (4), 473-481.

Baumeister, J., Reinecke, K., Schubert, M., Weiss, M., 2011. Altered electrocortical brain activity after ACL reconstruction during force control. J. Orthop. Res. 29 (9), 1383-1390.

Davis, K., Williams, J.J., Sanford, B.A., Zucker-Levin, A., 2019. Assessing lower extremity coordination and coordination variability in individuals with anterior cruciate ligament reconstruction during walking. Gait Posture [internet] 67 (February 2018). https://doi.org/10.1016/j.gaitpost.2018.01.010, 1560-1567. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6178909.

Decker, L.M., Moraiti, C., Stergiou, N., Georgoulis, A.D., 2011. New insights into anterior cruciate ligament deficiency and reconstruction through the assessment of knee kinematic variability in terms of nonlinear dynamics. Knee Surg Sports Traumatol Arthrosc [internet] 19 (10). Oct [Cited 2014 Apr 29], 1620-33. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21445594. Dekker, T.J., Godin, J.A., Dale, K.M., Garrett, W.E., Taylor, D.C., Riboh, J.C., 2017. The effect of anterior cruciate ligament reconstruction on stride-to-stride variability. Arthrosc - J Arthrosc Relat Surg [internet] 29 (10). https://doi.org/10.1016/j.arthro.2013.05.009, 1712-21. Available from: https://michael.shooman.jr, 2006 Jan. Psychological time-series analysis using approximate entropy and sample entropy. Am. J. Physiol. Heart Circ. Physiol. 287 (6), H2009-H2049.

Roelofsen, E.G.J., Boga, J., Rosenbaum, D.A., Nijhuis-van der Sanden, M.W.G., Hullegie, W., van Cingel, R., et al., 2016. Haptic feedback helps bipedal coordination. Exp Brain Res [internet] 234 (10) https://doi.org/10.1007/s00221-015-4369-3, 1293-1306. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26954952.

Swanik, C.B., Lephart, S.M., Giannantonio, F.P., Fu, F.H., 1997. Reestablishing muscle activation in women after ACL reconstruction. Knee Surgery, Sport Traumatol Arthrosc [internet] 5 (6), 291-294. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9291605.

Swanik, C.B., 2015. Brains and sprains: the brain plasticity of knee ligamentization.” Development and validation of the Photographic Series of Sports Activities for Functional Performance and Second ACL Injury After ACL Reconstruction and Return to Sport: a pilot study. Sports, Health. 10 (3), 228-233.

Tong, V.K., Murganahan, M.L., Nyhof-Young, J.M., Ogilvie-Harris, D.J., 2014. A qualitative investigation of the decision to return to sport after anterior cruciate ligament reconstruction. J. Physiotherapy. 60 (3), 180-187. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24934805.

Van Lankveld, W., Van Melick, N., Habez, B., Roelofsen, E., Staal, J.B., Van Cingel, R., 2017. Measuring individual hierarchy of anxiety invoking sports related activities. Arthrosc - J Arthrosc Relat Surg [internet] 33. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28332935.
Anterior Cruciate Ligament Reconstruction (PHOSA-ACLR). BMC Musculoskeleton Disord 18 (1).
van Melick, N., van Cingel, R.E.H., Brooijmans, F., Neeter, C., van Tienen, T., Hullegie, W., et al., 2016. Evidence-based clinical practice update: practice guidelines for anterior cruciate ligament rehabilitation based on a systematic review and multidisciplinary consensus. Br J Sports Med [Internet] 50 (24). Dec 1. 1506 LP – 1515. Available from: http://bjsm.bmj.com/content/50/24/1506.abstract.
Vlaeyen, J.W.S., Linton, S.J., 2000. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. Pain. 85 (3), 317–332.
Webster, K.E., Hewett, T.E., 2019. What is the evidence for and validity of return-to-sport testing after anterior cruciate ligament reconstruction surgery? A systematic review and meta-analysis. Sports Med [Internet] 49 (6). https://doi.org/10.1007/s40279-019-01093-x, 917–29. Available from:
Wiggins, M.E., Fadale, P., Barrach, H., Ehrlich, M., 2016. WW. Risk of secondary injury in younger athletes after anterior cruciate ligament reconstruction: a systematic review and meta-analysis. Am J Sport Med. 44 (7), 1861–1876.
Yentes, J.M., Hunt, N., Schmid, K.K., Kaipust, J.P., McGrath, D., Stergiou, N., 2013 Feb. The appropriate use of approximate entropy and sample entropy with short data sets. Ann. Biomed. Eng. 41 (2), 349-365.
Young, S.W., Valladares, R.D., Loi, F., Dragoo, J.L., 2016. Mechanoreceptor reinnervation of autografts versus allografts after anterior cruciate ligament reconstruction. Orthop J Sport Med. 4 (10), 1–5.