Adductor co-contraction during abduction: a friend or foe

Overbeek, C.L.

6

Reduced force entropy in Subacromial Pain Syndrome: a cross-sectional analysis.

Celeste L. Overbeek, MD[1, 2]
Willemijn E. Tiktak, BSc.[1, 2]
Arjen Kolk, MD[1, 2]
Jochem Nagels, MD, PhD[1]
Rob G.H.H. Nelissen, MD, PhD[1]
Jurriaan H. de Groot, Msc., PhD[1, 2]

[1]Department of Orthopaedics, Leiden University Medical Centre, Postzone J-11-R, PO box 9600, 2300RC Leiden, the Netherlands.
[2]Laboratory for Kinematics and Neuromechanics, department of Orthopaedics and Rehabilitation, Leiden University Medical Centre, Postzone J-11-R, PO box 9600, 2300RC Leiden, the Netherlands.

Clin Biomech; 2020; DOI: 10.1016/j.clinbiomech.2020.105137.

ABSTRACT

Background

Generating a force at the hand requires moments about multiple joints by a theoretically infinite number of arm and shoulder muscle force combinations. This allows for learning and adaptation and can possibly be captured using the complexity (entropy) of an isometrically generated force curve. Patients with Subacromial Pain Syndrome have difficulty to explore alternative, pain-avoiding, motor strategies and we questioned whether loss of motor complexity may contribute to this. We assessed whether patients with Subacromial Pain Syndrome have reduced entropy of an isometrically generated abduction and adduction force curve.

Methods

Forty patients and thirty controls generated submaximal isometric ab- and adduction force at the wrist. The force curve was characterized by the magnitude of force variability [standard deviation and coefficient of variation], and the entropy (complexity) of force variability [approximate entropy].

Findings

Patients showed reduced entropy both during the abduction (-0.16, confidence interval: [-0.33 ; -0.00], *p*: 0.048) and adduction task (-0.20, confidence interval: [-0.37 ; -0.03], *p*: 0.024) and reduced force variability during abduction (standard deviation: -0.006, confidence interval: [-0.011 ; -0.001], *p*: 0.013 and coefficient of variation: -0.51, confidence interval: [-0.93 ; -0. 10], *p*: 0.016).

Conclusions

Isometric force curves of patients with Subacromial Pain Syndrome show reduced complexity compared to asymptomatic controls, which may indicate more narrow and stereotype use of motor options. In future studies, it should be investigated whether the finding of reduced force (motor) entropy indicates functional decline, contributing to decreased ability to acquire and optimise motor strategies in Subacromial Pain Syndrome.

INTRODUCTION

Healthy physiological systems have an infinite number of solutions for a given task, resulting in a measurable complexity of the system's output[1,2]. This output complexity (entropy) reflects the spectrum of motor solutions available, which is fundamental for the acquisition of skills, adaptation to changing environments and equal distribution of load among tissues[3-6]. Loss of complexity has been interpreted as one of the driving principles for functional decline and measuring output complexity has been proven useful in identifying pre-clinical changes in aging, pain and disease[1,2,7,8]. In the musculoskeletal system, loss of complexity manifests by declined ability to generate precise levels of force, declined walking ability, disrupted (balance) control and frailty[1,2,7,9-11]. Loss of motor output complexity has been associated with the clinical course of pain conditions involving amongst others, the low back[7,9-14]. We questioned whether the most common chronic pain condition of the shoulder (Subacromial Pain Syndrome, SAPS), is associated with reduced motor output complexity.

In SAPS, there are no specific anatomic abnormalities that could explain complaints (e.g., acromioclavicular osteoarthritis, calcific tendinitis, full thickness rotator cuff tears), but movement factors including scapular dyskinesia and reduced humerus depression during abduction relate to pain[15-19]. Physical therapy for SAPS in which these factors are targeted have been shown effective, however, patients report persisting complaints in up to 40%[20-23]. We propose that loss of motor output complexity may contribute to the perpetuation of pain in patients with SAPS, as patients may not have the possibility to explore alternative motor strategies and avoid subacromial pain[24]. Few studies have looked into this aspect of motor control in SAPS by analysing the dispersion of force output using measures like the standard deviation (SD) or coefficient of variation (CV)[25-28]. These studies showed unaltered force steadiness (i.e., the degree of variability of force variability) in patients with SAPS, leading to the conclusion that force control is preserved[25-28]. However, information on a different, potentially important, aspect of motor control lying in the entropy (i.e., structure) of force variability, was disregarded in these studies and may provide further insight[1,2,25-29].

In this paper, we extend the analyses of variability by quantifying the complexity of isometric force curves using Approximate Entropy (ApEn) in patients with SAPS and controls[30]. We hypothesise that compared to asymptomatic controls, patients with SAPS have reduced force entropy in the shoulder indicated by lower ApEn values. Force entropy will be determined during an isometric abduction task, because the resulting movement is associated with pain in SAPS. We will furthermore determine

force entropy during isometric adduction, to provide insight into whether a potential loss of force entropy is specific to the abduction movement, or more systemic for the arm.

PATIENTS AND METHODS

This was a level II prognostic study in which the entropy of force curves was compared between patients with SAPS and asymptomatic controls.

Participants with SAPS

SAPS was defined as shoulder pain of subacromial origin, lasting for longer than 3 months with no other specific anatomic abnormalities that could explain complaints and require specific treatment (e.g., acromioclavicular osteoarthritis, calcific tendinitis, full thickness rotator cuff tears)[15]. From April 2010 through September 2016, 40 patients with SAPS were recruited at the Leiden University Medical Centre, Haaglanden Medical Centre and Alrijne Hospital, under a registered and published protocol (Trial register no. NTR2283)[31]. Patients were selected through a medical interview, clinical examination, radiographs and a Magnetic Resonance Imaging Arthrogram (MRA). Inclusion criteria were unilateral shoulder complaints for at least three months, positive Hawkins-Kennedy test (passive anteflexion of the shoulder to 90° with subsequent internal rotation of the shoulder to provoke subacromial pain complaints) and Neer lidocaine impingement test (looking for immediate relieve of pain after subacromial infiltration with Lidocaine). Further, patients had to have at least one of the following symptoms: pain during daily life activities with arm abduction, extension, and/or internal rotation, pain at night or incapable of lying on the shoulder, painful arc, diffuse pain at palpation of the greater tuberosity, scapular dyskinesis, and positive full or empty can test or positive Yocum test[31]. Patients were excluded in case of insufficient language skills, age under 35 or over 60 years, no written informed consent, any form of inflammatory arthritis of the shoulder, clinical signs of glenohumeral (GH) or acromioclavicular osteoarthritis, GH instability, decreased passive GH mobility (e.g., frozen shoulder), history of shoulder surgery, fracture or dislocation of the affected shoulder, cervical radiculopathy, and presence of a pacemaker or other electronic implants. Additionally, patients were excluded in case of an alternative diagnosis on radiographs or MRA, e.g., calcific tendinitis, full-thickness rotator cuff tear, labrum or ligament pathology, pulley lesion, biceps tendinopathy, os acromiale, tumour, cartilage lesion, and a bony cyst. Notably, general findings associated with subacromial pain (bursitis and tendinopathy) were no exclusion criteria. All MRAs were evaluated by an independent radiologist[18]. Included patients with SAPS were

allowed to have participated in earlier studies for varying purposes[17,18,32-35].

Asymptomatic controls

Under a separate protocol, asymptomatic controls were recruited at the Leiden University Medical Centre between January 2016 through November 2016. Spouses of patients with musculoskeletal complaints were invited to volunteer in case they were aged between 35-60 years and had no current or past shoulder complaints. We selected participants according to their age and sex to make sure that there were no differences between the SAPS and control groups in these characteristics. Exclusion criteria were impaired passive and active shoulder function during clinical examination, insufficient Dutch language skills, prior shoulder surgery, injections, shoulder fracture or dislocation, radiculopathy, frozen shoulder, osteoarthritis or rheumatoid arthritis and neurologic or muscle disease. No additional imaging was performed in the control group, as this was only of interest in the SAPS-group to exclude specific anatomic conditions that could give an alternative explanation for the symptoms.

The study was undertaken with the understanding and written consent of each subject, and that the study conforms with The Code of Ethics of the World Medical Association (Declaration of Helsinki), printed in the British Medical Journal (18 July 1964). The review board of the institutional ethical medical commission approved these study protocols (P09.227 & P15.046) and all participants provided written informed consent.

Measurement set-up

Force entropy is generally measured during isometric force tasks[29]. The movement associated with SAPS is abduction[15]. Because of the multiple joints (i.e., degrees of freedom) within the arm-shoulder complex, we postulate that if there exists a relation between SAPS and force entropy this would manifest at the hand (end point) and be observable during the abduction force direction which would result in the painful abduction motion. We also determined force entropy during isometric adduction to control for whether a potentially reduced force entropy is isolated for the pain related force or more systemic in the arm. During measurements, participants were in standing position facing a computer for force feedback, with the target arm in external rotation at the side attached to a one-dimensional force transducer at the wrist[31]. In this setup, participants performed isometric force tasks in ab- and adduction (figure of measurement set-up in[32]). The force task magnitude was similar for both abduction and adduction and equal to 60% of the maximal voluntary force (MVF), defined as the lowest absolute value of the MVF in abduction or adduction.

Signal processing

Post-processing of the (2500 Hz sampled) force signal had to result in a signal with

a sample rate of at least 200 Hz, accounting for sufficient Motor Unit recruitment induced variance[36]. The sampled force signal was therefore low-pass filtered using a third order Butterworth filter with a cut-off frequency of 125 Hz and down-sampled to 250Hz using custom made software (Matlab 2018b, MathWorks inc., Natick, USA). The data-vector used for the analyses consisted of consecutive force data points within a tolerance of 10% below or above the force task level (60% MVF). To exclude initial overestimation and undershooting of the force task (i.e., steering), the first 17.5% and last 2.5% of data were removed from the data-vector[26]. To have sufficient data length for the ApEn-analysis (i.e., >1000 samples), selected data vectors shorter than 4 seconds were discarded[37].

Outcome measures

Magnitude of force variability

The magnitude of force variability was assessed by calculating the Standard Deviation (SD) and the Coefficient of Variation (SD/mean force x 100, CV). These measures respectively represent the absolute and relative variability of the force about the mean, indicating higher force variability with higher values[25-27].

Complexity of force variability

The complexity of force variability was assessed with the Approximate Entropy value (ApEn). ApEn has been used in a wide range of pathologies and describes whether a system operates in a predictive, stereotype way or in a more chaotic, dynamic way, using many degrees of freedom[1,2]. The ApEn-value ranges between 0 and (about) 2. In general, healthy systems would reveal high ApEn-values, whereas functional decline is associated with low ApEn-values[1,2]. The ApEn-value was calculated according to articles of Pincus et al. with the function ApproximateEntropy in Matlab (Matlab 2018b, MathWorks inc., Natick, USA) and parameters set at $m = 2$ and $r = 0.2*SD$[30,38].

Statistical analysis

The data was stored and analysed using the Statistical package of social sciences (SPSS®) version 23 (IBM® Corp, Armonk, NY, USA). Categorical data are described with numbers and percentages and continuous parameters with means and either 95%-confidence intervals (CIs), standard deviations (SDs), or medians with the 25th and 75th percentiles, depending on data distributions. Demographic data, force task characteristics (data length and exerted force level) and the magnitude of force variability (SD and CV) were compared with the chi-square test and independent samples t-tests or Mann-Whitney U test depending on the distribution of data. The structure of force variability (ApEn) was compared between patients with SAPS and controls in a multivariate regression analysis with controlling for the data length associated with the force task. Results are presented as mean differences, estimated

regression coefficients, 95% CI's and *p*-values. A two-sided *p*-value of 0.05 or less was considered statistically significant.

RESULTS

Cohort and task characteristics

Forty patients with SAPS and 30 asymptomatic participants were included. There were no differences in baseline or task characteristics, except for the data length during the abduction task, which was 1.5 seconds (i.e., 375 samples) shorter (CI: [-2.76; -0.22], *p*: 0.022) in patients with SAPS (**Table 1**). Because of corrupt data (e.g., 50 Hz noise), the abduction data of 4 patients with SAPS and the adduction data of 5 patients with SAPS and two controls were unsuitable for the analysis.

Table 1 | Patient characteristics of patients with SAPS and asymptomatic controls

	SAPS	**Controls**	***Group difference***		
	n=40	*n=30*	*Mean*	*95% CI*	*p-value*
Age, yrs (mean, SD)	50 (6.38)	51 (5.71)	-0.49	[-3.43 ; 2.45]	0.740
Female (n, %)	23 (58)	17 (57)	Chi-square value: 0.005		0.944
Right side dominance (n, %)	35 (88)	25 (83)	Chi-square value: 0.243		0.622
Dominant side measured/affected (n, %)	25 (63)	17 (57)	Chi-square value: 0.243		0.622
Duration of complaints (median, IQR)	18 (12-29)	-	-	-	-
Abduction task					
Data length (sec.)	7.38 (2.32)	7.50 (2.80)	-0.12	[-1.38 ; 1.14]	0.850
Exerted force (N)	0.92 (0.35)	0.99 (0.31)	-0.07	[-0.23 ; 0.09]	0.400
Adduction task					
Data length (sec.)	7.38 (2.25)	8.87 (2.80)	-1.5	[-2.76 ; -0.22]	**0.022**
Exerted force (N)	0.93 (0.35)	1.0 (0.31)	-0.07	[-0.24 ; 0.10]	0.406

SAPS, Subacromial Pain Syndrome; n, number; N, Newton; SD, standard deviation.

Magnitude of force variability

Patients with SAPS had reduced magnitude of variability during the abduction task as assessed with the SD (group-difference: -0.006 N (CI: [-0.011; -0.001], *p*: 0.013) and CV (group-difference: -0.51 (CI: [-0.93; -0.10], *p*: 0.016). We did not observe differences in magnitude of variability during the adduction task (**Table 2**).

Complexity of force variability

Patients with SAPS had lower ApEn-values during the abduction task (-0.16, 95% CI: [-0.33 ; -0.00], *p*: 0.048) and adduction task (-0.20, 95% CI: [-0.37 ; -0.03], *p*: 0.024) (**Table 3, Figure 1**).

Table 2 | Difference in magnitude of force variability between patients with SAPS and controls

	SAPS	*Controls*	*Group difference*		
	Mean (SD)	*Mean (SD)*	*Mean*	*95% CI*	*p-value*
Abduction task					
SD (N)	0.019 (0.010)	0.026 (0.010)	-0.006	[-0.011 ; -0.001]	**0.013**
CV (%)	2.16 (0.76)	2.68 (0.92)	-0.51	[-0.93 ; -0.10]	**0.016**
Adduction task					
SD (N)	0.025 (0.013)	0.029 (0.011)	-0.004	[-0.010 ; 0.002]	0.229
CV (%)	2.62 (0.88)	2.93 (0.76)	-0.31	[-0.73 ; 0.11]	0.143

SAPS, Subacromial Pain Syndrome; n, number; N, Newton; SD, standard deviation.

Table 3 | Difference in structure of force variability between patients with SAPS and controls

	ApEn-value		
	Beta	*95% CI*	*p-value*
Abduction task			
Intercept	0.78	[0.52 ; 1.0]	NA
SAPS (ref. is control)	-0.16	[-0.33 ; -0.00]	**0.048**
Data length (seconds)	0.02	[-0.01 ; 0.05]	0.216
Adduction task			
Intercept	0.94	[0.67 ; 1.21]	NA
SAPS (ref. is control)	-0.20	[-0.37 ; -0.03]	**0.024**
Data length (seconds)	-0.01	[-0.05 ; 0.02]	0.392

Estimated group difference in Approximate Entropy value (ApEn) between patients with Subacromial Pain Syndrome (SAPS) and controls, adjusted for the data length associated with the task.

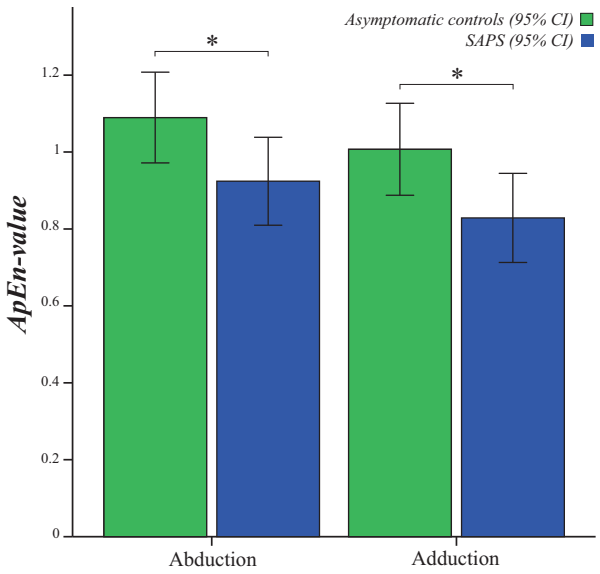

Figure 1 | Difference in force entropy between patients with SAPS and controls

Approximate Entropy values (ApEn) in patients with Subacromial Pain Syndrome (SAPS) and controls. Asterixis indicate significant adjusted estimated group differences in ApEn-values between patients with SAPS and controls, adjusted for the data length associated with the task

DISCUSSION

This cross-sectional evaluation showed that patients with SAPS have reduced motor output complexity during isometric abduction and adduction tasks, which may indicate functional decline. Furthermore, patients with SAPS showed reduced magnitude of force variability during isometric abduction.

In recent years, there has been an expansion of research on the subject of how musculoskeletal complaints can be discordant with observable pathology and become chronic. The focus has shifted from peripheral processes to factors as cognition, pain sensitisation and more recently, the adaptability of the motor system (e.g., assessed by the structure of motor control variability)[39-41]. The latter has already been investigated in various musculoskeletal disorders, and predominantly in low back pain there is a growing body of evidence suggesting that impaired adaptability of the motor system plays a role in the perpetuation of pain[12,14,41]. Furthermore, it has been shown that individuals who are involved in repetitive movements (e.g. butchers, assembly line workers) are more likely to develop overuse disorders if they have less complex variability between repetitions[12,14,42]. In SAPS, complaints become chronic in approximately 40% of patients, and reduced complexity of the motor system may contribute to the frequent perpetuation of complaints[40].

Only a few studies have investigated variability of force output in SAPS, with a focus on the magnitude hereof, discarding time-dependent characteristics[25-28]. In contrast to these previous studies that showed no alteration in magnitude of force variability and minor changes in control in SAPS, we did observe reduced magnitude of variability during isometric abduction. Our finding may be explained by a protective pain mechanism. It has been proposed that patients with pain minimise micro-movements at the painful joint by co-contracting with antagonists, to avoid damage and pain, resulting in a decrease of movement variability on a smaller scale[43-45]. In our study we measured force variability with the arm at the side, where patients experience least pain, to reduce direct pain interference. We assumed that the exertion of the abduction force that would lead to arm abduction elicits protective behaviour, because this movement is associated with pain exacerbation (painful arc)[15].

The main finding of our study was reduced motor complexity in patients with SAPS. There is yet no clarity on the nature of the association between pain and complexity of motor variability. In experiments with pain inducement, sudden alterations in motor complexity have been observed, suggesting that changes in motor output complexity are the consequence of pain[46]. On the contrary, reduced motor output complexity has been suggested as a cause of functional decline, overuse and pain[1,2,7,8]. To gain further

insight into the cause-and-effect relationship and into the potential prognostic value of assessing motor output complexity in SAPS, future studies should assess whether patients with SAPS who have reduced motor output complexity, are less able to develop successful motor strategies and hence more at stake of developing chronic complaints[6,24,47].

In this study we acknowledge the following limitations. First, inherent to the definition of SAPS, the cause of symptoms present in the SAPS-group were not related to observable anatomic derivatives, and thus could have been heterogeneous[15]. Our findings may therefore not be applicable to every individual SAPS-patient. Second, this study was based on a comparison of two separate study-cohorts for which no *a-priori* power analysis was performed. Third, the results of this study are based on measurements performed in a single posture. Future assessments with varying postures may provide more insight into whether a loss of complexity is isolated or systemic. Lastly, due to our measurement set-up there were differences in data-length between the SAPS and control group. As the ApEn-value is sensitive to differences in signal length and the choice of parameters, we corrected for data length in the ApEn analysis and chose parameters in conjunction with the literature[37,38,48].

To conclude, this cross-sectional evaluation of isometric force output signals suggests that patients with SAPS have reduced complexity of isometric force curves than asymptomatic controls, which may indicate more narrow and stereotype use of motor options. In future studies, it should be investigated whether the finding of reduced force (motor) entropy indicates functional impairment and decreased ability to acquire and optimise motor strategies in patients with SAPS[3-6].

ACKNOWLEDGEMENTS

The institution of one or more of the authors (R.G.H.H.N) has received funding from the Dutch Arthritis Foundation (grant number 13-1-303). There were no conflicts of interest. All authors had substantial contributions to the research design, acquisition, analysis and/or interpretation of data; drafting the paper and/or revising it critically; approval of the submitted and final versions. This study was performed at the Laboratory for Kinematics and Neuromechanics, department of Orthopaedics and Rehabilitation,Leiden University Medical Centre, Leiden, the Netherlands

REFERENCES

1. Lipsitz LA. Dynamics of stability: the physiologic basis of functional health and frailty. *Journals of Gerontology Series A: Biological Sciences and Medical Sciences*. 2002;57(3):B115-125.
2. Lipsitz LA, Goldberger AL. Loss of 'complexity' and aging. Potential applications of fractals and chaos theory to senescence. *JAMA*. 1992;267(13):1806-1809.
3. Lipsitz LA. Physiological complexity, aging, and the path to frailty. *Sci Aging Knowledge Environ*. 2004;2004(16):pe16. 10.1126/sageke.2004.16.pe16.
4. Therrien AS, Wolpert DM, Bastian AJ. Increasing Motor Noise Impairs Reinforcement Learning in Healthy Individuals. *eNeuro*. 2018;5(3)10.1523/ENEURO.0050-18.2018.
5. Barbado Murillo D, Caballero Sanchez C, Moreside J, Vera-Garcia FJ, Moreno FJ. Can the structure of motor variability predict learning rate? *J Exp Psychol Hum Percept Perform*. 2017;43(3):596-607. 10.1037/xhp0000303.
6. van Dieen JH, Flor H, Hodges PW. Low-Back Pain Patients Learn to Adapt Motor Behavior With Adverse Secondary Consequences. *Exerc Sport Sci Rev*. 2017;45(4):223-229. 10.1249/JES.0000000000000121.
7. Morrison S, Newell KM. Aging, neuromuscular decline, and the change in physiological and behavioral complexity of upper-limb movement dynamics. *J Aging Res*. 2012;2012:891218. 10.1155/2012/891218.
8. Vaillancourt DE, Newell KM. Changing complexity in human behavior and physiology through aging and disease. *Neurobiology of Aging*. 2002;23(1):1-11.
9. Hausdorff JM. Gait dynamics, fractals and falls: finding meaning in the stride-to-stride fluctuations of human walking. *Hum Mov Sci*. 2007;26(4):555-589. 10.1016/j.humov.2007.05.003.
10. Madeleine P, Madsen TM. Changes in the amount and structure of motor variability during a deboning process are associated with work experience and neck-shoulder discomfort. *Appl Ergon*. 2009;40(5):887-894. 10.1016/j.apergo.2008.12.006.
11. Sosnoff JJ, Rice IM, Hsiao-Wecksler ET, Hsu IM, Jayaraman C, Moon Y. Variability in Wheelchair Propulsion: A New Window into an Old Problem. *Front Bioeng Biotechnol*. 2015;3:105. 10.3389/fbioe.2015.00105.
12. Georgoulis AD, Moraiti C, Ristanis S, Stergiou N. A novel approach to measure variability in the anterior cruciate ligament deficient knee during walking: the use of the approximate entropy in orthopaedics. *Journal of Clinical Monitoring and Computing*. 2006;20(1):11-18. 10.1007/s10877-006-1032-7.
13. Terada M, Kosik K, Johnson N, Gribble P. Altered postural control variability in older-aged individuals with a history of lateral ankle sprain. *Gait & posture*. 2018;60:88-92. 10.1016/j.gaitpost.2017.11.009.
14. van den Hoorn W, Bruijn SM, Meijer OG, Hodges PW, van Dieen JH. Mechanical coupling between transverse plane pelvis and thorax rotations during gait is higher in people with low back pain. *J Biomech*. 2012;45(2):342-347. 10.1016/j.jbiomech.2011.10.024.
15. Diercks R, Bron C, Dorrestijn O, Meskers C, Naber R, de Ruiter T, Willems J, Winters J, van der Woude HJ, Dutch Orthopaedic A. Guideline for diagnosis and treatment of subacromial pain syndrome: a multidisciplinary review by the Dutch Orthopaedic Association. *Acta Orthop*. 2014;85(3):314-322. 10.3109/17453674.2014.920991.
16. Graichen H, Bonel H, Stammberger T, Haubner M, Rohrer H, Englmeier KH, Reiser M, Eckstein F. Three-dimensional analysis of the width of the subacromial space in healthy subjects and patients with impingement syndrome. *AJR American journal of roentgenology*. 1999;172(4):1081-1086. DOI:10.2214/ajr.172.4.10587151.
17. Kolk A, Henseler JF, de Witte PB, van Arkel ERA, Visser CPJ, Nagels J, Nelissen R, de Groot JH. Subacromial anaesthetics increase asymmetry of scapular kinematics in patients with subacromial pain syndrome. *Man Ther*. 2016;26:31-37. 10.1016/j.math.2016.07.002.
18. de Witte PB, Overbeek CL, Navas A, Nagels J, Reijnierse M, Nelissen RG. Heterogeneous MR arthrography findings in patients with subacromial impingement syndrome - Diagnostic subgroups? *J Electromyogr Kinesiol*. 2016;29:64-73. 10.1016/j.jelekin.2015.06.006.
19. Vecchio P, Kavanagh R, Hazleman BL, King RH. Shoulder pain in a community-based rheumatology clinic. *Br J Rheumatol*. 1995;34(5):440-442. 10.1093/rheumatology/34.5.440.
20. Croft P, Pope D, Silman A. The clinical course of shoulder pain: prospective cohort study in primary care. Primary Care Rheumatology Society Shoulder Study Group. *BMJ*. 1996;313(7057):601-602. 10.1136/bmj.313.7057.601.
21. Kuijpers T, van Tulder MW, van der Heijden GJ, Bouter LM, van der Windt DA. Costs of shoulder pain

in primary care consulters: a prospective cohort study in The Netherlands. *BMC Musculoskelet Disord.* 2006;7:83. 10.1186/1471-2474-7-83.
22. van der Windt DA, Koes BW, Boeke AJ, Deville W, De Jong BA, Bouter LM. Shoulder disorders in general practice: prognostic indicators of outcome. *Br J Gen Pract.* 1996;46(410):519-523.
23. Hanratty CE, McVeigh JG, Kerr DP, Basford JR, Finch MB, Pendleton A, Sim J. The effectiveness of physiotherapy exercises in subacromial impingement syndrome: a systematic review and meta-analysis. *Semin Arthritis Rheum.* 2012;42(3):297-316. 10.1016/j.semarthrit.2012.03.015.
24. Moseley GL, Hodges PW. Reduced variability of postural strategy prevents normalization of motor changes induced by back pain: a risk factor for chronic trouble? *Behavioral Neuroscience.* 2006;120(2):474-476. 10.1037/0735-7044.120.2.474.
25. Bandholm T, Rasmussen L, Aagaard P, Jensen BR, Diederichsen L. Force steadiness, muscle activity, and maximal muscle strength in subjects with subacromial impingement syndrome. *Muscle Nerve.* 2006;34(5):631-639. 10.1002/mus.20636.
26. Camargo PR, Avila MA, de Oliveira AB, Asso NA, Benze BG, de Fatima Salvini T. Shoulder abduction torque steadiness is preserved in subacromial impingement syndrome. *Eur J Appl Physiol.* 2009;106(3):381-387. 10.1007/s00421-009-1030-9.
27. Maenhout AG, Palmans T, De Muynck M, De Wilde LF, Cools AM. The impact of rotator cuff tendinopathy on proprioception, measuring force sensation. *J Shoulder Elbow Surg.* 2012;21(8):1080-1086. 10.1016/j.jse.2011.07.006.
28. Zanca GG, Camargo PR, Oliveira AB, Serrao PRMS, Matiello-Rosa SM. Isometric medial and lateral rotations torque steadiness in female workers with shoulder impingement. *Isokinet Exerc Sci.* 2010;17:1-4. 10.3233/IES-2009-0368.
29. Slifkin AB, Newell KM. Noise, information transmission, and force variability. *J Exp Psychol Hum Percept Perform.* 1999;25(3):837-851. 10.1037//0096-1523.25.3.837.
30. Pincus SM. Approximate entropy as a measure of system complexity. *Proceedings of the National Academy of Sciences of the United States of America.* 1991;88(6):2297-2301.
31. de Witte PB, Nagels J, van Arkel ER, Visser CP, Nelissen RG, de Groot JH. Study protocol subacromial impingement syndrome: the identification of pathophysiologic mechanisms (SISTIM). *BMC Musculoskelet Disord.* 2011;12:282. 10.1186/1471-2474-12-282.
32. Overbeek CL, Kolk A, Nagels J, de Witte PB, van der Zwaal P, Visser CPJ, Fiocco M, Nelissen R, de Groot JH. Increased co-contraction of arm adductors is associated with a favorable course in subacromial pain syndrome. *J Shoulder Elbow Surg.* 2018;27(11):1925-1931. 10.1016/j.jse.2018.06.015.
33. de Witte PB, Henseler JF, van Zwet EW, Nagels J, Nelissen RG, de Groot JH. Cranial humerus translation, deltoid activation, adductor co-activation and rotator cuff disease - different patterns in rotator cuff tears, subacromial impingement and controls. *Clin Biomech (Bristol, Avon).* 2014;29(1):26-32. 10.1016/j.clinbiomech.2013.10.014.
34. Overbeek CL, Kolk A, de Groot JH, de Witte PB, Gademan MGJ, Nelissen R, Nagels J. Middle-aged adults cocontract with arm ADductors during arm ABduction, while young adults do not. Adaptations to preserve pain-free function? *J Electromyogr Kinesiol.* 2019;49:102351. 10.1016/j.jelekin.2019.102351.
35. Overbeek CL, Kolk A, de Groot JH, Visser CPJ, van der Zwaal P, Jens A, Nagels J, Nelissen R. Altered Cocontraction Patterns of Humeral Head Depressors in Patients with Subacromial Pain Syndrome: A Cross-sectional Electromyography Analysis. *Clin Orthop Relat Res.* 2019;477(8):1862-1868. 10.1097/CORR.0000000000000745.
36. Forrest SM, Challis JH, Winter SL. The effect of signal acquisition and processing choices on ApEn values: towards a "gold standard" for distinguishing effort levels from isometric force records. *Med Eng Phys.* 2014;36(6):676-683. 10.1016/j.medengphy.2014.02.017.
37. Yentes JM, Hunt N, Schmid KK, Kaipust JP, McGrath D, Stergiou N. The appropriate use of approximate entropy and sample entropy with short data sets. *Ann Biomed Eng.* 2013;41(2):349-365. 10.1007/s10439-012-0668-3.
38. Forrest SM, Challis JH, Winter SL. The effect of signal acquisition and processing choices on ApEn values: towards a "gold standard" for distinguishing effort levels from isometric force records. *Medical Engineering and Physics.* 2014;36(6):676-683. 10.1016/j.medengphy.2014.02.017.
39. Chester R, Jerosch-Herold C, Lewis J, Shepstone L. Psychological factors are associated with the outcome of physiotherapy for people with shoulder pain: a multicentre longitudinal cohort study. *Br J Sports Med.* 2018;52(4):269-275. 10.1136/bjsports-2016-096084.

40. Sanchis MN, Lluch E, Nijs J, Struyf F, Kangasperko M. The role of central sensitization in shoulder pain: A systematic literature review. *Semin Arthritis Rheum.* 2015;44(6):710-716. 10.1016/j.semarthrit.2014.11.002.
41. Moseley GL, Hodges PW. Reduced variability of postural strategy prevents normalization of motor changes induced by back pain: a risk factor for chronic trouble? *Behav Neurosci.* 2006;120(2):474-476. 10.1037/0735-7044.120.2.474.
42. Hamill J, van Emmerik RE, Heiderscheit BC, Li L. A dynamical systems approach to lower extremity running injuries. *Clinical Biomechanics (Bristol, Avon).* 1999;14(5):297-308.
43. Seidler-Dobrin RD, He J, Stelmach GE. Coactivation to reduce variability in the elderly. *Motor Control.* 1998;2(4):314-330. 10.1123/mcj.2.4.314.
44. Vallbo AB, Wessberg J. Organization of motor output in slow finger movements in man. *J Physiol.* 1993;469:673-691. 10.1113/jphysiol.1993.sp019837.
45. Cote JN, Raymond D, Mathieu PA, Feldman AG, Levin MF. Differences in multi-joint kinematic patterns of repetitive hammering in healthy, fatigued and shoulder-injured individuals. *Clin Biomech (Bristol, Avon).* 2005;20(6):581-590. 10.1016/j.clinbiomech.2005.02.012.
46. Hodges PW, Moseley GL. Pain and motor control of the lumbopelvic region: effect and possible mechanisms. *J Electromyogr Kinesiol.* 2003;13(4):361-370. 10.1016/s1050-6411(03)00042-7.
47. Lund JP, Donga R, Widmer CG, Stohler CS. The pain-adaptation model: a discussion of the relationship between chronic musculoskeletal pain and motor activity. *Canadian Journal of Physiology and Pharmacology.* 1991;69(5):683-694.
48. Pincus SM. Approximate entropy as a measure of irregularity for psychiatric serial metrics. *Bipolar Disord.* 2006;8(5 Pt 1):430-440. 10.1111/j.1399-5618.2006.00375.x.