Book of Abstracts

Presented at the 4th AMS Annual Research Meeting

March 13, 2020

@ KIT (Royal Tropical Institute) Amsterdam
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P1: Sports
Tammie van Biemen

INTO THE EYES OF THE REFEREE: A COMPARISON OF ON-FIELD VISUAL SEARCH BEHAVIOUR BETWEEN ELITE AND SUB-ELITE FOOTBALL REFEREES

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Introduction: In the decision making of foul situations by a football referee, visual information plays a crucial role. Although visual search behaviour is an important skill to gain visual information to determine whether a foul has occurred, little is known whether better decisions are underpinned by more optimal visual search behaviour, particularly when tested on-field.

Purpose: This study therefore aimed to examine on-field visual search behaviour of football referees while assessing foul situations between elite and sub-elite referees.

Method: Elite (N=5) and sub-elite (N=9) referees participated in the study, each officiated a football game while wearing a mobile eye-tracker to assess their visual search behaviour during an on-field game. Their visual search behaviour during the assessment of foul situations was analysed by comparing search rate (number and duration of fixations) and search location.

Results: Results showed elite referees have a higher search rate with more fixations of less duration compared to sub-elite referees, but both spend a similar amount of time viewing the contact zones of both foul receiver and foul committer.

Conclusions: The elites’ higher search rate might attribute the overall superior decision-making accuracy in foul situations compared to sub-elites. This may indicate it is not where elites are looking, rather how they gain visual information, which can be used to train referees in on-field foul decision making in football matches.
Introduction: Visually guided braking has been investigated through information-based control approach; however, the role of affordances on cyclist’s braking control is still unclear. Purpose: To investigate whether cyclists take into account the perception of their action capabilities (affordances) during the braking task.

Method: Ten cyclists were asked to brake in order to stop as close as possible to an obstacle. Cycling speed was manipulated by varying initial distances: low-speed 21.6m and high-speed 37m. Brake strength was manipulated by adding weights on the bike: strong-brake, none; medium-brake, +5kg; weak-brake, +10kg. Bicycle motion was captured by GoPro camera (60 Hz). Ideal deceleration at braking onset (Dideal), Dideal relative to the Maximum deceleration (% Dmax) and Maximum velocity (Velmax) were submitted to brake vs. speed ANOVA-RM. Results: Cyclists showed higher Velmax in high- than low-speed (p < .001) (low-speed: 2.35 ± 0.05 m/s; high-speed: 3.84 ± 0.16 m/s). Increasing brake strength provoked higher Dmax (p < .001) (weak-brake: 0.97 ± 0.03 m/s²; medium-brake: 1.57 ± 0.06 m/s²; strong-brake: 2.24 ± 0.09 m/s²), indicating that cyclist’s action capabilities changed. Dideal at brake onset was higher in strong-brake (1.05 ± 0.01 m/s²) than medium-brake (0.67 ± 0.02 m/s²) and weak-brake (0.47 ± 0.01 m/s²) (p < .001); and high-speed (0.89 ± 0.01 m/s) than low-speed (0.58 ± 0.02 m/s) (p < .001). However, Dideal relative to Dmax showed similar results (p = 0.094).

Conclusion: The cyclist scaled braking deceleration to maximal achievable deceleration. These observations support the hypothesis movement control in braking tasks is affordance-based.
Paul Kuijer

KNEE OSTEOARTHRITIS & WORK: THE DUTCH PATIENT JOURNEY BEFORE SURGERY

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Introduction: Guidelines for managing knee osteoarthritis (OA) advise extensive non-surgical treatment to delay surgery.

Purpose: We evaluated how many Dutch knee OA patients received non-surgical treatment before surgery, and assessed their satisfaction regarding symptoms and participation.

Method: A multi-centre questionnaire study was performed among knee OA patients that were listed for or had recently undergone knee surgery. Questions concerned received non-surgical treatment modalities according to the Dutch Stepped Care Strategy, and satisfaction with received treatment modalities, rated from 1 (very unsatisfied) to 10 (very satisfied). A cut-off point of ≥6 was labelled as ‘satisfied’. Satisfaction rates were enquired concerning pain, swelling, stiffness, activities of daily life (ADL), work and sport/leisure time.

Results: The questionnaire was completed by 92 of 112 eligible patients. Mean age was 65 years, 62% female, 87% were overweight and 33% had paid employment. Step 1 treatments, consisting of Acetaminophen, education and lifestyle advice, were most received by patients (62-79%). Exercise-based therapy, NSAIDs, dietary therapy and Tramadol (step 2) were received by 19-59% of patients. Intra-articular injection (Step 3) was received by 47% of patients. Patients were mostly satisfied with NSAIDs, exercise-based therapy and intra-articular injection for pain and ADL. Patients with paid employment were most satisfied with NSAIDs (56%) and intra-articular injection (54%) for work participation.

Conclusions: Non-surgical treatment modalities appear underutilised and received the highest satisfaction rates for pain and generally low satisfaction rates for work and sports participation. Better insight in patients’ satisfaction regarding treatment effects on symptoms and participation could support better adherence.
Mohammadreza Mahaki

THE EFFECTS OF GENERAL FATIGUE INDUCED BY INCREMENTAL EXERCISE TEST AND ACTIVE RECOVERY MODES ON ENERGY COST, GAIT VARIABILITY AND STABILITY IN MALE SOCCER PLAYERS

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Introduction

The aerobic endurance is considered as an important physiological capacity of soccer players which is examined by the Incremental Exercise Test (IET). However, it is not clear how IET influences gait features in soccer players and how players recover optimally at post-IET.

Purpose

The effect of IET on energy cost, gait variability and stability in soccer players was investigated. Moreover, to identify an optimal recovery mode at post-IET, the effect of walking at Preferred Walking Speed (PWS), running at Individual Ventilation Threshold (IVT) (as two active recoveries), and Rest (as a passive recovery) on aforementioned features were studied.

Methods

Nine male soccer players participated in this study during three sessions for each recovery. Participants performed a 4-min walking trial at PWS on a treadmill prior IET (PreT), which was followed by four 4-min walking trials (PosT-0, 1, 2, and 3) with three 4-min recovery mode intervals (PWS, IVT, or Rest) between them (Fig 1. A). Energy cost, gait variability and stability were examined at PreT and PosT-0, 1, 2, and 3.

Results

IET significantly increased energy cost and gait variability. However, gait stability was not significantly influenced by IET. Energy cost significantly decreased by recovery modes. IVT induced significantly higher energy cost than PWS at PosT-2 and also significantly higher energy cost than Rest at PosT-3 (Fig 1. B).

Conclusion

Gait stability of soccer players was not affected by IET, despite increases in gait variability and energy cost. All the recovery modes decreased the energy cost, however PWS and Rest produced faster recovery of energy cost than IVT.

Keywords: gait stability, energy cost, active recovery, gait, soccer.
Anouk Nijs

CADENCE MODULATION IN EXPERIENCED RUNNERS: PACING STEPS OR STRIDES?

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Introduction A change in cadence during walking or running might be indicated for a variety of reasons, including mobility improvement and injury prevention. Auditory pacing may be used to modulate cadence.

Purpose In this study, we compared the effectiveness of step-based and stride-based auditory pacing for cadence modulation in both walking and running.

Method Sixteen experienced runners walked and ran on a treadmill while synchronizing with step-based and stride-based pacing at slow, preferred and fast pacing frequencies in synchronization-perturbation and synchronization-continuation trials. We quantified the variability of the relative phase between pacing cues and footfalls and the responses to perturbations in the pacing signal as measures of coordinative stability; the more stable the auditory-motor coordination, the stronger the modulating effect of pacing. Furthermore, we quantified the deviation from the prescribed cadence after removal of the pacing signal as a measure of internalization.

Results Synchronization was reached less often in running, especially in the conditions with a slow pacing frequency. If synchronization was reached, coordinative stability was similar for preferred and fast pacing frequencies, indicating that pacing is an effective method to increase cadence. Participants showing synchronization showed good internalization of the paced cadence in all conditions. Step-based auditory pacing led to more stable auditory-motor coordination in both walking and running.

Conclusions Based on the results, we conclude that step-based auditory pacing can be used to increase cadence in walking and running, provided that the user can synchronize to an external beat.
P2: Musculoskeletal Health
H.I. Berends

RISK-FACTORS FOR NEUROPHYSIOLOGICAL EVENTS DUE TO TRACTION IN SCOLIOSIS SURGERY

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Background: During corrective spine surgery, the integrity of the spinal cord, nerve roots and nerves is at risk. Damage to these structures might cause severe disability, like paraplegia. The integrity of the motor pathway is monitored intraoperatively to prevent, or limit, neurological damage. This is done using a multi-modal approach including motor evoked potentials (MEPs). Halofemoral traction is applied intraoperatively to improve the post-operative spinal correction and balance. However, it carries additional neurophysiological risks. This study examines patient characteristics predicting the chance of neurophysiological events by using traction.

Methods: This retrospective study included 81 patients (15.6 years±2.4, 47 idiopathic, 17 cerebral palsy, and 17 other pathology) where scoliosis correction using traction was performed. Outcome measure was the occurrence of a neurophysiological event caused-by-traction (>80% MEP amplitude decrease in >1 muscle [arm, abdomen, 4 leg muscles, bilaterally], which can be reversed by releasing traction). Possible predictors are pathology, body height, body weight, body mass index, (location of) largest Cobb angle, flexibility of curve (% correction by bending), amount of traction, and timing of event. Differences between patients with and without event, and predictive factors were statistically evaluated, using ANOVA and logistic regression analyses.

Results: We identified 11 patients (13.6%, 5 idiopathic scoliosis, 3 cerebral palsy, 3 other) in whom an event was caused by traction. Events occurred before incision (n=7), during pedicle screw (n=2), and rod (n=2) placement. Time between application of traction and event was 11-248 minutes. Events were found in both arm and leg muscles (n=3), in both legs (n=4), in one leg (n=1), or in just 1 or 2 muscles (n=1). Recovery time of the MEP responses after release of traction was 1-14 minutes. Patients with event-by-traction had a significantly shorter body height (153cm±13.8) and had stiffer curves (23.8%±9.7) compared to patients without events (164cm±15.2, 36.5%±14.4).

Logistic regression analysis showed that body height was a predictive factor for event-by-traction (p=0.014, OR=0.941, CI: 0.896, 0.988). A body height lower than 163cm gives 4 times more chance on event by traction. “Flexibility of the curve” showed a trend, indicating that when the flexibility of the curve increases, the chance on an event decreases (p=0.057, OR=0.932, 95% CI: 0.866, 1.002).

Conclusion: Patients with small body height have higher intra-operative risk on neurophysiological events due to halofemoral traction. All events resolved after release of traction, and no patient suffered from neurological damage caused by traction.
Meghan Koop

THE MOST IMPORTANT CONFOUNDERS FOR THE ASSOCIATION BETWEEN LOW-GRADE SYSTEMIC INFLAMMATION AND MUSCULOSKELETAL PAIN: A DELPHI STUDY

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Introduction

The association between low-grade systemic inflammation and musculoskeletal pain has been frequently studied in the past two decades. However, rarely do studies statistically correct for confounders that may disturb this association and literature about confounding factors for this association is lacking.

Purpose

A modified Delphi study was conducted to identify and provide consensus on the most important confounders when studying the association between low-grade systemic inflammation and musculoskeletal pain.

Methods

Three Delphi rounds were performed. Potential experts were identified in PubReminer and published at least two articles on the association between inflammatory markers and pain or inflammatory markers and other factors. In Round 1, the experts were asked to list the most important confounders that should be assessed. In Round 2, the experts were asked if they considered the listed confounder as important or not. In Round 3, the experts ranked the listed confounder’s level of importance on a 7-point Likert scale.

Results

The panel consisted of 48 experts. The experts suggested 120 confounders which were summarized into 38 confounders. In Round 2, 35 experts participated (response rate 72.9%) and reached consensus (>50%) for 33 confounders. In Round 3, 40 experts participated (response rate 83.3%) and reached consensus (>50%) for 8 extremely important confounders: immune disease, use of medication, acute illness/trauma, additional musculoskeletal diseases, experimental handling of blood samples, body composition, cancer and endocrine/nutritional/metabolic diseases.

Conclusions

These confounders are recommended to consider when assessing the association between low-grade systemic inflammation and musculoskeletal pain in future studies.
Moira van Leeuwen

ACTIVE STEP-BY-STEP CONTROL OF FOOT PLACEMENT DOMINATES GAIT STABILITY, BUT DOES NOT COMPENSATE FOR A CONSTRAINED ANKLE STRATEGY

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Introduction: The foot placement and ankle strategy are complementary mechanisms in coordinating the center of pressure (CoP) with respect to the center of mass (CoM), to maintain (mediolateral) gait stability.

Purpose: We intended to (1) replicate earlier findings demonstrating step-by-step neural control of foot placement and (2) investigate whether a constrained ankle strategy would tighten foot placement control as a compensatory strategy.

Method: 30 Healthy participants walked on a treadmill, while wearing a shoe limiting the CoP displacement during stance. Predictability of foot placement based on swing phase gluteus medius activity and CoM state, was compared against normal treadmill walking.

Results: We (1) replicated the relationship between gluteus medius activity and foot placement and (2) showed that the coordination of foot placement to CoM state was not tightened to compensate for a constrained ankle strategy. Instead, exploratory analysis revealed that compensatory foot placement encompassed an overall increase in step width.

Conclusions: We found an actively driven step-to-step foot placement strategy to maintain stability in walking. When compensating for a limited ankle strategy, average step width, rather than the degree of control was adjusted. Further research is required to unravel the contribution of other strategies and whether the compensatory strategy adapts over time. These fundamental insights can help to understand and/or intervene upon balance control in elderly, pathological or prosthetic gait and may contribute to the control of walking exoskeletons.
Content Validity of Patient Reported Outcome Measurement Instruments for Patient Satisfaction in Primary Care; a Systematic Review in Patients With Musculoskeletal Complaints

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Background
In the evaluation and treatment of patients with musculoskeletal disorders, the measurement of patient satisfaction plays an important role. As satisfied patients seem to gain more benefits from healthcare and adhere better to medical regimes, also, outcome assessment of patient satisfaction is used to assess the quality of healthcare and health care providers, and thus an important role in policy making. Although patient satisfaction is very frequently measured, it is unclear which instrument is the best to use. Therefore, existing instruments may only partly measure the patient satisfaction construct. The first measurement property that should be assessed when selecting an instrument is content validity, as it allows making a link between the content of the instrument and that of the construct to be measured.

Objective
To systematically review the literature on content validity of patient-reported outcome measurement (PROM) instruments used to assess satisfaction in patients with musculoskeletal complaints treated in primary care.

Method
- A literature search in MEDLINE, EMBASE and Cinahl was undertaken (up to January 2020) to identify studies on the development or evaluation of the content validity of a PROM aimed to assess patient satisfaction.
- A PROM was included if aiming to measure satisfaction of adult patients with musculoskeletal complaints for primary care services (e.g. physiotherapy, chiropractic). Two independent reviewers performed study selection, quality assessment, and data extraction.
- PROMs were assessed according the COSMIN guidelines.

Results
- Initially, 572 studies were identified. After screening the results on title and abstract, 40 studies were retrieved for full-text assessment. Seven different PROMs were eligible for assessment of content validity.
- All studies included scored ‘adequate’ for the total quality of the PROM development.
- No studies evaluating their content validity were retrieved.
- In rating the PROMs against the criteria of content validity all PROMs rated ‘insufficient’ for relevance, comprehensiveness, and comprehensibility.

Discussion
- In the development of PROMs, mainly clinicians were involved.
- Most PROMs were based on a formatistic model, which assumes that all items included fully form the framework patient satisfaction.
- None of the PROMs included items that were related to ‘shared decision making’, which is above all, a key issue in current health care.
- The low quality of evidence was partly due to the lack of original content validity studies.
- It is very likely that a number of PROMs were not included in this study, as not all PROMs used to measure patient satisfaction are published.

Conclusion
- None of the identified PROMs is recommended.
- Future studies should address the different aspects of content validity and emphasize patient involvement during the development of new instruments.

Data synthesis
The content validity of all of PROMs was rated as ‘insufficient’ and was supported by very low quality of evidence.

More details...
Check out the full protocol at PROSPERO (registration number CRD42189132623).
Available at: https://www.crd.york.ac.uk/PROSPERO/


References

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Anuja P. Satam

KNEE EXTENSOR MUSCLE STEADINESS IN RELATION TO MAXIMAL TORQUE AND PHYSICAL FUNCTIONING IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Introduction: While muscle function is quantified by maximal voluntary muscle torque (MVT), its quality is reflected in fluctuations observed on a torque-time curve. The extent of fluctuations is termed muscle steadiness. Whether muscle steadiness is associated with MVT and consequently with pain and activity limitations in patients of knee osteoarthritis (OA), is unknown.

Purpose: To explore the association of muscle steadiness with MVT and with physical functioning in patients with knee OA.

Method: Data of 172 patients with knee OA were used for this study. Torque-time curve data were obtained on an isokinetic dynamometer, and processed into MVT, torque fluctuations as coefficient of variance (CV), and as peak power frequency (PPF). Physical functioning was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire, the Get-Up & Go test, the 6-minute-walk test and the Stair-climb test. Associations were determined using correlation and regression analyses.

Results: Lower CV and PPF were significantly associated (p< 0.01 and p<0.05, respectively) with higher MVT, but associations were weak. Lower CV was significantly associated with better WOMAC score (p<0.05), also after correction for relevant confounders. CV was not associated with other tests. PPF approached significant association with physical functioning.

Conclusion: Muscle steadiness is, to some extent, related to better physical functioning, but not consistently across all tests in this study. It appears to be a weak relationship requiring further exploration. No previous study of muscle steadiness in relation to physical functioning in knee OA patients was found to compare our results.
Bernard J Smilde

STOPFOP: A EUROPEAN PHASE II CLINICAL TRIAL USING SARACATINIB TO TREAT FOP

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Background: Fibrodysplasia ossificans progressiva (FOP) is a genetic, progressive and devastating disease characterized by severe heterotopic ossifications (HO), contractures and early death. There are no approved medications yet. Our STOPFOP team identified AZD0530 (saracatinib) as a potent inhibitor of the ALK2-kinase which plays a key role in this rare bone disease. AZD0530 was proven to be effective in FOP mouse models. The EU Innovative Medicines Initiative provided funding to investigate the repurposing of AZD0530, originally designed for ovarian cancer treatment, to treat patients with FOP.

Methods: This is a phase 2a study, designed as European, multicentre, 6-month double blind randomized controlled trial of AZD0530 versus placebo, followed by a 12 month trial comparing open-label extended AZD0530 treatment with control data from a previous trial. We will include 20 FOP patients, aged 18-65 years, with the classic FOP mutation (R206H). Endpoints are objective change in heterotopic bone volume measured by low-dose whole-body computer tomography (CT), [18F] NaF PET activity and patient reported outcome measures.

Discussion: Drug repurposing – using existing clinical molecules for new disease indications - represents an ideal solution for limiting risks in early clinical studies. This is especially useful in rare diseases with limited study populations. Using existing assets may also allow more affordable pricing once an indication is approved.

With positive study outcome, AZD0530 may provide a rapidly translatable therapy for FOP due to the availability of extensive safety data from 28 registered clinical trials with AZD0530 involving over 600 patients.

Trial registration: EudraCT number 2019-003324-20
Introduction. A 44-year old woman presented with pain and nerve compression in the face due to Eagle syndrome. Eagle syndrome was diagnosed after many years of unexplained pain in the jaw and neck. The Eagle syndrome is due to elongation of the styloid process or calcification of the stylohyoid ligament. In this patient Eagle syndrome was diagnosed on both sides of the neck, which is very rare. Previously performed surgery, at the age of 39, to relieve complaints was not successful. At the age of 42, a second surgery took place to remove bone formed by the Eagle syndrome on the right side of the neck. Two years later, surgical removal of the calcified tissue on the left side of the neck was performed successfully.

Purpose. Analysis and description of the removed calcified tissue from the neck.

Method. Preoperatively a [18F]NaF PET/CT scan was conducted. Histologic examination and microCT was performed on removed tissue.

Results. [18F]NaF PET/CT scan prior to surgery showed no increased uptake of [18F] NaF in the styloid hyoid region, indicating active bone formation was not present at this site. The tissue removed during surgery is classified as calcified tissue. Histologic examination and microCT revealed cortical and trabecular bone and some areas of cartilage tissue.

Conclusion. The molecular mechanism leading to calcification in the styloid region in Eagle syndrome is still unknown. This case-report suggested an endochondral process of bone formation. Further examination of the calcified tissue will take place to investigate the properties of this material.
Mariana Vázquez-Cruz

LIPOTOXICITY CONTRIBUTES TO SKELETAL MUSCLE INSULIN RESISTANCE AND MITOCHONDRIAL DYSFUNCTION AFTER PHYSICAL INACTIVITY: A NARRATIVE REVIEW

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Physical inactivity is known to cause skeletal muscle atrophy and altered metabolism. Long term inactivity is associated with the development of metabolic syndrome, characterized by obesity, insulin resistance and development to type 2 diabetes mellitus. Short term inactivity in (hospitalized) humans indicates that insulin resistance can, however, develop within a week. As this is independent of obesity and over nutrition, it is currently unknown what the underlying mechanism of insulin resistance upon short term inactivity is. In this narrative literature review, supported by preliminary electron microscopy imaging, we observed that inactivity causes a cellular overload of substrate supply, relative to an underused substrate oxidation. This causes metabolic inflexibility, highlighted by a metabolic gridlock and elevated concentrations of acetyl-CoA. The increased intramyocellular lipids, such as diacylglycerol and ceramides, contribute to skeletal muscle lipotoxicity, and are known to inhibit IRS1/2 function and GLUT4 translocation to the membrane. This reduces insulin signaling and impairs glucose import, which can a positive adaptation to reduce a further nutritional overload during inactivity. Lipotoxicity likely contributes to mitochondrial dysfunction after inactivity, but this is poorly understood. In conclusion, short term inactivity causes insulin resistance and mitochondrial dysfunction via lipotoxicity, which can have severe consequences for hospitalized patients.

One sentence to highlight translational metabolism:

Physical inactivity during bedrest causes insulin resistance and mitochondrial dysfunction via metabolic inflexibility and lipotoxicity, which has negative consequences for the physical functioning in hospitalized patients.
Chen Zhang

ISOLATION OF HIGH QUALITY RNA FROM HUMAN BONE FOR RNA-SEQ ANALYSIS

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Introduction: Osteocytes in 3D-culture express a superior phenotype compared to osteocytes in monolayer culture(1). We have developed a protocol for culturing small human bone samples with primary osteocytes embedded in their native matrix. However, gene expression analysis in these bone samples is challenging, since the cell number is limited and RNA degradation and crosscontamination can occur.

Purpose: To develop a method to obtain a high yield RNA of high quality from human osteocytes embedded in their native matrix for RNA-seq analysis.

Method: Twenty-five human bone samples (surgical waste) from 2 donors (female, age: 79; male, age: 61) were collected. Bone samples were frozen in liquid N2, stored in RNAlater-ICE, and pulverized with frozen trizol using Freezer/Mill®-cryogenic-grinder. RNA was isolated and purified with chloroform and Direct-zol RNA-Miniprep-Plus-kit. RNA integrity (RNA integrity number (RIN)), was measured using Agilent-RNA-6000-Pico-Kit in a Bioanalyzer. RNA quantity was determined using NanoDrop spectrophotometer and Qubit®-RNA-HS-Assay-kits.

Results: The bone samples measuring 8.0x3.0x1.5 mm (length x width x height) were weighing 0.29±0.07 (mean±SD) g. RINranged from 2.8-7.6. RIN of 24% of RNA samples was >7, i.e. the minimum value required for RNA-seq. RNA yield/bone sample was 749±423 (mean±SD) ng, RNA yield of 72% of RNA samples was >500 ng, i.e. the minimum yield required for RNA-seq.

Conclusions: We developed a new method to isolate and purify RNA from small bone samples. Yieldand integrity of isolated RNA were adequate for RNA-seq analysis, as confirmed in a pilot RNA-seq run.

P3: Tissue Function & Regeneration
Wei Cao

κ-CARRAGEENAN-FUNCTIONALIZATION OF OCTACALCIUM PHOSPHATE-COATED TITANIUM DISCS ENHANCES PRE-OSTEOBLAST BEHAVIOR AND OSTEOGENIC DIFFERENTIATION

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Introduction: Octacalcium phosphate (OCP)-coated titanium implants are currently used for dental applications. Carrageenan is a sulfated-polysaccharide extracted from red edible seaweeds. It is highly hydrophilic and biocompatible.(1) Whether carrageenan can be used to functionalize OCP-coatings to enhance osseointegration of titanium dental implants is unclear.

Purpose: To characterize carrageenan-functionalized biomimetic OCP-coated titanium, and to test the effect of carrageenan on pre-osteoblast behavior and osteogenic differentiation.

Methods: Preparation and characterization of κ-carrageenan-functionalized OCP-coating: OCP-solution containing κ-carrageenan at 0.125, 0.25, 0.5, 1, and 2 mg/ml was used to precipitate OCP-coating onto titanium discs.(2) Characterization was performed using SEM, EDX, XRD, Raman-spectra, and contact-angle measurements. MC3T3-E1 pre-osteoblast behavior: Cell adhesion and spreading were determined using immunofluorescent staining (1,2h), and cell metabolic activity by PrestoBlue®-assay, and proliferation by CyQuant®-cell-proliferation-assay-kit (day 1,2,3). Osteogenic differentiation: Alkaline phosphatase-activity, osteogenic gene-expression, and matrix-mineralization (alizarin-red staining) were determined. Statistics: ANOVA (n=3-5), statistical significance: p<0.05.

Results: κ-Carrageenan (all concentrations) in OCP-coating changed the titanium disc coating’s morphology/microstructure by decreasing porosity compared to controls. κ-Carrageenan (2 mg/ml only) increased OCP-interplanar-crystal-distance (~1.5-fold). κ-Carrageenan did not affect hydrophilicity.

κ-Carrageenan (1+2mg/ml) significantly increased (6-7-fold) cell adhesion. All concentrations tested dose-dependently increased proliferation (max. 1.3-fold, day 3), metabolic activity (max. 1.5-fold, day 3), and alkaline phosphatase-activity (max. 1.8-fold, day 4).
Conclusions: β-Carrageenan modified morphology and microstructure of OCP-coating, and enhanced pre-osteoblast metabolic activity, proliferation, and osteogenic differentiation. This suggests that β-carrageenan might improve dental implant osseointegration in vivo.

References:
Background: There is controversy whether high-intensity resistance training (RT) is harmful to knee-joint tissues potentially exacerbating osteoarthritis (OA) symptoms. However, low-intensity RT may not be sufficient to increase muscle strength, thereby only provide short-term benefits. Mechanical loading influences the turnover of muscle extracellular matrix (ECM) proteins, including type VI collagen, that is involved in maintaining muscle integrity and force transmission. The biomarker PRO-C6 (C5-domain of the α3(VI) chain) is thought to reflect newly formed type VI collagen.

Purpose: Assessment of PRO-C6, and its association with changes in muscle strength, allows an objective indication of changes in muscle ECM in response to high-intensity or low-intensity RT.

Methods: 177 participants with knee OA conducted high-intensity (70%-80% 1RM) or low-intensity (40%-50% 1RM) RT (3 days/week for 12 weeks). PRO-C6 serum levels were quantified pre-intervention and post-intervention, and at 6-month follow-up using ELISA’s. Muscle strength was measured with an isokinetic dynamometer.

Results: PRO-C6 serum levels increased significantly from pre- to post-intervention, but did not change from post-intervention to follow-up. There were no significant between-group differences. Both groups improved over time for upper leg muscle strength. Elevated PRO-C6 serum levels were related to increased muscle strength.

Conclusions: Upregulated PRO-C6 serum levels likely reflects increased remodeling of muscle ECM in response to mechanical loading. Changes in PRO-C6 serum levels are related to improvements of upper leg muscle strength, which may be explained by the fact that in skeletal muscle type VI collagen is thought to provide reinforcement to ECM and to be involved in force transmission.
Jianfeng Jin

PULSATING FLUID SHEAR STRESS MODULATES BONE CELL SHAPE AND MITOCHONDRIAL STRUCTURE – IMPLICATIONS FOR BONE CELL FUNCTION?

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Introduction Bone cells respond to mechanical cues from the environment by changes in cellular morphology, which requires mitochondrial energy production. Mitochondria form an extensive highly dynamic network undergoing fission and fusion, with clusters moving along the cytoskeleton. Importantly, mitochondrial form and function are intimately linked. However, whether mechanical factors affecting cytoskeletal organization also affect mitochondrial network structure and function in bone cells is unknown.

Purpose To investigate whether live bone cell-deformation induced by mechanical loading is associated with changes in intracellular mitochondrial network structure.

Method Prior to 1h pulsating fluid shear stress (PFSS; peak-shear-stress-rate: 6.5Pa/s; amplitude: 1.0Pa; frequency: 1Hz), live MC3T3-E1 pre-osteoblasts were fluorescently stained for F-actin, nuclei, and mitochondria. Online live-cell imaging was employed (22 cells, 3 experiments) using LSCM, and various indices before/after applying PFSS computed. Cell-morphology (area), cell-movement (X,Y,Z-direction), cytoskeletal changes (F-actin fluorescence-intensity), and mitochondrial network structure and organization (number of branches, junctions, triple/quadruple-points, junction/slad/end-point-voxels, and branch-length in live-cell top-view images; every 10min) were determined.

Results PFSS reduced cell-surface-area gradually over time (0.85-fold, 10min; 0.50-fold, 60min). F-actin fluorescence-intensity remained unchanged. PFSS caused slight live-cell-movement periodically. PFSS modulated mitochondrial network structure and organization, e.g. number of branches, junctions, triple/quadruple-points, junction/slad-voxels, but not number of end-point-voxels or branch-length, was reduced after 6-7 sec but not thereafter.

Conclusions PFSS induced temporal and spatial changes in bone cell morphology, which was accompanied by significant changes in intracellular mitochondrial network structure. This suggests that mechanical load-induced bone cell deformation may drive mitochondrial function, and likely bone-cell function.
In vivo osteoconductivity of bovine serum albumin incorporated different crystalline calcium phosphate coatings

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Department of Oral Implantology and Prosthetic Dentistry

INTRODUCTION
Prosthetic implants and various fixation materials are commonly employed in dentistry(1). CaP coatings have been demonstrated to significantly improve the biological performances of metallic implants(2). Furthermore, the biomimetic incorporation of bovine serum albumin (BSA) could enhance the mechanical stiffness and the shear-force resistance of the mineral layer(3).

PURPOSE
The aim of the present study is to assess the bio-degradability and osteoconductivity of the amorphous, crystalline and hybrid coatings in rats, both in the absence and presence of BSA.

MATERIALS AND METHODS
To mimic the clinical titanium implant, a titanium pin with the groove (3mm in length) in the middle part of the pin was designed and coated with one of the three types of coatings. The coated pin was inserted into the femoral of rat (one sample per rat) for 3, 7, 14 and 21 days.

RESULTS
1. Scanning electron microscopy

2. Confocal laser-scanning microscopy

3. In vitro release profile of BSA

4. In vivo bone to implant contacts

DISCUSSIONS AND CONCLUSIONS
1. In vitro, the protein BSA, after incorporation, affected the morphology of crystalline calcium phosphate. The crystalline calcium phosphate could serve as a slow-release system for the incorporated protein.
2. In vivo, the amorphous CaP exhibited a similar BIC profile as the SLA surface and facilitated the highest BIC. In contrast, hybrid CaP and Crystalline favored an earlier significant increase of BIC.
3. BSA no matter of adsorbed or incorporated may compromise the osteoconductivity of both the three kinds of coatings and SLA surfaces of implant.

REFERENCES
Xumin Li

PROTECTIVE EFFECT OF CURCUMIN AGAINST OXIDATIVE STRESS-INDUCED DYSFUNCTION IN OSTEOBLASTS VIA GSK3β-NRF2 SIGNALING PATHWAY

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Introduction: Osteoblast dysfunction, induced by oxidative stress (OS), is one of major pathological mechanisms for osteoporosis. Curcumin (Cur), a bioactive antioxidant compound, isolated from Curcumin longa L, has been regarded as a strong reactive oxygen species (ROS) scavenger. However, it remains unveiled whether Cur can prevent osteoblasts from OS-induced dysfunction.

Purpose: To investigate the effects of Cur on oxidative stress-induced osteoblasts dysfunction and verify whether Glycogen synthase kinase (GSK3β) – Nuclear factor erythroid 2-related factor 2 (Nrf2) signaling pathway mediated the protective effect of Cur.

Methods: We adopted a well-established Hydrogen peroxide-induced oxidative damage model to investigate the preventive effect of Cur on osteoblast dysfunction by measuring intracellular ROS production, cell viability, apoptosis rate and expression levels of genes involved in osteoblastogenesis. Antagonist and agonist of Gsk3β-Nrf2 signaling were used to explore the role of this signaling pathway in OS-induced osteoblast dysfunction.

Results: Pretreatment of Cur significantly antagonized OS, i.e. suppressed endogenous ROS production, maintained osteoblasts viability and promoted osteoblastogenesis. The specific inhibitor of GSK3β and the activator of Nrf2 could significantly antagonize the destructive effects of OS, which indicated the critical role of GSK3β-Nrf2 signaling pathway. Furthermore, Cur mimicked the effects of these inhibitors and abolished the suppressive effects of OS on phosphorylated-GSK3β and Nrf2.

Conclusion: Our findings demonstrate that Cur protects osteoblasts against oxidative damages via retaining GSK3β-Nrf2 signaling and scavenging ROS production therefore maintains osteoblast function.
Human salivary cell-activating histatin 1 and histatin 2 target mitochondria and endoplasmic reticulum in live epithelial cells

Dandan Ma, Wei Sun, Kamran Nazmi, Enno C.G. Veerman, Floris J. Bikker, Richard T. Jaspers, Jan G.M. Bolhuis

Introduction
Human salivary histatin 1 (Hst1) and Hst2 exhibit cell-activating properties, whereas Hst3 shows an anti-fungal property. Hst1 and -2, as well as Hst5 accumulate in their target cells (epithelial cell and fungal cell, respectively), suggesting that their uptake and association with subcellular targets may play an important role in their functions.

Purpose
To explore the involvement of hist in mechanisms underlying the cell-activating functions is valuable for researchers within cell-based tissue engineering applications.

Method
Subcellular targets of histin were studied by using flow cytometry in combination with confocal laser scanning microscopy.

Results
Cellular uptake of the fluorescence (ATTO-647N)-labeled Histatin variants

Fluorescence microscopy revealed that a detectable accumulation of F-Hst1 to the intracellular space of HOS/HK epithelial cells was found as early as 5 min after starting the incubation (Fig. 1A). 60 min post incubation, the total fluorescence of cell-associated F-Hst1, as measured by flow cytometry, was significantly higher than those of F-Hst2 and F-Hst5. In contrast, the negative control — scrambled F-Hst1 (F-Hst1sc) — was virtually absent in the cells (Fig. 1B). In line with the FACS data, the highest level of accumulation in epithelial cells was observed by confocal laser-scanning microscopy (CLSM) with F-Hst1, followed by F-Hst2 > F-Hst5 > F-Hst1sc (Fig. 1C).

Using specific cell organelle markers, the subcellular location of the different Hsts was studied in more detail (Fig. 2A). F-Hst1, F-Hst2 and F-Hst5 colocalized with mitochondria with a P value of about 0.05. F-Hst1 showed a significantly (p<0.0001) higher colocalization (F value of 0.92 ± 0.02) with ER than F-Hst2 (P value of 0.51 ± 0.13) (Fig. 2A, 2B). In contrast, the P value of F-Hst3 and F-Hst1sc with the ER (0.40 ± 0.13 and 0.36 ± 0.05) were lower than 0.3, suggesting no co-localization of F-Hst1sc and F-Hst1sc with the ER (Fig. 2A, 2B). Neither of the tested Hst3 showed a co-localization with Golgi apparatus (Fig. 2A, 2B) and lysosomes (Fig. 2A, 2B).

Cellular uptake of the F-Hst1, F-Hst11-11, F-Hst112-22 and F-Hst123-38

Confocal images of subcellular targeted of F-Hst11-38 and F-Hst112-22

Confocal images of subcellular targeted of F-Hst1, F-Hst2 and F-Hst5

Conclusions
- F-Hst1, 2 and 5 co-localized with mitochondria.
- F-Hst1 and F-Hst2 but not F-Hst5 or F-Hst1sc showed a co-localization with the endoplasmic reticulum.
- The truncated fragment of F-Hst1, F-Hst112-22 co-localized with lysosomes, but not with mitochondria or with the endoplasmic reticulum.
- F-Hst1 and F-Hst2 increase cell metabolic viability.
- Our findings contribute to knowledge of histatin-cell interactions, which will help to further unravel the molecular mechanisms underlying the functions of histatin.
Introduction
Regulation of muscle fiber size and regeneration is critically determined by growth factors of the TGF-β superfamily, i.e. myostatin and TGF-β. Myostatin stimulates myofiber atrophy, while TGF-β stimulates collagen expression. It is presumed that myostatin acts via the Acvr1b (ALK4) and TGF-β via the Tgfbr1 (ALK5). Inhibition of one or both of the signaling pathways could potentially ameliorate muscle regeneration and prevent fibrosis. However, little is known about the impact of these receptors individually on muscle phenotype and regeneration as well as that of their combination.

Purpose
To investigate the role of ALK4 and ALK5 receptors solely and in combination in uninjured muscle and muscle during early regeneration after injury. Method A muscle fiber specific gene knockdown mouse model was generated in which ALK4 and/or ALK5 were knocked down. Muscle injury was induced in tibialis anterior muscle and qPCR, histological and immunohistochemical analyses were conducted in control and after 2, 4 days to examine myofiber size, regeneration and extracellular matrix deposition.

Results
In uninjured muscle, knockdown of combined receptors (ALK4/5−/−) substantially increased muscle fibers size (56.3%) and muscle mass (50%). Note that in ALK4/5−/− mice muscle, regeneration was detected in the absence of injury. Acutely after injury, both ALK4−/− and ALK5−/− mice decreased expression of muscle stem cells activators and myogenic regulatory factors. However, ALK4/5−/− increased fiber cross-sectional area and improved muscle regeneration index. Fibrotic genes expression remained unchanged in ALK4−/− and ALK5−/− mice, while it was significantly increased in ALK4/5−/− mice.

Conclusions
Individual muscle fiber specific knockdown of ALK4 and ALK5 impairs muscle regeneration, while combined knockdown of ALK4 and ALK5 stimulates myofiber hypertrophy and regeneration. Inhibition of ALK4 and ALK5 simultaneously may be a promising therapeutic approach for treatment of muscle wasting disorders and sarcopenia.
P4: Ageing & Vitality
Abstract

Introduction
It is known that balance training leads to improved balance in both young and older adults. However, in older adults, the mechanisms behind such improved balance is unclear.

Purpose
The influence of balance training (BT) on balance performance, spinal excitability, and muscle co-contraction were investigated in older adults.

Method
Twenty-two older adults participated in a 3-weeks BT program. Balance performance was quantified as mean absolute mediolateral center of mass velocity in perturbed and unperturbed unipedal stance on a robot-controlled platform, before and after the first session (SBT) and after ten sessions (LBT). In addition, durations of co-contraction in soleus and gastrocnemius lateralis (SOL/GL), as well as gluteus medius and adductor longus (GM/AL) muscles were assessed in perturbed and unperturbed unipedal balancing. H-reflex was acquired during the balancing tasks to obtain the H-reflex gain.

Results
We found improved balance performance in perturbed stance after SBT and improvements after LBT in both perturbed and unperturbed conditions. After SBT, duration of co-contraction of SOL/GL and GM/AL was increased in perturbed but not in unperturbed balancing and, after LBT co-contraction durations had returned to baseline values. H-reflex gains did not change with training.

Correlational analysis indicated that increasing co-contraction coincided with smaller improvements in balance performance and that increasing H-reflex gains coincided with bigger improvements in balance performance.

Conclusion
BT improves balance performance in older adults already after one session, with further slower improvements of three weeks of training. Ongoing analysis is aimed at elucidating the determinants of balance improvements with training in the short- and long-term.

Keywords: H-reflex, co-contraction, motor learning, balance training
Moritz Eggelbusch

INFLAMMATION-INDUCED SKELETAL MUSCLE WASTING: EMERGING ROLE OF THE NLRP3 INFLAMMASOME

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Introduction: Systemic low- and high-grade inflammation in various acute and chronic diseases is associated with skeletal muscle mass atrophy and metabolic dysfunction. While the nucleotide-binding oligomerization domain-like receptor family pyrin domain containing 3 (NLRP3) inflammasome is an integral component of the innate immune system, its role in skeletal muscle atrophy and metabolic dysfunction is poorly understood.

Purpose: Complicating factors in understanding molecular mechanisms underlying this loss, are that muscle wasting is a multifactorial process, and human tissue under well-controlled wasting conditions is sparse. Here we studied mechanistically how inflammation induces skeletal muscle atrophy and metabolic dysfunction.

Methods: We treated differentiated C2C12 myotubes with different concentrations of lipopolysaccharide (0,10,100-200 ng/ml LPS), and measured muscle fiber diameter, gene expression and protein concentrations.

Results: LPS reduced fiber diameter up to 42±6% (at 100 ng/ml LPS) after 24 hrs, which remained smaller up to 72 hrs. NLRP3 and downstream caspase-1 mRNA gene expression increased, resulting in a dose-dependent response in NLRP3 and cleaved (p20) caspase-1 effector protein concentration upon LPS treatment. The addition of 10 ng/ml TGF-b further induced NLRP3 gene expression upon LPS treatment. These data suggest an inflammation-induced priming of the NLRP3 inflammasome in myofibers, independent of immune cell involvement. Using STED fluorescent imaging, NLRP3 colocalized to mitochondria (66±5%), with unknown functional consequences. However, SS31 (stabilizing cardiolipin) mitigated LPS-induced fiber atrophy.

Conclusions: We show a mechanistic link between inflammation and mitochondrial dysfunction, highlighting the translational role of the NLRP3 inflammasome and mitochondrial dysfunction in the development of skeletal muscle wasting.
Moritz Eggelbusch

STUDYING MUSCLE ARCHITECTURE BY ULTRASOUND AND MAGNETIC RESONANCE IMAGING

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Introduction: The ability to non-invasively assess muscle morphology is very valuable in optimizing health care. Within Amsterdam Movement Sciences, researchers use either ultrasound or magnetic resonance imaging techniques to answer (pre)clinical research questions concerning muscles. At AUMC and Vrije University, 2D US images are converted into 3D voxel array using a motion caption system. Diffusion tensor imaging by magnetic resonance imaging (DTI-MRI) is available at AMC. Both measurement modalities have advantages and shortcomings, but no studies have compared these methodologies for the vastus lateralis (VL) muscle in detail.

Purpose: To compare muscle-related parameters (volume, anatomical cross-sectional area, pennation angle and fascicle length) using 2D, 3D ultrasound and DTI-MRI, as well as to determine repeatability and inter-/intra-observer-variability.

Methods: Up to 30 participants with a heterogenous muscle volume will be recruited in spring 2020. Muscle architecture of the vastus lateralis and gastrocnemius muscles will be assessed by 2D, 3DUS and DTI-MRI, and compared across modalities. Repeatability, and inter-/intra-observer-variability will be determined. Extrapolation of 2D US images will be used to estimate VL volume.

Results: Muscle volume assessed by 3D US and DTI-MRI likely gives very similar outcomes with a low variability, while extrapolation from 2D images estimates muscle architecture within a reasonable confidence interval.

Conclusions: With this study, we compare available techniques within Amsterdam Movement Sciences.
Sciences, and provide an overview of advantages and disadvantages of various techniques available to assess muscle morphology. Future studies at the intensive care, the hospital ward, in animals, astronauts and in (elite) athletes are in the planning.
Alan Jenks

STUDY OBJECTIVES: TO DO AN IPD META-ANALYSIS TO ASSESS THE EFFECT OF SMT IN OLDER ADULTS WITH CHRONIC LBP.

Alan Jenks, PhD student, Department of Health Sciences, Vrije Universiteit

Methods and material: Electronic databases from 2000 until April 2016, and reference lists of eligible trials and related reviews. Randomized controlled trials (RCT) which examined the effect of SMT in older adults with chronic LBP compared to any comparative treatment. We contacted authors from eligible trials for full data set. Two review authors (ADJ, SMR) independently conducted the study selection and risk of bias using the Cochrane Risk of Bias tool. We examined the effect of SMT versus recommended interventions (e.g. exercise); We used GRADE to assess the quality of the evidence. For the treatment effect, a one-stage approach (mixed model analysis, intention-to-treat principle) was used; sensitivity analyses were conducted to determine the robustness of the analyses further in a two-stage approach. Pain intensity and back-specific functional status; examined at 4, 13, 26 and 52 weeks.

Results: Of the 11 RCTs fulfilling the inclusion criteria, we obtained IPD from10(n=769). Most (n=x) compared SMT to recommended interventions. Compared to recommended interventions, there is moderate quality evidence that SMT results in similar outcomes at 4 weeks. (pain: mean difference -x, 95%CI: -x to x, ntrials, nparticipants, scale 0-100 point and functional status: z-score difference: -x, 95% CI -x to x, ntrials, nparticipants). These effects were similar to other follow-up measurements. Data for the other comparisons showed similar benefits. Sensitivity analyses confirmed the robustness of these findings.

Conclusion: SMT provides similar outcomes to recommended interventions for pain and functional status in older adults with chronic LBP. Therefore, SMT is an option for the treatment of chronic LBP.
In neuroscience, sensorimotor coordination is attributed solely to the neural control of movement. However, sports science reveals that improvements in athletic performance rely on muscular adjustments which change the body mechanics over weeks or months. Combining insights from neuroscience and biomechanics, I present the theory that efficient motor coordination relies on the nervous system finding the appropriate body mechanical properties to perform a motor task, through postural adjustments. I first show that in order to stand still in challenging balance conditions, the nervous system increases ankle stiffness and decreases the ankle sensorimotor gain in advance of perturbations. I then show that mobility relies on the nervous system adjusting the position of the center of mass to provide torque for movement. Moreover, elderly subjects use this ability to mobilise the center of mass in order to improve their balance. I finally show that balance during running benefits from the ability to adjust the leg biomechanics.
Isa Mast

DYNAMIC ARTERIAL SPIN LABELING MRI OF CEREBROVASCULAR PERFUSION DURING EXERCISE

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Introduction: Impaired cerebrovascular reactivity has been linked to cognitive decline found in aging and type 2 diabetes. Some hemodynamic changes can remain undetectable at rest, and may only become apparent during a cerebrovascular challenge. Spatial maps of the cerebrovascular reactivity can be obtained with pseudo-continuous arterial spin labeling (pCASL) MRI upon artificial vasodilator challenges. Alternatively, aerobic exercise can be used as a noninvasive physiological challenge.

Purpose: To evaluate the feasibility of dynamic pCASL-MRI for measuring the cerebrovascular response to exercise.

Methods: Nine volunteers (4/5 male/female; age 23.5 ± 1.5 years) were scanned during incremental exercise protocols on a MR-compatible bicycle ergometer (Lode-BV). Imaging was performed on a 3 Tesla MR system (Philips) using a 32-channel head coil. Cerebrovascular blood flow (CBF) was measured using pCASL with a 2D-EPI readout. Motion correction was performed by using statistical parametric mapping (SPM12).

Results: Data of a single measurement are displayed in Figure 1. Heart rate during exercise ultimately exceeded 160 bpm (Figure 2). We observed a transient 20-50% increase in CBF during exercise in all participants in both exercise protocols (Figure 3). In two measurements, control/label pairs were excluded due to excessive motion.
Conclusion: Our pilot experiments demonstrate that pCASL-MRI can detect dynamic changes in CBF during bicycle exercise, which may become a valuable modality to investigate cerebrovascular reactivity in health and disease.

Figure 1: Exercise intensity and dynamic CBF in one participant.

Figure 2: Heart rate response during exercise.

Figure 3: Maximal CBF changes per participant (median(IQR)).
Baroreflex Sensitivity and Cerebral Oxygenation During Standing Up in Younger and Older Adults

Arjen Mol

Baroreflex sensitivity and cerebral oxygenation during standing up in younger and older adults

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Purpose: The clinical consequences of orthostatic hypotension may be determined by baroreflex sensitivity and cerebral autoregulation. The aim of the present study was to compare these mechanisms between younger and older adults.

Methods: 34 younger (age < 65 years) and 31 older adults (age > 70 years) underwent continuous measurements of blood pressure, electrocardiogram and near-infrared spectroscopy measurements of cerebral oxygenation (as a proxy for cerebral perfusion) during active standing. Baroreflex sensitivity was defined as the drop of inter beat interval (the time between consecutive heart beats) after standing up divided by systolic blood pressure drop. The initial orthostatic drop (<30 seconds) and recovery (< 60 seconds) and late recovery (i.e. 60-180 seconds) of blood pressure and cerebral oxygenation were assessed.

Results: Initial systolic blood pressure drop was not significantly different between the age groups, while initial diastolic blood pressure drop was significantly larger in older adults (Δ13 mmHg, p < 0.001). Initial systolic blood pressure recovery was smaller in older adults (Δ12 mmHg, p < 0.05), but initial diastolic blood pressure recovery was not significantly different between the age groups. Baroreflex sensitivity was significantly lower in older adults (Δ8.0 ms/mmHg, p < 0.001). Oxygenated hemoglobin after standing up showed a smaller drop in older adults (Δ6 μmol/L, p < 0.001).

Conclusion: The lower baroreflex sensitivity in older compared to younger adults suggests a higher vulnerability for the consequences of orthostatic hypotension. The unexpected smaller cerebral oxygenation drop in older compared to younger adults might indicate a tighter cerebral autoregulation.

Keywords: ageing, baroreflex, blood pressure, cerebrovascular circulation, NIRS, orthostatic hypotension Baseline dev.: deviation from baseline.
Robert Memelink

SUSTAINED BODY COMPOSITION CHANGE DURING 6-MONTH FOLLOW-UP AFTER COMBINED LIFESTYLE INTERVENTION IN OLDER ADULTS WITH OBESITY AND TYPE 2 DIABETES

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Background:

Patients with obesity and type 2 diabetes (T2D) are advised to reduce their body weight to lose fat mass. We recently showed that older adults with obesity and T2D who consumed a whey protein drink enriched with leucine and vitamin D lost fat mass and preserved muscle mass during a 3m combined lifestyle intervention of hypocaloric diet and resistance exercise (PROBE study). We now evaluated to what extent body composition change was sustained after 6m follow-up without intervention.

Methods:

105 older adults with obesity and T2D completed the 3-month PROBE intervention and were followed from 3 to 9 months after baseline. 76 subjects participated at 9 months, of whom 38 had received the whey protein drink (test) and 38 had received an isocaloric control drink (control) during intervention. Body weight (scale), lean mass, appendicular muscle mass and fat mass (DXA), and dietary intake and physical activity level (3-day record) were assessed. Change over time was analysed using paired samples t-test. ANOVA was used for evaluation of differences in change in body composition between test and control.

Results:

At 9 months, an average of 2.1 kg (78%) of the initial 2.7 kg weight reduction at 3 months was maintained. Lean mass significantly increased (+0.60 ± 2.2 kg, p=0.026), whereas fat mass (+0.03 ± 2.8 kg, p=0.94) and appendicular muscle mass (+0.18 ± 0.98 kg, p=0.12) did not change. Protein intake (0.84 ± 0.32 g/kg body weight) returned to baseline level. The observed slight increase in physical activity level during intervention (+0.05 ± 0.02, p=0.009) was maintained during follow-up. There were no significant differences between the test and control group during follow-up.

Conclusions:

Body weight change during the 3-month combined lifestyle intervention in the PROBE study was sustained after 6 months follow-up without intervention. In addition, lean mass had increased, whereas fat mass remained unchanged.
Anna Rojer

ROBUSTNESS OF IN-LAB AND DAILY-LIFE GAIT SPEED MEASURES OVER ONE YEAR IN HIGH FUNCTIONING ADULTS AGED 61- TO 70-YEAR OLD

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Introduction: Gait speed is a simple and safe measure with strong predictive value for negative health outcomes in clinical practice, yet in-lab gait speed seems not representative for daily-life gait speed.

Purpose: This study aimed to investigate the interrelation between and robustness of in-lab and daily-life gait speed measures over 12 months in 61- to 70-year old adults.

Methods: Gait speed was assessed in-lab through standardized stop-watch tests and in daily life by 7 days of trunk accelerometry in the PreventIT cohort, at baseline, after 6 and 12 months. The interrelation was investigated using Pearson’s correlations between gait speed measures at each time point. For robustness, changes over time and variance components were assessed by Analyses of Variance (ANOVA) and measurement agreement over time by Bland-Altman analyses.

Results: Included were 189 participants (median age 67 years [IQR: 64-68], 52.2% females). In-lab and daily-life gait speed showed low correlations (Pearson’s r=0.045-0.455) at each time point. Moreover, both in-lab and daily-life gait speed appeared robust over time, with comparable and smaller within- than between-subjects variance (range 0.001-0.095 m/s and 0.032-0.397 m/s, respectively) and minimal differences between measurements over time (Bland-Altman) with wide limits of agreement (SD of mean difference range: 0.12-0.34 m/s).
Conclusion: In-lab and daily-life gait speed measures show robust assessments of gait speed over 12 months and are distinct constructs in this population of high functioning adults. This suggests that (a combination of) both measures may have added value in predicting health outcomes. Key words: accelerometry, walking speed, motor activity, longitudinal studies
P5: Rehabilitation & Development
Margit Bach

MODULAR CONTROL OF RUNNING IN CHILDREN

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Introduction

Muscle synergies are generally considered as the overall neural output of the central nervous system to evaluate motor control tasks like locomotion. We hypothesise that running gradually matures in children to resemble that of the adult pattern, i.e., increased number of synergies accompanied by a temporal shift related to a reduced stance phase.

Purpose

The purpose of this study was to investigate the fundamentals of the development of running in very young children. Methods In this cross-sectional study, we investigated comfortable treadmill running in twenty-four healthy children (2-8 yrs) and seven young adults (22-28 yrs). We measured EMG, kinematics, and performed a non-negative-matrix factorisation (NMF).

Results

Children younger than 6.5 years managed the running condition with a walk-run strategy. Children younger than 4.5 years had a longer burst duration of the medial gastrocnemius muscle (MG) compared to the older children and adults. The muscle synergy analysis using NMF revealed a similarity in the activation pattern representing the MG muscle with a shift corresponding to the reduced stance phase for running compared to walking. There were fewer muscle synergies needed to explain ~90% of the variance accounted for in children younger than 4.5 years old across all modalities.

Conclusions

The results of this study confirmed our hypotheses: the older the child the more the muscle synergy patterns resemble that of the adult pattern. Moreover, the development of running in children appeared gradual as the youngest children make use of a combination of a walk-run strategy to manage the running tasks.
Annike Bekius

MODULAR CONTROL IN CHILDREN WITH CEREBRAL PALSY DURING THE DEVELOPMENT OF WALKING

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Introduction

Cerebral palsy (CP) is a developmental motor disorder, caused by lesions in an immature brain, which affects the development of walking. In typically developing (TD) children the number of muscle synergies involved in walking increases throughout motor development from two during neonate stepping to four in toddlers when they start to walk independently. Children with CP who walk independently use fewer synergies than TD children. Purpose We investigated whether modular organization of muscle activation differed between CP and TD children, already in the early stage of development.

Method We recorded bilateral electromyography (EMG, 22 muscles) during treadmill and overground walking in 16 CP (uni- and bilateral) and 11 TD children (age: 6.5-47.2 months). Patients were included based on high-risk of developing CP with abnormalities in brain magnetic resonance imaging. Muscle synergies were estimated using non-negative matrix factorization to EMG envelopes pooled across steps. We compared their number between CP and TD children.

Results During supported walking, children with CP required two or three muscle synergies to describe bilateral muscle activation compared to three or four in TD children. Children with CP who walk independently required three or four synergies compared to four in TD children. Unilateral analysis of independent walkers with unilateral CP (n=5) revealed three synergies for the affected compared to four for the less-affected side.

Conclusions Our results suggest that children with CP use a ‘simpler’ motor control strategy during walking compared to TD children in the early stage of motor development. This appears to be sidespecific in children with unilateral CP.
Introduction

The final treatment option for knee osteoarthritis (KOA) is knee joint replacement and symptoms of KOA may reduce gait adaptability. Therefore, the capacity to adapt to a new joint may be a predicting factor in the outcome of replacement surgery. Gait adaptability can be tested using a Target-Stepping Test.

Purpose

To predict rehabilitation of gait after surgery, a Target-Stepping Test needs to be able to identify strong from weak adapters. Therefore, as a first step to validate this idea, we assessed gait adaptability of severe KOA patients compared to controls.

Method

Ten severe KOA patients, planned for knee replacement surgery and 21 age-matched asymptomatic controls were included.

The Target-Stepping Test imposed a constant asymmetric gait pattern, with constantly on one side 20% shorter steplength (for patients the side planned for surgery) and the other 20% longer than baseline steplength, at 130% of comfortable walking speed.

Performance (absolute stepping error = midfoot–midpoint target) was compared using the Mann-Whitney U Test.

Results

Patients (1.39 m/s, IQR1.2-1.5) walked slower than controls (1.57m/s, IQR1.4-1.8, p=0.026). Further, patients performed worse on precision stepping compared to controls (p=0.035, Figure). Performance of patients showed a large spread.

Conclusions

Target-Stepping Test imposing an asymmetric gait pattern at fast speed is sensitive enough to detect a worse stepping accuracy performance in patients compared to controls. Future research may investigate whether the Target-Stepping Test can be used for subgrouping patients in good versus poor gait adaptability, as a possible predictor for good versus bad outcome after joint replacement surgery.
Introduction: Balance interventions can improve balance control of children with cerebral palsy (CP), but effects on brain white matter (WM) are unknown. Diffusion tensor imaging (DTI) can be used to investigate integrity, by fractional anisotropy (FA), and volume of brain WM. Purpose: To investigate whether a 6-week balance intervention can alter DTI-derived measures, reflecting brain WM organization, in CP.

Method: 12 children with bilateral spastic CP (age:11.3±2.3y, GMFCS II) underwent balance evaluation and MRI acquisition, including DTI, at baseline and after a 6-week X-Box One Kinect balance intervention. 9 age-matched typically developing (TD) children underwent baseline measurements for reference. Balance control was evaluated clinically by GMFM-Challenge score. DTI was analyzed to obtain FA and volume of 8 WM regions (tensor-based segmentation analysis) and 5 WM tracts (probabilistic tractography analysis).

Results: Follow-up GMFM-Challenge scores were higher compared to baseline (Figure). Cerebral peduncle volume increased, whereas volumes of retro-lenticular limb of internal capsule and splenium of corpus callosum decreased. FA of corticospinal tract decreased.

Conclusions: Changes in FA and volume of WM regions were small but very consistent between children, indicating that neuroplastic changes can occur after a 6-week balance intervention in CP. Remarkably, the direction of the observed changes was not always towards TD. Reproducibility of the current findings should therefore be investigated in future studies. Overall, the results may provide new insights in the neural mechanisms contributing to balance control in CP, and indicate that the brain of children with CP may be more plastic than sometimes assumed.
THE EFFECT OF SELECTED MOTOR EXERCISES ON SENSORY ORGANIZATION OF CHILDREN WITH DEVELOPMENTAL COORDINATION DISORDER: A DUAL-TASK APPROACH

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Abstract
Postural control includes the efficient use of information on somatosensory, visual, and vestibular systems. Children with Developmental Coordination Disorder (DCD) have a lower balance ability compared to their typical peers and show a wide disadvantage in sensory organizing. The purpose of this study was to investigate the effect of selected balance exercises under dual task and single task conditions on the sensory organization of balance control in children with DCD. Participants included 39 children aged 9 to 7 years old with DCD who were randomly assigned to three groups, dual-task balance training (n = 13, Mage: 8.59 ± 0.82 years), single-task balance training (n = 13; Mage: 8.61 ± 0.83 years) and control (n = 13; Mage: 8.41 ± 0.86 years). The composite equilibrium scores, somatosensory ratio, visual ratio and vestibular ratio were measured by sensory organizing test in pretest, posttest (after 24 sessions) and follow-up (two months after intervention). To evaluate the sensory organization of participants, a computerized dynamic posturography device was used. There was a significant difference between the dual-task group and the single-task and control group in the composite equilibrium scores, visual and vestibular ratios. The dual task balance training program improved sensory organization of balance control in children with DCD (P <0.05). The balance exercises based on dual-task approaches can improve the sensory organization of children with DCD. It is suggested to mentors and occupational therapists to take advantage of this approach in designing their exercise programs in children with DCD.

Keywords: sensory organization, vestibular system, somatosensory system, visual system, dual-task
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Hamideh Jahanbakhsh

THE EFFECT OF TASK-SPECIFIC BALANCE TRAINING PROGRAM IN DUAL-TASK AND SINGLE-TASK CONDITIONS ON BALANCE PERFORMANCE IN CHILDREN WITH DEVELOPMENTAL COORDINATION DISORDERS

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Abstract

BACKGROUND: Among the disorders and developmental delays in children with developmental coordination disorder (DCD), the ability to maintain balance is important because of the impact on motor skills development, the falling risks and participating in various physical activities. The purpose of this study was to examine the effect of task-specific balance training in dual-task and single task conditions on balance performance in children with DCD.

METHODS: Thirty-nine children aged 7 to 9 years old with DCD were randomly assigned into 3 groups: 1- Dual-task training group (n = 13; mean age: 8.99 ± 0.82 years); 2. Single task training group (n = 13; mean age: 6.61 ± 0.83 years) and control group without any intervention (n = 13; mean age: 8.41 ± 0.86 years). The balance of all three groups was measured using the stork balance stand test and dynamic Y balance test in the pretest, posttest, and follow-up phases (2 months after the intervention).

RESULTS: There was a significant difference between the dual task and single task training program in static and dynamic balance tests score. The dual-task program significantly improved the balance performance of children with DCD (P <0.05).

CONCLUSIONS: Compared to single task approaches, task-specific balance training based on dual-task approaches can lead to a greater improvement in the balance of DCD children. This type of training is suggested to use for planning physical activity classes.

Keywords: static balance, dynamic balance, developmental coordination disorder, dual-task

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Robin Kwakman

METABOLIC LOAD OF MORNING CARE AND REHABILITATION ACTIVITIES IN CRITICALLY ILL PATIENTS; PRELIMINARY RESULTS

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Abstract

Introduction
Early rehabilitation is advocated but physically demanding for critically ill patients. In order to prescribe a well-balanced rehabilitation programme, more insight in the metabolic load of daily activities on the intensive care is needed.

Purpose
The aim of this study is to describe and compare the oxygen cost of morning care and rehabilitation activities in mechanically ventilated ill patients.

Method
We measured breath-by-breath gas exchange in ventilated (≥48hrs) intensive care patients during rest, morning care and rehabilitation activities. The absolute oxygen uptake attributable to the activity (net-VO2 in mlO2) was calculated by subtracting the area under the curve (AUC) of VO2 at rest from the AUC of VO2 of the total activity. Additionally, absolute net-VO2 was also expressed relatively (%) to resting VO2.
We used paired t-tests to compare absolute and relative net-VO2 between activities.

Results
We recruited 10 patients in this ongoing study (mean±SD age, 63±12y; MRC sum-score, 34±20). Median duration was 27min for morning care (range, 10–48min) and 9min for active bed exercises (range, 3–21min). The absolute net-VO2 differed significantly between active bed exercises (median: 37mlO2, IQR:-33 to 486) and morning care (499mlO2, 50 to 1318). The relative net-VO2 did not differ significantly between both activities (mean±SD: 7.2±12.7% and 9.0±9.0% respectively).

Conclusion
The metabolic load and duration of daily activities varies between patients. The absolute net-VO2 of morning care was higher when compared to bed exercises. This stresses the need to take the metabolic load of daily activities into account in intensive care rehabilitation programmes.
Mohammadreza Mahaki

HOW DOES EXTERNAL LATERAL STABILIZATION CONSTRAIN NORMAL GAIT, BESIDES FROM IMPROVING MEDIO-LATERAL GAIT STABILITY?

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Introduction: The effect of external lateral stabilization on medio-lateral gait stability has been investigated previously. However, existing lateral stabilization devices not only constrains lateral motions, but also transverse pelvis rotation.

Purpose: This study aimed to investigate the effect of external lateral stabilization with and without constrained transverse pelvis rotation on mechanical and metabolic gait features.

Methods: Kinematic, kinetic, and breath-by-breath oxygen consumption data were recorded during 3 walking conditions (Normal walking, lateral stabilization with (Free) and without transverse pelvis rotation (Restricted)) and 3 speeds (0.83, 1.25, and 1.66 m/s) for each condition (Fig 1.).

Results: External lateral stabilization significantly reduced the amplitudes of the transverse and frontal pelvis rotations, transverse thorax rotation, medio-lateral pelvis displacement, arm swing, and step width. The amplitudes of anterior-posterior and vertical pelvis displacements, step length, free vertical moment, and energy cost were not significantly influenced by external lateral stabilization. The removal of transverse pelvis rotation restriction by our experimental set-up resulted in significantly higher transverse pelvis rotation in Free condition than in Restricted condition (Fig 2.).

Conclusion: Existing lateral stabilization set-ups not only constrain medio-lateral motions (i.e. medio-lateral pelvis displacement and step width), but also constrains other gait patterns such as transverse pelvis and thorax rotations, frontal pelvis rotation, as well as arm swing. Our set-up restricted transverse rotation less than previous set-ups. Future studies are suggested to utilize set-ups without the aforementioned movement restrictions.

Keywords: Gait stability, external lateral stabilization, pelvis rotation, arm swing, step length, energy cost.
Introduction: Exploration is considered a key element in reward-based motor learning. Since both sensorimotor noise and exploration result in variability, exploration is difficult to measure.

Purpose: In order to quantify exploration, we compare three methods for estimating other sources of variability: sensorimotor noise.

Method: Participants (N=41) performed target-directed weight shifts. Following each trial they could receive stochastic binary reward feedback. Participants first performed 6 baseline blocks without feedback, and next twenty blocks alternating with and without feedback. We quantified variability by trial-to-trial changes in movement endpoint. We estimated sensorimotor noise by the median squared trial-to-trial change in movement endpoint for trials in which no exploration is expected: trials in baseline blocks, trials in blocks without feedback, and rewarded trials in blocks with feedback. We estimated exploration by the median squared trial-to-trial change following non-rewarded trials minus sensorimotor noise.

Results: Variability was larger following non-rewarded trials than following rewarded trials. This indicates that our reward-based weight-shifting task successfully induced exploration. Most importantly, our three estimates of sensorimotor noise differed: the estimate based on rewarded trials was significantly lower than the estimates based on the two types of trials without feedback. Consequently, the estimates of exploration also differed.

Conclusion: We conclude that the quantification of exploration depends critically on the type of trials used to estimate sensorimotor noise. We recommend the use of variability following rewarded trials.
MOTION ANALYSIS OF THE DRUJ AND QUANTIFICATION OF THE METHODOLOGICAL ERROR

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Introduction

A distal radio-ulnar joint (DRUJ) prosthesis is a treatment option in DRUJ arthroplasty. Unfortunately, implant-related complications often occur. Implant design improvement through integration of the patients unique kinematic properties could reduce complications.

Purpose

The research goal is to use 3D image analysis technology to investigate motion of the DRUJ while simultaneously uncovering the methodological error.

Methods

To evaluate the methodological error an arm was scanned 10 times without changing its position. Quantification of the methodological error was achieved by calculating the mean target registration error (mTRE), being the average distance between corresponding points of the bone polygons in frame 1 and each of the remaining frames.

Forearm rotation was assessed by rotating the arm in set increments from pronation to supination while scanning at every interval. After image analysis, the distal radius centroid was plotted for every timeframe (Fig. 2). A circle fit was performed to find the approximate center of rotation.

Results

mTRE for the radius and ulna were 0,018- and 0,015 millimeter respectively. Motion analysis of the centroid of the distal radius revealed a circular motion path suggesting a fixed rotation axis (Fig. 2)
Conclusions

The small methodological errors enable investigation of the motion path with a high reliability. Research into the kinematics of the DRUJ is ongoing with a focus on the axis of rotation.

Figure 1: The test setup.

Figure 2: Motion path of the distal radius (blue) and the center of rotation (green)
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Introduction
Knee ankle foot orthoses (KAFOs) are commonly prescribed in persons with quadriceps muscle weakness to reduce mobility problems such as instability, reduced speed and increased energy expenditure during walking. A stance-control KAFO (SC-KAFO) is a type of orthosis that locks during the stance phase, providing stability, and unlocks during the swing phase, allowing a more natural gait pattern. So far, the evidence on the efficacy of SC-KAFOs in polio survivors is very scarce.

Purpose
To investigate the efficacy of SC-KAFOs on walking speed, energy expenditure and satisfaction with walking in polio survivors with quadriceps muscle weakness compared to walking with shoes only.

Methods
We retrospectively analyzed data from 29 polio survivors who were prescribed with a SC-KAFO during clinical care at the Amsterdam UMC. The following assessments were performed before and at least 3 months after receiving the SC-KAFO: six-minute comfortable walk test with ambulant registration of gas-exchange to assess walking speed, walking energy expenditure, and a questionnaire on satisfaction with walking.

Results
Walking energy consumption decreased significantly with 7% while walking with the KAFO compared to shoes-only walking (p=0.006). No differences were found in walking speed and energy cost (p>0.05). Patients reported significant improvements on safety and stability during walking and walking satisfaction (p<0.035). No improvements were seen on walking effort, stair climbing and fear of falling (p>0.05)

Conclusions
This study shows that the SC-KAFO is beneficial in improving mobility in polio survivors with quadriceps muscle weakness by decreasing energy consumption of walking and improving satisfaction in walking.

Note:
Data will be more specified and visualized by using graphs on the poster.
Mique Saes

IS RESTING-STATE EEG LONGITUDINALLY ASSOCIATED WITH RECOVERY OF CLINICAL NEUROLOGICAL IMPAIRMENTS EARLY POST STROKE? A PROSPECTIVE COHORT STUDY

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Introduction The time course of cortical activation and its relation with clinical measures may elucidate mechanisms underlying spontaneous neurobiological recovery after stroke.

Purpose We aimed to investigate (1) the time course of cortical activation as revealed by EEG-based spectral characteristics during awake rest and (2) the development of these spectral characteristics in relation to global neurological and upper-limb motor recovery in the first six months post stroke.

Methods Resting-state EEG was measured serially in 41 patients after a first-ever ischemic stroke, within 3 and at 5, 12 and 26 weeks post stroke. We computed the brain symmetry index (BSI) and directional BSI (BSIdir) over different frequency bands (1-25Hz, delta, theta) and delta/alpha ratio (DAR). The National Institutes of Health Stroke Scale (NIHSS) and Fugl-Meyer motor assessment of the upper extremity (FM-UE) were determined as clinical reflections of spontaneous neurobiological recovery. Longitudinal changes in spectral characteristics and within- and between-subject associations with NIHSS and FM-UE were analyzed with linear mixed models.

Results Spectral characteristics showed a gradual normalization over time, within and beyond 12 weeks post stroke. Significant within- and between-subject associations with NIHSS were found for DAR of the affected hemisphere (DARAH) and BSIdirdelta. BSIdirdelta also demonstrated significant within- and between-subject associations with FM-UE.

Conclusions Changes in spectral characteristics are not restricted to the time window of recovery of clinical neurological impairments. The present study suggests that decreasing DARAH and BSIdirdelta reflect improvement of global neurological impairments, whereas BSIdirdelta was also specifically associated with upper-limb motor recovery early post stroke.

Fig 1. Development of clinical assessment scores (A, B) and EEG parameters (C, D) over time post stroke.
Fig 2. Measurement set-up in the especially equipped 4D-EEG van to visit patients at their place of residence.