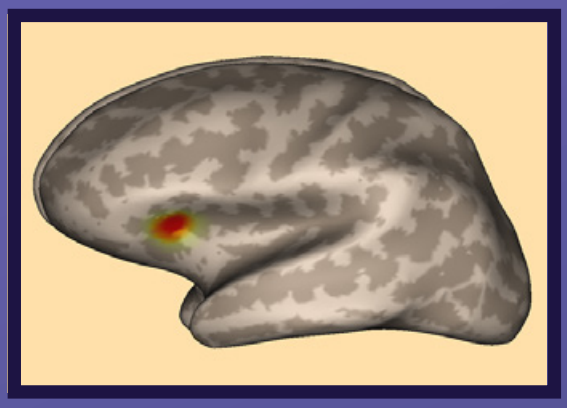


ANNUAL RESEARCH REPORT 2017

DEPARTMENT OF CLINICAL NEUROPHYSIOLOGY
AARHUS UNIVERSITY HOSPITAL

AARHUS UNIVERSITY

Aarhus University Hospital

CONTENT

DEPARTMENT OF **CLINICAL NEUROPHYSIOLOGY**

The research group:
Two professors
Three associate professors
Three post-docs
Three postgraduate (PhD) students
Two research-year (graduate) students

41 **Published papers** in peer-reviewed international journals listed on PubMed

18 **Oral presentations** at international congresses

14 **Textbook chapters**

Being the largest Danish neurophysiological department outside the capital area, the department of Clinical Neurophysiology at Aarhus University Hospital is internationally acclaimed for its highly specialised diagnostic services and comprehensive research and clinical development activities.

Research at the Neurophysiology Department is clinically oriented and focuses on developing, validating and implementing in clinical practice new methods for functional investigations of the central and peripheral nervous system and of the muscles. The goal is to achieve methods that are highly accurate and feasible, in order to increase the quality of care of the patients.

The research group comprises two professors, three associate professors, three post-docs and three postgraduate (PhD) students. The research group uses facilities at the Aarhus University Hospital Neurophysiology Department and at the Danish Neuroscience Center.

In 2017, we published 41 papers in peer-reviewed international journals listed on PubMed. At the European Congress of Clinical Neurophysiology (August 2017) our department had a record-high participation, with 18 oral and 6 poster presentations. In addition, we had oral presentations at the Congress of the European Academy of Neurology, International Epilepsy Congress and the German-Austiran-Swiss Epileptology Congress.

The department has close collaboration with centres in several international consortia: ESTEEM (lead), SCORE (lead) and EpiCare (lead of the Neurophysiology work-package). Our colleagues have several positions of trust in national and international scientific societies. We have close collaboration with other Danish research groups at the Danish Epilepsy Centre and Copenhagen University.

THE **RESEARCH** GROUP

Sándor Beniczky

MD and PhD from University of Szeged, Hungary (1997, 2004) .
Specialist in Neurology (2002).
Specialist in Clinical Neurophysiology (2006).
European certification as epileptologist (2010).

Current position: Professor, consultant

Research interests
- Electromagnetic source imaging
- Epilepsy surgery
- Automated seizure detection
- Wearable devices in epilepsy
- Standardization and quality assurance in clinical neurophysiology.

Supervisor of eight PhD students (currently supervising three); four EFNS/EAN research fellows; two IFCN research fellows; 12 EFNS/EAN educational fellows. 122 publications, 105 in peer-reviewed journals; H-index: 25.

Editorial board: Epilepsia, Epilepsy and Behavior.

Peter Orm Hansen

MD from Odense University (1992)
PhD from Aarhus University (2001)
Specialist in Clinical Neurophysiology (2008)

Current position: Head of Department of Clinical Neurophysiology, Aarhus University Hospital, Aarhus

Research interests
- Central and peripheral nervous system
- Magnetoencephalography
- Intraoperative monitoring.

Anders Fuglsang-Frederiksen

MD from University of Copenhagen (1972).
DMSc from University of Copenhagen (1981).
Director of Department of Clinical Neurophysiology (2000-2011).
Professor in Clinical Neurophysiology.
Department Chair, Aarhus University (2000-2016).

Current position: Professor Emeritus, Consultant in Clinical Neurophysiology, Aarhus University Hospital
Associate Editor of Clinical Neurophysiology (2003-2009)

Research interests
- Electrodiagnostics
- Guidelines and pathophysiology in neuromuscular disorders
- MEG and EEG in evaluation for epilepsy surgery.

196 publications, 167 in peer reviewed journals, H-index 38

Hatice Tankisi

MD from Uludag University, School of Medicine, Bursa, Turkey
Specialist in Neurology from Ankara University, Turkey (1995)
PhD from Aarhus University, Denmark (2004)
Specialist in Neurology, Denmark (2010)
Specialist in Clinical Neurophysiology, Denmark (2011)

Current position: Associate professor, consultant

Research interests
- Peripheral nervemuscle and cortical excitability tests with threshold tracking
- Quantitative EMG and Motor Unit Estimation (MUNE) methods in normal and diseased muscles/nerves
- Electrodiagnostics and pathophysiology in polyneuropathy and ALS.

Main supervisor for 2 and co-supervisor for 5 PhD students.
41 peer-reviewed and PubMed indexed articles, 6 book chapters, 2 thesis and 49 congress proceedings.

Birger Johnsen

MD from University of Copenhagen (1987)
PhD from University of Copenhagen (1997)
Specialist in Clinical Neurophysiology (2000)

Current position
Associate Professor, Consultant

Research interests
- Coma prognostication by neurophysiological methods
- Electrophysiological methods in neuromuscular diseases
- Diagnostic criteria for amyotrophic lateral sclerosis.

PhD supervisor for 5 completed PhD studies and two research year students, currently two PhD students. Also doing pre- and postgraduate teaching in clinical neurophysiology.

Published 53 scientific publications in peer-reviewed journals, 10 book chapters, 69 abstracts and 38 oral presentations.

Erisela Qerama

MD from University of Tirana (1997)
Aarhus University (1999), PhD from Aarhus University (2005)

Current position
Associate Professor, Specialist in Clinical Neurophysiology.

Research interests
- Nerve and muscle ultrasound in entrapment neuropathies and in neuromuscular disorders
- Epilepsy and status epilepticus
- Muscle pain and muscle fatigue mechanisms and treatment.

I am main supervisor for one research year student and one student in special honors research program, co-supervisor for two research year students and one PhD student, clinical supervisor for residents in research and clinical training, 1-2 residents per year. Previously, I had three research year students as main supervisor.

Marit Otto

MD from Kiel University (1995)
PhD from Odense University (2008)
Specialist in Neurology (2007)
Subspecialty in Clinical Neurophysiology (2010)
European certification as somnologist – Expert in Sleep Medicine (2014)
European board certification in neurology (2016).

Current position
Staff specialist and consultant

Research interests
- Sleep medicine
- Idiopathic REM sleep behaviour disorder
- Ear EEG in the evaluation of sleep, studies in patients with insomnia.

Kirsten Pugdahl

MSc in Molecular Biology from Aarhus University (2001)
PhD in Medicine from Aarhus University (2007).

Current position
Researcher and coordinator of a national quality improvement database and an international multicenter research database at Department of Clinical Neurophysiology, Institute of Clinical Medicine, Aarhus University

Research interests
- Cover electrodiagnostic examination strategies and patho physiology of neuromuscular disorders, in particularly amyotrophic lateral sclerosis
- Evidence-based quality improvement initiatives within clinical neurophysiology.

THE **RESEARCH** GROUP

Jesper Jeppesen

Master in Biomedical Engineering
Cand.scient.med. Aarhus University (2010).
PhD Faculty of Health, Aarhus University (2015)

Current position
Postdoc

Research interests
- Seizure detection
- Biosignal analysis
- Seizure alarm systems.

PhD entitled: Detecting epileptic seizures with hart rate variability (HRV) and near infrared
spectroscopy.
Winner: Young Investigator Award, Danish Epilepsy Society Annual Meeting 2013 & 2015.
Best European Student Paper and Finalist, 36th IEEE EMBS Chicago, USA, 2014

Lene Duez

MD from Aarhus University (2010)
Resident at Department of Internal Medicine (2010-2012).
PhD student at the department of Clinical Neurophysiology (until October 2017).

Current position
Resident at Department of Neurology

Research interests
- Electromagnetic source imaging
- Epilepsy surgery
- Epilepsy

Published 7 scientific publications in peer-reviewed journals, 2 book chapters, 9 abstracts and winner of Best poster presentation, PhD day Aarhus university 2014 and 2015 and the Mogens Fog price, Danish Neurology Society 2017

Alexander Gramm Kristensen

MD from Aarhus University (2016)

Current position
PhD student at Danish Pain Research Center, Department of Clinical Medicine, Aarhus University and Department of Clinical Neurophysiology, Aarhus University Hospital.

Research interests
- Nerve excitability
- Nerve conduction studies
- Motor unit number estimation
- Diabetic neuropathy
- Deep learning
- Neurology
- Neural implants.

Agnes Hauschultz Witt

MD from Aarhus University (2008)
Resident at Department of Internal Medicine and Neurology (2008-2016).

Current position
PhD student at Department of Clinical Neurophysiology.

Research interests
- The peripheral nervous system in patients with spinal cord injury using novel techniques as threshold tracking to examine nerve excitability and motor unit number estimation (axonal loss) to see if complications as spasticity and neuropathic pain are related to changes in the peripheral nervous system
- I also examine muscle membrane properties using muscle velocity recovery cycle after nerve lesion.

Aykut Mustafa Kural

MD from Cukurova University (2008)
Specialist in Neurology from Ankara University (2014)

Current position
Scientific Assistant

Research interests
- Epilepsy surgery
- Voltage mapping
- Connectivity analyses
- Nerve conduction studies
- Diabetic neuropathy.

Rikke Søgaard Kristensen

5th year medical student at Aarhus University. Has experience in teaching fellow medical students and from volunteer board work, but is novel in research.

Currently doing a research year project at the Department of Clinical Neurophysiology regarding: Two novel electrophysiological methods in the evaluation of ALS and myopathy patients, MScan MUNE and MVRC. This project will hopefully result in first scientific publication as a first author.

Was awarded 2nd place in oral presentation competition at "33rd National Congress of
Neurophysiology, EEG-EMG" (Antalya, Turkey) in April 2017.

Christina Shen-Zhuang Nielsen

4th year medical student (Bsc. Med 2017) at Aarhus University.

Current position
Research Year Student at Department of Clinical Neurophysiology, Aarhus University Hospital and Secretary at Selskab for Medicinsk Studenterforskning (student organisation) at Health, Aarhus University.

Research interests
- Pathophysiology in ALS
- Cortical hyperexcitability tests with threshold tracking TMS.

POSITIONS **OF TRUST**

Sándor Beniczky
- International League Against Epilepsy (ILAE), Commission on European Affairs (elected in 2013, re-elected in 2017, treasurer since 2017).
- ILAE Edication Commission (since 2012).
- ILAE Commission on Diagnostic Methods (since 2017).
- Chair of the Joint Taskforce on EEG of the ILAE and International Federation of Clinical Neurophysiology.
- Chair of the Congress Education Taskforce, ILAE.
- Danish Epilepsy Society:
  - board member since 2010
  - treasurer since 2014.
- Member of five working groups on international guidelines (ILAE, IFCN and EAN) – chair of two working groups.

Anders Fuglsang-Frederiksen
- President of Danish Society of Clinical Neurophysiology (1988-1996).
- Member of board of European Chapter of the International Federation of Clinical Neurophysiology (2005-2014).

Peter Orm Hansen
- Danish Society of Clinical Neurophysiology: board member and treasurer (since 2004).

Hatice Tankisi
- Secretary and treasurer of the Executive Committee, International Federation of Clinical Neurophysiology – European Chapter (since 2017).

Birger Johnsen
- Danish Society of Clinical Neurophysiology: member of the education committee (since 2007).

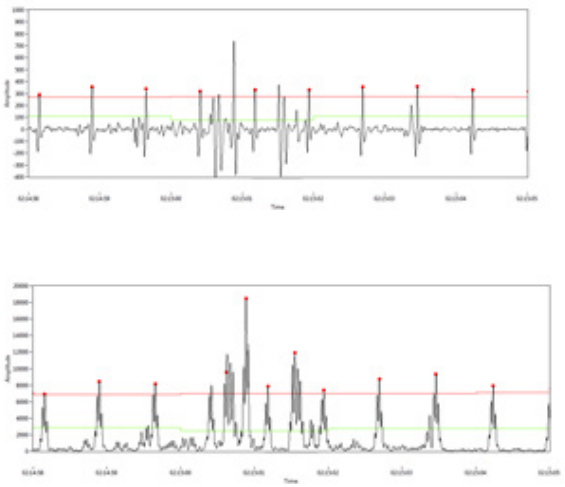
Erisela Qerama
- Danish Society of Clinical Neurophysiology: board member (since 2015).

Marit Otto
- Danish Neurological Society: board member (since 2017).

RESEARCH PROJECTS

Seizure detection using heart rate variability analyses of ECG

Earlier studies have shown that short term heart rate variability (HRV) analysis of ECG seems promising for detection of epileptic seizures. A precise and accurate automatic R-peak detection algorithm is a necessity in a real time, continuous measurement of HRV, in a portable ECG device. We used the portable CE marked ePatch® heart monitor to record the ECG of 14 patients who were enrolled in the video-EEG long term monitoring unit for clinical workup of epilepsy. Recordings of the first 7 patients were used as a data training set for the R-peak detection algorithm and the recordings of the last 7 patients (467.6 recording hours) were used to test the performance of the algorithm. The proposed R-peak detection algorithm showed a high sensitivity (Se = 99.979%) and positive predictive value (P+ = 99.976%). This was comparable with a previously published QRS-detection algorithm for the ePatch® ECG device when testing the same dataset. The novel R-peak detection algorithm designed to avoid jitter has a very high sensitivity and specificity and thus is a suitable tool for a robust, fast, real time HRV analysis in patients with epilepsy, creating the possibility for real time seizure detection for these patients.

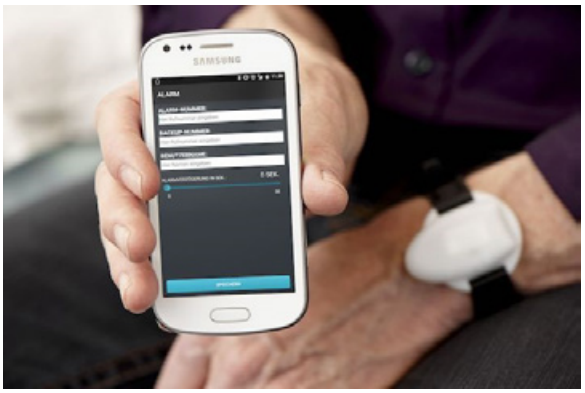


Example from training-patient 1. Redline is Thigh, green line Tlow threshold, Red dots are detections. A) The Rsearchpoint feature enables the detection of the real R-peaks as these are closer to the expected R-peak even though the noise in-between surpasses the threshold. B) QRS complex detection with Saadi et al. algorithm of same time as A. The noise in-between R-peaks creates false detections.

PAPERS

Jeppesen J, Beniczky S, Johansen P, Sidenius P, Fuglsang-Frederiksen A. Modified automatic R-peak detection algorithm for patients with epilepsy using a portable electrocardiogram recorder. Conf Proc IEEE Eng Med Biol Soc 2017; 4082-4085. doi: 10.1109/EMBC.2017.8037753

Automated seizure detection based on surface electromyography and accelerometry



Generalized tonic-clonic seizures (TCS) increase the risk of sudden unexpected death in epilepsy patients, especially when they are unattended. In sleep, they often remain unnoticed, which can result in suboptimal treatment decisions. Hence, there is a need for wearable devices that can automatically detect TCS, both to prevent injury and death, and to provide objective data on seizure frequency. We have developed and validated wearable devices, based on movement signals (accelerometry) and based on surface electromyography (EMG) for detection of TCS.

In a phase III, multicenter, prospective, blinded study using real time detection of TCS in epilepsy monitoring units, we demonstrated that the accelerometry device had a sensitivity of 90% and a false alarm rate of 0.2/day for detecting TCS. However, that study was conducted in an artificial environment. Therefore, we extended it with a phase IV open study to assess the performance, applicability and usability of the device in the home environment of patients, using a modified form of the standardized questionnaire developed by IBM to evaluate user satisfaction and applicability of technical/ computerbased devices: Post-Study System Usability Questionnaire (PSSUQ). The median time patients had been using the device was 15 months. In 10% of the cases patients stopped using the device due to reasons related to the device. Sensitivity (90%) and false alarm rate (0.1/day) were similar to what had been determined in the phase III trial. Patients and caregivers were overall satisfied with the device (median: 5.5 on the 7 point Likert scale). Adverse effects occurred in 11% of the patients, but were only mild. In 55% of the patients, the device influenced the number of seizures noted into the seizure diary, and in 40% it contributed to fewer seizure related injuries.

We found quantitative EMG changes that are specific for TCS. They are characterized by a dynamic evolution of low (LF) and high frequency (HF) signal components. Algorithms targeting increase in HF EMG signals are biomarkers of TCS. They can be used both for seizure detection and for distinguishing TCS from convulsive psychogenic non-epileptic seizures (PNES). We have conducted a large-scale, blinded, prospective multicenter, phase III study on the accuracy of real time seizure detection, using a wearable EMG-device, based on an algorithm with pre-defined threshold values. The device had a sensitivity of 94% and a false alarm rate of 0.7 / day.

Although recently there has been a considerable increase in the number of publications on seizure detection devices, the way studies were designed and reported was very heterogeneous and often confusing. We have developed standards for seizure detection clinical trial. Using a set of key features, the studies are categorized from I to IV, similar to the therapeutic studies.

PAPERS

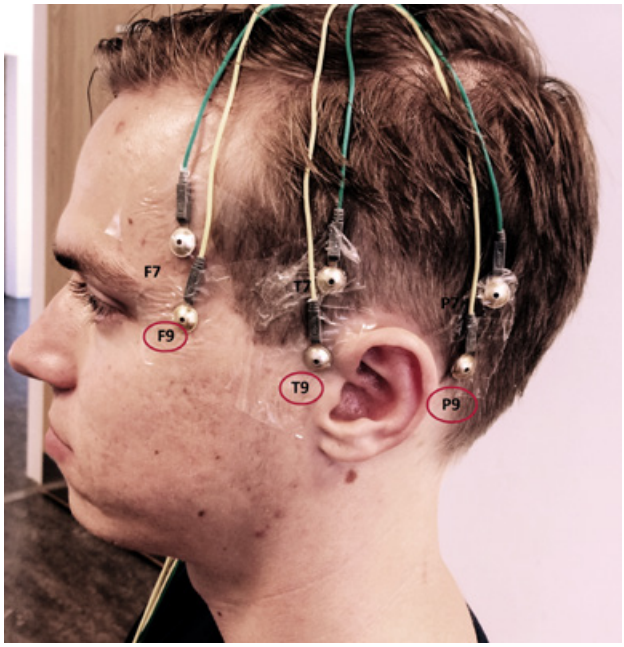
Beniczky S, Conradsen I, Henning O, Fabricius M, Wolf P.
Automated real-time detection of tonic-clonic seizures using a wearable EMG device. Neurology. 2018; 90:428-434.

Pirgit Meritam, Philippe Ryvlin, Sándor Beniczky.
User-based evaluation of applicability and usability of a wearable accelerometer device in detecting bilateral tonic-clonic seizures: a field study.
Epilepsia (in press)

Sándor Beniczky, Isa Conradsen, Peter Wolf.
Detection of convulsive seizures using surface electromyography.
Epilepsia (in press)

Sándor Beniczky and Philippe Ryvlin.
Standards for testing and clinical validation of seizure detection devices.
Epilepsia (in press).

Source localization and connectivity studies in epilepsy



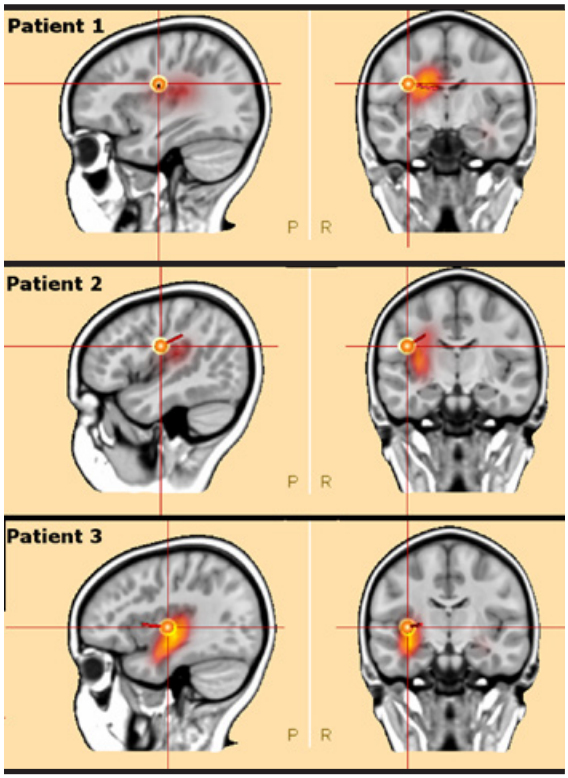
Electroencephalography (EEG) and magnetoencephalography (MEG) signals are generated in the cortex and recorded at the surface of the scalp. Traditionally, in clinical practice, EEG is recorded with 19 electrodes of the 10-20 array, covering the upper part of the head (scalp), and location of these signals is given as the location of the peak negativity on the scalp. However, this region on the scalp does not necessary correspond to the location of the source, thus there is need for better recordings and advanced methods of source localization.

We investigated the diagnostic added value of supplementing the 10-20 with six electrodes in the inferior temporal chain ("low-row). We analyzed 500 consecutive standard and sleep EEG recordings, using the 10-20 array and the extended array. We identified the recordings with EEG abnormalities that had peak negativities at the inferior temporal electrodes, and those that only were visible at the inferior temporal electrodes. We found that adding six electrodes in the inferior temporal electrode chain to the 10-20 array improved the localization and identification of EEG abnormalities, especially those located in the temporal region.

We have developed a standardized method of ictal source imaging, based on independent component analysis and averaging of the ictal waveforms. We applied this method to map the ictal activity in children with self-limited epilepsy with centrotemporal spikes. The ictal source localized to the operculo-insular area. The rhythmic EEG activity was time-locked to the contralateral focal motor seizure manifestations.

The seizures had fluctuating course with pauses of clinical and electrographic seizure activity, ranging from 0.4 to 7 seconds.

We investigated functional coupling between brain networks using spectral changes induced by single-pulse electric stimulation (SPES). We found an early excitation (10-60 ms) and a delayed inhibition (60-500 ms) response. In the delayed period, stimulation in primary visual and primary sensory cortex produced a higher gamma-inhibition in the default mode network (DMN), while stimulation in the seizure onset zone (SOZ) induced a higher inhibition in the epilepsy related higher frequencies (Ripples and Fast-Ripples). We concluded that physiologic and pathologic interactions in the brain can be assessed using spectral changes induced by SPES. This seems to be a promising method for connectivity studies in patients with drug-resistant focal epilepsy.



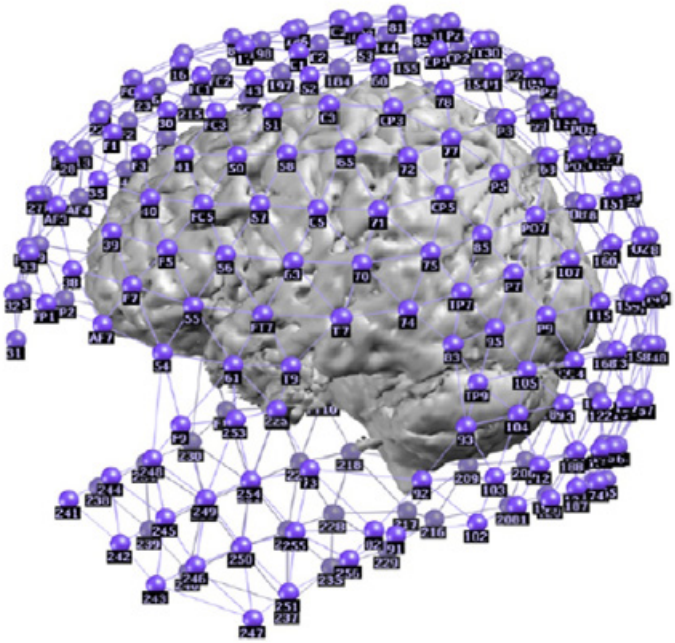
PAPERS

Bach Justesen A, Eskelund Johansen AB, Martinussen NI, Wasserman D, Terney D, Meritam P, Gardella E, Beniczky S.
Added clinical value of the inferior temporal EEG electrode chain.
Clin Neurophysiol. 2018;129:291-295.

Alving J, Fabricius M, Rosenzweig I, Beniczky S.
Ictal source imaging and electroclinical correlation in self-limited epilepsy with centrotemporal spikes. Seizure. 2017;52:7-10.

Mălîia MD, Donos C, Barborica A, Mindruta I, Popa I, Ene M, Beniczky S.
High frequency spectral changes induced by single-pulse electric stimulation: Comparison between physiologic and pathologic networks.
Clin Neurophysiol. 2017;128:1053-1060.

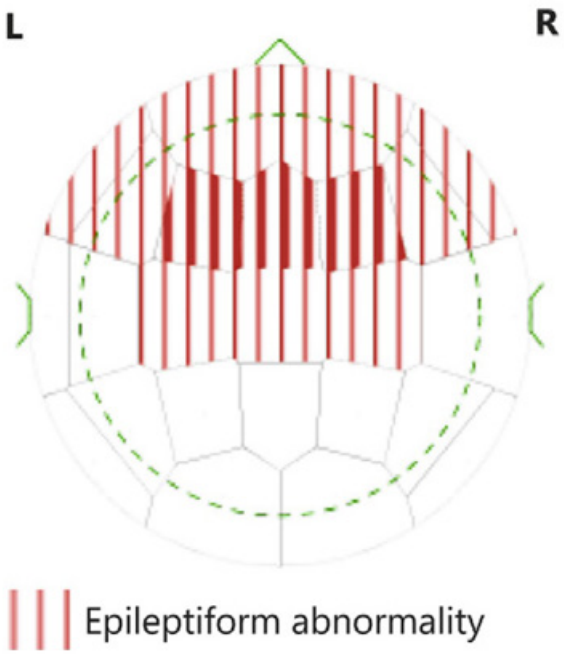
Standardization and quality assurance in clinical neurophysiology



Most of the neurophysiological methods in clinical neurophysiology are based on local traditions, expert-opinions and on old studies lacking proper reference standard and study design. To improve patient care it is important to revisit the old techniques and to validate new methods, using robustly designed diagnostic studies. Our group contributed to this in several areas of clinical neurophysiology.

Our group had a leading role in the taskforce of the International Federation of Clinical Neurophysiology, that developed the standardized, computer-based organized reporting system for clinical EEG (SCORE). The system has been validated on 12,160 EEG recordings. Standardized terms implemented in SCORE are used to report the features of clinical relevance. This automatically generates a report and feeds these features into a database. SCORE proved to be a useful clinical tool with potential impact on clinical care, quality assurance, data-sharing, research and education. It serves as the interactive online template for the most recent edition of the most authoritative textbooks in the field of EEG (Niedermeyer).

We have contributed to the development of new standards of the International Federation of Clinical Neurophysiology on the standardized electrode EEG electrode arrays. The basic array is of 25 electrodes including the inferior temporal chain. This should be used for all standard clinical recordings. High-density scalp EEG arrays (64–256 electrodes) allowing source imaging with even sub-lobar precision were developed.



We contributed to mapping the current practices and development of recommendations for long-term video-EEG recordings and clinical application of magnetoencephalography (MEG).

In a prospective study on quality and patient safety, we found that using wireless amplifiers allowing high patient mobility in the epilepsy monitoring units is a safe and efficient medical procedure.

In critically ill patients we have demonstrated that observation of subtle motor phenomena are insufficient for diagnosing status epilepticus, and there is a need for standardizing assessment of these patients using EEG.

PAPERS

Beniczky S, Aurlien H, Brøgger JC, Hirsch LJ, Schomer DL, Trinka E, Pressler RM, Wennberg R, Visser GH, Eisermann M, Diehl B, Lesser RP, Kaplan PW, Nguyen The Tich S, Lee JW, Martins-da-Silva A, Stefan H, Neufeld M, Rubboli G, Fabricius M, Gardella E, Terney D, Meritam P, Eichele T, Asano E, Cox F, van Emde Boas W, Mameniskiene R, Marusic P, Zárubová J, Schmitt FC, Rosén I, Fuglsang-Frederiksen A, Ikeda A, MacDonald DB, Terada K, Ugawa Y, Zhou D, Herman ST.
Standardized computer-based organized reporting of EEG: SCORE – Second version.
Clin Neurophysiol. 2017;128:2334-2346.

Seeck M, Koessler L, Bast T, Leijten F, Michel C, Baumgartner C, He B, Beniczky S.
The standardized EEG electrode array of the IFCN.
Clin Neurophysiol. 2017;128:2070-2077.

Hamandi K, Beniczky S, Diehl B, Kandler RH, Pressler RM, Sen A, Solomon J, Walker MC, Bagary M; with ILAE British Chapter Workshop Attendees.
Current practice and recommendations in UK epilepsy monitoring units. Report of a national survey and workshop.
Seizure. 2017;50:92-98.

De Tiège X, Lundqvist D, Beniczky S, Seri S, Paetau R.
Current clinical magnetoencephalography practice across Europe: Are we closer to use MEG as an established clinical tool?
Seizure. 2017;50:53-59.

Craciun L, Alving J, Gardella E, Terney D, Meritam P, Cacic Hribljan M, Beniczky S.
Do patients need to stay in bed all day in the Epilepsy Monitoring Unit? Safety data from a non-restrictive setting. S
eizure. 2017;49:13-16.

Florea B, Beniczky SA, Demény H, Beniczky S.
Semiology of subtle motor phenomena in critically ill patients.
Seizure. 2017;48:33-35.

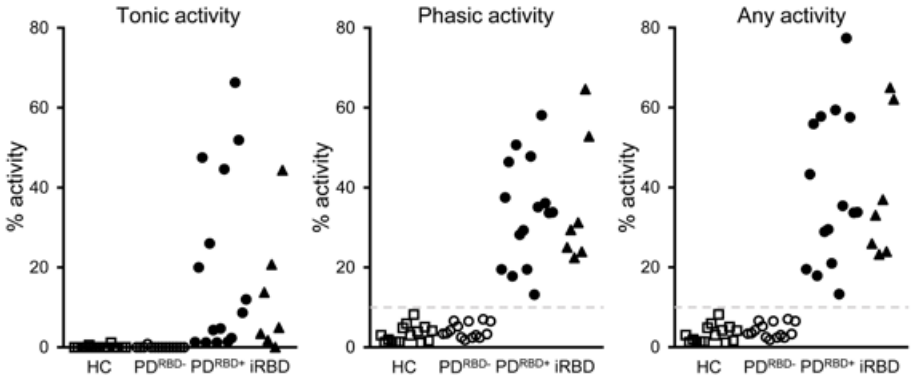
Semi-automatic scoring algorithm of muscle activity in REM sleep behavior disorder

Rapid eye movement (REM) sleep behavior disorder (RBD) is defined by dream enactment due to a failure of normal muscle atonia. Visual assessment of this muscle activity is time consuming and rater-dependent.

An EMG computer algorithm for scoring tonic, phasic and any submental muscle activity during REM sleep was evaluated compared with human visual ratings. Subsequently, 52 subjects were analyzed with the algorithm. Duration and maximal amplitude of muscle activity were assessed.

The computer algorithm showed high congruency with human ratings and all subjects with RBD were correctly identified by excess of submental muscle activity when artifacts were removed before analysis. Subjects with RBD exhibited prolonged bouts of 'phasic' muscle activity with high amplitude. Our proposed algorithm was able to detect and rate REM sleep without atonia allowing identification of RBD. Increased duration and amplitude of muscle activity bouts were characteristics of RBD. Quantification of REM sleep without atonia represents a marker of RBD severity.

Our EMG computer algorithm can support a diagnosis of RBD while the quantification of altered muscle activity provides a measure of its severity.



Correlation plot of human raters assessing percentage of 'tonic', 'phasic', and 'any' muscle activity during REM sleep; line of unity in light grey. Figure B: Correlation plot of computer algorithm scoring of percentage of 'tonic', 'phasic', and 'any' muscle activity during REM sleep against the two human raters from A; line of unity in light grey.

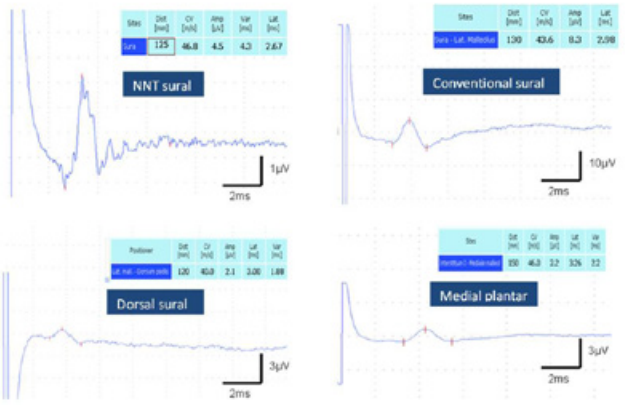
PAPERS

Jeppesen J, Otto M, Frederiksen Y, Hansen AK, Fedorova TD, Knudsen K, Nahimi A, Brooks DJ, Borghammer P, Sommerauer M. Observations on muscle activity in REM sleep behavior disorder assessed with a semi-automated scoring algorithm. Clinical Neurophysiology; In press. doi.org/10.1016/j.clinph.2017.12.029

Sommerauer M, Fedorova T D, Hansen A K, Knudsen K, Otto M, Jeppesen J, Frederiksen Y, Blicher J U, Geday J, Nahimi A, Damholdt M F, Brooks D J, Borghammer P. Evaluation of the noradrenergic system in Parkinson's disease: An 11C-MeNER positron emission tomography & neuromelanin magnetic resonance imaging study. Brain 2017; awx348. doi.org/10.1093/brain/awx348

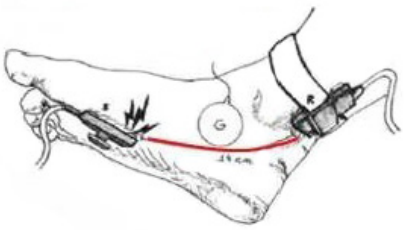
Diagnosis of polyneuropathy benefits from nerve conduction studies of distal nerves

Nerve conduction studies of the sural nerve with near-nerve needle recording is a very sensitive parameter in the electrodiagnosis of polyneuropathy (PNP). However, the technique requires an experienced examiner and may feel unpleasant for the patient. The study *"Diagnostic utility of distal nerve conduction studies and sural near-nerve needle recording in polyneuropathy"* showed a high sensitivity of examination of distal nerves (dorsal sural and medial plantar) with surface recording equaling that of needle examination of the sural nerve. The study concluded that the electrodiagnostic evaluation of patients with suspected PNP could benefit from including nerve conduction studies of the distal nerves.

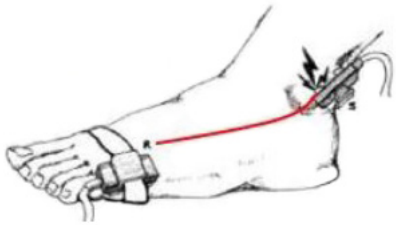


Abnormal nerve conduction study results of the sural nerve with near-nerve needle (NNT) recording and of the dorsal sural and medial plantar nerves in a patient with polyneuropathy. In contrast conventional surface studies of the sural nerve were normal.

Medial Plantar NCS



Dorsal Sural NCS



PAPERS

Kural MA, Karlsson P, Pugdahl K, Isak B, Fuglsang-Frederiksen A, Tankisi H.
Diagnostic utility of distal nerve conduction studies and sural near-nerve needle recording in polyneuropathy.
Clin Neurophysiol. 2017;128:1590-1595.

Outcome prediction of comatose patients by neurophysiological methods

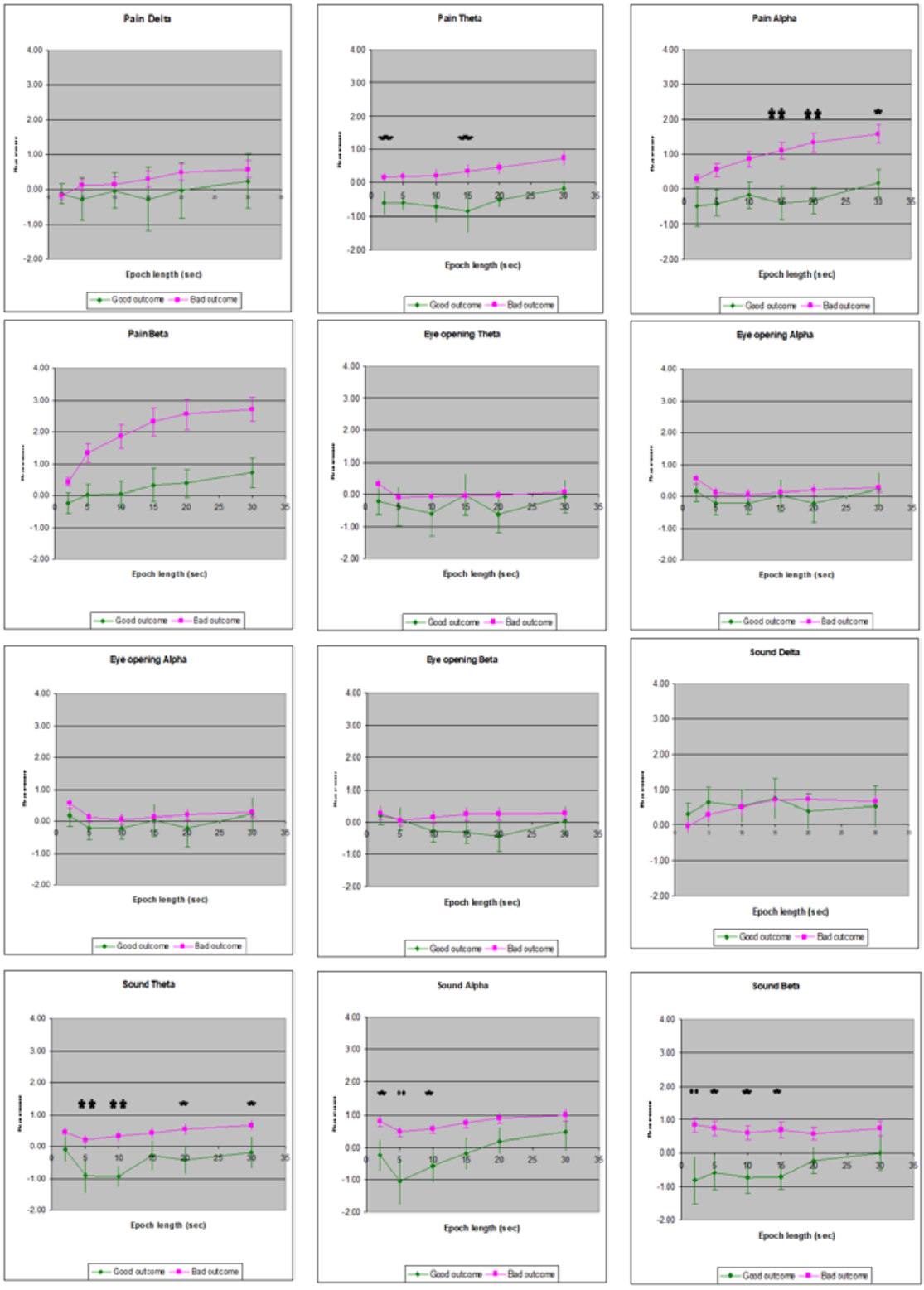
The prognosis of patients in coma after head trauma, intracranial bleedings, and cardiac arrest (CA) varies from waking up without any sequelae, survival with mild or severe cognitive deficits, to death. For the relatives and for the threatening physicians, the prediction of outcome is very important for the decision of how to continue treatment. There is no single test that reliably predicts the outcome in coma patients. Current routine methods include clinical examination and neurophysiological examinations by somatosensory evoked potentials (SSEP) and electroencephalography (EEG).

Several EEG findings such as background activity, epileptiform changes, and EEG-reactivity may be used in the prediction. The absence of EEG-R has been considered an important parameter for the prediction of poor outcome, and it has been suggested to use it in an algorithm for the decision of withdrawal of life sustaining therapy. However, more recently there has been some debate of the use of EEG-R because the methods used are very subjective and standardization of stimulation and analyzing methods lacks.

In order to overcome some of these limitations of the test for EEG-R, we have recently published the paper *"The Nature of EEG Reactivity to Light, Sound, and Pain Stimulation in Neurosurgical Comatose Patients Evaluated by a Quantitative Method"*. In this paper standardized stimulation methods and a method for quantitative analyses of the EEG-R are used in 39 comatose neurosurgical patients. It was shown that the kind of EEG change was important, as an increase in EEG activity was related to poor outcome and a decrease in EEG activity to good outcome. Pain and sound were the most provocative stimulation methods, and eye-opening did not discriminate between good and poor outcome. EEG reactivity in the theta and alpha bands of the first 5 to 15 seconds of stimulation performed best in the discrimination between good and poor outcome. The impact of the study is that it reveals new knowledge about the nature of EEG reactivity contributing to the development of more reliable and objective clinical procedures for outcome prediction.

PAPERS

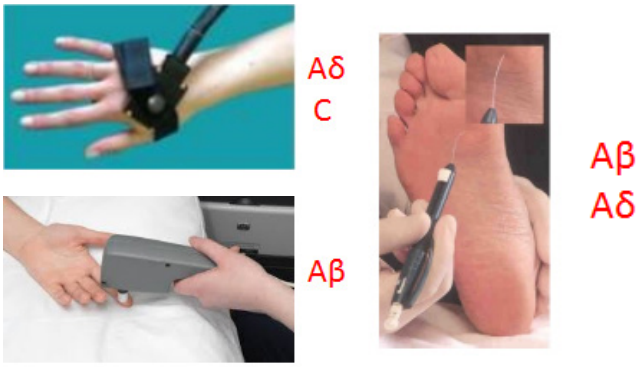
Johnsen B, Nøhr KB, Duez CHV, Ebbesen MQ. The Nature of EEG Reactivity to Light, Sound, and Pain Stimulation in Neurosurgical Comatose Patients Evaluated by a Quantitative Method.
Clin EEG Neurosci. 2017;48:428-437.



Normalised EEG-reactivity for good and poor outcome
EEG-reactivity in four different frequency bands due to pain stimulation (average of four stimulations), sound stimulation and eye-opening. Mean values of 33 comatose neurosurgical intensive care patients with poor outcome (pink filled squares) compared with mean values of 6 patients with good outcome (green open squares). EEG-reactivity is expressed in z-scores (mean±SEM); a positive z-score indicates an increase in activity due to stimulation and a negative z-score indicates a decrease in activity. Data analysed in epoch lengths of 2, 5, 10, 15, 20, and 30 seconds. Significant differences between means by Students t-test: * p< 0.05; ** p< 0.01.

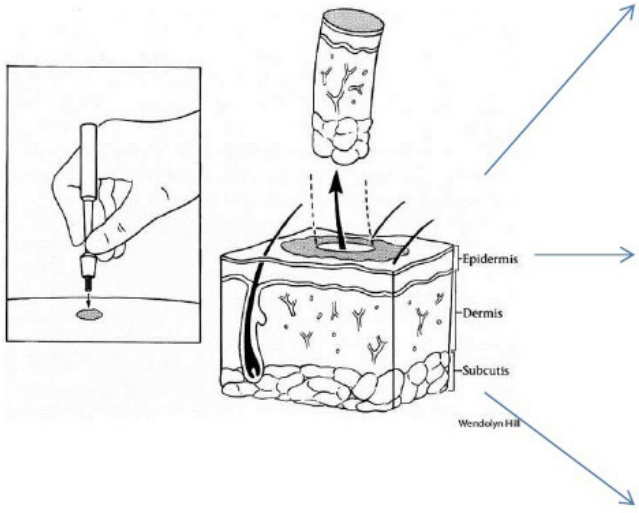
Sensory nerve affection in ALS

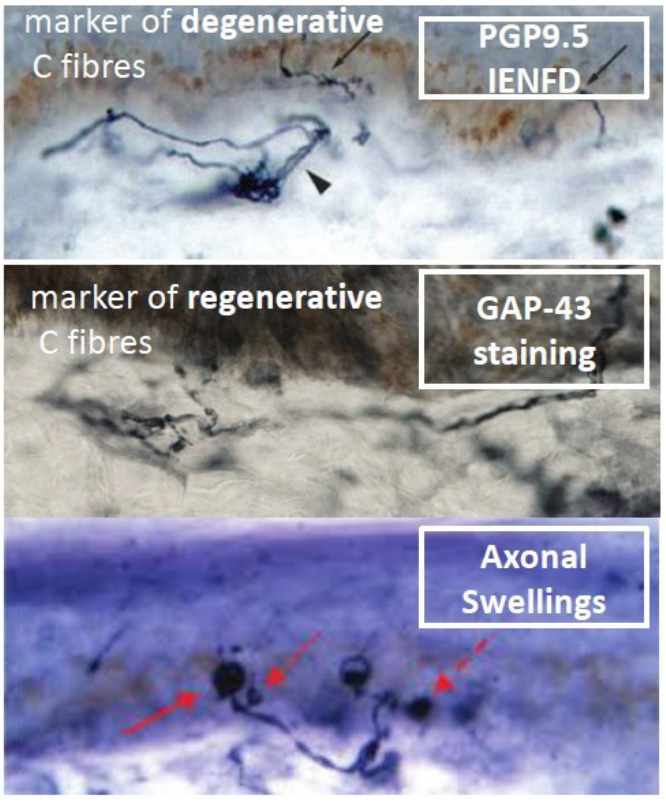
Amyotrophic lateral sclerosis (ALS) is a devastating disease characterised by degeneration of motor neurons. However, minor changes in also the sensory nervous system have previously been demonstrated by our research group amongst others. In the paper "Quantitative sensory testing and structural assessment of sensory nerve", mean values for quantitative sensory testing (QST) and intraepidermal nerve fibre density (IENFD) on skin biopsy were found to be similar to healthy controls in 32 ALS patients. However, increased axonal swelling ratios and negative growth-associated protein 43 (GAP-43) antibody staining were seen in the ALS patients, indicating presence of minor structural changes in the sensory nerves and insufficiency of regeneration in small sensory nerve fibres.



PAPERS

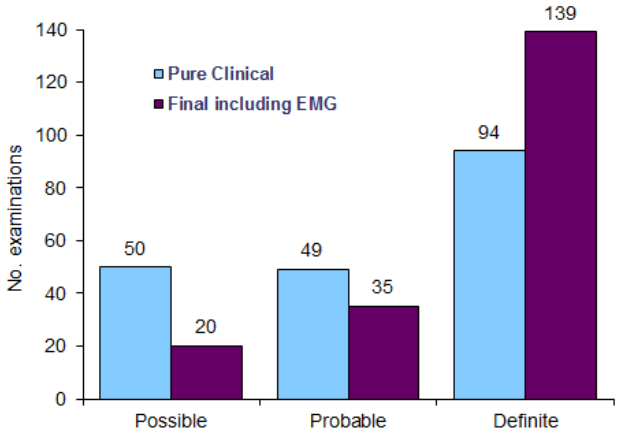
Isak B, Pugdahl K, Karlsson P, Tankisi H, Finnerup NB, Furtula J, Johnsen B, Sunde N, Jakobsen J, Fuglsang-Frederiksen A. Quantitative sensory testing and structural assessment of sensory nerve fibres in amyotrophic lateral sclerosis. J Neurol Sci. 2017;373:329-334.





Utility of EMG in myopathies

With the increasing development of new techniques for the diagnosis of myopathy, the results obtained from electromyography (EMG) may be considered less important. Nonetheless, in the European multicentre study "Added value of electromyography in the diagnosis of myopathy: A consensus exercise", EMG increased the probability of myopathy in 34.4% of 194 patients with expert consensus on the diagnosis. The conclusion of the study was that EMG is still a useful tool in the diagnostic work-up of patients with suspected myopathy. The added value was greatest on myopathies of unknown aetiology, while EMG generally supported the diagnosis in genetically or biopsy proven myopathies.

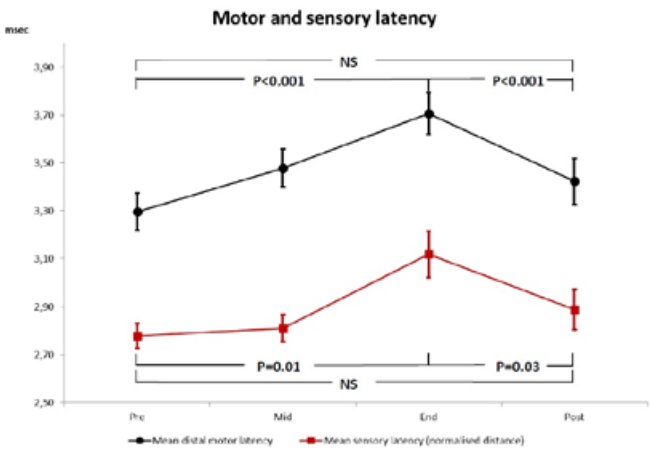


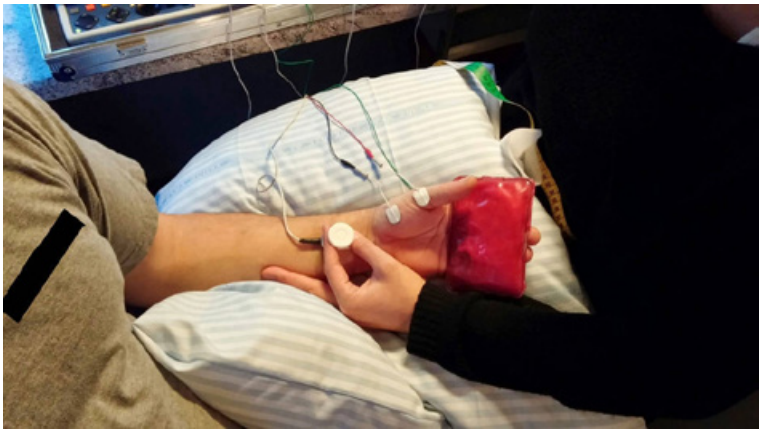
PAPERS

Pugdahl K, Johnsen B, Tankisi H, Camdessanché JP, de Carvalho M, Fawcett PR, Labarre-Vila A, Liguori R, Nix W, Schofield I, Fuglsang-Frederiksen A.
Added value of electromyography in the diagnosis of myopathy: A consensus exercise.
Clin Neurophysiol. 2017;128:697-701.

Reversible impairment of the median nerve

In the study "Reversible median nerve impairment after three weeks of repetitive work", conduction velocity of the median nerve was followed in 11 men doing hand-intensive seasonal work (mink skinning). After 22 days of work both sensory and motor conduction of the median nerve had decreased significantly and 5 of the workers fulfilled the criteria for carpal tunnel syndrome. At the follow-up 3-6 weeks post-season, the electrophysiological and clinical changes had reverted to normal. The study, for the first time, documented the existence of a subacute carpal tunnel syndrome with reversible changes of the median nerve and that sensory and motor changes run in parallel in this condition.



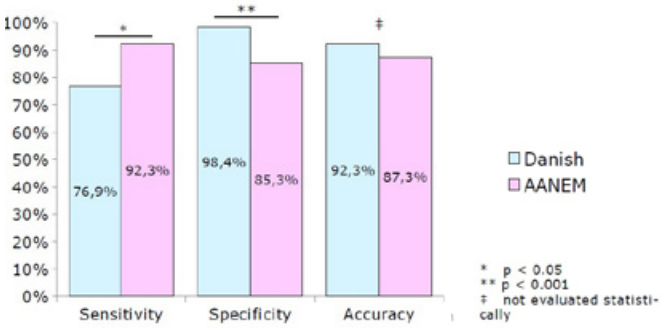


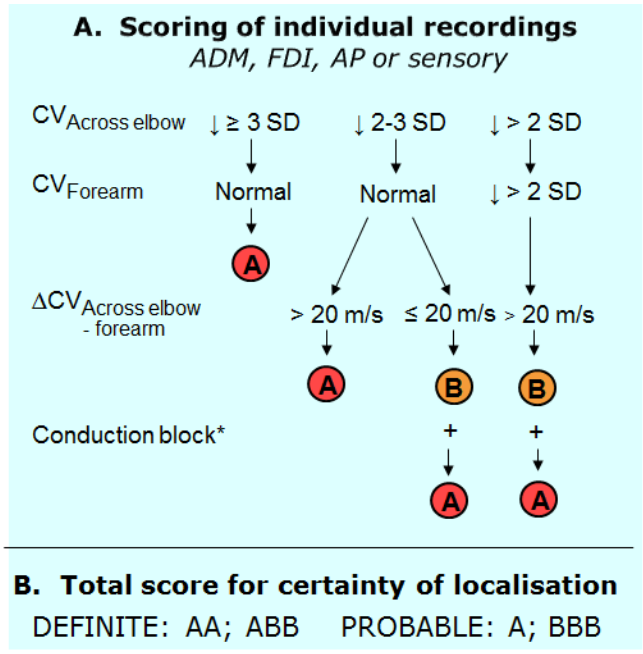
PAPERS

Tabatabaeifar S, Svendsen SW, Johnsen B, Hansson GÅ, Fuglsang-Frederiksen A, Frost P.
Reversible median nerve impairment after three weeks of repetitive work.
Scand J Work Environ Health. 2017;43:163-170.

Electrodiagnostic criteria for ulnar nerve lesion at the elbow

Ulnar neuropathy at the elbow is a frequent referral reason for electrodiagnostic examination. Nevertheless, published electrodiagnostic criteria are sparse. The Danish multicentre study *"Neurophysiological localisation of ulnar neuropathy at the elbow: Validation of diagnostic criteria developed by a taskforce of the Danish Society of clinical neurophysiology"* presented consensus criteria for localisation of ulnar nerve lesion at the elbow used at all major Danish neurophysiological departments since their development in 2011. The Danish criteria should also be suitable for international use at different centres as they are based on Z-scores. When validated on a mixed patient group with consensus on the diagnosis, the Danish criteria showed higher specificity (98.4%), but lower sensitivity (76.9%) than the existing criteria from the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM).



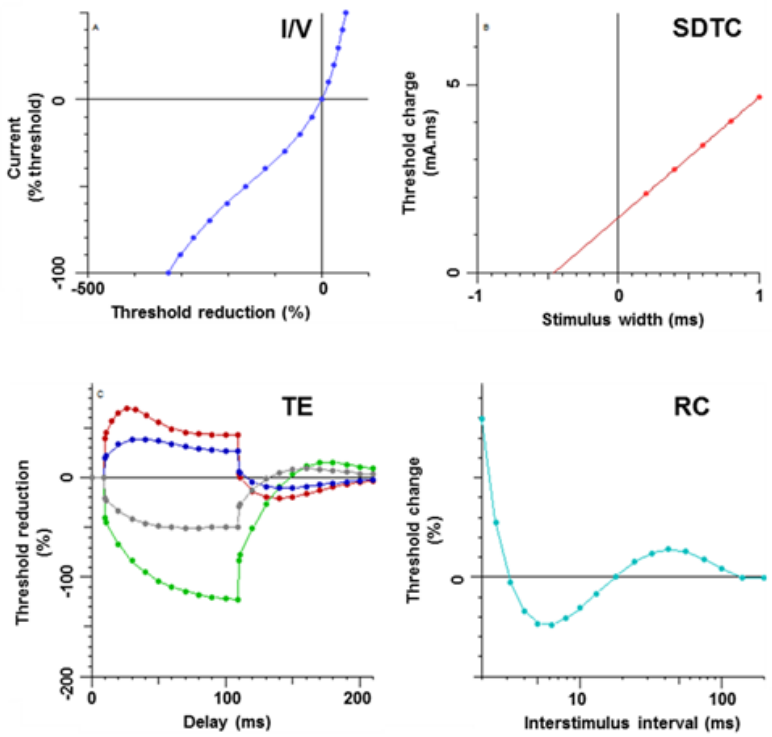


PAPERS

Pugdahl K, Beniczky S, Wanscher B, Johnsen B, Qerama E, Ballegaard M, Benedek K, Juhl A, Ööpik M, Selmar P, Sønderborg J, Terney D, Fuglsang-Frederiksen A. Neurophysiological localisation of ulnar neuropathy at the elbow: Validation of diagnostic criteria developed by a taskforce of the Danish Society of clinical neurophysiology.
Clin Neurophysiol. 2017;128:2205-2210.

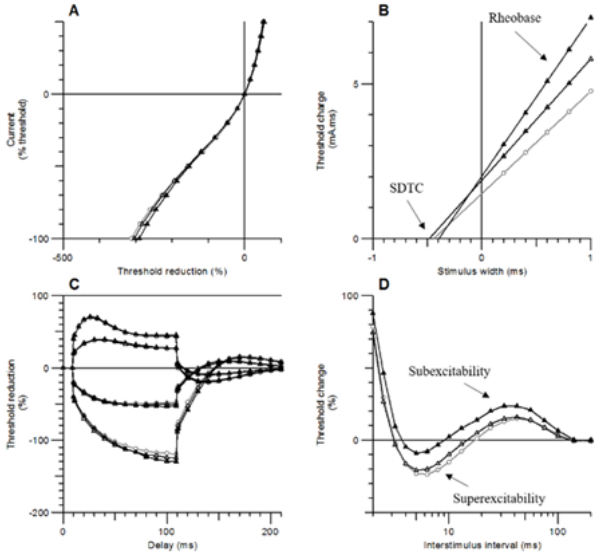
Aarhus Qtrac Study Group

Axonal excitability testing using threshold tracking technique provides complementary information to conventional nerve conduction studies. The method has been developed by Professor Hugh Bostock, Queen Square, London, United Kingdom. The software is called Qtrac and the method has recently been adapted to muscle membrane and cortical excitability, and a novel motor unit number estimation (MUNE) method, so-called MScanFit MUNE (MScan). Axonal excitability testing was established at the Department of Neurophysiology, Aarhus University Hospital in 2015 in close collaboration with Professor Hugh Bostock. Aarhus Qtrac Study Group is already the largest group in Europe and the only group in the world using all aspects of Qtrac. Different aspects of Qtrac are being used in 6 PhD and 5 research year projects for understanding disease pathophysiology as well as ealier and more accurate diagnosis of amyotrophic lateral sclerosis, spinal cord injury, epilepsy, chemotheraphy-induced neuropathy and myopathy. Additionally, excitability tests are beings used to understand underlying mechanisms of diabetic neuropathy as a part of International Diabetic Neuropathy Consortium (IDNC), a project constituted by Professor Troels Staehelin Jensen. Other interdisciplinary collaborators are Professor Nanna Finnerup at Danish Pain Research Center, Professor Henning Andersen and Associate professor Jakob Uldby Blicher at the Department of Neurology, Associate professor Helge Kasch at Spinal Cord Injury Centre of Western Denmark and Professor Michael Pedersen, Comparative Medicine Lab, Institute of Clinical Medicine.



Changes in axonal excitability following chemotherapy

Axonal excitability testing may be used to infer the activity of a variety of ion channels, energy-dependent pumps and ion exchange processes activated during the process of impulse conduction. By the use of the threshold tracking technique, we showed in a recent study *"Axonal excitability changes and acute symptoms of oxaliplatin treatment: In vivo evidence for slowed sodium channel inactivation"* that anti-cancer agent oxaliplatin induces reversible slowing of sodium channel inactivation in motor axons. The background for this study was two recent studies done in collaboration with Danish Pain Research Center: *"Chronic neuropathic pain following oxaliplatin and docetaxel: A 5-year follow-up questionnaire" and "Chronic Pain and Neuropathy Following Adjuvant Chemotherapy"* where we examined particularly the clinical profiles of oxaliplatin and docataxel neurotoxicity. We are conducting further studies to explore the mechanisms of acute and chronic neurotoxicity of oxaliplatin and chronic neurotoxicity of docetaxel using axonal excitability testing which we believe may improve prevention or treatment of chemoteraphy-induced neurotoxicity.



A: Current/threshold (I/V) relationship
B: Strength-duration time constant
C: Threshold electrotonus
D: Recovery cycle

○ Healthy controls
▲ Patients with post infusion examination
△ Patients with recovery examination

PAPERS

Heide R, Bostock H, Ventzel L, Grafe P, Bergmans J, Fuglsang-Frederiksen A, Finnerup NB, Tankisi H. Axonal excitability changes and acute symptoms of oxaliplatin treatment: In vivo evidence for slowed sodium channel inactivation.
Clin Neurophysiol. 2017; pii: S1388-2457(17)31162-8.

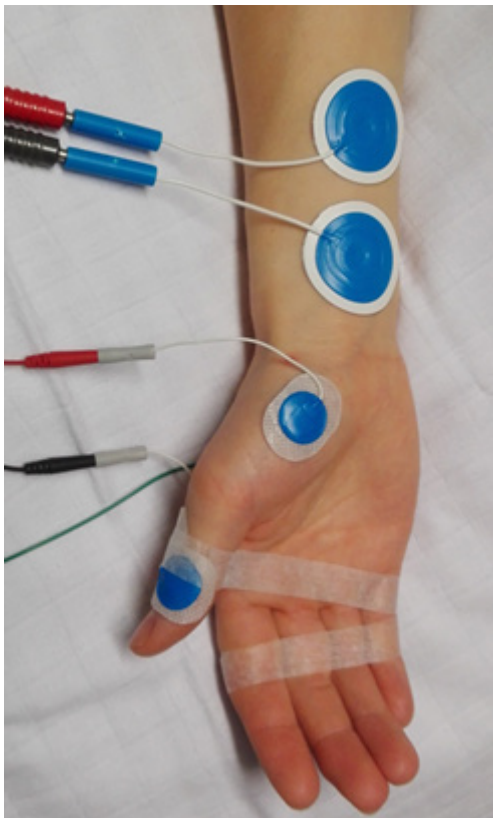
Ventzel L, Madsen CS, Karlsson P, Tankisi H, Isak B, Fuglsang-Frederiksen A, Jensen AB, Jensen AR, Jensen TS, Finnerup NB. Chronic Pain and Neuropathy Following Adjuvant Chemotherapy.
Pain Med. 2017; doi: 10.1093/pm/pnx231

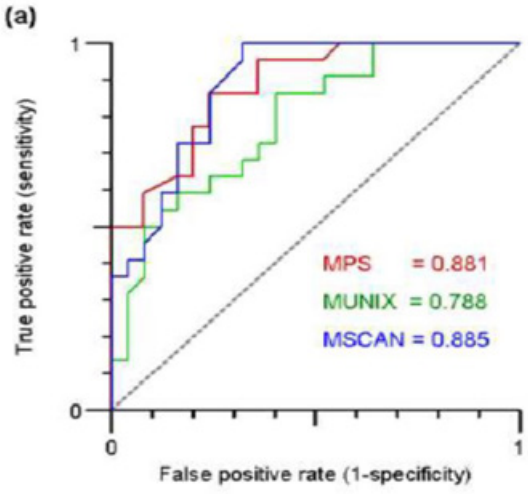
Bennedsgaard KJ, Ventzel L, Jensen AB, Jensen AR, Tankisi H, Finnerup NB. Chronic neuropathic pain following oxaliplatin and docetaxel: A 5-year follow-up questionnaire study.
Scandinavian Journal of Pain. 2017; 16:166

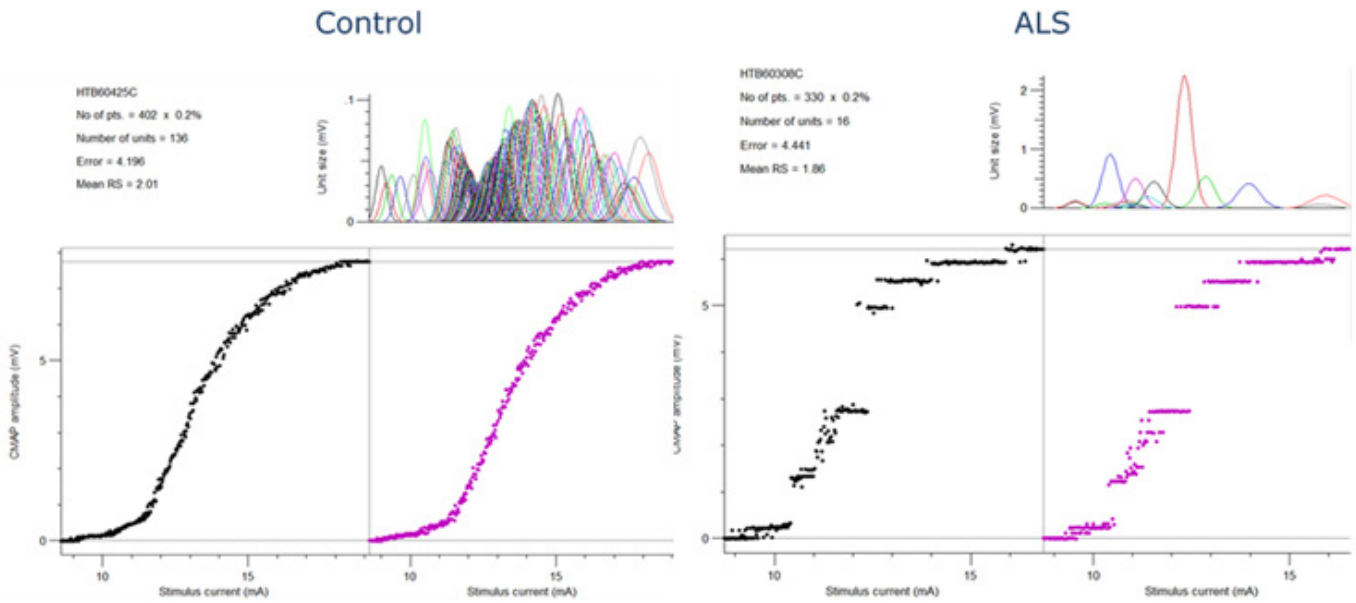
MScan: A new promising technique for assessing motor unit loss

Reliable detection of motor unit loss is important in diagnosing and monitoring disease progression in neuromuscular disorders, in particular amyotrophic lateral sclerosis (ALS). For this, the motor unit number estimation (MUNE) techniques, being non-invasive electrophysiological methods for estimating the number of functioning motor units in a muscle, are valuable tools. During the last years, Consultant Hatice Tankisi and co-workers have worked closely on the development of a novel MUNE method (MScan) together with its inventor Professor H. Bostock from London. MScan, unlike most other MUNE methods in use, assesses all the motor units in a muscle by fitting a model to a detailed stimulus-response curve. Furthermore , it is fast and simple to perform.

Several studies have been done on the reproducibility and diagnostic value of MScan. In *"CMAP Scan MUNE (MScan) – A Novel Motor Unit Number Estimation (MUNE) Method"* the protocol for using the technique was presented (video) and an excellent intra- and inter-rater reproducibility in both ALS patients and healthy controls was shown. An excellent reproducibility among different examiners was further confirmed in the study "Reproducibility, and sensitivity to motor unit loss in amyotrophic lateral sclerosis, of a novel MUNE method: MScanFit MUNE", which also showed a higher diagnostic sensitivity of MScan compared to two traditional MUNE methods: Multiple point stimulation MUNE and Motor Unit Number Index (MUNIX). The diagnostic utility of MScan in ALS was further assessed in the study "The utility of motor unit number estimation methods versus quantitative motor unit potential analysis in diagnosis of ALS" where MScan showed higher sensitivity than the traditionally used quantitative motor unit potentials (MUP) analysis in the abductor pollicis brevis muscle. In addition, MScan correlated with the clinical ALS functional rating scale. In conclusion, being a fast, convenient, and reproducible method, MScanFit MUNE is a highly promising tool for detecting and following motor unit loss and is suitable for both research and clinical use.







PAPERS

Jacobsen AB, Bostock H, Fuglsang-Frederiksen A, Duez L, Beniczky S, Møller AT, Blicher JU, Tankisi H.
Reproducibility, and sensitivity to motor unit loss in amyotrophic lateral sclerosis, of a novel MUNE method: MScanFit MUNE.
Clin Neurophysiol. 2017 Jul;128(7):1380-1388.

Jacobsen AB; Kristensen RS; Witt AH, Kristensen AG, Duez L, Beniczky S, Fuglsang-Frederiksen A, Tankisi H.
The utility of motor unit number estimation methods versus quantitative motor unit potential analysis in diagnosis of ALS.
Clin Neurophysiol. 2018 Mar;129(3):646-53

Jacobsen AB, Bostock H, Tankisi H.
CMAP Scan MUNE (MScan) - A Novel Motor Unit Number Estimation (MUNE) Method.
J Vis Exp. 2018 (Accepted).

Ultrasound of nerve and muscle alongside neurophysiology

Recent developments in the ultrasound technology with high-resolution tranducers(18-22MHz) have given ultrasound the possibility to play a significant role in diagnosis of nerve and muscle disorders alongside neurophysiological tests.

In our lab, we have conducted research with ultrasound techniques since 2008. The first topic has been to evaluate the role and utility of the entrapment neuropathies such as carpal tunnel syndrome and ulnar nerve entrapment at the elbow. High-resolution ultrasound of the nerves at the entrapment side has been shown to have a considerable supplementary value to the neurophysiological diagnosis of those conditions (Ellegaard H 2015). We have also examined the role of high-resolution ultrasound in brachial plexopathies which are conditions that can be challenging to diagnose with neurophysiological tests. We examined last year a wide range of patients with conditions involving the brachial plexus and are currently working on an article describing the role and value of ultrasound in those conditions is under preparation.

The neurophysiological examination of motor neuron disease is essential for the final diagnosis and in our lab we showed that ultrasound can play an important role in supplementing this diagnosis. Johannson et al (2017) found that ultrasound is a sensitive method in detecting fasciculations and even outperformed EMG in patients with nerve and muscle disorders. We have also looked at the elastography (a novel ultrasound technique that uses shear-waves to determine the elastic properties of the tissues) in evaluating chronic changes in muscles in patients with nerve and muscle disorders. An article is under preparation.

In collaboration with the Danish Pain research center at Aarhus University Hospital we examined the role of ultrasound in identifying neuromas following nerve injury . The neuromas are believed to be involved in both stump and phantom pain in patients with peripheral nerve injury. In the last decade ultrasound imaging applied to diagnose and localize neuromas accurately has gained ground. The data are part of a PhD project and several abstracts have been published with preliminary data.

PAPERS

JM.T. Johansson, H.R. Ellegaard, H. Tankisi, A. Fuglsang-Frederiksen, E. Qerama
Fasciculations in nerve and muscle disorders – A prospective study of muscle ultrasound compared to electromyography.
Clinical Neurophysiology 2017; 128:2250–2257.

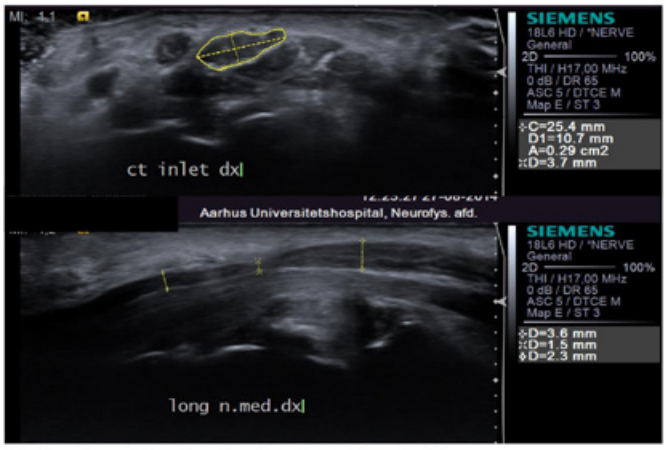


Figure shows a transverse ultrasound image of a swollen median nerve at the carpaltunnel inlet and a notch-tegn on the longitudinal scan , confirming the diagnosis of entrapment.

Guillain-Barré Syndrome

In relation to an international multicenter study, International GBS Outcome Study (IGOS), more than 60 patients were examined in Aarhus clinically at the Department of Neurology and electrophysiologically at the Department of Neurophysiology. The first paper regarding the description of the protocol was published recently and was entitled *"International Guillain-Barré Syndrome Outcome Study: protocol of a prospective observational cohort study on clinical and biological predictors of disease course and outcome in Guillain-Barré syndrome"*. More than 1.400 participants from 143 active centers in 19 countries across 5 continents were included in the IGOS study which is expected to shed light on most of the mysteries in GBS

PAPERS

Jacobs BC, van den Berg B, Verboon C, Chavada G, Cornblath DR, Gorson KC, Harbo T, Hartung HP, Hughes RAC, Kusunoki S, van Doorn PA, Willison HJ; IGOS Consortium.
International Guillain-Barré Syndrome Outcome Study: protocol of a prospective observational cohort study on clinical and biological predictors of disease course and outcome in Guillain-Barré syndrome.
J Peripher Nerv Syst. 2017;22:68-76.

Magnetic resonance imaging in visualizing peripheral nerves

Examination of peripheral nerves by magnetic resonance neurography (MRN) in combination with diffusion tensor imaging (DTI) may increase the diagnostic accuracy of neuromuscular disorders. In collaboration with the Department of Neurology, we showed that evaluation of sciatic and tibial nerves by MRN-DTI improves the detection of nerve abnormalities in patients with diabetic neuropathy "Magnetic Resonance Neurography Visualizes Abnormalities in Sciatic and Tibial Nerves in Patients With Type 1 Diabetes and Neuropathy" "Diffusion tensor imaging MR neurography for the detection of polyneuropathy in type 1 diabetes" and CMT1A "Magnetic resonance neurography and diffusion tensor imaging of the peripheral nerves in patients with Charcot-Marie-Tooth Type 1A".

PAPERS

Vaeggemose M, Vaeth S, Pham M, Ringgaard S, Jensen UB, Tankisi H, Ejskjaer N, Heiland S, Andersen H.
Magnetic resonance neurography and diffusion tensor imaging of the peripheral nerves in patients with Charcot-Marie-Tooth Type 1A.
Muscle Nerve. 2017;56:E78-E84.

Vaeggemose M, Pham M, Ringgaard S, Tankisi H, Ejskjaer N, Heiland S, Poulsen PL, Andersen H.
Magnetic Resonance Neurography Visualizes Abnormalities in Sciatic and Tibial Nerves in Patients With Type 1 Diabetes and Neuropathy.
Diabetes. 2017;66:1779-1788.

Vaeggemose M, Pham M, Ringgaard S, Tankisi H, Ejskjaer N, Heiland S, Poulsen PL, Andersen H.
Diffusion tensor imaging MR neurography for the detection of polyneuropathy in type 1 diabetes.
J Magn Reson Imaging. 2017;45:1125-1134.

PUBLICATIONS

List of peer reviewed articles

1 **Beniczky S**, Conradsen I, Henning O, Fabricius M, Wolf P. Automated real-time detection of tonic-clonic seizures using a wearable EMG device. Neurology. 2018 Jan 30;90(5):e428-e434. doi: 10.1212/WNL.0000000000004893. *Epub* 2018 Jan 5.

2. Pirgit Meritam, Philippe Ryvlin, **Sándor Beniczky**. User-based evaluation of applicability and usability of a wearable accelerometer device in detecting bilateral tonic-clonic seizures: a field study. *Epilepsia* (in press)

3. **Sándor Beniczky**, Isa Conradsen, Peter Wolf. Detection of convulsive seizures using surface electromyography. *Epilepsia* (in press).

4. **Sándor Beniczky** and Philippe Ryvlin. Standards for testing and clinical validation of seizure detection devices. *Epilepsia* (in press).

5. Bach Justesen A, Eskelund Johansen AB, Martinussen NI, Wasserman D, Terney D, Meritam P, Gardella E, **Beniczky S**. Added clinical value of the inferior temporal EEG electrode chain. *Clin Neurophysiol.* 2018;129:291-295.

6. **Jeppesen J, Otto M**, Frederiksen Y, Hansen AK, Fedorova TD, Knudsen K, Nahimi A, Brooks DJ, Borghammer P, Sommerauer M. Observations on muscle activity in REM sleep behavior disorder assessed with a semi-automated scoring algorithm. *Clinical Neurophysiology*; In press. doi.org/10.1016/j.clinph.2017.12.029.

7. Sommerauer M, Fedorova T D, Hansen A K, Knudsen K, **Otto M**, **Jeppesen J**, Frederiksen Y, Blicher J U, Geday J, Nahimi A, Damholdt M F, Brooks D J, Borghammer P. Evaluation of the noradrenergic system in Parkinson's disease: An 11C-MeNER positron emission tomography & neuromelanin magnetic resonance imaging study. *Brain* 2017; awx348. doi.org/10.1093/brain/awx348.

8. **Jacobsen AB; Kristensen RS; Witt AH, Kristensen AG, Duez L, Beniczky S, Fuglsang-Frederiksen A, Tankisi H**. The utility of motor unit number estimation methods versus quantitative motor unit potential analysis in diagnosis of ALS. *Clin Neurophysiol.* 2018 Mar;129(3):646-53.

9. **Jacobsen AB, Bostock H, Tankisi H**. CMAP Scan MUNE (MScan) – A Novel Motor Unit Number Estimation (MUNE) Method. J *Vis Exp.* 2018 (in press).

10. Heide R, **Bostock H**, Ventzel L, Grafe P, Bergmans J, **Fuglsang-Frederiksen A**, Finnerup NB, **Tankisi H**. Axonal excitability changes and acute symptoms of oxaliplatin treatment: In vivo evidence for slowed sodium channel inactivation. *Clin Neurophysiol.* 2017; pii: S1388-2457(17)31162-8.

11. Bennedsgaard KJ, Ventzel L, Jensen AB, Jensen AR, **Tankisi H**, Finnerup NB. Chronic neuropathic pain following oxaliplatin and docetaxel: A 5-year follow-up questionnaire study. *Scandinavian Journal of Pain.* 2017; 16:166.

12. Jacobs BC, van den Berg B, Verboon C, Chavada G, Cornblath DR, Gorson KC, Harbo T, Hartung HP, Hughes RAC, Kusunoki S, van Doorn PA, Willison HJ; **IGOS Consortium**. International Guillain-Barré Syndrome Outcome Study: protocol of a prospective observational cohort study on clinical and biological predictors of disease course and outcome in Guillain-Barré syndrome. *J Peripher Nerv Syst.* 2017;22:68-76.

13. Alving J, Fabricius M, Rosenzweig I, **Beniczky S**. Ictal source imaging and electroclinical correlation in self-limited epilepsy with centrotemporal spikes. *Seizure – European Journal of Epilepsy* 2017; 52: 7-10.

14. **Beniczky, Sándor**; Aurlien, Harald; Brøgger, Jan C; Hirsch, Lawrence J; Schomer, Donald L; Trinka, Eugen; Pressler, Ronit M; Wennberg, Richard; Visser,Gerhard H; Eisermann, Monika; Diehl, Beate; Lesser, Ronald P; Kaplan, Peter W; Nguyen The Tich, Sylvie; Lee, Jong Woo; Martins-da-Silva, Antonio; Stefan, Hermann; Neufeld, Miri; Rubboli, Guido; Fabricius, Martin; Gardella, Elena; Terney, Daniella; Meritam, Pirgit; Eichele, Tom; Asano, Eishi; Cox, Fieke; van Emde Boas, Walter; Mameniskiene, Ruta; Marusic, Petr; Zárubová, Jana; Schmitt, Friedhelm C; Rosén, Ingmar; **Fuglsang-Frederiksen**, **Anders**; Ikeda, Akio; MacDonald, David B; Terada, Kiyohito; Ugawa, Yoshikazu; Zhou, Dong; Herman, Susan T: Standardized computer-based organized reporting of EEG SCORE – Second version. *Clinical neurophysiology* : official journal of the International Federation of Clinical Neurophysiology, 2017; Bind 128, Nr. 11, 11.2017, s. 2334-2346.

15. Craciun, Laura; Alving, Jorgen; Gardella, Elena; Terney, Daniella; Meritam, Pirgit; Hribljan, Melita Cacic; **Beniczky**, **Sándor**: Do patients need to stay in bed all day in the Epilepsy Monitoring Unit? Safety data from a non-restrictive setting. *Seizure – European Journal of Epilepsy,* Bind 49, 07.2017, s. 13-16.

16. De Tiège, Xavier; Lundqvist, Daniel; **Beniczky**, **Sándor**; Seri, Stefano; Paetau, Ritva: Current clinical magnetoencephalography practice across Europe: Are we closer to use MEG as an established clinical tool? Seizure – *European Journal of Epilepsy*, Bind 50, 08.2017, s. 53-59.

17. Florea, Bogdan; Beniczky, Simona Alexandra; Demény, Helga; **Beniczky, Sándor**: Semiology of subtle motor phenomena in critically ill patients. *Seizure – European Journal of Epilepsy*, Bind 48, 05.2017, s. 33-35.

18. Foged, Mette Thrane; Lindberg, Ulrich; Vakamudi, Kishore; Larsson, Henrik B W; Pinborg, Lars H; Kjær, Troels W; Fabricius, Martin; Svarer, Claus; Ozenne, Brice; Thomsen, Carsten; **Beniczky, Sándor;** Paulson, Olaf B; Posse, Stefan: Safety and EEG data quality of concurrent high-density EEG and high-speed fMRI at 3 Tesla. *PLoS ONE*, Bind 12, Nr. 5, 26.05.2017, s. e0178409.

19. Hamandi, Khalid; **Beniczky, Sándor;** Diehl, Beate; Kandler, Rosalind H; Pressler, Ronit M; Sen, Arjune; Solomon, Juliet; Walker, Matthew C; Bagary, Manny; with ILAE British Chapter Workshop Attendees: Current practice and recommendations in UK epilepsy monitoring units. Report of a national survey and workshop. *Seizure – European Journal of Epilepsy*, Bind 50, 08.2017, s. 92-98.

20. **Isak, Baris**; **Pugdahl, Kirsten**; Karlsson, Pall; **Tankisi, Hatice**; Finnerup, Nanna Brix; **Furtula, Jasna**; **Johnsen, Birger**; Sunde, Niels; Jakobsen, Johannes Klitgaard; **Fuglsang-Frederiksen, Anders**: Quantitative Sensory Testing and Structural Assessment of Sensory Nerve Fibres in Amyotrophic Lateral Sclerosis. *Journal of the Neurological Sciences*, Bind 373, 15.02.2017, s. 329-334.

21. **Jacobsen, A B**; **Bostock, Hugh**; **Fuglsang-Frederiksen, A**; **Duez, L**; **Beniczky, S**; **Møller, A T**; **Blicher, Jakob**; **Tankisi, H**: Reproducibility, and sensitivity to motor unit loss in amyotrophic lateral sclerosis, of a novel MUNE method : MScanFit MUNE. *Clinical neurophysiology*: official journal of the International Federation of Clinical Neurophysiology, Bind 128, Nr. 7, 07.2017, s. 1380-1388.

22. **Jeppesen, J**; **Beniczky, S**; **Fuglsang Frederiksen, A**; Sidenius, P; Johansen, P: Modified automatic R-peak detection algorithm for patients with epilepsy using a portable electrocardiogram recorder. *I E E E Engineering in Medicine and Biology Society. Conference Proceedings*, Bind 2017, 07.2017, s. 4082-4085.

23. **Johansson, Maria Therese Thelin**; **Ellegaard, Hanne Rheder**; **Tankisi, Hatice**; **Fuglsang-Frederiksen, Anders**; **Qerama, Erisela**: Fasciculations in nerve and muscle disorders - A prospective study of muscle ultrasound compared to electromyography. *Clinical Neurophysiology*, Bind 128, Nr. 11, 11.2017, s. 2250-2257.

24. **Johnsen, Birger**; Backman Nøhr , Kristoffer ; Duez, Christophe Henri Valdemar; Ebbesen, Mads Qvist: The Nature of EEG reactivity to light, sound and pain stimulation in neurosurgical comatose patients evaluated by a quantitative method. *Clinical EEG and Neuroscience*, Bind 48, Nr. 6, 11.2017, s. 428-437.

25. **Kural, Mustafa Aykut;** Karlsson, Pall; **Pugdahl, Kirsten**; **Isak, Baris**; **Fuglsang-Frederiksen, Anders**; Tankisi, Hatice: Diagnostic utility of distal nerve conduction studies and sural near-nerve needle recording in polyneuropathy. *Clinical Neurophysiology*, Bind 128, Nr. 9, 09.2017, s. 1590-1595.

26. Leitinger, Markus; Trinka, Eugen; Gardella, Elena; Kalss, Gudrun; **Beniczky, Sándor**: Salzburg criteria: can we extend validation to critical care? *Lancet Neurology*, Bind 16, Nr. 1, 01.2017, s. 25-26.

27. Mikkelsen, Kaare; Villadsen, David Bové; **Otto, Marit**; Kidmose, Preben: Automatic sleep staging using ear EEG. *BioMedical Engineering OnLine*, Bind 16, 111, 19.09.2017.

28. Mălîia, Mihai Dragos; Donos, Cristian; Barborica, Andrei; Mindruta, Ioana; Popa, Irina; Ene, Mirela; **Beniczky, Sándor**: High frequency spectral changes induced by single-pulse electric stimulation : Comparison between physiologic and pathologic networks. *Clinical Neurophysiology*, Bind 128, Nr. 6, 06.2017, s. 1053-1060.

29. Nahimi, Adjmal; Sommerauer, Michael; Kinnerup, Martin B; Østergaard, Karen; Winterdahl, Michael; Jacobsen, Jan; Schacht, Anna; **Johnsen, Birger;** Damholdt, Malene F; Borghammer, Per; Gjedde, Albert: Noradrenergic deficits in Parkinson's disease imaged with (11) C-MeNER. *Journal of Nuclear Medicine*, 28.08.2017.

30. **Otto, Marit**; Markvardsen, Lars Høj; **Tankisi, Hatice;** Jakobsen, Johannes Klitgaard; **Fuglsang-Frederiksen, Anders**: The electrophysiological response to immunoglobulin therapy in chronic inflammatory demyelinating polyneuropathy. *Acta Neurologica Scandinavica*, Bind 135, Nr. 6, 25.04.2017, s. 656-662.

31. **Pugdahl, Kirsten**; **Johnsen, Birger**; **Tankisi, Hatice**; Camdessanche, J.-P.; Carvalho, Mamede de; Fawcett, P.R.W.; Labarre-Vila, A.; Liguori, R.; Nix, W.; Schofield, Ian; **Fuglsang Frederiksen, Anders**: Added value of electromyography in the diagnosis of myopathy: A consensus exercise. *Clinical Neurophysiology*, Bind 128, Nr. 5, 05.2017, s. 697-701.

32. **Pugdahl, Kirsten**; **Beniczky, Sándor**; Wanscher, Benedikte; **Johnsen, Birger**; **Qerama, Erisela**; Ballegaard, Martin; Benedek, Krisztina; Juhl, Anne ; Ööpik, Merle; Selmar, Peter E; Sønderborg, Jørgen; Terney, Daniella; **Fuglsang-Frederiksen, Anders**. Neurophysiological localisation of ulnar neuropathy at the elbow: validation of diagnostic criteria developed by a taskforce of the Danish Society of Clinical Neurophysiology. *Clinical Neurophysiology*, Bind 128, Nr. 11, 11.2017, s. 2205-2210.

33. Seeck, Margitta; Koessler, Laurent; Bast, Thomas; Leijten, Frans; Michel, Christoph; Baumgartner, Christoph; He, Bin; **Beniczky, Sándor**: The standardized EEG electrode array of the IFCN. *Clinical Neurophysiology*, Bind 128, Nr. 10, 10.2017, s. 2070-2077.

34. Springer, Jeanette; Karlsson, Pall; Madsen, C S; **Johnsen, Birger**; Finnerup, Nanna Brix; Jensen, Troels Staehelin; Nikolajsen, Lone Functional and structural assessment of patients with and without persistent pain after thoracotomy. *European journal of pain* (London, England), Bind 21, Nr. 2, 02.2017, s. 238-249.

35. Sridharan, Kousik Sarathy; Højlund, Andreas; Johnsen, Erik Lisbjerg; Sunde, Niels Aagaard; Johansen, Lars Gottfried; **Beniczky, Sándor**; Østergaard, Karen: Differentiated effects of deep brain stimulation and medication on somatosensory processing in Parkinson's disease. *Clinical neurophysiology*: official journal of the International Federation of Clinical Neurophysiology, Bind 128, Nr. 7, 07.2017, s. 1327-1336.

36. Stokholm, Morten Gersel; Iranzo, Alex; Østergaard, Karen; Serradell, Mónica; **Otto, Marit**; Svendsen, Kristina Bacher; Garrido, Alicia; Vilas, Dolores; Borghammer, Per; Santamaria, Joan; Møller, Arne; Gaig, Carles; Brooks, David J; Tolosa, Eduardo; Pavese, Nicola: Assessment of neuroinflammation in patients with idiopathic rapid-eye-movement sleep behaviour disorder: a case-control study. *Lancet Neurology*, Bind 16, Nr. 10, 10.2017, s. 789-796.

37. Tabatabaeifar, Sorosh; Svendsen, Susanne Wulff; **Johnsen, Birger**; Hansson, Gert-Åke; **Fuglsang-Frederiksen, Anders**; Frost, Poul: Reversible median nerve impairment after three weeks of repetitive work. *Scandinavian Journal of Work, Environment & Health*, Bind 43, Nr. 2, 01.03.2017, s. 163-170.

38. Vaeggemose, Michael; Pham, Mirko; Ringgaard, Steffen; **Tankisi, Hatice**; Ejskjaer, Niels; Heiland, Sabine; Poulsen, Per L; Andersen, Henning: Diffusion tensor imaging MR neurography for the detection of polyneuropathy in type 1 diabetes. *Journal of Magnetic Resonance Imaging*, Bind 45, Nr. 4, 04.2017, s. 1125-1134.

39. Vaeggemose, Michael; Pham, Mirko; Ringgaard, Steffen; **Tankisi, Hatice**; Ejskjaer, Niels; Heiland, Sabine; Poulsen, Per L; Andersen, Henning: Magnetic Resonance Neurography Visualizes Abnormalities in Sciatic and Tibial Nerves in Patients with Type 1 Diabetes and Neuropathy. *Diabetes*, Bind 66, Nr. 7, 07.2017, s. 1779-1788.

40. Vaeggemose, Michael; Vaeth, Signe; Pham, Mirko; Ringgaard, Steffen; Jensen, Uffe B; **Tankisi, Hatice**; Ejskjær, Niels; Heiland, Sabine; Andersen, Henning: Magnetic resonance neurography and diffusion tensor imaging of the peripheral nerves in patients with Charcot-Marie- Tooth Type 1A. *Muscle & Nerve*, Bind 56, Nr. 6, 12.2017, s. E78-E84.

41. Ventzel, Lise; Madsen, Caspar S; Karlsson, Pall; **Tankisi, Hatice**; **Isak, Baris**; **Fuglsang-Frederiksen, Anders**; Jensen, Anders B; Jensen, Anni R; Jensen, Troels S; Finnerup, Nanna B: Chronic Pain and Neuropathy Following Adjuvant Chemotherapy. Pain Medicine, 23.09.2017.

Book Chapters

Book: Niedermeyer's Electroencephalography. Basic Principles, Clinical Applications, and Related Fields. Seventh edition. Oxford University Press

Chapters:
Chapter 9: Validating Biomarkers and Diagnostic Tests in Clinical Neurophysiology: Developing Strong Experimental Designs and Recognizing Confounds. /Ewen, Joshua B and **Beniczky, Sándor**

Chapter 26: Standardizing EEG Interpretation and Reporting. / **Beniczky, Sándor**, Aurlien, Harald, Brøgger, Jan, Pressler, Ronit and Hirsch, Lawrence J.

Book: Klinisk neurofysiologi. 1. udg. København: Munksgaard, 2017

Chapters:
Kapitel 2.1 Basal neurofysiologi – EEG. / Benedek, Krisztina; **Beniczky, Sándor**; Kjær, Troels Wesenberg. s. 19-23.

Kapitel 2.2: Basal EEG-teknologi. / **Beniczky, Sándor**; Duez, Lene; Kjær, Troels Wesenberg. s. 23-29.

Kapitel 2.4: EEG-abnormiteter. / **Beniczky, Sándor**; Meritam, Pirgit; Kjær, Troels Wesenberg. s. 45-55.

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Book: Textbook of Electrodiagnosis/Elektrodiagnoz. 2017.

Chapters:
Motor Unit Number Estimation (MUNE)/Motor Ünite Sayimi. / **Tankisi, Hatice**. s. 203-206
Special EMG methods/Özel elektromiygrafik Incelemeler. / Tankisi, Hatice; Pugdahl, Kirsten; Fuglsang-Frederiksen, Anders. Surface EMG/Yüzeyel EMG. / **Qerama, Erisela**; **Fuglsang-Frederiksen, Anders**. s. 135-152.

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