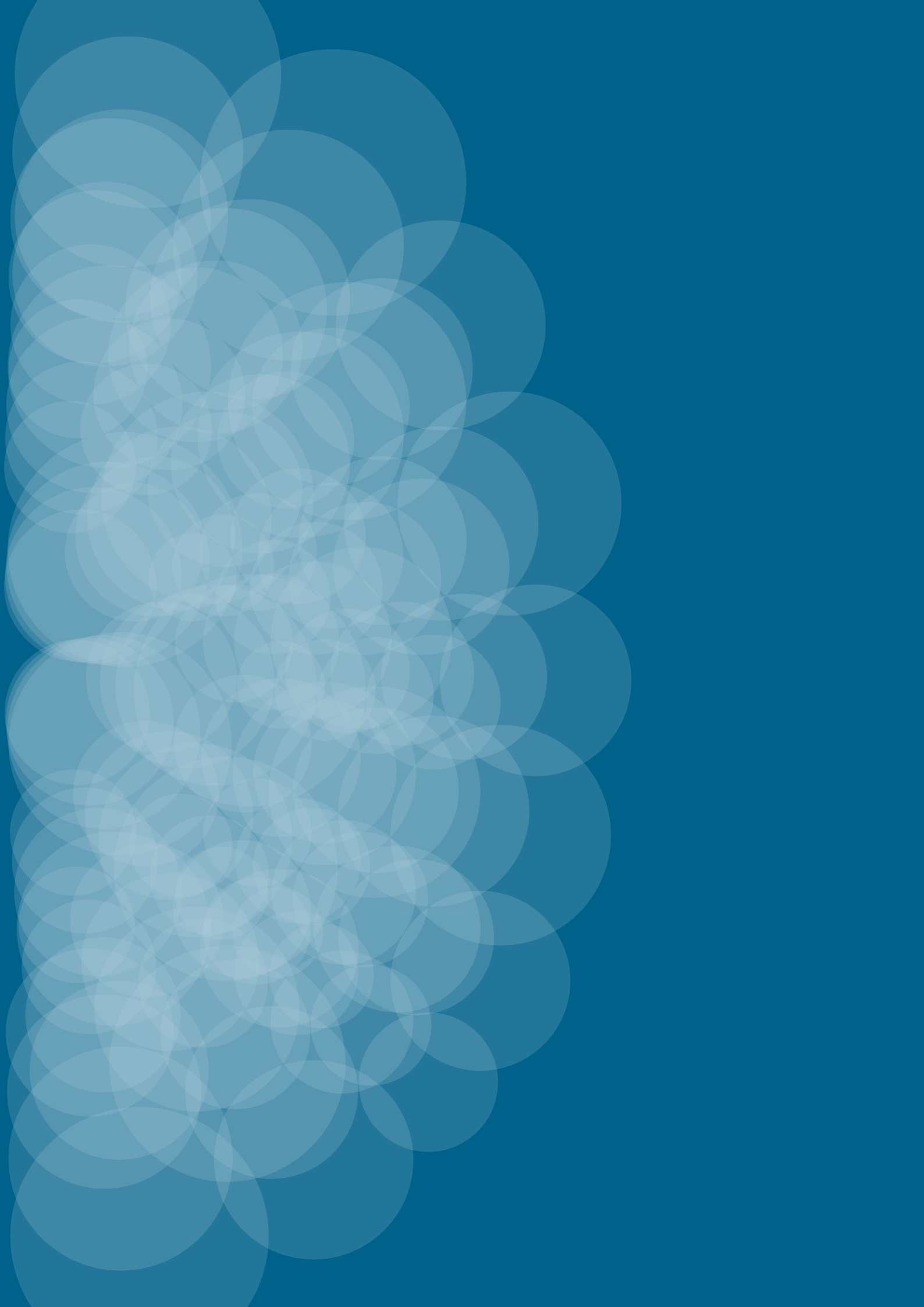


ANNUAL RESEARCH REPORT 2022-2023

DEPARTMENT OF
CLINICAL NEUROPHYSIOLOGY
AARHUS UNIVERSITY HOSPITAL



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DEPARTMENT OF CLINICAL NEUROPHYSIOLOGY

As the largest Danish neurophysiology department outside the capital area, the Clinical Neurophysiology department at Aarhus University Hospital enjoys international acclaim for its highly specialized diagnostic services, extensive research and clinical development activities.

Research at the Neurophysiology Department is clinically oriented and focuses on developing, validating, and implementing new methods for functional investigations of the central and peripheral nervous system, as well as muscles, with the goal of achieving highly accurate and feasible diagnostic approaches to enhance the quality of patient care.

The research group comprises two professors, one professor emeritus, two associate professors, one assistant professor and five postgraduate (PhD) students, utilizing facilities at Aarhus University Hospital.

In 2022 and 2023, we published 129 papers in peer-reviewed international journals listed on PubMed. Our department also actively contributed to international congresses and meetings with 80 presentations, posters, and teaching courses.

Furthermore, the department collaborates closely with several international consortia, leading ESTEEM and SCORE and serving as the lead of the Neurophysiology work-package in EpiCare. Our colleagues hold positions of trust in national and international scientific societies, and we maintain a strong collaboration with other Danish research groups at the Danish Epilepsy Centre and Copenhagen University.

THE RESEARCH GROUP

TWO PROFESSORS
ONE PROFESSOR EMERITUS
TWO ASSOCIATE PROFESSORS
ONE ASSISTANT PROFESSOR
FIVE POSTGRADUATE (PHD) STUDENTS
ONE RESEARCH ASSISTANT

129

PUBLISHED PAPERS
IN PEER-REVIEWED JOURNALS,
LISTED ON PUBMED

80

CONTRIBUTIONS OF
INTERNATIONAL CONGRESSES



Foto: Jesper Larsen



The research group

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)
Fellow of the European Academy of Neurology (2020)
Fellow of the American Clinical Neurophysiology Society (2023)

Current positions

Professor, consultant, Aarhus University Hospital
Head of Clinical Neurophysiology, Danish Epilepsy Centre, Filadelfia
Editor-in-chief, Epileptic Disorders

Research interests

- Seizure detection
- Video-EEG monitoring
- Epilepsy surgery
- Electromagnetic source imaging and quantitative EEG analysis
- Standardisation and quality assurance in clinical neurophysiology
- Artificial intelligence and decision support systems in epilepsy

PhD projects

Completed in 2022-2023

- Bogdan Florea: Electroencephalography in patients with disturbed level of consciousness. University of Szeged, Hungary. Main supervisor: Sándor Beniczky. Co-supervisor: Péter Klivényi.
- Karin Westin: Extending the clinical applications of magnetoencephalography. Karolinska Institute, Stockholm. Co-supervisor: Sándor Beniczky. Main supervisor: Daniel Lundquist.

Ongoing

- Maria Vlachou: Evaluation of electro-clinical findings using standardised feature extraction and machine learning. Aarhus University. Main supervisor: Sándor Beniczky.
- Sidsel Armand Larsen: Digital Technology in Epilepsy. Aarhus University. Main supervisor: Sándor Beniczky.
- Levente Hadady: Assessment of the clinical impact of electronic applications and wearable devices on the clinical management of patients with epilepsy. University of Szeged, Hungary. Main supervisor: Sándor Beniczky.
- Amir Baroumand: Automated EEG Source imaging. Ghent University, Belgium. Main supervisor: Pieter van Mierlo. Co-supervisor: Sándor Beniczky

251 publications in peer-reviewed journals; 9711 citations; H-index: 53.



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

Consultant at Aarhus University Hospital, and clinical professor at Aarhus University

Research interests

- Peripheral nerve-muscle 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
- Neuromuscular manifestations of long-term Covid-19.

PhD projects

Has been main supervisor for 2 PhD students and co-supervisor for 7 PhD students.

Ongoing PhD projects as main supervisor

- Anna Bystrup Jacobsen: Neurophysiological biomarkers for early diagnosis of ALS. Aarhus University.
- Benjamin Khan: Long-term neuromuscular manifestations of COVID-19. Aarhus University
- Gaia Fanella: Disclosing the most effective therapeutic TMS strategy for reducing cortical excitability in ALS. Aarhus University

Peer reviewed and PubMed indexed 165 articles. Google Scholar: H-index: 34, Total citations: 3796



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, 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.

192 publications in peer-reviewed journals, H-index 53,
citations 8648



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.

Published 70 scientific publications in peer-reviewed journals,
12 book chapters, 79 abstracts and 42 oral presentations.



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

**Erisela Qerama**

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

Current position

Associate Professor, Aarhus University
Consultant in Clinical Neurophysiology, Aarhus University Hospital

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.

Co-supervisor for three PhD students, two from AUH and one PhD student from Kaunas University Hospital, Lithuania

Main supervisor for seven medical students with their 4th semester research thesis and main clinical supervisor for four medical students for the 3-rd semester clinical project.

Clinical supervisor for residents in research and clinical training, 1-2 residents/ year.

Main supervisor for five research-year students

**Jesper Jeppesen**

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

Current position

Assistant Professor, Aarhus University

Research interests

- Seizure detection
- Biosignal analysis
- Seizure alarm systems.

PhD entitled: Detecting epileptic seizures with heart 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

**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

**Alexander Gramm Kristensen**

MD from Aarhus University (2016)
PhD from Aarhus University Clinical Institute (2020)

Current position

MD at Department of Neurology and Clinical Neurophysiology, Aarhus University Hospital

Research interests

- Microneurography
- Nerve excitability
- Nerve conduction studies
- Motor unit number estimation
- Diabetic neuropathy
- Deep learning



Maria Vlachou

MD from Aristotle University, Thessaloniki,
Greece (2012)
Specialist in Neurology, Denmark (2021)

Current Position

PhD-student at Department of Clinical Neurophysiology,
Aarhus University Hospital

Research Interests

- Epilepsy
- Epilepsy Surgery
- Standardization in EEG reporting
- Seizure Severity-Postictal generalized EEG suppression
- Clinical Relevance of ictal electro-clinical features
- Supervised machine learning in epilepsy research



Anna Bystrup Jacobsen

MD from Aarhus University (2018)

Current position

PhD-student at Department of Clinical Neurophysiology,
Aarhus University Hospital

Research interests

- TMS
- MScanFit MUNE
- Motor unit number estimation
- ALS, Nerve excitability
- Nerve conduction studies



Hossein Pia

MD from Tabriz University of Medical Sciences,
Iran (2006)
Specialist in Neurology from Ege University,
Faculty of Medicine, Turkey (2016)

Current Position

Research Assistant at Department of Clinical Neurophysiology and
Neurology, Aarhus University Hospital

Research Interests

- Neurology
- Nerve conduction studies
- Cortical excitability
- Transcranial magnetic Stimulation



Sara Silkjær Bak

MD from Aarhus University (2020)

Current position

Resident at Department of Neurology, Regional Hospital of Viborg
Former research year student at Department of Clinical
Neurophysiology

Research interests

- Nerve and muscle ultrasound
- The diagnostic work-up of scapulae alatae patients in regard
to the clinical examination, electrodiagnostic examination
and ultrasound

Published 2 scientific publications in peer-reviewed journals.

**Torsten Vinding Merinder**

MD from Aarhus University (2021)

Current position

Medical doctor at Department of Neurophysiology / Neurology,
Aarhus University Hospital
Former research student at Department of Clinical Neurophysiology

Research Interests

- Connectivity analyses
- Electromagnetic source imaging
- Functional cortical mapping
- Long-term monitoring of epilepsy seizure manifestations
- Artificial intelligence and integrated health solutions
- Automated EEG interpretation / machine learning in epilepsy research

**Benjamin Khan**

Specialist in Neurology, Denmark (2020)

Current Position

PhD Student at Department of Clinical Neurophysiology, Aarhus
University Hospital

Research interests

- COVID 19
- Post Covid Syndrome "Long Covid"
- Myopathy
- Neuromuscular Transmission Defects

**Anders Stouge**

MD from Aarhus University (2020)

Current position

PhD student at the Department of Neurology and Steno Diabetes
Center Aarhus: 'Understanding muscle failure of diabetic myopathy'
Former research year student at the department of neurology:
'Structural and compositional changes of skeletal muscles in
participants with type 2 diabetes with and without diabetic
polyneuropathy'

Research Interests

- Diabetic neuropathy
- Diabetic myopathy
- Muscle Failure
- Muscle mitochondrial function and bioenergetics

**Atle Vigild Lomstein**

MD from Aarhus University (2018)

Current position

Resident specializing in neurology at the Department of Clinical
Neurophysiology, Aarhus University Hospital

Research interests

- Myopathy and muscular dystrophy
- Inherited ataxias and neuropathies
- Long COVID
- Multiple sclerosis and epilepsy
- Brain-machine-interfacing

Research activity

2 publications. Manager of MASTER-PCM, clinical trial at the
Department of Neurology, Aarhus University Hospital. Investigator in
DANMNORMS Clinical Trial.



Gaia Fanella

MD from La Sapienza University of Rome, Italy (2018)
Specialist in Neurology from Milano Bicocca University, Italy (2023)

Current position

PhD student at Department of Clinical Neurophysiology, Aarhus University Hospital

Research interests

- Transcranial Magnetic Stimulation
- Neuromodulation
- Nerve conduction studies
- ALS
- Neuromuscular manifestations of post-COVID condition



Thorbjørn Søndergaard Engedal

MD from University of Aarhus (2010)
Ph.D. from University of Aarhus (2017)
Specialist in Neurology (2021)
Specialist in Clinical Neurophysiology (2023)

Current position

Senior Registrar, Department of Clinical Neurophysiology, Aarhus University Hospital

Research interest

- Electrodiagnostics
- Neuromuscular disease
- Epilepsy in children
- Non-convulsive status epilepticus



Peter Andreas Andersen

MD

Current position

PhD-student

Research interests

- Neuropathic pain in syringomyelia and radiculopathy
- Electrophysiological assessment of pain related neuronal pathways



Magdalena Mroczek

MD from Medical University of Warsaw, Poland (2013)

Current position

Neurologist in training, Department of Neurology, University Hospital Basel, Switzerland

Former guest researcher at Department of Clinical Neurophysiology, Aarhus University Hospital: Effects of sleep deprivation on cortical excitability: A threshold-tracking TMS study

Research interests

- Neuromuscular diseases
- Neurogenetics

**Zahra Nochi**

M.Sc in Cell & Molecular Biology, Azad University, Iran (2007)

PhD in Molecular Medicine, Aarhus University, Denmark (2016)

Current position

Assistant Professor of Mechanistic Pain and Fatigue Research
Danish Pain Research Center & Research Unit for Molecular Medicine,
Department of Clinical Medicine, Aarhus University

Research interests

- Pain and chronic fatigue
- Mitochondrial function
- Neuroinflammation

**Diletta Fratini****Current position**

V year Medicine and Surgery Student at Campus Bio-Medico
University of Rome (2019-2025)

Former Researcher Student at Department of Clinical
Neurophysiology at Aarhus
University Hospital in August-November 2023

Research interests

- TMS
- EMG
- Nerve conduction studies

**Martina Cannazza****Current position**

V year Medicine and Surgery Student at Campus Bio-Medico
University of Rome (2019-2025)

Former Researcher Student at Department of Clinical
Neurophysiology at Aarhus
University Hospital in August-November 2023

Research interests

- TMS
- EMG
- Nerve conduction studies

**Camilla Carrozzo****Current position**

V year Medicine and Surgery Student at Campus Bio-Medico
University of Rome (2019-2025)

Former Researcher Student at Department of Clinical
Neurophysiology at Aarhus
University Hospital in August-November 2023

Research interests

- TMS
- EMG
- Nerve conduction studies



Amedeo De Grado
Doctor, Neurologist (2023)

Current position

Inherited Neuropathy Consortium Fellow at Fondazione Istituto Carlo Besta

Former guest researcher at Department of Clinical Neurophysiology at Aarhus University Hospital

Research interests

- Inherited neuropathies, neurophysiology and rare neurometabolic diseases



Sidsel Armand Larsen
MSc in Human Physiology,
University of Copenhagen (2016)

Current Position

PhD student, Aarhus University and Filadelfia Epilepsy Hospital

Research interests

- Mobile health and seizure Detection



Tim Østerkjerhuus
Neurophysiology Assistant/EEG Technician from
Aarhus University Hospital & SDE College

Current position

Neurophysiology Assistant/EEG Technician at Department of Clinical Neurophysiology, Aarhus University Hospital

Research interests

- Automated analysis and detection of epileptic seizures in recordings using artificial intelligence
 - Long-term EEG monitoring of epilepsy seizure manifestation and semiology
-

POSITIONS OF TRUST

SANDOR BENICZKY

- Editor-in-Chief, Epileptic Disorders
 - Chair, ILAE Neurotechnology Section (2022-2023)
 - Chair, EEG Task Force, ILAE Commission on Big Data
 - Past-chair, Joint Taskforce on EEG of the International Federation of Clinical Neurophysiology (IFCN) and the International League Against Epilepsy (ILAE)
 - Member, ILAE Commission on Diagnostic Methods
 - Member, ILAE Education Council; coordinator of the Virtual Epilepsy Academy (VIREPA)
 - Member, ILAE Publication Council
 - Member, ILAE Congress Council
 - Member, IFCN Guidelines Committee
-

PETER ORM HANSEN

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

HATICE TANKISI

- President of the Europe-Middle East-Africa Chapter-IFCN (EMEAC-IFCN), 2022-
 - Executive Committee Member of International Federation of Clinical Neurophysiology (IFCN)- 2023-
 - Co-chair of the Clinical Neurophysiology Panel Management Group, EAN, 2019-2023 Co-chair of the ALS/FTD Panel Management Group, EAN, 2024-
 - Co-Chair of the Research Committee of IFCN, 2023-
 - Co-Chair of the Nerve and Muscle Excitability Special Interest Group of IFCN, 2022-
 - Steering Group member of the Teaching Course Sub-committee of the EAN, 2022-
 - Steering Group member of NeuroCampus Aarhus, 2022-
 - Associate Editor of Clinical Neurophysiology Practice, 2020-
 - Associate Editor of Neurophysiologie Clinique/Clinical Neurophysiology- 2024
 - Co-Editor of IFCN Handbook Series, Volume 2: Clinical Neurophysiology of MND, 2023-2024
 - Editorial board member of Clinical Neurophysiology- 2020-
 - Editorial board member of Journal of Clinical Neurophysiology- 2020-
 - Lead of the European Multicenter EMG network ESTEEM 2021-
-

ERISELA QERAMA

- Danish Society of Clinical Neurophysiology: board member and secretary (since 2015).
-

The background of the entire image is a solid dark blue. Overlaid on this background is a pattern of numerous overlapping circles in a lighter shade of blue. These circles are of varying sizes and are arranged in a way that they create a complex, layered effect, particularly concentrated on the right side of the image.

RESEARCH PROJECTS

Standardization and quality assurance in Clinical Neurophysiology

by Sándor Beniczky

Standardization is essential for improving the quality of care. Clinical Practice Guidelines are important tools to achieve this goal. Guidelines must be developed using a robust methodology, based on systematic review of published evidence. Developing guidelines is resource demanding, yet much needed for clinical practice. We were happy to contribute to the clinical practice guideline on standards for inpatient long-term video-electroencephalographic monitoring. The guideline has been endorsed both by the International League Against Epilepsy and the International Federation of Clinical Neurophysiology.

We contributed to development of international guidelines on minimum standards for routine and sleep EEG, endorsed by both the International Federation of Clinical Neurophysiology and the International League Against Epilepsy.

A significant technical impediment in clinical EEG is the lack of a universal data format. This makes shared-care and collaborative research difficult. Under the auspices of the International Federation of Clinical Neurophysiology, a working group developed a new, international standard for a universal data format, using DICOM. Our group contributed to this work.

Bias from clinical data (the text of the EEG referral) is detrimental for an objective interpretation of clinical EEG. We showed the discrepancy between what experts consider optimal, and their own clinical practice. We published a manifesto for changing the practice and improve the quality of clinical EEG interpretation.

PAPERS

Tatum WO, Mani J, Jin K, Halford JJ, Gloss D, Fahoum F, Maillard L, Mothersill I, Beniczky S.

Minimum standards for inpatient long-term video- electroencephalographic monitoring: A clinical practice guideline of the International League Against Epilepsy and International Federation of Clinical Neurophysiology.

Dual publication in:

Clin Neurophysiol. 2022 Feb;134:111-128. doi: 10.1016/j.clinph.2021.07.016.

Epilepsia. 2022 Feb;63(2):290-315. doi: 10.1111/epi.16977.

Halford JJ, Brinkmann BH, Clunie DA, Gotman J, Beniczky S, Rampp S, Rémi J, Husain A, Andrew Ehrenberg J, Winkler S.

Continued progress in DICOM neurophysiology standardization.

Clin Neurophysiol. 2023 Mar;147:11-13. doi: 10.1016/j.clinph.2022.12.008.

Nascimento FA, Jing J, Beniczky S, Olandoski M, Benbadis SR, Cole AJ, Westover MB.

EEG reading with or without clinical information - a real-world practice study. Neurophysiol Clin. 2022 Oct;52(5):394-397. doi: 10.1016/j.neucli.2022.08.002

Nascimento FA, Jing J, Beniczky S, Benbadis SR, Gavvala JR, Yacubian EMT, Wiebe S, Rampp S, van Putten MJAM, Tripathi M, Cook MJ, Kaplan PW, Tatum WO, Trinka E, Cole AJ, Westover MB.

One EEG, one read - A manifesto towards reducing interrater variability among experts.

Clin Neurophysiol. 2022 Jan;133:68-70. doi: 10.1016/j.clinph.2021.10.007.

Peltola ME, Leitinger M, Halford JJ, Vinayan KP, Kobayashi K, Pressler RM, Mindruta I, Mayor LC, Lauronen L, Beniczky S.

Routine and sleep EEG: Minimum recording standards of the International Federation of Clinical Neurophysiology and the International League Against Epilepsy. Dual publication in:

Clin Neurophysiol. 2023 Mar;147:108-120. doi: 10.1016/j.clinph.2023.01.002.

Epilepsia. 2023 Mar;64(3):602-618. doi: 10.1111/epi.17448.

Leitinger M, Gaspard N, Hirsch LJ, Beniczky S, Kaplan PW, Husari K, Trinka E.

Diagnosing nonconvulsive status epilepticus: Defining electroencephalographic and clinical response to diagnostic intravenous antiseizure medication trials. Epilepsia. 2023 Sep;64(9):2351-2360. doi: 10.1111/epi.17694.

Electro-clinical phenomena in epileptic seizures

by Sándor Beniczky

Accurate feature extraction and characterization of the EEG and clinical phenomena (semiology) observed in epileptic seizures is of paramount importance.

Postictal generalized electroencephalography (EEG) suppression (PGES) is a surrogate marker of sudden unexpected death in epilepsy (SUDEP). In our large dataset, we demonstrated that progressive slowing of clonic phase (PSCP) in generalized tonic-clonic seizures, predicts prolonged PGES, emphasizing the importance of gradually increasing inhibitory phenomena at the end of the seizures. Our findings shed more light on the ictal phenomena leading to increased risk of SUDEP. These phenomena may provide basis for algorithms implemented into wearable devices for identifying GCS with increased risk of SUDEP.

We lead an international working group which, under the auspices of the International League Against Epilepsy revised the semiology glossary. This work was based on systematic search of the published literature. The paper includes video-examples of the various semiology phenomena, and is an important educational resource.

PAPERS

Vlachou M, Ryvlin P, Arbune AA, Armand Larsen S, Skraep Sidaros A, Cacic Hribljan M, Fabricius M, Beniczky S.

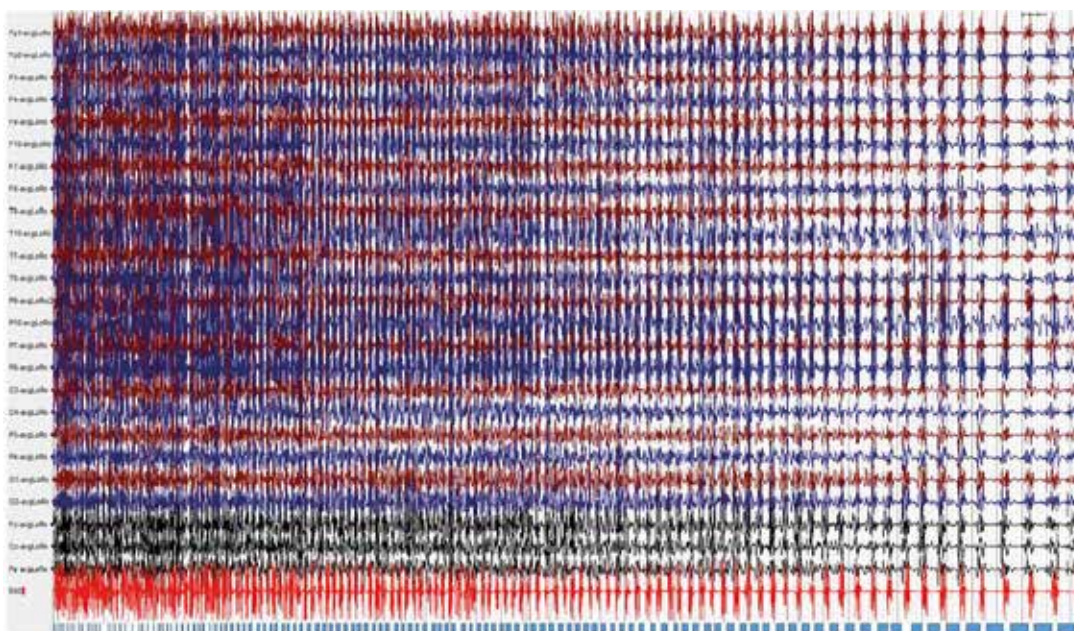
Progressive slowing of clonic phase predicts postictal generalized EEG suppression.

Epilepsia. 2022 Dec;63(12):3204-3211. doi: 10.1111/epi.17434. Epub 2022 Oct 29.

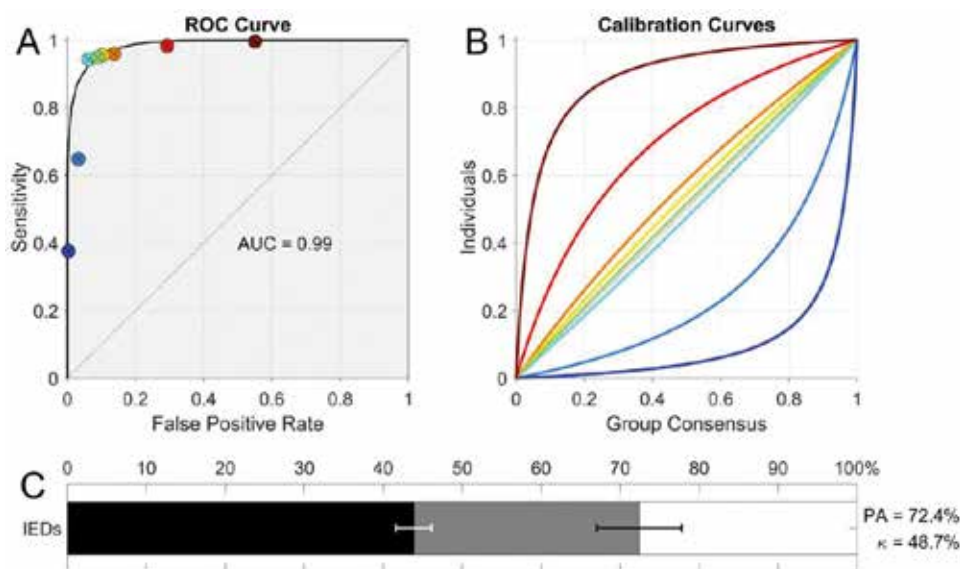
Beniczky S, Tatum WO, Blumenfeld H, Stefan H, Mani J, Maillard L, Fahoum F, Vinayan KP, Mayor LC, Vlachou M, Margitta S, Ryvlin P, Philippe K.

Seizure semiology: ILAE glossary of terms and their significance.

Epileptic Disord. 2022 Jun 1;24(3):447-495. doi: 10.1684/epd.2022.1430. PMID: 35770761.



Progressive slowing of the clonic phase in generalized tonic-clonic seizures.



Inter-rater reliability
A: Receiver operating characteristic curve fit to all experts' scores.
B: Parametric calibration curve fit to the binary scores of each expert.
C: Inter-rater reliability (IRR): Kappa (κ) values in relation to percent agreement.

Big Data and Standardized Computer-based Organized Reporting of EEG: SCORE

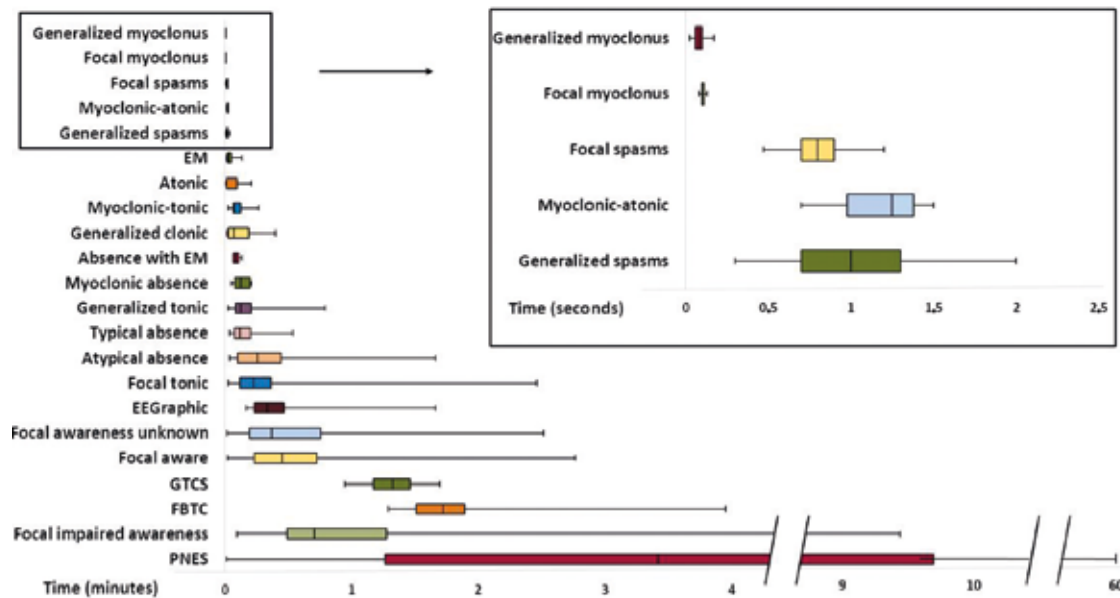
by Sándor Beniczky

Large structured datasets are essential for medical research. They make possible datamining and addressing clinical questions, based on a data-driven approach. Standardized Computer-based Organized Reporting of EEG (SCORE) is a digital tool developed using the international standards. The tool helps improving the quality of clinical EEG interpretation and in the same time facilitates research, by building a database. We helped colleagues in an underprivileged area of the world, to implement a free version of the SCORE software. In a prospective study, we showed that this contributed to improving the quality of patient care.

We extracted data from the anonymized clinical dataset, to investigate the prevalence of normal variants. We compiled comprehensive list and characterized the normal variants in our database. To make this useful for postgraduate training we included typical examples of each normal variant. This paper gives a realistic picture about the frequency of EEG normal variants, and it is a valuable resource for trainees.

From our large database, we extracted data on the duration of various seizure-types. Our data-driven approach resulted in accurate characterization of this important feature of the epileptic seizures. Our results are useful for accurate identification of the seizure types in clinical practice, and in setting time-limits for status epilepticus.

Based on a large international dataset with de-identified data from epilepsy surgery programs, we have validated and conducted a head-to-head comparison of tools for predicting outcome after surgery. We developed and validated a method for risk-stratification in this group of patients. We contributed to the analysis of a large Swiss dataset, to evaluate the diagnostic yield of prolonged EEG and MRI after the first seizures.



Duration of epileptic seizure types, extracted from a large SCORE dataset

PAPERS

Japaridze G, Kasradze S, Aurlen H, Beniczky S.

Implementing the SCORE system improves the quality of clinical EEG reading. Clin Neurophysiol Pract. 2022 Sep 1;7:260-263. doi: 10.1016/j.cnp.2022.07.004

Wüstenhagen S, Terney D, Gardella E, Meritam Larsen P, Rømer C, Aurlen H, Beniczky S.

EEG normal variants: A prospective study using the SCORE system. Clin Neurophysiol Pract. 2022 Jun 30;7:183-200. doi: 10.1016/j.cnp.2022.06.001.

Meritam Larsen P, Wüstenhagen S, Terney D, Gardella E, Aurlen H, Beniczky S.

Duration of epileptic seizure types: A data-driven approach. Epilepsia. 2023 Feb;64(2):469-478. doi: 10.1111/epi.17492.

Hadady L, Sperling MR, Alcala-Zermeno JL, French JA, Dugan P, Jehi L, Fabó D, Klivényi P, Rubboli G, Beniczky S.

Prediction tools and risk stratification in epilepsy surgery. Epilepsia. 2023 Dec 7. doi: 10.1111/epi.17851.

De Stefano P, Ménétré E, Stancu P, Mégevand P, Vargas MI, Kleinschmidt A, Vulliémoz S, Wiest R, Beniczky S, Picard F, Seeck M.

Added value of advanced workup after the first seizure: A 7-year cohort study. Epilepsia. 2023 Dec;64(12):3246-3256. doi: 10.1111/epi.17771.

EEG Source Imaging

by Sándor Beniczky

Using mathematical algorithms, the source of the EEG signal can be estimated in the brain. EEG Source Imaging (ESI) has been one of the research topics our group has been focusing on for more than a decade. In 2022-2023 we continued this work, using ESI for presurgical evaluation of patients with drug-resistant focal epilepsy.

We investigated the performance of automated and semi-automated spike-detection, in relation to their localization accuracy. We found that these methods show significant agreement with visually detected spikes in the long-term recordings and concordance with the seizure onset zone. In short-term, high-density EEG, semi-automated detection of spikes is concordant with the visually detected ones, and the seizure-onset zone if high spike-counts were detected.

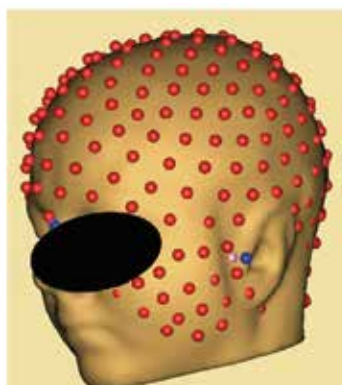
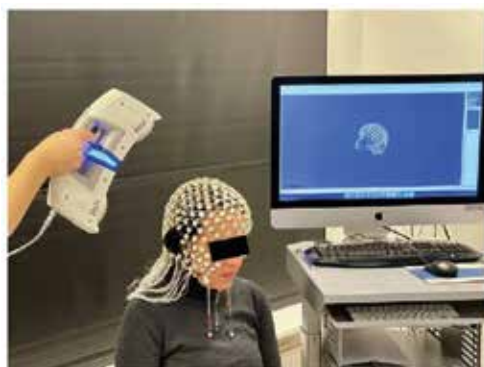
We assessed the accuracy of high-density EEG electrode position measurement, using an optical scanner compared with the classical, photogrammetry method. We found that the handheld optical scanner is more accurate and feasible, compared to the photogrammetry method. This warrants for the clinical implementation of the novel method.

We have validated the accuracy of a novel method of source localization – the relative source power (RSP) imaging of extratemporal interictal epileptiform discharge. A source region with 20 mm radius contained lesioned tissue in all cases. Using localization of the resection site and operation outcome as gold standard, we achieved a sensitivity of 82% and specificity of 50%.

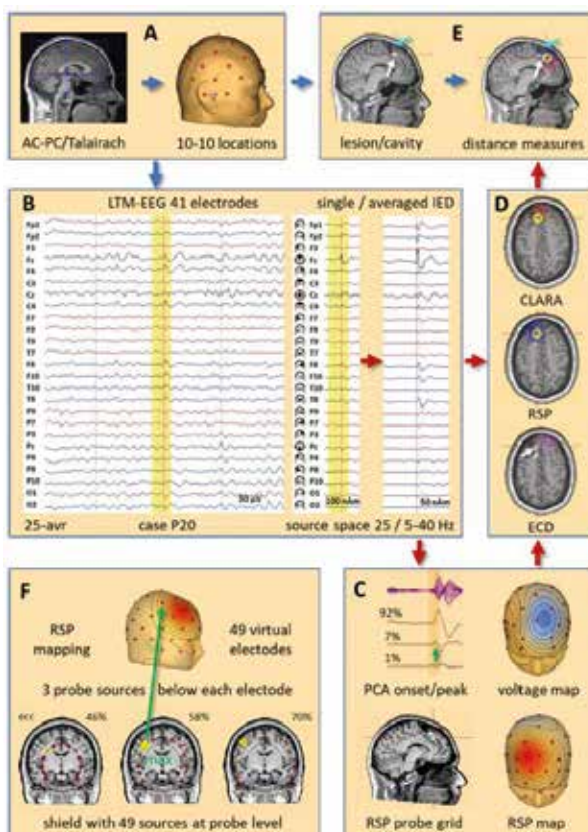
We have investigated the diagnostic utility of ESI in the presurgical evaluation of children with focal cortical dysplasia, and to compared it with other imaging techniques. Highest localization accuracy (80%) was obtained with ESI, followed by PET and ictal SPECT (75%). Our findings demonstrate that ESI using a high-density EEG array allows accurate localization of the epileptogenic zone in children with focal cortical dysplasia.

In spite of a standardized analysis pipeline, several aspects tailored to the individual patient involve subjective decisions of the expert performing the analysis. We investigated the inter-analyzer agreement of ESI in presurgical evaluations of epilepsy, using the same software and analysis pipeline. The overall agreement among experts for the ESI methods was substantial, and there was no significant difference between the methods. Our results suggest that using a standardized analysis pipeline, newly trained experts reach similar ESI solutions, calling for more standardization in this emerging clinical application in neuroimaging.

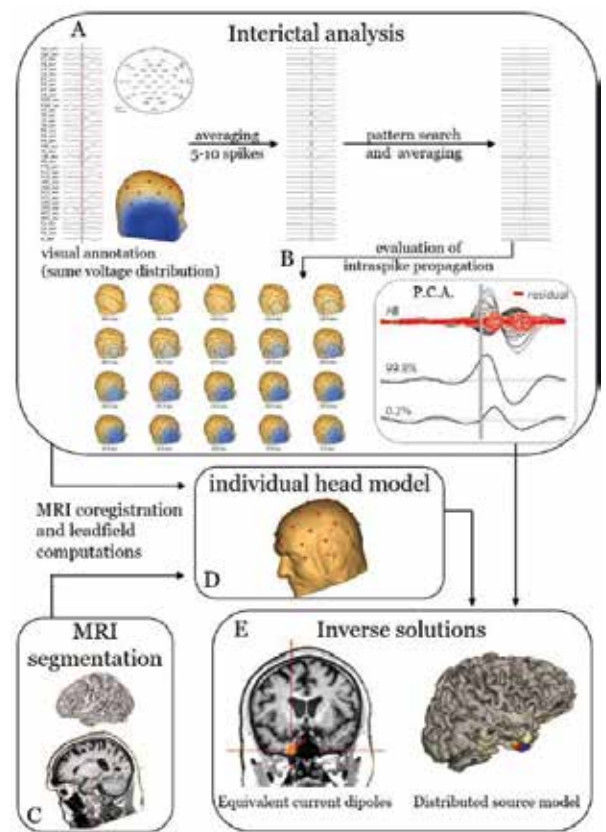
ESI requires special expertise and it is underutilized. To circumvent this, automated analysis pipelines have been previously developed and validated for the interictal discharges. In a new study published in 2022, we presented the clinical validation of an automated ESI for ictal EEG signals. The accuracy of the automated ESI was 74%. Automating the ESI of the ictal EEG signals will facilitate implementation of this tool in the presurgical evaluation.



Optical scanner for rapid and accurate measurement of the three-dimensional positions of 256 EEG electrodes in a high-density array.



Analysis pipeline of a novel ESI method:
Relative Source Power.



Standardized analysis pipeline of the
interictal EEG source imaging.

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Postgraduate education and research in adult learning

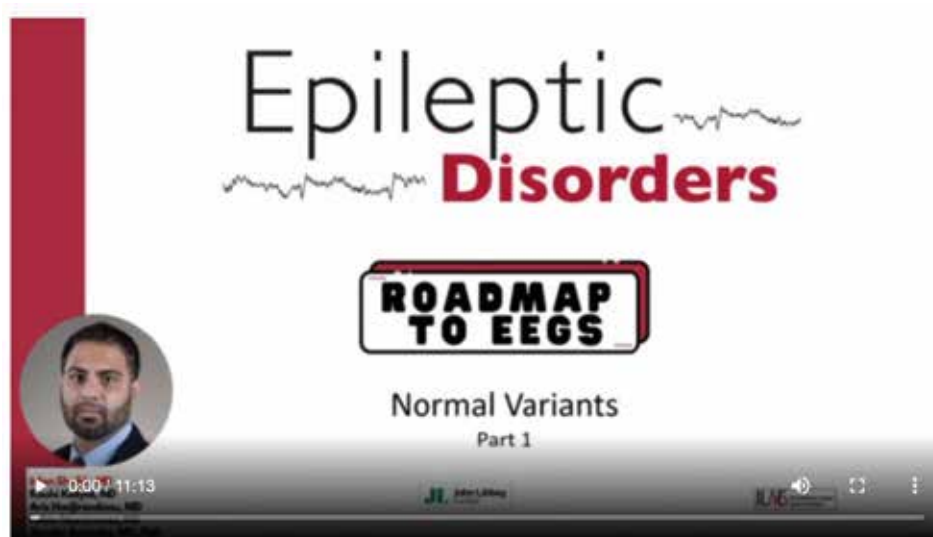
by Sándor Beniczky

Postgraduate education utilizes important new knowledge in the field of adult learning. We have contributed to the development of interactive, online, self-paced learning elements, addressing the learning objectives of the ILAE curriculum in epileptology, and we have summarized these educational offerings and their performance in a paper published in 2022.

Based on a consensus discussion of a broad, international expert panel, we compiled a curriculum for the EEG patterns which neurology residents must learn during their training. We have developed an internship program at Epileptic Disorders, the official educational journal of the ILAE. One of the main objectives were to promote the educational activities and improve the outreach. With the interns, we developed a series of educational videos, addressing important learning objectives

in EEG. These videos are available now on our YouTube channel too. We published a comprehensive, educational review paper on how to read voltage maps in EEG. We have evaluated and reported the results of the student evaluation of the educational courses, which we organized at 34th International Epilepsy Congress. This content was available online too. We showed that an online interactive teaching session about the operational criteria of epileptiform discharges, significantly improved the accuracy of young trainees in interpreting EEG.

We published educational review papers and multimedia teaching material to spread the new knowledge cumulated in our field. We critically addressed the impact and efficacy of various curricula and teaching methods.



Screenshot of the online educational material on EEG normal variants.

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Artificial intelligence in epilepsy diagnosis and monitoring

by Sándor Beniczky

Medical applications of artificial intelligence (AI) are likely to be a game-changer in our field too. We contributed to training and validation of AI models for automated and semi-automated analyses of videos and EEGs.

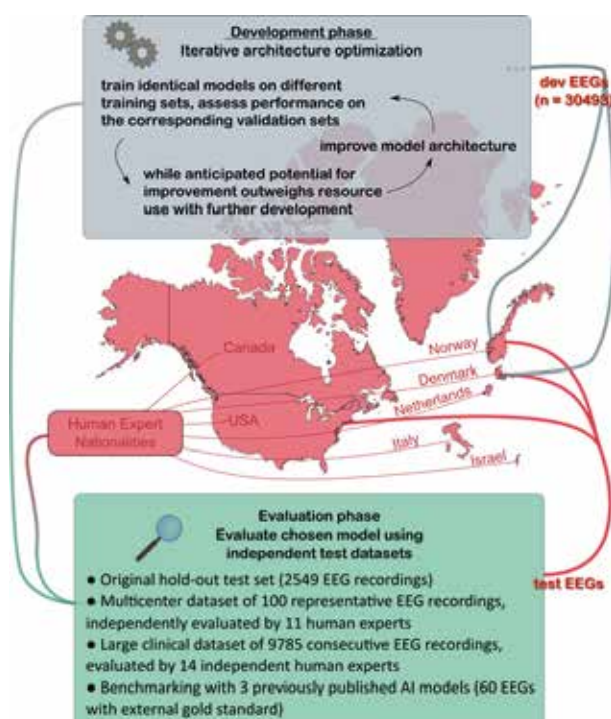
In collaboration with University of Bergen and Holberg-EEG, we developed an AI-model for automated interpretation of routine, clinical EEGs. The AI-model was developed using an artificial neural network, based on large EEG datasets (over 30 thousand de-identified recordings), systematically labeled using the SCORE software (Standardized Computer-based Organized Reporting of EEG). SCORE-AI was tested on a multicenter test dataset, assessed by international experts, and a large, independent dataset from Oslo University Hospital. SCORE-AI reached performance equivalent to human experts in distinguishing normal from abnormal EEGs, and then classifying the abnormal EEGs into the categories with clinical relevance (focal epileptiform, generalized epileptiform, focal non-epileptiform, diffuse non-epileptiform).

The paper reporting SCORE-AI received much attention internationally. It appeared in numerous editorials, news, posts, tweets and blogs, giving an Altmetric score of 318. It was one of the most viewed articles in JAMA Neurology in 2023 (with close to 30 thousand views in less than 5 months).

Automated video analyses was sensitive for detecting major motor seizures, such as generalized tonic-clonic seizures. However, for assessment and classification of the other seizure-types, a semi-automated ("hybrid") approach was necessary, where human experts inspected the video-epochs highlighted by the AI model. The hybrid approach significantly reduced the workload of the human experts.

We found similar outcome for AI models detecting interictal epileptiform discharges. The fully automated application of the AI model gave high specificity, but the sensitivity was too low for clinical implementation. However, the hybrid system in which human experts inspected the automated detections, have high sensitivity and specificity, and significantly decreased the workload.

We contributed to training and validation of an AI model which predicts impaired consciousness in absence epilepsy, based on analysis of the EEG signals.



Receiver Operating Characteristic (ROC) curve of SCORE-AI, in the development and test datasets, demonstrating the high performance and generalizability of the model.

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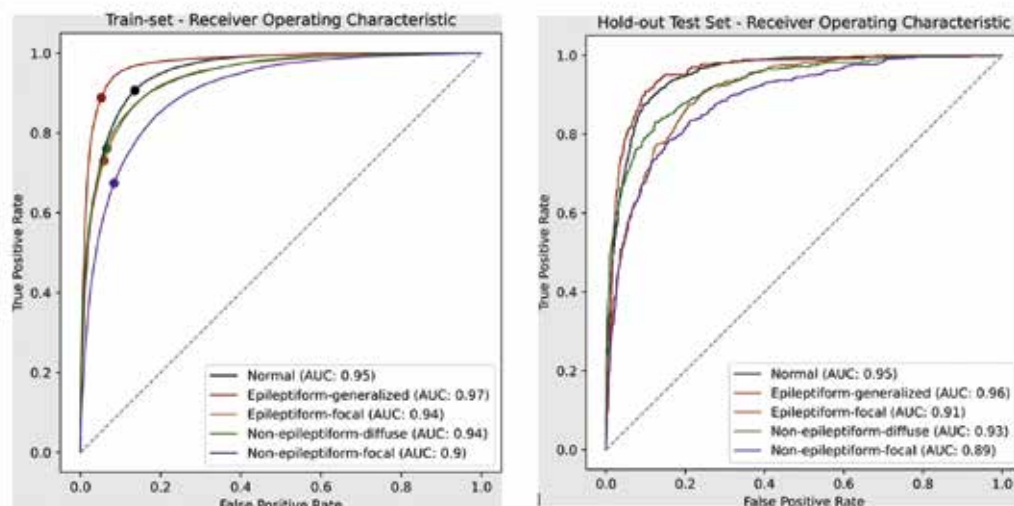
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SCORE-AI: Flowchart of validation.



Graphical user interface view of the video-analysis system using artificial intelligence

Wearable devices in epilepsy monitoring

by Sándor Beniczky

One of the main research topics of our group is development and validation of wearable devices for automated seizure detection and characterization. In 2022-2023 we continued working on numerous projects in this area.

We have validated an artificial intelligence-based algorithm for automated detection of absence seizures, using a wearable non-invasive EEG device. In a proof of principle study, we demonstrated the feasibility and clinical utility of automated behavioral testing triggered by automated seizure detection. We contributed to a multicenter study on detection of temporal lobe seizures using ultra-long term monitoring with a subcutaneously implanted EEG device. Our findings demonstrated that semi-automated seizure detection/review process can be performed with high sensitivity and clinically applicable specificity. In a large, international survey study on the ultra-long-term experience of patients with using wearable devices, we showed the clinical utility of these devices, and we found that

the devices formally validated in phase-3 studies performed better than the other devices.

Using machine learning, we optimized our heart-rate variability (HRV) based seizure detection algorithm, which helped us decrease the false alarm rate. We conducted a proof-of-principle study and published a seminal paper on using subcutaneously implanted electrocardiogram (ECG) for automated seizure detection of epileptic seizure. This application has huge potential in clinical practice. It combines a hardware which is well-established in cardiology, with a novel algorithm for seizure detection.

We have reviewed the state-of-the-art and current clinical practices in using wearables for seizure detection. These results will likely promote further research and development in this important field.



Wearable electroencephalographic (EEG) device for detection of absence seizures using artificial intelligence.



Automated seizure detection using subcutaneously implanted ECG.

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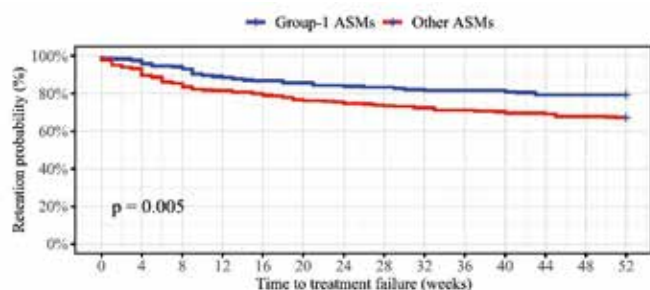
Epipick: a web-based decision support system for optimal, patient-tailored choice of antiseizure medication

by Sándor Beniczky

We developed the Epipick – a freely accessible web-based application (<https://epipick.org>) to help health care professionals select the most appropriate, patient-tailored antiseizure medication (ASM) in patients with epilepsy (seizure onset at 10 years of age or older). EpiPick considers seizure types and patient-specific variables to provide treatment recommendations, ranking ASMs in order of appropriateness based on the available scientific evidence and expert judgement. The app also provides a summary of prescribing information for each of the ASMs being suggested.

After the original publication of the application in 2021, we continued monitoring the published evidence and we updated

the application accordingly in 2022. We completed a large-scale validation study on 425 consecutive patients with newly diagnosed epilepsy, who were followed for at least 1 year after starting medication. ASMs classified by the algorithm as best options had a significantly higher retention rate, higher seizure freedom rate and lower rate of discontinuation due to adverse effects than ASMs ranked as less desirable by the algorithm. We concluded that the use of the freely available decision support system is associated with improved outcomes. This drug selection application can provide valuable assistance to health care professionals prescribing medication for individuals with epilepsy.



Kaplan-Meier analysis of the time to treatment failure. Patients treated with best option antiseizure medications (ASMs) recommended by the algorithm (Group 1) versus patients treated with other drugs

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Myopathy in long-term COVID-19

by Hatice Tankisi

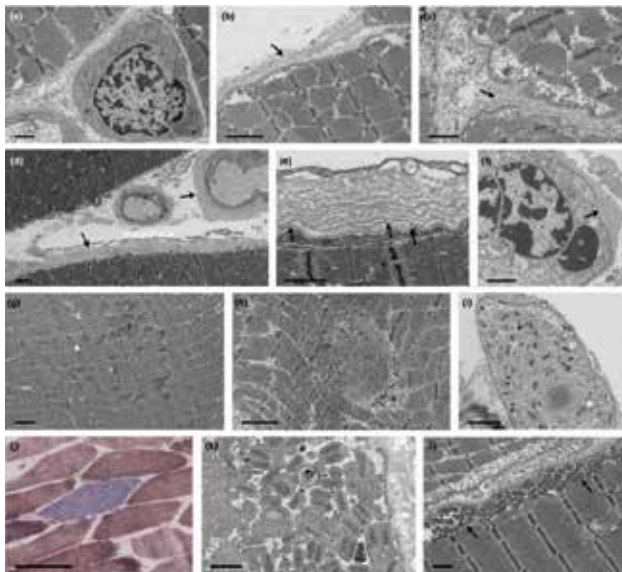


Figure 1

Histopathological changes in muscle fibers. (a, b) Muscle fiber atrophy. (a) Atrophic fiber and (b) folds in the basal lamina. (c-f) Muscle fiber damage indicated by basal lamina proliferation. (c) Basal lamina duplication (arrow) (d, e) Multiple myofiber basal lamina (d) and (e) higher magnification showing continuity between the different layers (arrows) (f) Aggregation of nuclei, and multiple layers of myofiber basal lamina (arrow). (g-i) Myofibrillary disorganization: (g) streaming of Z-bands (h) disorganized myofibrils and (i) myofibril disorganization and a cytoplasmic body (j-l) Mitochondrial changes: (j) a cytochrome c oxidase-negative fiber (blue) and (k) subarcolemmal accumulation of structurally abnormal mitochondria, and (l) subarcolemmal accumulation of ultrastructural normal-appearing mitochondria. Scale bars: k = 500 nm; c, e, h, and l = 1 μ m; a, b, d, f, g, and i = 2 μ m; j = 100 μ m

Long term symptoms following COVID-19 (Long COVID) now affects a large number of patients with estimates of up to 100 million people world-wide.

As a part of the MULTICOV Consortium, we showed that in patients with long-term muscular complaints or fatigue after mild or moderate SARS-CoV-2 infection, myopathy was a common finding (Agergaard et al., 2021). Later, we showed in electron microscopy of muscle biopsies a wide variety of histological changes with signs of mitochondrial changes, inflammation and capillary injury (Figure 1) suggesting that skeletal muscles may be a major target of SARS-CoV-2 causing muscular post-COVID-19 symptoms (Hejbøl et al., 2023) including changes in motor end-plate (Agergaard et al., 2023). In a large cohort of 84 patients with Long Covid, myopathic changes were common. Single-fiber electromyography was less common but correlated with clinical scores suggesting that fatigue may be due to neuromuscular transmission failure (Agergaard et al., 2023).

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Conventional and Threshold-Tracking Transcranial Magnetic Stimulation (TMS)

by Hatice Tankisi

Most single-pulse transcranial magnetic stimulation (TMS) parameters (e.g., motor threshold, stimulus-response function, cortical silent period) are used to examine corticospinal excitability. Paired-pulse TMS paradigms (e.g., short- and long-interval intracortical inhibition (SICI/LICI), short-interval intracortical facilitation (SICF), and short- and long-latency afferent inhibition (SAI/LAI)) provide information about intracortical inhibitory and facilitatory networks.

This has long been done by the conventional TMS method of measuring changes in the size of the motor-evoked potentials (MEPs) in response to stimuli of constant intensity, so-called amplitude SICI (A-SICI). An alternative threshold-tracking approach has recently been introduced whereby the stimulus intensity for a target amplitude is tracked, so-called for example

threshold tracking SICI (T-SICI). The limitations of the conventional methodologies are manual operation, poor reproducibility, and time consumption. To overcome these limitations, our research group developed a menu-driven suite of semi-automatic programs to facilitate the broader use of threshold-tracking TMS techniques and to enable direct comparisons with conventional amplitude measurements (Figure 1).

We have shown good reliability and repeatability of various TMS measures and good sensitivity and specificity of A-SICI and T-SICI in ALS (Tankisi et al., 2023) (Figure 2). There was no influence of caffeine on SICI (Strunge et al., 2023). Sleep deprivation did not have any influence on SICI, SICF, and LICI but there was a decrease in SAI (Mroczek et al., 2023).

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Figure 1

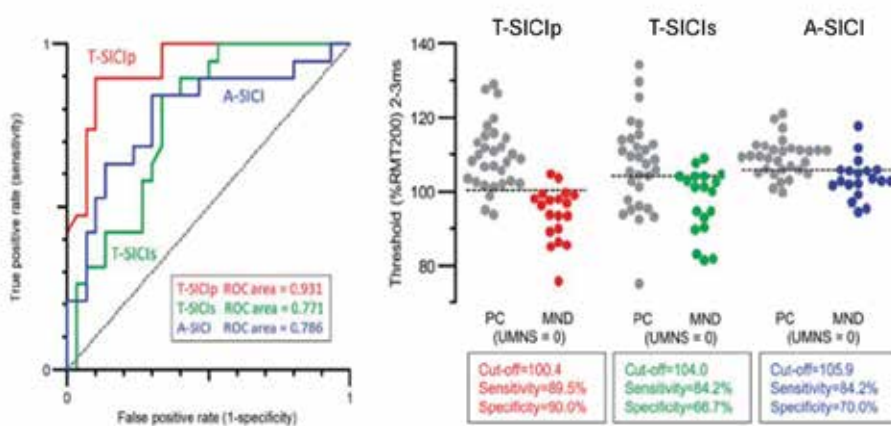


Figure 2

Threshold tracking short-interval intracortical inhibition (T-SICI) using a parallel tracking protocol (T-SICIp) has higher sensitivity and specificity than serial protocol (TSICIs) and conventional amplitude SICI (A-SICI).
PC: Patient controls, MND: Motor neuron disorders, UMNS: upper motor neuron scores.

Muscle velocity recovery cycles and MScanFit motor unit number estimation (MUNE) in neuromuscular disorders

by Hatice Tankisi

Nerve conduction studies (NCS) and electromyography (EMG) are the conventional electrophysiological methods that are used for the diagnosis of neuromuscular disorders. However, NCS or EMG have limitations that can be overcome by the use of novel electrophysiological methods.

The method, Muscle Velocity Recovery Cycles (MVRC) enables in vivo assessment of changes in muscle membrane potential and alterations of muscle ion channel function in pathology (Figure 1) while MUNE methods provide information about

number of functioning motor units in a nerve. Among MUNE methods, MScanFit (Figure 1) is the most recent one, developed by Professor H. Bostock from London in close collaboration with our research group. Our recent studies applied MVRCs in immobilisation (Zeppelin et al., 2023), critical illness myopathy (CIM) (Rodriguez et al., 2022) and in myopathy (Meldgaard et al., 2023), and MScanFit in immobilisation (Zeppelin et al., 2023) and in multicentre studies (Sørensen et al., 2022; Sørensen et al., 2023).

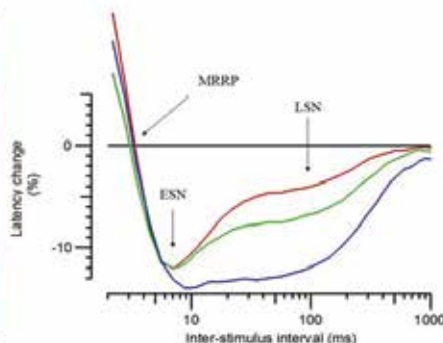
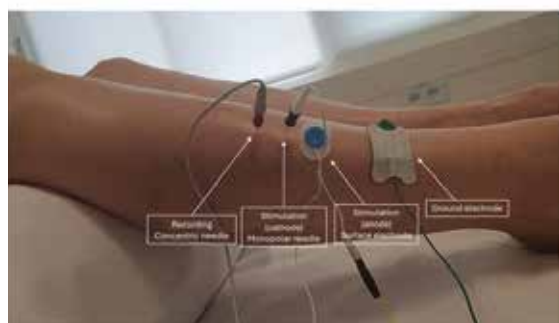


Figure 1

Kaplan-Meier analysis of the time to treatment failure. Patients treated with best option antiseizure medications (ASMs) recommended by the algorithm (Group 1) versus patients treated with other drugs

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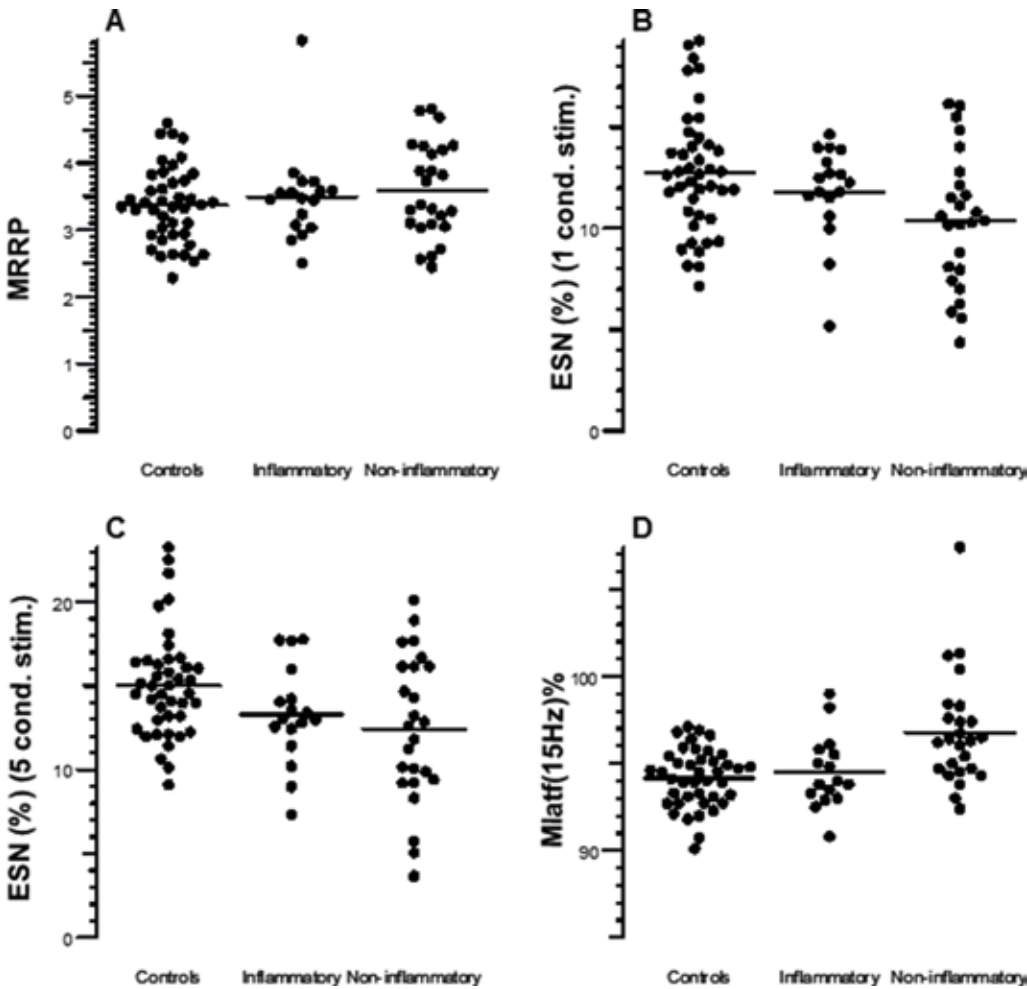


Figure 2
Muscle velocity recovery cycles (MVR) and frequency ramp measures presented in dot-plots in healthy controls and inflammatory myopathy and non-inflammatory myopathy patient groups for some selected variables. A) muscle relative refractory period (MRRP), B) Early supernormality, C) 5XLSN: extra late supernormality after 5 conditioning stimuli and D) Mlatf 15 Hz: latency to the first response in the train of 15 Hz in percentage change from baseline. ESN: early supernormality up to 15 ms. interstimulus intervals.

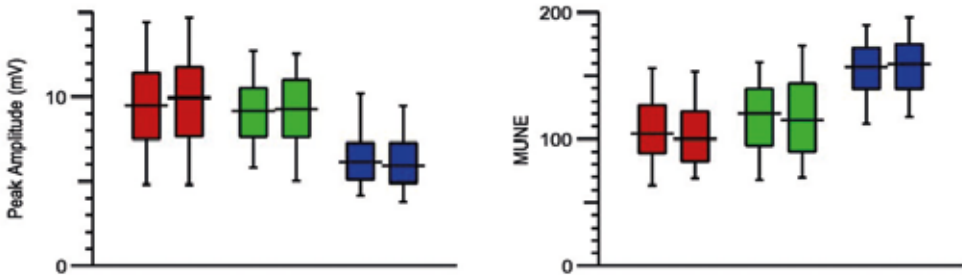


Figure 3
MScanFit comparisons between 2 recordings from each of 3 muscles. Each box plot indicates median, interquartile range and 90% confidence limits for the 148 subjects. Compound muscle action potential (CMAP) peak amplitudes were consistently smaller for tibialis anterior (TA) than abductor pollicis brevis (APB) or abductor digiti minimi (ADM) (left), whereas motor unit number estimation (MUNE) values were consistently higher (right).

Nerve excitability testing

by Hatice Tankisi

Peripheral nerve excitability testing (NET) performed using the threshold-tracking technique can be used to infer changes in the membrane potential of sensory and/or motor fibres underlying the site of stimulation. Our research group has explored the impact of NET in various conditions (Lugg et al., 2023; 2023; Hansen et al., 2023; Themistocleous et al., 2022; Krøigård et al., 2022).

Standard NET predominantly assesses A α - and A β -fiber

function, but a method examining small afferents would be of great interest in pain studies. We have examined the properties of a novel perception threshold tracking (PTT) method that preferentially activates A δ -fibers using weak currents delivered by a novel multipin electrode and compared its reliability with NET (Pia et al., 2023) (Figure 1). This was a part of the multicentre Bio-Pain Study (Nochi et al., 2022).

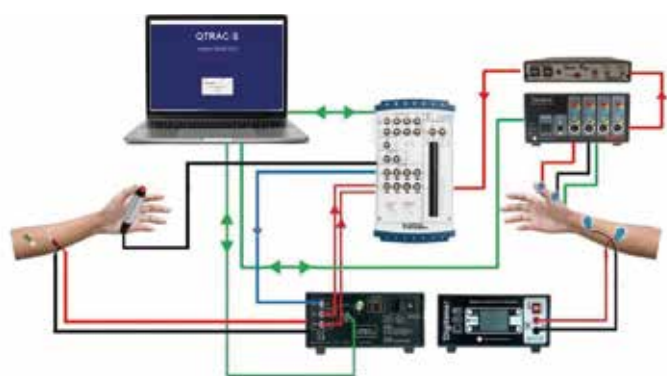


Figure 1

Illustration of motor and sensory nerve excitability testing and perception threshold tracking. The equipment set-up and the placement of stimulation and recording electrodes are shown.

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Nerve and muscle ultrasound

by Erisela Qerama

High resolution ultrasound is an important part of our diagnostic work-up. We are examining its feasibility in visualisation of muscles and nerves in different diseases.

We have looked at our routine ultrasound examinations in patients referred for the ulnar neuropathy at the elbow and found that ultrasound supplements the electrodiagnostic examination with a high sensitivity and specificity. An article is under preparation.

Disease of the diaphragm can be challenging to diagnose with electrodiagnostic methods, so we are conducting a project of ultrasound of the diaphragm muscles in healthy subjects. Ultrasound guided EMG examination of the diaphragm can help to increase the yield of our diagnostic ability.

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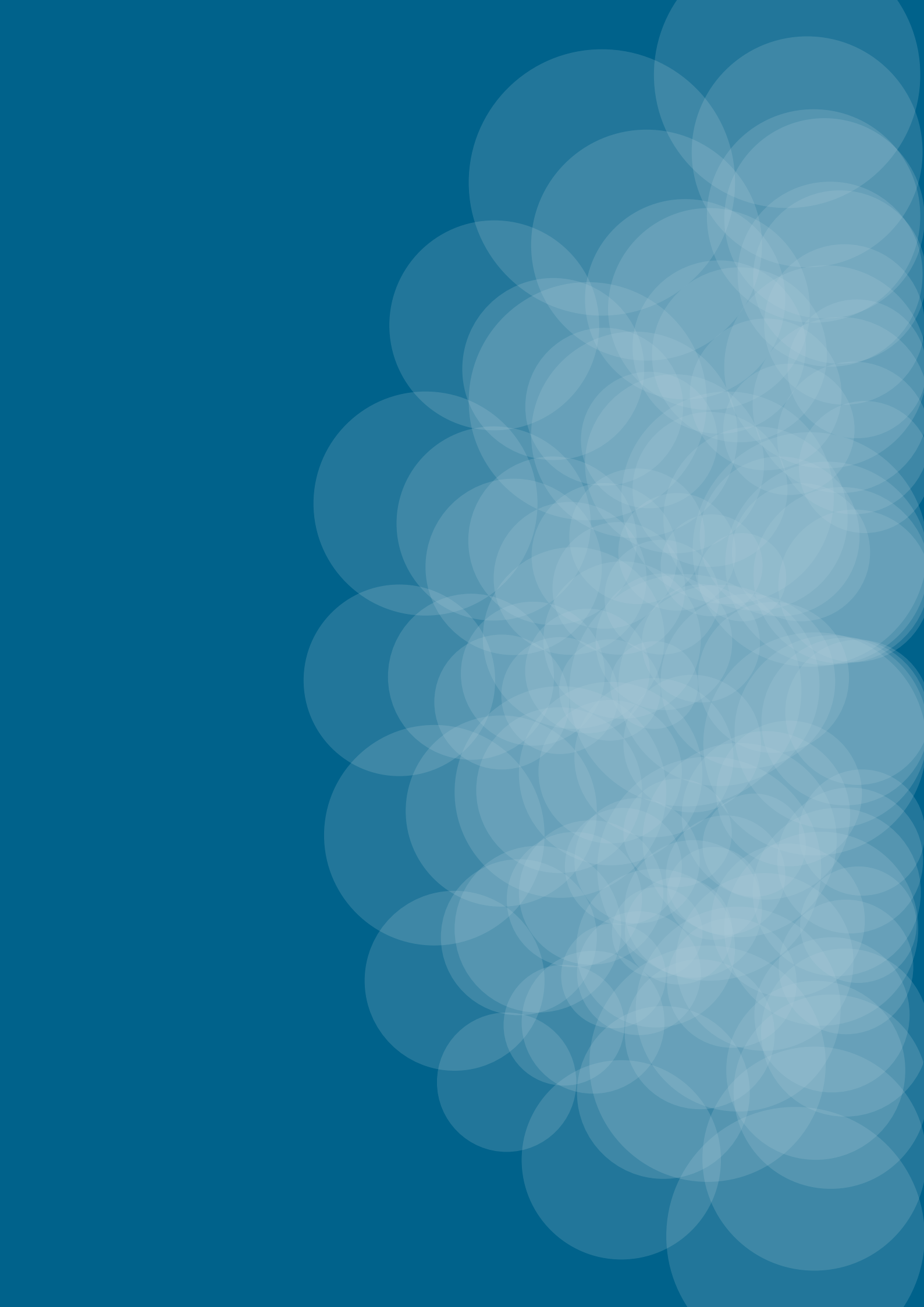
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