32nd Neurodiab Annual Meeting

15 - 18 September 2022

Bergen, Norway

32ND
ANNUAL MEETING
DIABETIC NEUROPATHY
STUDY GROUP.

INDEX

NEURODIAB

COMMITTEE

Chair:
Vincenza Spallone

Secretary:
Eirik Søfteland

Honorary Treasurer:
Peter Kempler

Executive Committee

Professor:
Triantafyllos Didangelos

MD:
Anna Körei

MD:
Fabiana Picconi

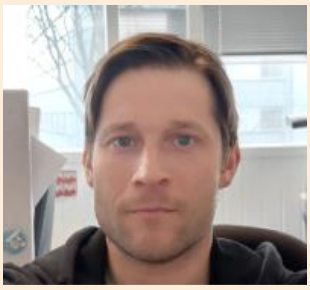
Professor:
Rodica Pop-Busui

Professor:
Gerry Rayman

NEURODIAB

Local Organising Committee

Associate Professor:
Eirik Søfteland



MD:
Sondre Meling

Professor:
Christina Brock

Dr. Prashanth Vas

WELCOME

Dear Neurodiab Members, Friends, and Colleagues,

It is a great pleasure to welcome you to the 32nd Annual Meeting of Neurodiab in Bergen, Norway.

This year, we can meet again face-to-face after 3 years and take advantage of the traditional points of strength of Neurodiab meetings: the opportunity of cooperation between specialists, the interaction between basic and clinical science, and the exchanges between leader scientists and young researchers.

The annual meeting of Neurodiab is the most important annual event in the field of diabetic neuropathy.

This year, there are all the ingredients for a fruitful meeting: a promising scientific program with symposia on epigenetics and omics, neuropathic pain, cardiorenal syndrome, COVID-19, diabetes drugs and neural diseases, and presentations of original research, a significant presence of young researchers in the faculty, numerous participants from many countries, an attractive social program in the wonderful city of Bergen, and the hospitality of Norwegian people.

With the whole Executive Committee, I hope that you enjoy this meeting and can experience the friendly atmosphere as most of us did in this 32-year long life of Neurodiab, and find new energy, ideas, and renewed inspiration for your research and clinical work.

On behalf of the Executive Committee of Neurodiab

Vincenza Spallone
Chair of Neurodiab

NEURODiab

Dear friends and colleagues,

I am very excited to welcome you all to the 32nd Neurodiab conference! The meeting is taking place in beautiful surroundings in the centre of the historical UNESCO city of Bergen in Norway, well worth a visit in itself, also known as the "Gateway to the Fjords".

The aim of this Neurodiab meeting is to combine exciting and perhaps provocative symposia and lectures on diabetic neuropathy with ample opportunities for the presentation of the latest research results.

With a great venue and programme, we hope to encourage you all to "take the leap" and attend on-site in Bergen. We have all suffered through more than two years of restrictions due to the pandemic, so we are sure that you will find the opportunity to socialise, discuss and interact face-to-face most stimulating and inspiring.

We would also like to extend a special invitation to younger colleagues, with reduced costs and great opportunities to get up-to-date on the field. Also, we aim to have a global reach within diabetic neuropathy, so new participants from around the world will be warmly welcomed!

We cannot promise warm weather, polar bears or northern lights. BUT, we do promise a rewarding time both scientifically and personally – and who knows – maybe even the sun will shine on us.

See you in Bergen!

Eirik Søfteland

Leader of the local organising committee

PROGRAMME OVERVIEW

15 / SEPTEMBER / 2022

17:00 – 20:00	**Neurodiab Hospitality desk open for registration** **Location**: Ground floor, Main hall area	

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07:30 – 17:00	**Neurodiab Hospitality desk open for registration**	
07:30 – 17:00	**Posters are on display throughout the whole duration of the conference** **Location**: First floor, Studio 1+2+3 (up the stairs in the main hall outside the conference area)	
08:15 – 08:25	**Welcome** **Location**: Ground floor, Ballroom	Eirik Søfteland (Bergen, NO) and Vincenza Spallone (Rome, IT)
08:25 – 10:00	**Symposium: The future of diabetic neuropathy** **Location:** Ground floor, Ballroom	Chairs: Christian Stevns Hansen (Herlev, DK) and Mark Yorek (Iowa City, US)
08:25 – 08:45	Epigenetics – is that the missing link?	Stephanie Eid (Ann Arbor, US)
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09:05 – 09:25	Proteomics and diabetic neuropathy	Karolina Sulek (Copenhagen, DK)
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10:30 – 11:30	**Oral presentations** (O1-O4) **Pathogenesis** **Location**: Ground floor, Ballroom	Chairs: Dan Ziegler (Düsseldorf, DE) and Thorbjørn Åkerstrom (Måløv DK)
11:30 – 12:40	**Symposium: Role of thiamine in diabetes and diabetic polyneuropathy** **Location**: Ground floor, Ballroom	Wörwag Pharma symposium Chair: Peter Kempler (Budapest, HU)
11:30 – 11:40	Introduction	Peter Kempler (Budapest, HU)
11:40 – 12:10	Association of transketolase SNPs with diabetic polyneuropathy: The KORA Study	Dan Ziegler (Düsseldorf, DE)
12:10 – 12:40	Association of thiamine status with diabetes: a systematic review and meta-analysis	Rima Obeid (Homburg, DE)
12:40 – 13:20	**Lunch break** **Location**: Second floor, Restaurant NOVA (We have reserved the inner part of the restaurant. Follow Neurodiab signs.)	
13:20 – 15:00	**Oral presentations** (O5-O11) Young investigators award for the best presentation **Location**: Ground floor, Ballroom	Chairs: Triantafyllos Didangelos (Thessaloniki, GR) and Niels Ejskjaer (Aalborg, DK)
15:00 – 15:20	**Coffee break and industry stands** **Location**: Ground floor, mingle-area outside Ballroom	

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15:20 – 17:00	**Oral Presentations** (O12-O18) Young investigators award for the best presentation **Location:** Ground floor, Ballroom	Chairs: Fabiana Picconi (Rome, IT) and Peter Kempler (Budapest, HU)
17:30	**Guided tour of Bergen where we will end up at Haakonshallen for the Official Opening** If you have signed up for the guided tour, you will have received an email confirming your GROUP NUMBER. Your guide will be meeting his/her group outside the hotel with a sign/group number. Please join your guide/your number. Each group will have separate itineraries.	
18:30 – 19:45	**Official opening by the Mayor of Bergen. Canapes and welcome drink**	
20:00 -	**Dine-around**, only reserved table/restaurant for those who have signed up. Arrangement on own expense.	

Day 2
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08:00 – 18:00	**Neurodiab Hospitality desk open** **Location**: Ground floor, mingle-area outside Ballroom	
08:00 – 18:00	**Posters are on display throughout the whole duration of the conference** **Location**: First floor, Studio 1+2+3 (up the stairs in the main hall outside the conference area)	
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09:45 – 10:00	**Coffee break and visit industry stands** Location: Ground floor, mingle-area outside Ballroom	
10:00 – 11:15	**Symposium: Pain in diabetic neuropathy, partly supported by Sanofi** **Location**: Ground floor, Ballroom	Chairs: Rodica Pop-Busui (Ann Arbor, US) and Anders Stouge (Aarhus, DK)
10:00 – 10:20	It's the nerves!	Rayaz Malik (Doha, QR)
10:20 – 10:40	It's the brain!	Dinesh Selvarajah (Sheffield, UK)
10:40 – 11:00	It's depression!	Bruce Perkins (Toronto, CA)
11:00 – 11:15	Panel discussion	
11:15 – 11:30	**Coffee break and visit industry stands** **Location:** Ground floor, mingle-area outside Ballroom	
11:30 – 12:30	**Oral presentations** (O24-O27) Small fiber and painful neuropathy **Location:** Ground floor, Ballroom	Chairs: Dinesh Selvarajah (Sheffield, United Kingdom) and Tae Sun Park (Seoul, KR)

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12:30 – 13:30	**Lunch break** **Location:** Second floor, Restaurant NOVA (We have reserved the inner part of the restaurant. Follow Neurodiab signs.)	
13:30 – 14:30	**Poster presentations** (P2-P11) Young investigators award for the best poster presentation **Location**: First floor, Studio 1+2 (up the stairs in the main hall outside the conference area)	Chairs: Tamas Varkonyi (Szeged, Hungary) and Sondre Meling (Stavanger, NO)
	Poster presentations (P12-P22) Young investigators award for the best poster presentation **Location**: First floor, Studio 3 (up the stairs in the main hall outside the conference area)	Chairs: Gerry Rayman (Ipswich, United Kingdom) and Ioannis Nikolaos Petropoulos (Doha, QR)
14:30 – 15:30	**Symposium: Autonomic nervous system and the cardiorenal metabolic syndrome** **Location:** Ground floor, Ballroom	Boehringer gold sponsor Chairs: Kåre Birkeland (Oslo, NO) and Paul Valensi (Bondy, FR)
14:30 – 14:40	Introduction to the cardiorenal metabolic syndrome	Kåre Birkeland (Oslo, NO)
14:40 – 15:00	The synergistic effect of SGLT2 /aldosterone antagonism on cardiac outcome	Peter Rossing (Copenhagen, DK)
15:00 – 15:20	Is the autonomic nervous system the missing piece of a puzzle?	Vincenza Spallone (Rome, IT)
15:20 – 15:30	Panel discussion	

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15:30 – 15:50	**Coffee break and visit industry stands** **Location:** Ground floor, mingle-area outside Ballroom	
15:50 – 16:40	The Göran Sundkvist Young Investigators Award for Clinical Science Location: Ground floor, Ballroom	Chair: Vincenza Spallone (Rome, IT)
15:50 – 16:15	Is corneal confocal microscopy a viable endpoint in clinical trials of diabetic neuropathy?	Shazli Azmi (Manchester, UK)
16:15 – 16:40	On pins and needles: how neuropathy guided my career in medicine	Lynn Ang (Ann Arbor, US)
16:40 – 17:50	**General Assembly Neurodiab** **Location**: Ground floor, Ballroom	
18:45	Departure from your hotel to the port; Dreggekaien, Skur 8.	
19:00	Departure private boat to Restaurant Cornelius by the Fjords.	
19:30	Estimated time of arrival Cornelius.	
19:30 – 23:00	Neurodiab Conference Dinner	
23:00	Approx. return from Cornelius towards Bergen. Walk back to your hotel.	

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08:00 – 14:00	**Neurodiab Hospitality desk open** **Location**: Ground floor, mingle-area outside Ballroom	
08:00 – 14:00	**Posters are on display throughout the whole duration of the conference** **Location**: First floor, Studio 1+2+3 (up the stairs in the main hall outside the conference area)	
08:30 -09:30	**Oral presentations** (O28-O31) **Autonomic neuropathy and treatment** **Location**: Ground floor, Ballroom	Chairs: Triantafyllos Didangelos (Thessaloniki, GR) and Gidon Bönhof (Düsseldorf, DE)
09:30 – 10:10	**Symposium: Diabetes and COVID-19** **Location**: Ground floor, Ballroom	Chairs: Gerry Rayman (Ipswich, UK) and Anne-Marie Wegeberg (Aalborg, DK)
09:30 – 09:50	Mediators and adverse outcome in individuals with diabetes hospitalized for COVID-19	Rodica Pop-Busui (Ann Arbor, US)
09:50 – 10:10	COVID-19 and the peripheral nervous system	Giuseppe Lauria (Milan, IT)
10:10 – 10:30	**Coffee break and visit industry stands** **Location**: Ground floor, mingle-area outside Ballroom	
10:30 – 11:20	**Symposium: Translational science in pain treatment** **Location**: Ground floor, Ballroom	Chair: Bruce Perkins (Toronto, CA)
10:30 – 10:50	Mechanism-based treatment	Uazman Alam (Liverpool, UK)
10:50 – 11:10	Clinical treatment of neuropathic pain	Solomon Tesfaye (Sheffield, UK)
11:10 – 11:20	Panel discussion	

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11:20 – 12:20	**Poster presentations** (P24-P34) Pathogenesis, epidemiology, and diagnosis **Location:** First floor, Studio 1+2 (up the stairs in the main hall outside the conference area)	Chairs: Mitra Tavakoli (Exeter, United Kingdom) and Luca D'Onofrio (Rome, IT)
	Poster presentations (P1, P35-P45) Autonomic neuropathy and treatment **Location:** First floor, Studio 3 (up the stairs in the main hall outside the conference area)	Chairs: Sanjeev Sharma (Ipswich, UK) and Georgios Ponirakis (Doha, QR)
12:20 – 13:30	Key Notes Location: **Ground floor, Ballroom**	Novo Nordisk gold sponsor Chair: Christina Brock (Aalborg, DK)
	GLP-1 in inflammation, neuroinflammation and Alzheimer's Disease	Lotte Bjerre Knudsen (Måløv, DK)
	Not all insulins are created equal. The differential effects of insulins on diabetic peripheral neuropathy	Thorbjørn Åkerstrom (Måløv, DK)
13:30 – 13:45	Final words **Location**: Ground floor, Ballroom	Vincenza Spallone and Eirik Søfteland
13:45 – 14:15	**Grab´n´Go lunch and departure** **Location**: Ground floor, mingle-area outside Ballroom	

DAILY PROGRAMME

15 / SEPTEMBER / 2022

17:00 – 20:00	**Neurodiab Hospitality Desk open for Registration** **Location:** Ground floor, Main hall area	

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08:25 – 08:45	Epigenetics – is that the missing link?	Stephanie Eid (Ann Arbor, US)
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09:45 – 10:00	Discussion	
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10:30 – 11:30	**Oral presentations (O1-O4)** **Pathogenesis** **Location:** Ground floor, Ballroom	Chairs: Dan Ziegler (Düsseldorf, DE) and Thorbjørn Åkerstrom (Måløv DK) - (TBC)
	O1. Update: omega-3 polyunsaturated fatty acids in the treatment of diabetic peripheral neuropathy (DPN) *Mark Yorek* (Iowa City, USA)	
	O2. Collagen turnover is associated with cardiovascular autonomic and peripheral neuropathy in type 1 diabetes – novel pathophysiological mechanism? *Christian Stevns Hansen*, Daniel K Rasmussen, Tine W Hansen, Signe H Nielsen, Simone Theilade, Morten A Karsdal, Frederica Genovese, Peter Rossing (Herlev, Denmark; Lyngby, Denmark; Copenhagen, Denmark)	
	O3. Diabetic neuropathy, DNA damage and mutagen-induced sensitivity in vitro *Laura Šiaulienė*, Žydrūnė Visockienė, Veronika Dedonytė, Ieva Sereikė, Juozas Rimantas Lazutka (Vilnius, Lithuania)	
	O4. Lack of association between fasted C-peptide and neuropathy in longstanding type 1 diabetes (T1D): analysis of the Canadian Study of Longevity in Type 1 Diabetes Sebastien O. Lanctôt, Leif Erik Lovblom, Evan J. H. Lewis, Michelle Morris, Nancy Cardinez, Daniel Scarr, Julie A. Lovshin, Yuliya Lytvyn, Geneviève Boulet, Alexandra Bussières, Michael H. Brent, Narinder Paul, David Z. I. Cherney, Vera Bril, *Bruce A. Perkins* (Toronto, Canada; Sherbrooke, Canada; London, Canada	
11:30 – 12:40	**Symposium: Role of thiamine in diabetes and diabetic polyneuropathy** **Location**: Ground floor, Ballroom	Wörwag Pharma symposium Chair: Peter Kempler (Budapest, HU)
11:30 – 11:40	Introduction	Peter Kempler (Budapest, HU)

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11:40 – 12:10	Association of transketolase SNPs with diabetic polyneuropathy: The KORA Study	Dan Ziegler (Düsseldorf, DE)
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12:40 – 13:20	Lunch break Location: Second floor, Restaurant NOVA (We have reserved the inner part of the restaurant. Follow Neurodiab signs.)	
13:20 – 15:00	**Oral presentations** (O5-O11) Young investigators award for the best presentation **Location**: Ground floor, Ballroom	Chairs: Triantafyllos Didangelos (Thessaloniki, GR) and Niels Ejskjaer (Aalborg, DK)
	O5. Systemic inflammation is more pronounced when peripheral neuropathy is present *Anne-Marie Wegeberg*, Tina Okdahl, Joachim Størling, Birgitte Brock, Christina Brock (Aalborg, Denmark)	
	O6. Declining incident rates of distal polyneuropathy in a cohort study, but with distinct age-related patterns between diabetes types in the period 1996-2018 *Hatice Isik Mizrak*, Hanan Amadid, Peter Rossing, Dorte Vistisen, Christian Stevns Hansen (Herlev, Denmark)	

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O7. Normative corneal nerve values for corneal confocal microscopy Maryam Ferdousi, ***Alise Kalteniece***, Ioannis N Petropoulos, Georgios Ponirakis, Hoda Gad, Adnan Khan, Shazli Azmi, Golnoosh Motamedi-Ghahfarokhi, Handrean Soran, Bruce Perkins, Dan Ziegler, Daniele Pacaud, Andrew JM Boulton, Nathan Efron, Rayaz A Malik (Manchester, United Kingdom; Doha, Qatar; Toronto, Canada; Düsseldorf, Germany; Calgary, Canada; Brisbane, Australia)

O8. Greater small nerve fibre deficits in participants with diabetic neuropathic foot ulcers compared to diabetic neuropathy in type 1 diabetes
Jonathan Zhang Ming Lim, Jamie Burgess, Anne Marshall, David Riley, Daniel Cuthbertson, Cheong Guan Ooi,
Maryam Ferdousi, Alise Kalteniece, Rayaz Malik, Uazman Alam (Liverpool, United Kingdom; Manchester, United Kingdom; Doha, Qatar)

O9. Distal corneal small nerve fibre damage in subjects with obesity Zohaib Iqbal, ***Maryam Ferdousi***, Alise Kalteniece, Shazli Azmi, Safwaan Adam, Jan Ho, Yifen Liu, Rachelle Donn, Akheel Syed, Basil Ammori, Rayaz Malik, Handrean Soran (Manchester, United Kingdom; Salford, United Kingdom; Abu Dhabi, UAE; Doha, Qatar)

O10. Subclinical large fibre-, small fibre- and autonomic neuropathy in adolescents with type 1 diabetes and associated risk factors
Vinni Faber Rasmussen, Mathilde Thrysøe, Hatice Tankisi, Pall Karlsson, Esben Thyssen Vestergaard, Kurt Kristensen, Jens Randel Nyengaard, Klaus Krogh, Christina Brock, Astrid Juhl Terkelsen (Aarhus, Denmark; Randers, Denmark; Aalborg, Denmark)

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	O11. The impact of diabetic neuropathy definition on the diagnostic performance of corneal confocal microscopy *Ioannis N. Petropoulos*, Maryam Ferdousi, Shazli Azmi, Georgios Ponirakis, Omar Asghar, Alise Kalteniece, Maria Jeziorska, Andrew Marshall, Caroline Abbott, Uazman Alam, Handrean Soran, Rayaz A. Malik (Doha, Qatar; Manchester, United Kingdom; Liverpool, United Kingdom)
15:00 – 15:20	Coffee break and visit industry stands Location: Ground floor, mingle-area outside Ballroom
15:20 – 17:00	Oral Presentations (O12-O18) Young investigators award for the best presentation Location: Ground floor, Ballroom Chairs: Fabiana Picconi (Rome, IT) and Peter Kempler (Budapest, HU)
	O12. Systemic low-grade inflammation in diabetes is associated with gastrointestinal transit times *Tina Okdahl*, Anne-Marie Wegeberg, Anne Birthe Helweg Jensen, Sarah Thorius Jensen, Helene Riis Pontoppidan Andersen, Joachim Størling, Birgitte Brock, Christina Brock (Aalborg, Denmark, Herlev, Denmark)
	O13. Visceral adiposity is associated with autonomic dysfunction in adults with autoimmune diabetes Ernesto Maddaloni, *Luca D'Onofrio*, Mikiko Watanabe, Raffaella Cassano, Davide Masi, Rocco Amendolara, Sara Sterpetti, Chiara Moretti, Antonio Siena, Lucio Gnessi, Raffaella Buzzetti (Rome, Italy)
	O14. Corneal confocal microscopy detects small nerve fibre damage in patients with heterozygous familial hypercholesterolemia which ameliorated after treatment with PCSK9 inhibitor therapy. *Maryam Ferdousi*, Alise Kalteneice, Ruth Eatough, Kirsty Nicholson, Rayaz Malik, Handrean Soran (Manchester, United Kingdom; Doha, Qatar)
	O15. Does a simple clinical scoring system complement COMPASS 31 in predicting cardiovascular autonomic neuropathy in type 1 and type 2 diabetes? *Ilenia D'Ippolito*, Marika Menduni, Cinzia D'Amato, Carla Greco, Martina Leoni, Davide Lauro, Vincenza Spallone (Rome, Italy)

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	O16. Functional alterations in brain regions involved in sensory processing in diabetic peripheral neuropathy and neuropathic pain Suganthiya S Croosu, ***Johan Røikjer***, Carsten Dahl Mørch, Niels Ejskjaer, Jens Brøndum Frøkjær, Tine Maria Hansen (Aalborg, Denmark)
	O17. Neurotransmitter enriched resting state functional MRI – a new mechanistic-informed biomarker for predicting treatment response in diabetic painful neuropathy ***Kevin The***, James McAllister, Arpana Anandhanarayanan, Gordon Sloan, Solomon Tesfaye, Dinesh Selvarajah (Sheffield, United Kingdom)
	O18. A novel data-driven machine learning approach to identify subtypes of painful diabetic neuropathy from resting-state functional magnetic resonance imaging ***Kevin The***, James McAllister, Aparna Anandhanarayanan, Gordon Sloan, Solomon Tesfaye, Dinesh Selvarajah (Sheffield, United Kingdom)
17:30	**Guided tour of Bergen where we will end up at Haakonshallen for the Official Opening** If you have signed up for the guided tour, you will have received an email confirming your GROUP NUMBER. Your guide will be meeting his/her group outside the hotel with a sign/group number. Please join your guide/your number. Each group will have separate itineraries.
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O19. Autonomic and sensory neuropathy with multiple etiology in kidney transplanted patients
Tamás Várkonyi, Anna Vágvölgyi, Bernadett Borda, Andrea Orosz, Mónika Szűcs, Attila Nemes, György Lázár, István Baczkó, Péter Kempler, Csaba Lengyel (Szeged, Hungary; Budapest, Hungary)

O20. Clinical phenotypes of neuropathic symptoms in type 2 diabetic patients: A multicenter study
Yu Ji Kim, *Tae Sun Park*, Heung Yong Jin, Kynung Ae Lee, Dong Sun Kim, Kyu Jeung Ahn, Jong Chul Won (Jeonju, Republic of Korea; Seoul, Republic of Korea)

O21. Painful diabetic peripheral neuropathy in type 1 diabetes (T1D) in the Epidemiology of Diabetes Interventions and Complications (EDIC) study
Barbara Braffett, Laure El Ghormli, James Albers, Eva Feldman, Rose Gubitosi-Klug, William Herman, Catherine Martin, Trevor Orchard, Bruce Perkins, Neil White, John Lachin, *Rodica Pop-Busui* (Rockville, MD, USA; Ann Arbor, USA; Cleveland, USA; Pittsburg, USA; Toronto, Toronto, Canada; St Louis, USA)

O22. Is it depression? Depressive symptoms at baseline are associated with the onset of diabetic peripheral neuropathy within 10 years following T2DM diagnosis
Dulce Alarcon Yaquetto, Prashanth Vas, Kirsty Winkley-Bryant, Michael Edmonds, Khalida Ismail (London, United Kingdom)

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	O23. Determining the Sequence of Microvascular Complications: Results of Multistate Markov Modelling in the Diabetes Control and Complications Trial (DCCT) *Leif Erik Lovblom*, Laurent Briollais, George Tomlinson, Bruce A. Perkins (Toronto, Canada)	
09:45 – 10:00	**Coffee break and visit industry stands** **Location:** Ground floor, mingle-area outside Ballroom	
10:00 – 11:15	**Symposium: Pain in diabetic neuropathy, partly supported by Sanofi** **Location**: Ground floor, Ballroom	Chairs: Rodica Pop-Busui (Ann Arbor, US) and Anders Stouge (Aarhus, DK)
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11:30 – 12:30	**Oral presentations** (O24-O27) Small fiber and painful neuropathy **Location**: Ground floor, Ballroom	Chairs: Dinesh Selvarajah (Sheffield, United Kingdom) and Tae Sun Park (Seoul, KR)
	O24. The LDIFLAREmethod predicts the development of incipient diabetes polyneuropathy (DPN) – results of the 5-year longitudinal Ipswich NeuroDiab study *Sanjeev Sharma*, Jenna Cross, Gerry Rayman (Ipswich, United Kingdom)	
	O25. Three-years follow up of retinal neurodegeneration and neuropathic characteristics in paediatric type 1 diabetic patients Marika Menduni, *Fabiana Picconi*, Maria Cristina Parravano, Benedetta Russo, Alessio Maiorino, Laura Chioma, Dorina Ylli, Stefano Cianfarani, Patrizia Ippolita Patera, Simona Frontoni (Rome, Italy; Washington DC, USA)	

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	O26. Spinal disinhibition: evidence for a hyperpathia phenotype in painful diabetic neuropathy Anne Marshall, Alise Kalteniece, Maryam Ferdousi, Shazli Azmi, Edward Jude, Clare Adamson, Luca D'Onofrio, Shaishav Dhage, Handrean Soren, Corinne Lee-Kubl, Shaheen Hamdy, Uazman Alam, Rayaz Malik, Nigel Calcutt, ***Andrew Marshall*** (Liverpool, United Kingdom; Manchester, United Kingdom; Rome, Italy; La Jolla, USA; Doha, Qatar)	
	O27. Thalamic neuronal and mitochondrial function in painful and painless diabetic peripheral neuropathy: a multimodal magnetic resonance spectroscopy study ***Gordon Sloan***, Adriana Anton, Iain Wilkinson, Dinesh Selvarajah, Solomon Tesfaye (Sheffield, United Kingdom)	
12:30 – 13:30	**Lunch break** **Location**: Second floor, Restaurant NOVA (We have reserved the inner part of the restaurant. Follow Neurodiab signs.)	
13:30 – 14:30	**Poster presentations** (P2-P11) Young investigators award for the best poster presentation **Location**: First floor, Studio 1+2 (up the stairs in the main hall outside the conference area)	Chairs: Tamas Varkonyi (Szeged, Hungary) and Sondre Meling (Stavanger, NO)
	P2. Non-Alcoholic Fatty Liver Disease Is not Related to the Prevalence of Diabetic Polyneuropathy in Diabetes ***Carla Greco***, Stefano Boni, Silvia Coluccia, Massimiliano Colzani, Daniele Santi, Manuela Simoni (Modena, Italy)	

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P3. Particularities of a Roma population with type 2 diabetes mellitus, obesity and peripheral neuropathy
Andrada Cosoreanu, Emilia Rusu, Gabriela Radulian (Bucharest, Romania)

P4. The presence of chronic complications in prediabetes
Claudia Sivu, Ion-Vlad Vinereanu, Alexandru Nechita, Vasilica Enache, Florina Ciobanu, Gabriela Radulian (Bucharest, Romania)

P5. Predicting neuropathy using routine eye and kidney test results: An application of novel statistical methods in the Diabetes Control and Complications Trial (DCCT) *Leif Erik Lovblom*, Laurent Briollais, George Tomlinson, Bruce A. Perkins (Toronto, Canada)

P6. Genetic factors that increase the risk of diabetic neuropathy
Dóra Tordai, Noémi Hajdú, Orsolya Erzsébet Vági, Miklós Kempler, Magdolna Békeffy, Anna Erzsébet Körei, Ildikó Istenes, Viktor Horváth, Péter Kempler, Zsuzsanna Putz (Budapest, Hungary)

P7. Genetic factors that reduce the risk of diabetic neuropathy
Noémi Hajdú, Dóra Tordai, Orsolya Erzsébet Vági, Miklós Kempler, Magdolna Békeffy, Anna Erzsébet Körei, Ildikó Istenes, Viktor Horváth, Péter Kempler, Zsuzsanna Putz (Budapest, Hungary)

P8. Plasma levels of vitamin B12 and Neurofilament light chain in adolescents with type 1 diabetes with and without neuropathy
Mathilde Thrysøe Jespersen, Tina Parkner, Hatice Tankisi, Astrid Juhl Terkelsen, Jens Randel Nyengaard, Esben Thyssen Vestergaard, Kurt Kristensen, Vinni Faber Rasmussen (Aarhus, Denmark)

P9. Small nerve fibre pathology in people with obesity at high risk of non-alcoholic fatty liver disease (NAFLD): preliminary baseline
David Riley, *Azlinda Hamid*, Leandros Rapteas, Anne Marshall, Jamie Burgess, Ioannis Petropolous, Rayaz Malik, Theresa Hydes, Dan Cuthbertson, Uazman Alam (Liverpool, United Kingdom; Doha, Qatar)

P10. A New Diagnostic Method to Assess Small Fiber Neuropathies at Early Stages – An Experimental study investigating perception threshold stability
Mette Krabsmark Borbjerg, Elin Antonsson, Johan Roeikjer, Niels Ejskjaer, Carsten Dahl Moerch (Aalborg, Denmark)

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P11. Perception threshold tracking: A novel method for assessing the function of large and small nerve fibers in diabetic peripheral neuropathy
Johan Røikjer, Suganthiya S Croosu, Jens B Frøkjær, Tine M Hansen, Niels Ejskjaer, Carsten D Mørch (Aalborg, Denmark)

Poster presentations (P12-P22)
Young investigators award for the best poster presentation
Location: First floor, Studio 3 (up the stairs in the main hall outside the conference area)

Chairs: Gerry Rayman (Ipswich, UK) and Ioannis Nikolaos Petropoulos (Doha, QR)

P12. Subclinical corneal nerve loss in obese children and adolescents *Hoda Gad*, Hajar Dauleh, Shiga Chirayath, Basma Haris, Houda Afyouni, Goran Petrovski, Saira Shehzad, Amel Khalifa, Fawziya Al-Khalaf, Parul Sing, Souhaila AlKodor, Mohamed A. Hendaus, Einas Elgassim, Ioannis N. Petropoulos, Georgios Ponirakis, Khalid Hussain, Rayaz A. Malik (Doha, Qatar; Manchester, United Kingdom)

P13. People with type 1 diabetes mellitus and significant small nerve fibre loss have greater loss of grey matter volume in brain regions associated with pain and cognition
Jamie Burgess, Jonathan Lim, Christophe De Bezenac, Anne Marshall, David Riley, Cheong Ooi, Daniel Cuthbertson, Simon S Keller, Uazman Alam (Liverpool, United Kingdom)

P14. Equivalent neuropathic deficits, differing pain. A study of small fibre pathology and sensory phenotypes in patients with diabetic neuropathy and fibromyalgia syndrome
Leandros Rapteas, Anne Marshall, Jamie Burgess, David Riley, Alise Kalteniece, Maryam Ferdousi, Shazli Azmi, Rayaz Malik, Nigel Calcutt, Andrew Marshall, Uazman Alam (Liverpool, United Kingdom; Manchester, United Kingdom; Doha, Qatar; San Diego, USA)

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P15. Early corneal nerve fiber regeneration with the weekly GLP-1 agonist semaglutide*Hoda Gad*, Einas Elgassim, Adnan Khan, Ioannis N. Petropoulos, Georgios Ponirakis, Rayaz A. Malik (Doha, Qatar; Manchester, United Kingdom)

P16. Determinants of orthostatic hypotension in type 2 diabetes: is still cardiac autonomic neuropathy the main factor? *Ilenia D'Ippolito*, Cinzia D'Amato, Carla Greco, Davide Lauro, Vincenza Spallone (Rome, Italy)

P16. Determinants of orthostatic hypotension in type 2 diabetes: is still cardiac autonomic neuropathy the main factor? *Ilenia D'Ippolito*, Cinzia D'Amato, Carla Greco, Davide Lauro, Vincenza Spallone (Rome, Italy)

P17. Clinical characteristics in diabetic gastroparesis – the DIAGAS study *Elisabeth K. Steinsvik*, Dag Sangnes, Georg Dimcevski, Trygve Hausken, Odd Helge Gilja, Eirik Søfteland (Bergen, Norway)

P18. Glycemic variability is associated with diastolic dysfunction in patients with type 2 diabetes Yana Dzhun, Georgiy Mankovsky, Nadiya Rudenko, Yevgen Marushko, *Yanina Saienko*, Borys Mankovsky (Kyiv, Ukraine)

P19. Meal-induced gallbladder emptying in diabetic, prediabetic, and control patients – preliminary results from the PanGut-study *Tæraneh Jouleh*, Ingrid Kvåle Nordaas, Erling Tjora, Sondre Meling, Georg Dimcevski, Odd Helge Gilja, Eirik Søfteland (Bergen, Norway; Stavanger, Norway)

P20. Effectiveness of Treatment with Vitamins B12 and D in Patients with Diabetic Peripheral Neuropathy by Sudoscan *Tamar Maghradze*, Elena Shelestova, Ramaz Kurashvili (Tbilisi, Georgia)

P21. Study Protocol For Neuromuscular Electrical Stimulation For The Treatment Of Diabetic Peripheral Neuropathy: A Multi-centre, Double-blinded, Randomised Controlled Trial *Sasha Smith*, Tristan Lane, Pasha Normahani, Catarina Carvalho, Ian Mak, Cain Clark, David David Hohenschurz-Schmidt, Nick Oliver, Alun Davies (London, United Kingdom; Cambridge, United Kingdom; Coventry, United Kingdom)

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	P22. Effects of progressive resistance training in individuals with type 2 diabetes and severe motor dysfunction following diabetic polyneuropathy***Anders Stouge***, Karolina S. Khan, Henning Andersen (Aarhus, Denmark)	
14:30 – 15:30	**Symposium: Autonomic nervous system and the cardiorenal metabolic syndrome** **Location**: Ground floor, Ballroom	Boehringer gold sponsor Chairs: Kåre Birkeland (Oslo, NO) and Paul Valensi (Bondy,FR)
14:30 – 14:40	Introduction to the cardiorenal metabolic syndrome	Kåre Birkeland (Oslo, NO)
14:40 – 15:00	The synergistic effect of SGLT2 /aldosterone antagonism on cardiac outcome	Peter Rossing (Copenhagen, DK)
15:00 – 15:20	Is the autonomic nervous system the missing piece of a puzzle?	Vincenza Spallone (Rome, IT)
15:20 – 15:30	Panel discussion	
15:30 – 15:50	**Coffee break and visit industry stands** **Location:** Ground floor, mingle-area outside Ballroom	
15:50 – 16:40	**The Göran Sundkvist Young Investigators Award for Clinical Science** **Location**: Ground floor, Ballroom	Chair: Vincenza Spallone (Rome, IT)
15:50 – 16:15		Shazli Azmi (Manchester, UK)
16:15 – 16:40	On pins and needles: how neuropathy guided my career in medicine	Lynn Ang (Ann Arbor, US)

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16:40 – 17:50	**General Assembly Neurodiab** **Location:** Ground floor, Ballroom
18:45	Departure from your hotel to the port, Dreggekaien, Skur 8
19:00	Departure private boat to Restaurant Cornelius by the Fjords
19:30	Estimated time of arrival at Cornelius by the Fjords
19:30 – 23:00	Neurodiab Conference dinner
23:00	Approx. return from Cornelius towards Bergen. Walk back to your hotel.

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08:00 – 14:00	**Neurodiab Hospitality desk open** **Location**: Ground floor, mingle-area outside Ballroom
08:00 – 14:00	**Posters are on display throughout the whole duration of the conference** **Location**: First floor, Studio 1+2+3 (up the stairs in the main hall outside the conference area)
08:30 -09:30	**Oral presentations** (O28-O31) Autonomic neuropathy and treatment **Location**: Ground floor, Ballroom Chairs: Triantafyllos Didangelos (Thessaloniki, GR) and Gidon Bönhof (Düsseldorf, DE) O28. Association of microangiopathic complications and cardiac autonomic neuropathy with cardiac structure and function in asymptomatic patients with type 2 diabetes *Paul Valensi*, Minh Tuan Nguyen, Sara Pinto, Patricia Poignard (Bondy, France) O29. The PanGut-study: Evoked potentials following rectal balloon distention, a new way of diagnosing diabetic autonomic neuropathy in the gut? *Sondre Meling*, Erling Tjora, Heike Eichele, Rasmus Bach Nedergaard, Niels Ejskjær, Eirik Søfteland (Stavanger, Norway; Bergen, Norway; Aalborg, Denmark)

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	0=30. Sodium Glucose Cotransporter-2 Inhibitor Protects against Diabetic Neuropathy and Nephropathy in Modestly Controlled Type 2 Diabetes: Follow-up Study Fukashi Ishibashi, Aiko Kosaka, ***Mitra Tavakoli*** (Hiroshima, Japan; Exeter, United Kingdom)	
	O31. Effects of a cardiac rehabilitation programme on heart rate response to exercise and on aerobic performance in patients with newly-detected glycemic disorders Kamel Abdennbi, Minh Tuan Nguyen, Guy Amah, Sylvie Gagey, Nérimaine Chaib, Chabnam Guiti, Marie Sylva, ***Paul Valensi*** (Paris, France; Bondy, France)	
09:30 – 10:10	**Symposium: Diabetes and COVID-19** **Location:** Ground floor, Ballroom	Chairs: Gerry Rayman (Ipswich, UK) and Anne-Marie Wegeberg (Aalborg, DK)
09:30 – 09:50	Mediators and adverse outcome in individuals with diabetes hospitalized for COVID-19	Rodica Pop-Busui (Ann Arbor, US)
09:50 – 10:10	COVID-19 and the peripheral nervous system	Giuseppe Lauria (Milan, IT)
10:10 – 10:30	**Coffee break and visit industry stands** **Location:** Ground floor, mingle-area outside Ballroom	
10:30 – 11:20	**Symposium: Translational science in pain treatment** **Location:** Ground floor, Ballroom	Chair: Bruce Perkins (Toronto, CA)
10:30 – 10:50	Mechanism-based treatment	Uazman Alam (Liverpool, UK)
10:50 – 11:10	Clinical treatment of neuropathic pain	Solomon Tesfaye (Sheffield, UK)
11:10 – 11:20	Panel discussion	
11:20 – 12:20	**Poster presentations** (P24-P34) Pathogenesis, epidemiology, and diagnosis **Location**: First floor, Studio 1+2 (up the stairs in the main hall outside the conference area)	Chairs: Mitra Tavakoli (Exeter, United Kingdom) and Luca D'Onofrio (Rome, IT)

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P24. Clinical characteristics of diabetic peripheral neuropathy in type 2 diabetes: results of a national health insurance service, 2012-2017

Chong Hwa Kim, Tae Sun Park, Ji Hyun Lee (Bucheon, Republic of Korea; Jeonju, Republic of Korea; Daegu, Republic of Korea)

P25. The co-existence of peripheral and autonomic neuropathy in type 1 diabetes with and without pain

Johan Røikjer, Suganthiya Santhiapillai Croosu, Tine Maria Hansen, Jens Brøndum Frøkjær, Christina Brock, Carsten Dahl Mørch, Niels Ejskjaer (Aalborg, Denmark)

P26. Inflammatory markers are associated with prevalent cardiac autonomic neuropathy 10 years after diagnosis with type 2 diabetes: Observation from the multi-ethnic SOUth London Diabetes (SOUL-D) study

Prashanth Vas, Dulce Alarcon Yaquetto, Kirsty Winkley-Bryant, Michael Edmonds, Khalida Ismail (London, United Kingdom)

P27. Inflammatory Markers and Cardiovascular Autonomic Neuropathy in Type 1 Diabetes

Lynn Ang, Sejal Gunaratnam, Yiyuan Huang, Catherine Martin, Aaron Burant, Jacob Reiss, Pennelope Blakely Kunkle, Alexi Vasbinder, Christopher Launius, Lily Zhao, Kara Mizokami-Stout, Eva Feldman, Salim Hayek, Rodica Pop-Busui (Ann Arbor, USA)

P28. The Effect of Statins on Peripheral Neuropathy in Diabetic Patients

Raabya Pasha, Maryam Ferdousi, Shazli Azmi, Alise Kalteniece, Handrean Soran, Rayaz A Malik (Manchester, United Kingdom; Doha, Qatar)

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P29. Determinants of prolonged sensory neuropathy after severe COVID-19 infection
Ariel Odriozola, Lucía Ortega, Lidia Martinez, Samantha Odriozola, Ainhoa Torrens, David Corroleu, Silvia Silvia, Xavier Sans, Meritxell Ponce, Yolanda Meije, Mercedes Presas, Alejandra Duarte, M Belén Odriozola, Georgios Ponirakis, Rayaz Malik (Barcelona, Spain; Doha, Qatar)

P30. Diabetic neuropathy is a generalized phenomenon with significant impact on hand functional performance and quality of life *Zoltan Kender*, Dimitrios Tsilingiris, Lukas Schimpfle, Alba Sulaj, Ekaterina von Rauchhaupt, Peter Nawroth, Julia Szendroedi, Stefan Kopf (Heidelberg, Germany; München-Neuherberg, Germany; Munich, Germany

P31. Retinal neurodegeneration as a marker of diabetic peripheral neuropathy and cognitive impairment in type 2 diabetes mellitus *Fabiana Picconi*, Marika Menduni, Alessio Maiorino, Mariacristina Parravano, Benedetta Russo, Noemi Lois, Rafael Simò, Simona Frontoni (Rome, Italy; Belfast, United Kingdom; Barcelona, Spain)

P32. The association between prevalent sensory neuropathy and age or diabetes duration in people cared for type 2 diabetes mellitus in an internal medicine outpatient clinic – a cross-sectional study *Viktor J Horváth*, Noémi Hajdú, Csaba G Koós, Magdolna Békeffy, Beatrix A Domján, Márk M Svébis, Anna E Körei, Péter Kempler, Ádám Gy Tabák (Budapest, Hungary; Biatorbágy, Hungary; London, United Kingdom)

P33. Multiple musculoskeletal complications as a consequence of diabetic polyneuropathy in one patient - a case report
Anna Körei, Noémi Hajdú, Zsuzsanna Putz, Ildikó Istenes, Viktor Horváth, Orsolya Vági, Dóra Tordai, Magdolna Békeffy, Karola Osgyán, Adrienn Menyhárt, Péter Kempler (Budapest, Hungary)

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P34. Assessing diabetes polyneuropathy using a 5.07/10g Semmes-Weinstein monofilament
Øystein Dunker, Marie Bu Kvaløy, Martin Uglem, Sissel Løseth, Ina Elen Hjelland, Sara Maria Allen, Inge Petter Kleggetveit, Maria Dehli Vigeland, Trond Sand, Kristian Bernhard Nilsen (Oslo, Norway; Stavanger, Norway; Trondheim, Norway; Tromsø, Norway; Bergen, Norway)

Poster presentations (P1, P35-P45) Autonomic neuropathy and treatment **Location**: First floor, Studio 3 (up the stairs in the main hall outside the conference area)	Chairs: Sanjeev Sharma (Ipswich, UK) and Georgios Ponirakis (Doha, QR)

P1. Prevalence and risk factors for diabetic peripheral neuropathy, neuropathic pain and foot ulceration in the Arabian Gulf Region
Georgios Ponirakis, Tarik Elhadd, Ebaa Al Ozairi, Imad Brema, Rayaz Malik (Doha, Qatar; Kuwait City, Kuwait; Riyadh, Saudi Arabia)

P35. Predictors of erectile dysfunction in type 2 diabetes in secondary care in Qatar *Georgios Ponirakis*, Tarik Elhadd, Subitha Chinnaiyan, Zeinab Dabbous, Mashhood Siddiqu, Hamad Al-muhannadi, Ioannis Petropoulos, Adnan Khan, Khaled A. E. Ashawesh, Khaled M. O Dukhan, Ziyad R. Mahfoud, Rayaz A. Malik (Doha, Qatar)

P36. Influence of body composition on cardiovascular autonomic neuropathy in patients with type 2 diabetes mellitus
Andra-Elena Nica, Carmen Dobjanschi, Emilia Rusu, Vlad Vinereanu, Gabriela Radulian (Bucharest, Romania)

P37. Clinical Characteristics of Diabetic Cardiovascular Autonomic Neuropathy in Republic of Korea *Jong Chul Won*, Chong Hwa Kim, Ie Byung Park, Jihyun Lee, Kyu Jeung Ahn, Dong Sun Kim, Tae Sun Park (Seoul, Republic of Korea; Bucheon, Republic of Korea; Incheon, Republic of Korea; Daegu, Republic of Korea; Jeonju, Republic of Republic of Korea)

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P38. Role of the Nerve Check Master to identify diabetic patients with cardiac autonomic neuropathy
Paul Valensi, Raffaele Galiero, Amel Rezki, Emmanuel Cosson, Domenico Beccia, Maria Alfano, Ferdinando Carlo Sasso (Bondy, France; Naples, Italy)

P39. Predicting diabetic cardiac autonomic neuropathy using advanced machine learning algorithms in type 2 diabetes patients
Tae Sun Park, Heung Yong Jin, Kyung Ae Lee, Jong Chul Won, Chong Hwa Kim (Jeonju, Korea, Jeonju, Republic of Korea; Seoul, Korea, Republic of Korea; Bucheon, Korea, Republic of Korea)

P40. The Composite Autonomic Symptom Score 31 (COMPASS 31) in a Norwegian population of longstanding type 2 diabetes, early diabetes, and healthy controls. A part of the PanGut study.
Sondre Meling, Erling Tjora, Heike Eichele, Niels Ejskjær, Siri Carlsen, Pål Rasmus Njølstad, Eirik Søfteland (Stavanger, Norway;Bergen, Norway; Aalborg, Norway)

P41. Renal Hemodynamic Dysfunction and Neuropathy in Longstanding Type 1 Diabetes: Results from the Canadian Study of Longevity in Type 1 Diabetes
Yuliya Lytvyn, Rehab Albakr, Petter Bjornstad, Leif Erik Lovblom, Hongyan Liu, Julie A. Lovshin, Geneviève Boulet, Mohammed A. Farooqi, Alanna Weisman, Hillary A. Keenan, Michael H. Brent, Narinder Paul, Vera Bril, David Z.I. Cherney, Bruce A. Perkins (Toronto, Canada; Aurora, USA)

P42. Early witnesses of sympathetic activation during hypopneic episodes induced by the slow breathing test in obese or diabetic patients with obstructive sleep apnoea syndrome (OSAS)
Paul Valensi, Sofia Domanovic, Mohamed Zerguine, Nada Younes, Aboubacarine Wangara, Sandrine Millasseau, Sara Pinto (Bondy, France; Saint Leu La Forêt, France)

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	P43. Life threatening recurring hypoglycemic episodes in a type-1 diabetic patient with severe autonomic neuropathy and chronic malabsorption ***Szabolcs Nyiraty***, Katalin Fehértemplomi, Andrea Orosz, Csaba Lengyel, Péter Kempler, Tamás Várkonyi (Szeged, Hungary; Budapest, Hungary)	
	P44. Venesection Improves Small Fiber Nerve Function in Diabetics with Elevated Ferritin ***Hani Naiem Ibrahim***, Marina Israel, Christine Mourad (Cairo, Egypt)	
12:20 – 13:30	**Invited Key Note** **Location**: Ground floor, Ballroom	Novo Nordisk gold sponsor Chair: Christina Brock (Aalborg, DK)
	GLP-1 in inflammation, neuroinflammation and Alzheimer's Disease	Lotte Bjerre Knudsen (Måløv, DK)
	Not all insulins are created equal. The differential effects of insulins on diabetic peripheral neuropathy	Thorbjørn Åkerstrom (Måløv, DK)
13:30 – 13:45	**Final words** **Location**: Ground floor, Ballroom	Vincenza Spallone and Eirik Søfteland
13:45 – 14:15	**Grab´n´Go lunch and departure** **Location**: Ground floor, mingle-area outside Ballroom	

ORAL ABSTRACTS

Day 1

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Oral presentations (O1-O4) Pathogenesis

Chairs: Dan Ziegler and Thorbjørn Åkerstrom

O1. Update: omega-3 polyunsaturated fatty acids in the treatment of diabetic peripheral neuropathy (DPN)

Mark Yorek

University of Iowa, Iowa City, USA. Iowa City Veterans Health Care System, Iowa City, USA

Aim: Good glycemic control delays the onset of DPN in type 1 diabetes but is less effective in those with type 2 diabetes. Thus, there is a critical need of a treatment. Our pre-clinical studies have demonstrated that treating diabetic rodents with fish oil, a natural source of omega-3 polyunsaturated fatty acids (PUFA), initiates nerve damage repair and reverses DPN. Anti-inflammatory mediators of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the predominate omega-3 PUFA found in fish oil, also elicit repair of nerve damage caused by diabetes when administered endogenously. However, is fish oil the best source of omega-3 PUFA for the treatment of DPN or are alternative sources such as krill oil, algal oils that are naturally enriched in EPA and/or DHA, or ethyl ester derivatives of EPA and/or DHA more efficacious?

Methods: Obese (pre-diabetes model) and type 2 diabetic rats were treated with diets enriched with omega-3 PUFA derived from these alternative sources using an early and late intervention protocol and afterwards multiple endpoints for vascular, neural, and behavioral dysfunction determined.

Results: Omega-3 PUFA derived from krill oil, algal oils or ethyl esters were effective treatments for DPN. EPA or DHA alone targeted different vascular and neural endpoints with the combination being most efficacious.

Conclusion: The etiology of DPN is complex, it is likely that sources of omega-3 PUFA that contain both EPA and DHA will be the more effective. Environmental and supply issues should be considered when selecting an omega-3 PUFA treatment for DPN.

O2. Collagen turnover is associated with cardiovascular autonomic and peripheral neuropathy in type 1 diabetes – novel pathophysiological mechanism?

Christian Stevns Hansen[1], Daniel K Rasmussen[2], Tine W Hansen[1], Signe H Nielsen[2,3], Simone Theilade[1,4], Morten A Karsdal[5], Frederica Genovese[5], Peter Rossing[1,4]

[1]Steno Diabetes Center Copenhagen, Herlev, Denmark. [2]Nordic Bioscience, Herlev, Denmark. [3]Technical University of Denmark, Lyngby, Denmark. [4]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark. [5]Nordic Biosceince, Herlev, Denmark

Aims: Collagen type VI (COL6) and III (COL3) have been associated with nerve function. We aim to investigate the possible associations between serum markers of COL6 and COL3 and diabetic neuropathy in people with type 1 diabetes (T1DM).

Methods: In a cross-sectional study 300 people with T1DM, serum PRO-C6 (marker of COL6 formation) and C3M (marker of COL3 degradation) were obtained. Cardiovascular autonomic neuropathy(CAN) was assessed by cardiovascular reflex tests(CARTs) Distal peripheral sensimotor neuropathy(DSPN) was assessed by biothesiometry.

Results: Patients were (mean (SD)) 55.7 (9.3) years, 51% where males, diabetes duration was 40.1 (8.9) years, HbA1c was 62.9 (1.9) mmol/mol, serum PRO-C6 7.8 (6.2;11.0) ng/ml and C3M 8.3 (7.1;10.0) ng/ml. CAN and DSPN were present in 34% and 43% of participants, respectively. When adjusted for age, sex (model 1) and additionally adjusted (model 2), a doubling of serum PRO-C6, was associated with odds ratio (OD) >2 for CAN and > 1 for DSPN, respectively. Significance was retained after adjustment for eGFR (model 3) for CAN (OD 1.7 (95%CI 1.0;2.7 p=0.035), but not for DSPN (Figure 1, Panel A). A doubling of serum C3M was associated with a higher OD for CAN only in model 1 and 2, (OD 1.7 (95%CI 1.2;2.6 p=0.004) and 1.8 (95%CI 1.2;2.7 p=0.040)).

Conclusion: Our results show associations between collagen biomarkers and CAN and DSPN in T1DM, where higher serum levels were associated with both CAN and DSPN.

Figure 1

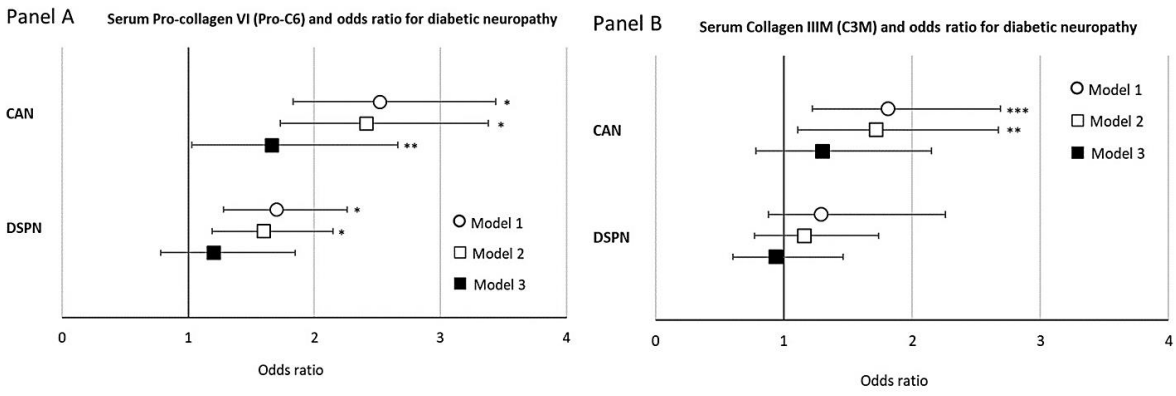


Figure 1. Logistic regression analyses (OD (95% CI)) for presence of diabetic neuropathy in T1DM for the biomarkers PRO-C6 (Panel A) and C3M (Panel B) measured in serum. ORs are presented as a doubling of determinants: model 1 is adjusted for age and sex, model 2 is further adjusted for diabetes duration, HbA_{1c}, BMI, smoking, systolic blood pressure, serum LDL and beta blocker use (only for CAN), model 3 is additionally adjusted for eGFR. * = $p < 0.001$, ** = $p<0.05$, ***=$p<0.005$.

O3. Diabetic neuropathy, DNA damage and mutagen-induced sensitivity in vitro

Laura Šiaulienė[1,2], Žydrūnė Visockienė[3,2], Veronika Dedonytė[1], Ieva Sereikė[3,2], Juozas Rimantas Lazutka[1]

[1]Vilnius University, Life Sciences Center, Vilnius, Lithuania. [2]Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania. [3]Vilnius University Faculty of Medicine, Vilnius, Lithuania

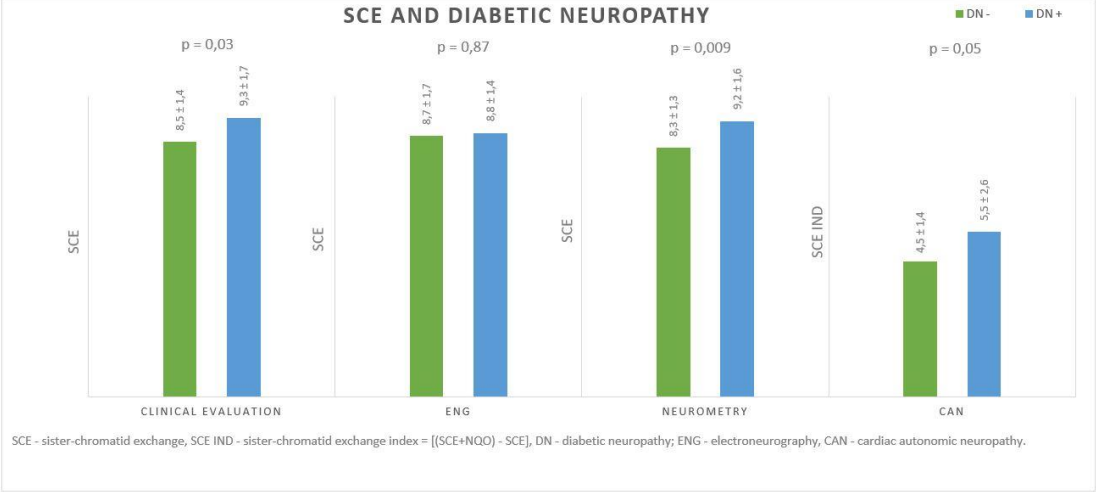
Aim: To evaluate the difference of DNA damage and in vitro 4-nitroquinoline-1-oxide (NQO) induced mutagen sensitivity in patients with and without diabetic neuropathy (DN).

Methods: DNA oxidative damage was evaluated analyzing sister-chromatid exchange (SCE) and micronucleus (MN) frequency in blood lymphocytes. Mutagen-induced sensitivity test was performed treating cells with 0.1 μg/ml of 4NQO and calculating difference of SCE and MN in treated and untreated cultures. Diabetic polyneuropathy (DPN) was evaluated by clinical examination using neuropathy symptom score (NSS) and neuropathy disability score (NDS), neurometry (NM) and electroneurography (ENG). Cardiac autonomic neuropathy (CAN) was assessed by performing cardiovascular autonomic reflex tests (CARTS).

Results: There were 76 patients enrolled in to the study – 42 (55,3%) with type 1 and 34 (44,7%) with type 2 diabetes mellitus. Mean age of participants was 48,3 ± 17,4 yrs., disease duration – 13,0 ± 11,6 yrs., average HbA1c – 9,9 ± 2,4%, male/female ratio – 40 (52,6%)/36 (47,4%). Significantly higher SCE frequency was observed in patients with DPN, diagnosed by clinical examination and NM (Figure 1). Also, significantly higher frequency of mutagen-induced SCEs was observed in patients with CAN compared with those without CAN. There were no significant differences in MN frequency among patients with and without DN.

Conclusions: In our study DN was linked to higher frequency of DNA damage in lymphocytes of diabetic patients as revealed by SCE analysis. Moreover, patients with CAN exhibited reduced DNA repair capacity, since their lymphocytes were more sensitive to NQO treatment.

Figure 1. Sister-chromatid exchange (SCE) and diabetic neuropathy



SCE - sister-chromatid exchange, SCE IND - sister-chromatid exchange index = [(SCE+NQO) - SCE], DN - diabetic neuropathy; ENG - electroneurography, CAN - cardiac autonomic neuropathy.

O4. Lack of association between fasted C-peptide and neuropathy in longstanding type 1 diabetes (T1D): analysis of the Canadian Study of Longevity in Type 1 Diabetes

Sebastien O. Lanctôt[1], Leif Erik Lovblom[1], Evan J. H. Lewis[1], Michelle Morris[1], Nancy Cardinez[1], Daniel Scarr[1], Julie A. Lovshin[2], Yuliya Lytvyn[3], Geneviève Boulet[1], Alexandra Bussières[4], Michael H. Brent[5], Narinder Paul[6,7], David Z. I. Cherney[3], Vera Bril[8], *Bruce A. Perkins*[1,2]

[1]Lunenfeld-Tanenbaum Research Institute, Toronto, Canada. [2]Division of Endocrinology and Metabolism, Department of Medicine, University of Toronto, Toronto, Canada. [3]Department of Medicine, Division of Nephrology, University of Toronto, Toronto, Canada. [4]Faculty of Medicine and Health Sciences, University of Sherbrooke, Sherbrooke, Canada. [5]Department of Ophthalmology and Vision Sciences Faculty of Medicine, University of Toronto, Toronto, Canada. [6]Joint Department of Medical Imaging, University of Toronto, Toronto, Canada. [7]Department of Medical Imaging, Western University, London, Canada. [8]Department of Medicine, Division of Neurology, University Health Network, University of Toronto, Toronto, Canada

Aims: Although insulin production is reportedly retained in many with longstanding T1D, the magnitude and relevance of C-peptide production are not known with certainty. We aimed to define fasted C-peptide distributions and associated peripheral nerve measures and clinical factors.

Methods: In this cross-sectional analysis, fasted serum and urinary high-sensitivity C-peptide assays were measured in 74 patients with longstanding T1D and 75 age- and sex-matched controls. Extensive phenotyping for neuropathy and other complications were conducted.

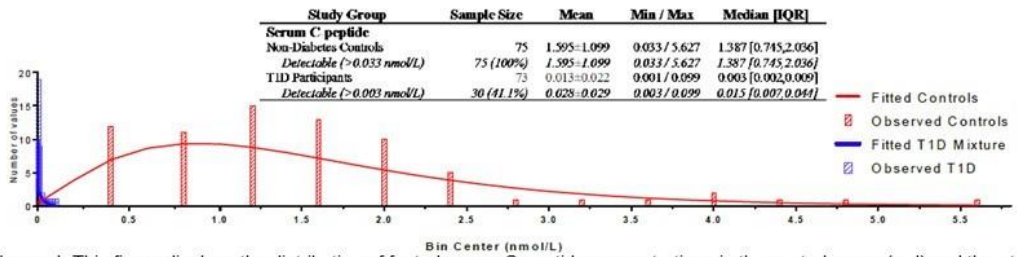
Results: T1D participants had mean±SD age 66±8 years, median[Q1-Q3] duration of diabetes 54[52,58] years, and HbA1C 7.4±0.8%; controls had mean age 65±8 years and HbA1C 5.7±0.4%. T1D had lower fasted serum C-peptide than controls (0.013±0.022 vs. 1.595±1.099 nmol/L, p<0.001, Figure 1). In T1D, C-peptide was detectable in 30/73(41%) of serum samples, 32/74(43%) of urine samples, and 48/74(65%) in either serum or urine.

Variables independently associated with detectable serum or urinary C-peptide included lower total daily insulin requirement (OR 2.351 for 1 lower unit/kg, p=0.013) and lower hypoglycemia worry (OR 1.059 for 1 point lower on the hypoglycemia fear survey

worry sub-score, p=0.030). After adjustment, C-peptide levels were not associated with measures of neuropathy (Table 1).

Conclusions: While detectable C-peptide in longstanding diabetes was common, the magnitude of concentration was extremely low compared to age-and sex-matched controls. Despite minimal detectability, its presence was validated by lower insulin requirements and strongly associated with lower hypoglycemia worry. Cross-sectional associations with neuropathy were not observed.

Figure 1. Distribution of fasted serum C-peptide in the non-diabetes control group and T1D participants



Legend: This figure displays the distribution of fasted serum C-peptide concentrations in the control group (red) and the study group (blue). Descriptive measures are included in the table above.

Table 1. Selected characteristics of the study participants.

Variable	Non-Diabetes Control (n=75)	Detectable C-peptide (n=48);	Non-detectable C-peptide (n=26)	p-Value C+ vs C-
Age, years	64 ± 8	65 ± 8	67 ± 8	0.46
Diabetes duration, years	-	54 [51.5,58]	54 [52,57]	0.87
TCNS (out of 19)	2 [0,4]	7 [3.5,10]	5 [4,9]	0.62
Nerve conduction studies				
Sural Amplitude (μV)	11.03 ± 5.91	3.30 ± 3.29	2.29 ± 1.99	0.1
Peroneal F-Wave Latency (msec)	51.42 ± 7.46	61.98 ± 8.25	64.49 ± 6.51	0.17
Heart-Rate Variability Measures				
SDNN (msec)	56.9 ± 32.34	43.74 ± 40.84	33.03 ± 16.40	0.12
LF:HF Ratio	1.71 ± 1.41	2.48 ± 1.96	2.43 ± 2.41	0.93
Corneal Confocal Microscopy (automated protocol)				
CNFL (mm/mm^2)	13.5 ± 4.5	8.4 5.0	8.0 3.3	0.74
CNFD (fibers/mm^2)	19.75 ± 9.26	10.76 ± 9.91	8.00 ± 6.93	0.22

16 / SEPTEMBER / 2022 / 13:20 – 15:00

Oral presentations (O5-O11) Young investigators award for the best presentation

Chairs: Simona Frontoni (Rome, Italy) and Niels Ejskjaer (Aalborg, Denmark)

O5. Systemic inflammation is more pronounced when peripheral neuropathy is present

Anne-Marie Wegeberg[1,2], Tina Okdahl[1], Joachim Størling[3,4], Birgitte Brock[3], Christina Brock[1,5]

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Aim: Systemic inflammation may contribute to the pathogenesis of diabetic neuropathies, but whether it is more pronounced in specific clinical manifestations remains unclear. Our objective was to investigate if inflammatory markers differ between clinical distinct neuropathy groups.

Methods: One-hundred and fifty-six adults with type 1 or type 2 diabetes were classified into four groups (no, autonomic, peripheral, and autonomic+peripheral (concomitant) neuropathy) based on abnormal biothesiometry (>20V) and cardiovascular autonomic reflex test score (>0). Circulating inflammatory marker levels of (interleukin (IL)-6, IL-8, IL-10, tumor necrosis factor α and interferon γ) were measured using multiplex technology (Mesoscale Discovery). Participants with elevated C-reactive protein (>10mg/L, n=18) were excluded.

Results: Data is presented in Table1. Participants with exclusive or concomitant peripheral neuropathy were older ($p<0.001$) and had worse estimated glomeruli filtration rate ($p<0.024$) than participants with no or exclusive autonomic neuropathy. Differences in proinflammatory IL-6 and IL-8 between groups were seen ($p=0.001$ and $p=0.015$), specifics presented in Figure 1. No difference was seen for tumor necrosis factor α ($p=0.22$), and interferon γ ($p=0.12$) or the anti-inflammatory IL-10 ($p=0.32$). Age was a confounding factor for the link between peripheral neuropathy and IL-6 or IL-8, while eGFR confounded the link with IL-6.

Conclusions: We showed that systemic proinflammatory levels of IL-6 and IL-8 were increased in people with peripheral neuropathy, but not in those with exclusively autonomic neuropathy. This may suggest that neuroinflammation in long peripheral axons is reflected in the systemic inflammatory level of certain inflammatory markers to a higher degree than vagalopathy.

Table 1	**No Neuropathy**	**Autonomic Neuropathy**	**Peripheral Neuropathy**	**Peripheral/ autonomic Neuropathy**	**p-value**
Number	54	17	34	33	
Diabetes type (T1/T2)	29/25	6/11	7/27	10/23	**0.012**
Age (years)	49 (29-63)	49 (43-57)	69 (64-72)	66 (62-69)	**<0.001**
Sex (male %)	46%	65%	68%	69%	0.09
Disease Duration (years)	13 (6-20)	10 (4-20)	15 (9-20)	19 (8-25)	0.12
Height (cm)	171 ± 9	176 ± 9	172 ± 10	174 ± 9	0.12
Weight (kg)	84 ± 15	87 ± 18	83 ± 19	90 ± 14	0.32
Body mass index (kg/cm^2)	28.9 ± 5.3	27.9 ± 3.9	28.3 ± 5.6	29.9 ± 4.3	0.53
Smoker (yes)	17%	12%	6%	12%	0.52
Vibration perception threshold (V)	13 ± 4	13 ± 3	35 ± 10	36 ± 11	**<0.001**
CAN score (borderline/abnormal)	0/0	14/3	0/0	22/11	**<0.001**
Systolic BP (mmHg)	132 ± 14	131 ± 13	139 ± 16	141 ± 19	**0.025**
Diastolic BP (mmHg)	75 ± 9	79 ± 9	74 ± 8	74 ± 9	0.21
Heart rate (beats pr min)	69 (62-75)	67 (63-77)	68 (60-72)	69 (65-73)	0.71
Hemoglobin A1c (mmol/mol)	57 (48-63)	57 (54-66)	54 (48-61)	60 (52-67)	0.18
Fasting glucose (mmol/L)	9.1 (7.5-11.2)	9.5 (8.6-10.1)	8.5 (7.0-10.4)	9.2 (7.9-11.5)	0.36
eGFR	90 (90-90)	90 (90-90)	81 (73-89)	86 (75-90)	**<0.001**
Cholesterol (mmol/L)	4.2 (3.3-4.5)	4.0 (3.8-4.7)	3.8 (3.3-4.3)	4.1 (3.2-4.7)	0.51
Interleukin 6 (pg/mL)	0.6 (0.4-0.9)	0.4 (0.3-0.6)	0.8 (0.7-1.1)	0.9 (0.5-1.2)	**0.001**
Interleukin 8 (pg/mL)	10.1 (7.6-13.7)	9.9 (8.6-13.3)	13.0 (10.2-16.6)	13.4 (10.2-17.2)	**0.015**
Interleukin 10 (pg/mL)	0.3 (0.2-0.4)	0.2 (0.2-0.3)	0.2 (0.2-0.4)	0.3 (0.2-0.5)	0.32
Tumor necrosis factor α (pg/mL)	1.2 (0.9-1.6)	1.2 (0.9-1.7)	1.5 (1.2-1.7)	1.4 (1.1-1.6)	0.22
Interferon γ (pg/mL)	3.8 (2.4-6.7)	3.2 (2.8-4.3)	5.4 (3.5-7.2)	4.7 (3.1-6.8)	0.12

Data is presented as mean ± standard deviation, median (Q1-Q3) or percentage based on data characteristics. One-way ANOVA, Kruskal-Wallis rank test or Chi-square were used to calculate overall p-values. Smoker includes current and previous smoking. T1: Type 1 diabetes, T2: Type 2 diabetes, CAN: cardiovascular autonomic neuropathy, BP: blood pressure, eGFR: estimated glomeruli filtration rate.

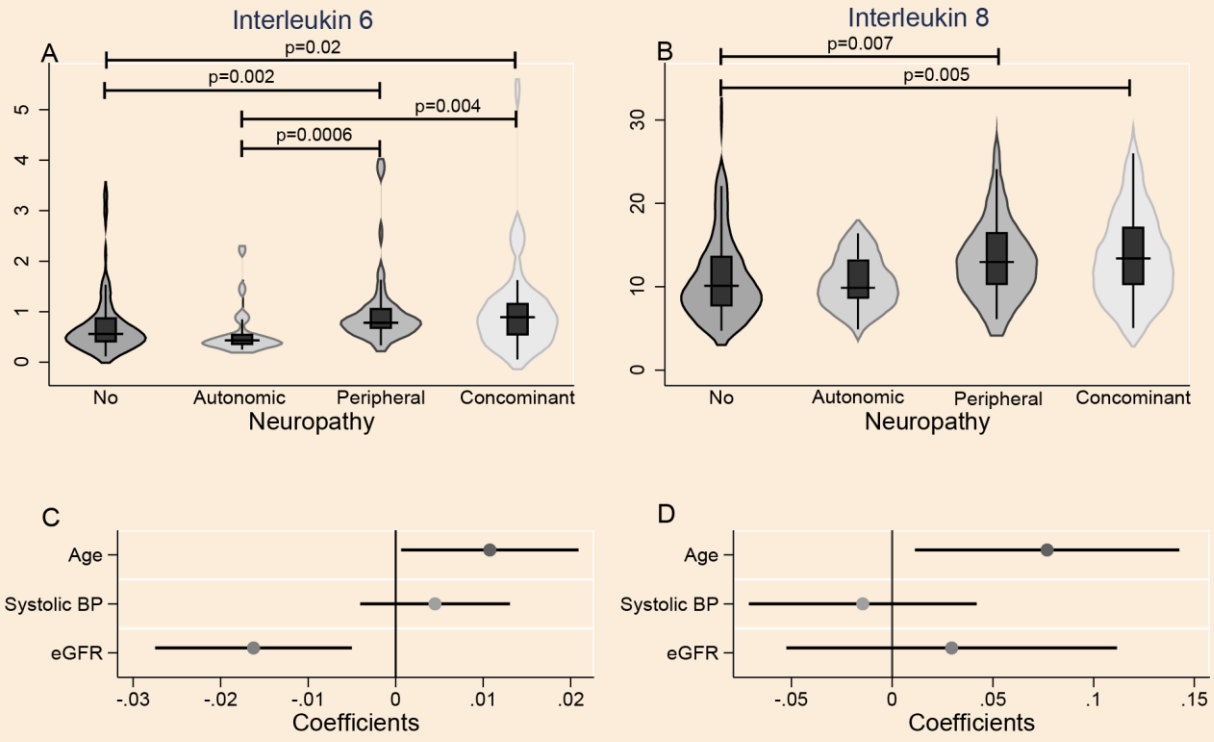

***Figure 1**: (A + B) violin plots for interleukin 6 and 8 based on the four neuropathy groups, unadjusted for possible confounding factors. Statistical significance between groups were evaluated using Kruskal-Wallis test with Dunns test as posthoc. (C + D) coefficient plots for correlation between biothesimetry and IL6 or IL8, respectively, showing effects of age, systolic blood pressure (BP) and estimated glomeruli filtration rate (eGFR). Produced using regression models.*

O6. Declining incident rates of distal polyneuropathy in a cohort study, but with distinct age-related patterns between diabetes types in the period 1996-2018

Hatice Isik Mizrak, Hanan Amadid, Peter Rossing, Dorte Vistisen, Christian Stevns Hansen

Steno Diabetes Center Copenhagen, Herlev, Denmark

Aim: To estimate temporal changes in incidence rates of Distal symmetrical polyneuropathy (DSPN) in individuals with type 1 diabetes (T1D) and type 2 diabetes (T2D) in a longitudinal cohort followed at a tertiary diabetes treatment clinic. Moreover, differences in age-related incidence rates were investigated

Methods: In the period 1996-2018, we identified 2783 individuals, 1071 with T1D and 1712 with T2D, with repeated measures of vibration perception threshold (VPT) and no DSPN at first measurement. VPT was measured with Bio-Thesiometer and age- sex- and height-specific cut-off values were used to assess the presence of DSPN. Incidence rates of DSPN, sex, age and calendar time were modelled by Poisson regression for time-split data and separate for T1D and T2D.

Results From 1996 to 2018 we observe an overall incidence rate of 19.5/100 PY and 15.6/100PY for individuals with T1D and T2D, respectively. For both T1D and T2D, we observe a decreasing incidence rate in the period 2007-2017, similar in all ages (figure 1A,1C). For T1D the incidence rate was decreasing with higher age, but without sex differences (figure 1B). Whereas for T2D we observe an increasing incidence rate with higher age, also without sex differences (figure 1D).

Conclusion This cohort study demonstrated a declining incidence rate of DSPN in both T1D and T2D since 2007. With increasing age, individuals with T1D and T2D have, respectively, declining and increasing incidence rates of DSPN.

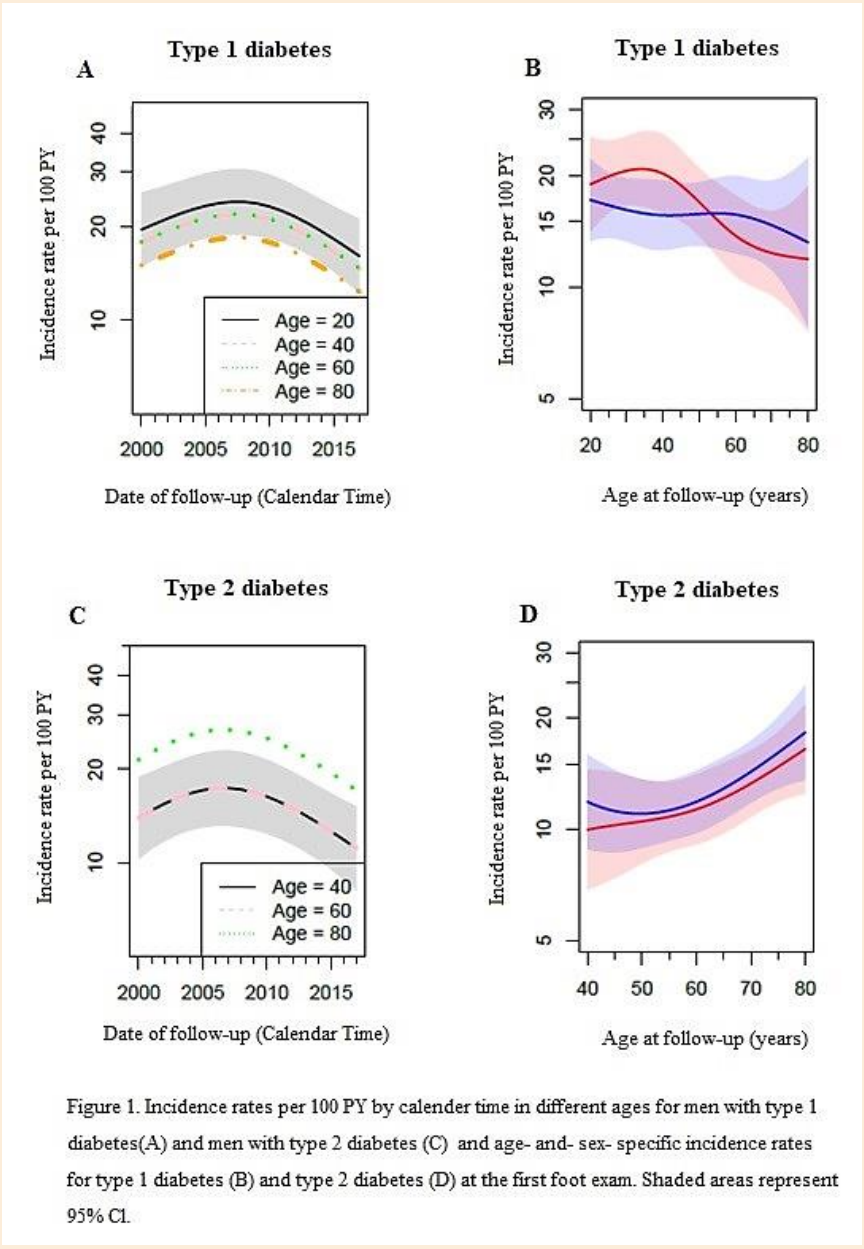

Figure 1. Incidence rates per 100 PY by calender time in different ages for men with type 1 diabetes(A) and men with type 2 diabetes (C) and age- and- sex- specific incidence rates for type 1 diabetes (B) and type 2 diabetes (D) at the first foot exam. Shaded areas represent 95% CI.

O7. Normative corneal nerve values for corneal confocal microscopy

Maryam Ferdousi[1], *Alise Kalteniece*[1], Ioannis N Petropoulos[2], Georgios Ponirakis[2], Hoda Gad[2], Adnan Khan[2], Shazli Azmi[1], Golnoosh Motamedi-Ghahfarokhi[3], Handrean Soran[1], Bruce Perkins[4], Dan Ziegler[5], Daniele Pacaud[6], Andrew JM Boulton[1], Nathan Efron[7], Rayaz A Malik[2,1]

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Aim: Corneal confocal microscopy (CCM) is an established ophthalmic imaging tool for the evaluation of neurodegeneration in peripheral and central neurodegenerative diseases. Age-adjusted normative values for CCM parameters are required to enable clinicians to rapidly identify normal from pathological changes. Healthy controls were enrolled from 7 international study centres using a common adopted method to capture, export and analyse CCM images.

Methods: 464 healthy controls from Manchester, Doha, Brisbane, Calgary, Dusseldorf, Toronto, and Utah underwent CCM with the Heidelberg Retina Tomograph III. Six to eight images of the sub-basal corneal nerve plexus were exported and analysed using automated software (ACCMetrics). Three corneal nerve parameters were analysed – corneal nerve fibre density (CNFD), branch density (CNBD) and length (CNFL).

Results: There was a negative association between age and CNFD (r= -0.31, P<0.001), CNBD (r=-0.20, P<0.001) and CNFL (r= -0.25, P<0.001). BMI>30 was negatively associated with CNBD (r=-0.3, P=0.04) and CNFL (r= -0.36, P=0.01. The 0.05th percentile for CCM parameters has been considered as the cut-off points, which are presented in the table 1.

Conclusions: The current study establishes corneal nerve parameter cut-off values to enable clinicians to identify nerve damage.

Table 1. Corneal nerve normative values

Age group (years)	Number of subjects	CNFD (no/mm2)	CNBD (no/mm2)	CNFL (mm/mm2)
5-20	78	29.16 (14.58)	37.50 (10.42)	17.04 (11.27)
20-40	148	28.66 (13.75)	36.74 (9.37)	16.98 (10.34)
40-60	120	24.11 (12.50)	29.16 (6.25)	14.64 (9.20)
>60	84	22.19 (12.50)	27.08 (6.25)	14.24 (7.14)

The results are presented as mean (0.05th percentile)

O8. Greater small nerve fibre deficits in participants with diabetic neuropathic foot ulcers compared to diabetic neuropathy in type 1 diabetes

Jonathan Zhang Ming Lim[1], Jamie Burgess[1], Anne Marshall[1], David Riley[1], Daniel Cuthbertson[1], Cheong Guan Ooi[1], Maryam Ferdousi[2], Alise Kalteniece[2], Rayaz Malik[3], Uazman Alam[1]

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Aim: The development of diabetic foot ulcers (DFU) has an association with peripheral neuropathy (DPN) in type 1 diabetes (T1D). However, there remains a paucity of data on quantification of small nerve deficits in people with DFU.

Objectives: To characterize neuropathy in healthy volunteers (HV), T1D, T1D-DPN, T1D-DFU in relation to neuropathy phenotyping including corneal nerve fibres using corneal confocal microscopy (CCM).

Methods: Neuropathy status of 110 participants HV (n=32),T1D (n =25),T1D-DPN (n=28), and T1D-DFU (n=25) were quantified with McGill-visual analogue score (VAS), neuropathy symptom profile (NSP), neuropathy disability score (NDS), vibration perception threshold (VPT) and sural nerve conduction velocity (SNCV) and amplitude (SNAmp). Corneal nerve fibre length (CNFL), fibre density (CNFD), branch density (CNBD) were quantified.

Results: T1D-DPN and T1D-DFU were older ($p<0.001$), increased duration of diabetes ($p<0.001$) and HbA1c ($p<0.001$) compared to T1D. There were no significant difference in BMI (P=NS), total cholesterol (P=NS), triglycerides (P=NS), and eGFR (P=NS). T1D-DPN and T1D-DFU had greater symptoms: NSP($p<0.0001$), NDS($p<0.0001$), VAS ($p<0.001$). Higher VPT ($p<0.001$) and reduced SNAmp ($P<0.001$) and SNCV ($P<0.001$) was observed in T1D-DPN & T1D-DFU versus T1D. CNFL ($p<0.001$), CNFD ($p<0.001$) and CNBD ($p<0.001$) were reduced in T1D-DPN and T1D-DFU. Comparing DFU vs DPN: CNFD($p=0.009$) and CNFL($p=0.006$) was reduced but not CNBD($p=0.183$).

Conclusion: CCM demonstrates greater deficits in T1D-DFU compared to T1D-DPN. Progressive small nerve fibre loss predicts neuropathic foot ulceration in T1D, thus CCM may risk stratify individuals at risk of foot ulceration.

	HV	T1D	T1D-DPN	T1D-DFU	P value between DPN vs DFU	P value between all groups
Demographics						
Age (years)	41.1±11.3	43.4±13.2	48.3±7.8	49.8±9.2	0.988	**0.012**
Duration Diab (year)	0	16.2±12.3	25.5±11.7	26.9±10.9	0.998	**<0.001**
BMI	24.50±3.8	27.8±4.9	28.9±5.7	28.2±5.7	1.000	0.415
Biochemistry						
HbA1c, mmol/mol	37±4	69±13	78±16	80±17	1.000	**<0.001**
Cholesterol, mmol/L	4.7±0.7	4.4±1.0	4.8±1.2	4.9±0.5	1.000	0.215
HDL, mmol/L	1.4±0.4	1.7±0.4	1.7±0.5	1.5±0.3	1.000	0.212
LDL, mmol/L	2.6±0.8	2.0±0.8	2.4±0.9	2.2±0.6	1.000	0.053
Triglycerides, mmol/L	1.4±0.7	1.5±0.8	1.7±1.1	1.4±0.5	1.000	0.607
eGFR, ml/min/1.73m^2	82±13	81±17	74±20	75±20	1.000	0.298
Symptoms						
VAS (-/10)	0±0	0.6±1.2	5.3±3.0	5.8±2.6	1.000	**<0.001**
NSP (-/38)	0±0	2.1±2.6	11.9±7.2	18.2±5.1	**<0.001**	**<0.001**
NDS (-/10)	0±0	0.6±0.8	5.0±3.1	7.7±2.4	**<0.001**	**<0.001**
VPT, Volts	6.7±2.8	9.2±2.4	15.6±9.0	23.1±8.5	**<0.001**	**<0.001**
SNCV, m/s	49.4±6.7	49.8±5.5	37.6±9.5	33.6±7.0	0.319	**<0.001**
SNAP, ∝V	8.8±3.3	7.5±3.5	3.1±2.0	2.6±2.0	1.000	**<0.001**
Corneal Confocal Microscopy						
CNFL, no./mm^2	16.07±3.79	16.46±3.69	9.20±6.54	5.17±1.82	**0.006**	**<0.001**
CNFD, no./mm^2	24.39±7.16	20.26±6.65	11.33±5.15	6.12±2.90	**0.009**	**<0.001**
CNBD, no./mm^2	25.50±9.62	22.33±11.06	11.13±7.05	6.03±4.24	0.183	**<0.001**

O9. Distal corneal small nerve fibre damage in subjects with obesity

Zohaib Iqbal[1,2], *Maryam Ferdousi*[1,2], Alise Kalteniece[1,2], Shazli Azmi[1,2], Safwaan Adam[1], Jan Ho[1], Yifen Liu[1], Rachelle Donn[1], Akheel Syed[1,3], Basil Ammori[1,4,5], Rayaz Malik[1,6], Handrean Soran[1,2]

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Background: Subjects with obesity have central corneal nerve loss and patients with diabetic neuropathy have greater corneal nerve loss at the inferior whorl. In this study, we assessed whether there is evidence for a dying-back neuropathy in subjects with obesity with and without diabetes.

Methods: 57 obese subjects, with and without diabetes (DM+, n=30; DM-, n=27 respectively) and age- and sex-matched controls (n=21) underwent quantitative sensory and autonomic nerve function testing and corneal confocal microscopy (CCM) including measurement of the inferior whorl length (IWL).

Results: Neuropathy Symptom Profile and Neuropathy Disability Sscore were significantly elevated in obese DM+ ($p<0.0001$; $p=0.001$) and DM- ($p<0.0001$; $p=0.001$) subjects. Vibration perception threshold was significantly higher in DM+ ($p=0.001$). Deep breathing heart rate variability was significantly lower in DM+ ($p=0.01$). Corneal nerve fibre density [26.8 ±6.22 vs 26.8 ±6.01 vs 35.3 ±7.41, $p<0.0001$], branch density [55.4 ±28.2 vs 58.4 ±28.5 vs 88.2 ±31.1, $p<0.001$], fibre length (CNFL) [17.6 ±4.43 vs 19.9 ±5.43 vs 26.7 ±5.31, $p<0.0001$], inferior whorl length (IWL) [17.9 ±6.10 vs 18.6 ±7.42 vs 35.3 ±9.70, $p<0.0001$] and total nerve fibre length (TNFL) [35.5 ±9.58 vs 38.5 ±11.0 vs 62.0 ±12.3, $p<0.0001$] were significantly lower in obese subjects without and with diabetes. In comparison to controls, there was a greater relative difference in IWL compared to CNFL in DM+ (47.3% vs 25.4%) and DM- (49.3% vs 34.1%).

Conclusion: Small fibre nerve damage is greater in the inferior region of cornea as compared to central in obese subjects with or without diabetes.

O10. Subclinical large fibre-, small fibre- and autonomic neuropathy in adolescents with type 1 diabetes and associated risk factors

Vinni Faber Rasmussen[1,2], Mathilde Thrysøe[1], Hatice Tankisi[3], Pall Karlsson[4,5], Esben Thyssen Vestergaard[6], Kurt Kristensen[6], Jens Randel Nyengaard[5], Klaus Krogh[7], Christina Brock[8], Astrid Juhl Terkelsen[1,9]

[1]Danish Pain Research Center, Department of Clinical Medicine, Aarhus University, Aarhus, Denmark. [2]Department of Pediatrics and Adolescents, Randers Regional Hospital, Randers, Denmark. [3]Department of Neurophysiology, Aarhus University, Aarhus, Denmark. [4]Department of Clinical Medicine, Aarhus University, Aarhus, Denmark. [5]Core Centre for Molecular Morphology, Section for Stereology and Microscopy, Aarhus University, Aarhus, Denmark. [6]Steno Diabetes Center Aarhus, Aarhus, Denmark. [7]Department of Hepatology and Gastroenterology, Aarhus University Hospital, Aarhus, Denmark. [8]Department of Gastroenterology, Aalborg University Hospital, Aalborg, Denmark. [9]Department of Neurology, Aarhus University Hospital, Aarhus, Denmark

Aim: To estimate the prevalence of large fibre- (LFN), small fibre- (SFN), and autonomic neuropathy in a selected group of adolescents with type 1 diabetes.

Methods: Sixty adolescents with type 1 diabetes (15-18 years, diabetes duration >5 years) and 23 control subjects were enrolled. Gold standard diagnostic tests for LFN, SFN, and autonomic neuropathy were performed, including nerve conduction studies, skin biopsies determining intraepidermal nerve fibre density, quantitative sudomotor axon reflex test, cardiovascular reflex tests, tilt table test analyzing orthostatic parameters, and wireless motility capsule recording gastrointestinal transit times.

Results: The prevalence of diabetic subclinical LFN was 39%, SFN up to 38% depending on diagnostic methods, and early and definite cardiovagal neuropathy were 32% and 8%, respectively. Orthostatic intolerance and -hypotension were present in 7% and 27%, respectively, and one participant syncopated. Abnormal gastrointestinal transit times was seen in 42%. Higher height, plasma triglycerides, total daily and basal insulin dose, systolic blood pressure, HbA1c, and less time in hypoglycemia were observed in the group with neuropathy compared with patients without. Higher relative risk for neuropathy were found in patients with triglycerides ≥2 mmol/l and an alcohol consumption ≥8 units per week.

Conclusion: We found a relative high prevalence of subclinical neuropathy in adolescents with type 1 diabetes. This highlights the need for more focus on how to avoid, screen, and monitor neuropathy in adolescents with diabetes. Identifying risk factors for developing neuropathy and progression seems relevant to prevent accompanying symptoms.

O11. The impact of diabetic neuropathy definition on the diagnostic performance of corneal confocal microscopy

Ioannis N. Petropoulos[1], Maryam Ferdousi[2], Shazli Azmi[2,3], Georgios Ponirakis[1], Omar Asghar[2], Alise Kalteniece[2], Maria Jeziorska[2], Andrew Marshall[4,2], Caroline Abbott[5], Uazman Alam[6,2], Handrean Soran[2,3], Rayaz A. Malik[1,]

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Aims: There is an exponential increase in studies worldwide exploring the diagnostic utility of corneal confocal microscopy (CCM) as a biomarker of diabetic peripheral neuropathy (DPN). However, the diagnostic yield of CCM depends on how DPN is assessed. We aimed to determine the impact of different case definitions of DPN on the diagnostic performance of CCM.

Methods: 418 patients with T1/T2D and 72 controls underwent assessment for DPN and CCM for corneal nerve fiber length (CNFL, mm/mm2). DPN definitions were as follows: visual analogue scale (VAS)>2; neuropathy symptom profile (NSP)>1; neuropathy disability score (NDS)>2; vibration perception threshold (VPT)>15V; peroneal motor nerve conduction velocity (PMNCV)<40m/s;

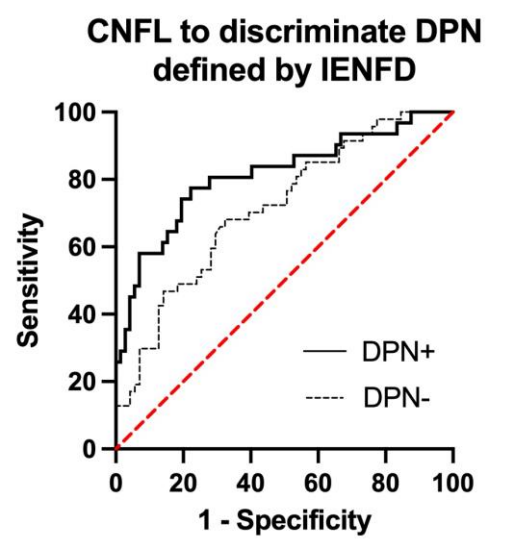
Toronto

criteria for confirmed DPN; and abnormal intra-epidermal nerve fiber density (IENFD). Area under the receiver operating characteristic (AUROC) curve analysis was performed to assess CNFL ability to discriminate between controls, patients without (DPN-) / with (DPN+).

Results: For DPN defined by VAS: CNFL for DPN- AUROC=0.71, sensitivity/specificity=0.65/0.63; for DPN+ AUROC=0.79,

sensitivity/specificity=0.7/0.7. DPN by NSP: CNFL for DPN- AUROC=0.72, sensitivity/specificity=0.7/0.6; for DPN+ AUROC=0.75, sensitivity/specificity=0.71/0.7. DPN by NDS: CNFL for DPN- AUROC=0.68, sensitivity/specificity=0.7/0.5; for DPN+ AUROC=0.74, sensitivity/specificity=0.7/0.69. DPN by VPT: CNFL for DPN- AUROC=0.64, sensitivity/specificity=0.6/0.6; for DPN+ AUROC=0.8, sensitivity/specificity=0.77/0.7. DPN by PMNCV: CNFL for DPN- AUROC=0.69, sensitivity/specificity=0.68/0.62; for DPN+ AUROC=0.8, sensitivity/specificity=0.76/0.71. DPN by Toronto: CNFL for DPN- AUROC=0.68, sensitivity/specificity=0.7/0.53; for DPN+ AUROC=0.81, sensitivity/specificity=0.8/0.7. DPN by IENFD: CNFL for DPN- AUROC=0.7, sensitivity/specificity=0.64/0.63; for DPN+ AUROC=0.81, sensitivity/specificity=0.81/0.72.

Conclusions: The diagnostic performance of CCM improves when objective criteria, such as IENFD, are used to define DPN.



16 / SEPTEMBER / 2022 / 15:20-17:00

Oral presentations (O12-O18) Young investigators award for the best presentation

Chairs: Fabiana Picconi (Rome, Italy) and Peter Kempler (Hungary)

O12. Systemic low-grade inflammation in diabetes is associated with gastrointestinal transit times

Tina Okdahl1, Anne-Marie Wegeberg1,2, Anne Birthe Helweg Jensen1, Sarah Thorius Jensen1, Helene Riis Pontoppidan Andersen1, Joachim Størling3, Birgitte Brock3, Christina Brock1,4,5

1Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg University Hospital, Aalborg, Denmark. 2Thisted Research Unit, Aalborg University Hospital Thisted, Thisted, Denmark. 3Steno Diabetes Center Copenhagen, Herlev, Denmark. 4Department of Clinical Medicine, Aalborg University, Aalborg, Denmark. 5Steno Diabetes Center Northern Jutland, Aalborg, Denmark

Aim: Gastroparesis is a common complication to diabetes and may be the result of neuronal damage to the enteric nervous system. Systemic low-grade inflammation is known to facilitate neurotoxicity, and an association between circulating proinflammatory factors and peripheral neuropathy have previously been reported. The aim was to explore whether an association between systemic inflammation and objective measures of gastroenteropathy is present.

Methods: 156 people with diabetes (type 1: 56, type 2: 100) were included. Plasma levels of interleukin (IL)-6, IL-8, IL-10, tumor necrosis factor (TNF)-α, and interferon (IFN)-γ were measured by multiplex technology. A wireless motility capsule was used for assessment of segmental transit times of the gastrointestinal tract. Differences in cytokine concentrations between participants with normal or prolonged transit times were investigated by statistical appropriate methods.

Results: Concentrations of pro-inflammatory cytokines IL-8 and TNF- α were significantly elevated in people with diabetes and prolonged gastric emptying (IL-8: median 15.2 vs. 11.0, p=0.011, TNF- α : median 1.6 vs. 1.3, p=0.021). Contrary, participants with prolonged colonic transit had lower levels of IL-6 (median 0.3 vs. 0.7, p=0.037). No differences were observed for IL-10, IFN- γ , or small bowel transit.

Conclusions: Diabetes-induced prolonged gastric emptying was associated with increased levels of IL-8 and TNF- α , while low levels of IL-6 were associated with prolonged colonic transit. These findings warrant further research within the area and raise the question as to whether anti-inflammatory strategies could be applied in the therapeutic management of gastroparesis and constipation.

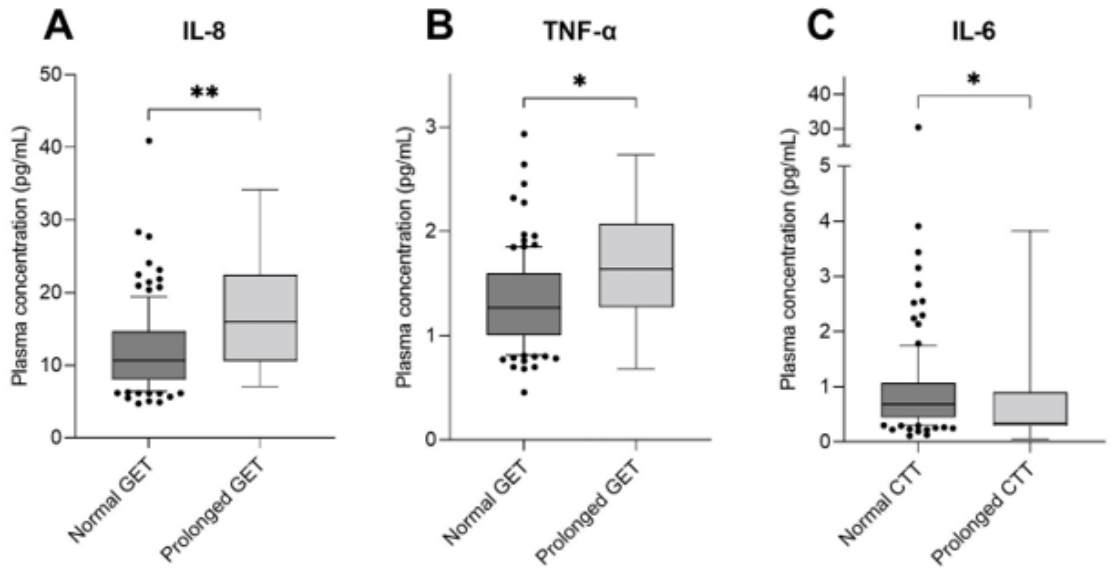


Figure 1: Plasma concentrations of selected cytokines in diabetes (type 1 and type 2) with A/B) normal GET (n=116) and prolonged GET (n=17), and C) normal CTT (n=122) and prolonged CTT (n=11). * p<0.05; ** p<0.01. GET: Gastric emptying time; CTT: Colonic transit time

O13. Visceral adiposity is associated with autonomic dysfunction in adults with autoimmune diabetes

Ernesto Maddaloni, *Luca D'Onofrio*, Mikiko Watanabe, Raffaella Cassano Cassano, Davide Masi, Rocco Amendolara, Sara Sterpetti, Chiara Moretti, Antonio Siena, Lucio Gnessi, Raffaella Buzzetti

Department of Experimental Medicine, "Sapienza" University of Rome, Rome, Italy

Aim: In this study we aimed to evaluate whether visceral adiposity is associated with autonomic dysfunction and cardiac autonomic neuropathy (CAN) in people with autoimmune diabetes (AD).

Methods: Body mass composition was assessed in 63 adults with AD (37 females; mean age ±SD: 49.7±12.5years; BMI: 25.7±4.9Kg/m2) using dual-energy X-ray absorptiometry (DXA). The Composite Autonomic Symptom Score 31 (COMPASS31) was used to assess the presence of symptoms of autonomic dysfunction in six domains (orthostatic, vasomotor, secretomotor, gastrointestinal, bladder and pupillomotor). Cardiac autonomic reflex tests (CART) were performed to investigate the presence of CAN in 49 participants (14 subjects were not able to perform CART). Medical history and biochemical data were retrieved from medical records.

Results: Mean weighted COMPASS31 was 15.9±13.2 and CAN was diagnosed in 22(44.9%) participants. After adjustment for age, sex, HbA1c and HDL cholesterol, higher visceral adipose tissue (VAT) mass was associated with higher COMPASS31 in the gastrointestinal domain (adjusted beta coefficient [95%-CI]: 1.69 [0.14-3.23], p=0.033), but not with total COMPASS31 (adjusted beta coefficient [95%-CI]: -0.30 [-0.76-16.0], p=0.19). Subjects with CAN showed higher VAT mass than those without CAN (512.8±217.2g vs 366.0±221.9g, p=0.037 after adjustment for age, sex, HbA1c and HDL cholesterol). Conversely, total body fat mass was not associated with COMPASS31 nor with the presence of CAN.

Conclusion: This study shows that VAT, but not total body fat, is associated with autonomic dysfunction in people with AD, highlighting the need for research into the interrelated consequences of obesity among individuals with AD.

O14. Corneal confocal microscopy detects small nerve fibre damage in patients with heterozygous familial hypercholesterolemia which ameliorated after treatment with PCSK9 inhibitor therapy

Maryam Ferdousi[1], Alise Kalteneice[1], Ruth Eatough[2], Kirsty Nicholson[2], Rayaz Malik[3], Handrean Soran[4]

[1]The University of Manchester, Manchester, United Kingdom. [2]Manchester University NHS Foundation Trust, Manchester, United Kingdom. [3]3Weill Cornell Medicine-Qatar, Doha, Qatar. [4]Manchester University Hospitals, Manchester, United Kingdom

Background: Hyperlipidaemia may play an important role in the development and progression of small fibre neuropathy. We aimed to assess if small nerve fibre damage occurs in patients with Heterozygous Familial Hypercholesterolemia (HeFH) and to determine if treatment with PCSK9 monoclonal antibodies, improves nerve damage, utilising corneal confocal microscopy (CCM).

Methods: Fifty four patients with FH and twenty-one age-matched healthy controls underwent assessment of fasting lipid profile and HbA1c. CCM was undertaken at baseline and 12 months after starting the treatment with PCSK9 monoclonal antibodies and corneal nerve fibre density (CNFD)(no./mm^2), branch density (CNBD)(no./mm^2), length (CNFL)(mm/mm^2), and inferior whorl length (IWL)(mm/mm$^{2)}$ were quantified.

Results: At baseline, total cholesterol (7.57±1.93 vs. 5.29.±0.82 mmol/L,P<0.0001) and LDL-cholesterol (5.44±1.8 vs. 2.93±0.67 mmol/L,P<0.0001) were higher while CNFD (24.44±4.53 vs. 34.87±8.13,P<0.0001), CNBD (64.03±25.9 vs. 85.46±32.56,P=0.01), CNFL (21.43±4.72 vs. 26.18±6.21,P=0.001) and IWL (25.36±8.54 vs. 33.92±10.32,P=0.001) were lower in patients compared to controls. Treatment with PCSK9 monoclonal antibodies resulted in a significant reduction in LDL-cholesterol (P<0.0001) and an increase in CNFD (P<0.0001), CNBD (P<0.0001), CNFL (P<0.0001) and IWL (P=0.03) comparing baseline to 12 months.

Conclusions/implications: This study shows that patients with HeFH have evidence of small fibre neuropathy and treatments with PCSK9 monoclonal antibodies promote corneal nerve fibre regeneration. This may suggest a potential therapeutic target for the treatment of diabetic peripheral neuropathy.

O15. Does a simple clinical scoring system complement COMPASS 31 in predicting cardiovascular autonomic neuropathy in type 1 and type 2 diabetes?

Ilenia D'Ippolito, Marika Menduni, Cinzia D'Amato, Carla Greco, Martina Leoni, Davide Lauro, Vincenza Spallone

Endocrinology, Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy

Aim: The Composite Autonomic Symptom Score (COMPASS) 31 is a validated questionnaire for autonomic symptoms of diabetic neuropathy. A clinical-based scoring system (CAN Risk Score) has been built to predict cardiovascular autonomic neuropathy (CAN) in type 1 (T1D) and type 2 diabetes (T2D). This study aimed to evaluate if the combined use of CAN Risk Score and COMPASS-31 allows a better diagnostic performance for CAN than their single use.

Methods: Seventy-one patients with T1D (age 42±13 years, duration 25±11 years, 26 men) and 101 with T2D (age 62±9 years, duration 10±8 years, 71 men), free from conditions affecting autonomic function, completed COMPASS-31 before undergoing four cardiovascular reflex tests (CARTs). CAN Risk Score was based on resting heart rate, HbA1c, retinopathy, nephropathy, cardiovascular disease in both T1D and T2D, and on HDL cholesterol, systolic blood pressure, and smoking in T1D or insulin treatment and physical activity in T2D (range 0-10).

Results: Confirmed CAN was present in 22.5% of T1D and 10.9% of T2D. The combined use of COMPASS-31 and CAN Risk Score obtained an area under the ROC curve (AUC) in predicting confirmed CAN significantly greater compared to COMPASS-31 in both T1D (0.841±0.053 Vs. 0.701±0.075, P=0.0161) and T2D (0.875±0.063 Vs. 0.591±0.099, P=0.005) and better diagnostic characteristics (Table).

Conclusions: The combined use of COMPASS-31 and CAN Risk Score improves their diagnostic performance and allows a screening strategy for CAN, suggesting CAN absence with combined normality, and increasing the odds of CAN with combined abnormality.

Table. Diagnostic characteristics for confirmed CAN of COMPASS 31 Total Weighted Score and CAN Risk Score when used alone or in combination. PPV: positive predictive value; NPV: negative predictive value. 95% confidence intervals in brackets.

Type	Abnormality	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
T1D	CAN Risk Score (≥4)	81.2 (62.1-100.4)	70.9 (58.9-82.9)	44.8 (26.7-62.9)	92.9 (85.1-100.6)
	COMPASS 31 (≥16.44)	81.2 (62.1-100.4)	58.2 (45.1-71.2)	36.2 (20.4-51.8)	91.4 (82.1-100.7)
	COMPASS 31+CAN Risk Score	68.7 (46.0-91.5)	**87.3** (78.5-96.1)	61.1 (38.6-83.6)	90.6 (82.7-98.4)
	COMPASS 31 and/or CAN Risk Score	**93.7** (81.9-105.6)	41.8 (28.8-54.8)	31.9 (18.6-45.2)	95.8 (87.8-103.8)
T2D	CAN Risk Score (≥4)	81.8 (59.0-104.6)	73.3 (64.2-82.5)	27.3 (12.1-42.5)	97.1 (93.0-101.1)
	COMPASS 31 (≥16.44)	54.5 (25.1-84.0)	48.9 (38.6-59.2)	11.5 (2.85-20.2)	89.8 (81.3-98.3)
	COMPASS 31+CAN Risk Score	45.5 (16.0-74.9)	**86.7** (79.6-93.4)	29.4 (7.75-51.1)	92.9 (87.3-98.4)
	COMPASS 31 and/or CAN Risk Score	**90.9** (73.9-107.9)	35.6 (25.7-45.4)	14.7 (6.29-23.1)	97.0 (91.1-102.8)

O16. Functional alterations in brain regions involved in sensory processing in diabetic peripheral neuropathy and neuropathic pain

Suganthiya S Croosu[1,2,3], Johan Røikjer[2,4], Carsten Dahl Mørch[4], Niels Ejskjaer[2,5,3], Jens Brøndum Frøkjær[1,3], Tine Maria Hansen[1,3]

[1]Aalborg University Hospital, Department of Radiology, Aalborg, Denmark. [2]Aalborg University Hospital, Steno Diabetes Center North Denmark, Aalborg, Denmark. [3]Aalborg University, Department of Clinical Medicine, Aalborg, Denmark. [4]Aalborg University, Center for Neuroplasticity and Pain (CNAP), SMI, Department of Health Science and Technology, Aalborg, Denmark. [5]Aalborg University Hospital, Department of Endocrinology, Aalborg, Denmark

Aim: This study investigated functional connectivity of brain regions involved in sensory processing in diabetes with and without diabetic peripheral neuropathy(DPN) and neuropathic pain. The associations between the functional connectivity to peripheral nerve function and pain scores were further investigated.

Methods: This cross-sectional study included 60 type 1 diabetes individuals and 20 healthy controls. Resting-state functional magnetic resonance imaging were utilized to investigate functional connectivity. Nineteen individuals with type 1 diabetes and neuropathic pain, 19 with type 1 diabetes and DPN, 18 with type 1 diabetes without DPN, and 20 healthy controls were included in the seed-based connectivity analysis for thalamus, postcentral gyrus, and insula. The connectivity parameters were used for correlation analysis to peripheral nerve functions and pain scores.

Results: Overall, thalamus and postcentral gyrus showed higher connectivity to motor areas in diabetes without DPN compared to diabetes with neuropathic pain and healthy controls (all $p \leq 0.029$). Poorer peripheral nerve functions and higher pain scores were associated with lower connectivity of thalamus and postcentral gyrus (all $p \leq 0.043$). No connectivity differences were found in insula (all $p \geq 0.071$).

Conclusions: Higher functional connectivity of thalamus and postcentral gyrus only appeared in diabetes without neuropathic complications. Thalamic/postcentral gyral connectivity demonstrated an association with peripheral nerve functions. Based on thalamic connectivity, it was possible to

distinguish between type 1 diabetes with DPN/neuropathic pain and type 1 diabetes without DPN. The current study may contribute to a further understanding of functional alterations of regions involved in sensory processing in diabetes.

O17. Neurotransmitter enriched resting state functional MRI - a new mechanistic-informed biomarker for predicting treatment response in diabetic painful neuropathy

Kevin Teh[1], James McAllister[1], Arpana Anandhanarayanan[1], Gordon Sloan[2], Solomon Tesfaye[2], Dinesh Selvarajah[1]

[1]University of Sheffield, Sheffield, United Kingdom. [2]Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom

Aim: The neurobiological mechanisms underlying treatment response in painful diabetic neuropathy are poorly understood. We have demonstrated that responders to neuropathic pain treatment have greater functional connectivity between the insula cortex and the corticolimbic system compared to non-responders. Activity within these networks is mediated by endogenous opioid receptor systems and may hold clues to possible future treatment targets.

Methods: 43 painful-DN subjects [responders (VAS<4; n=29) and non-responders (VAS>4; n=14)] underwent detailed clinical and neurophysiological assessment, and RS-fMRI. Data analysis was performed using the NITRC Functional ConnectivityToolbox and SPM8 in MatLab. RS-fMRI data was masked and binarised using an opioid receptor atlas to restrict the analysis to the voxels with high receptor density. Subject-specific spatial maps of responders and non-responders were compared.

Results: Compared to painful-DN non-responders, responders had greater functional connectivity between the corticolimbic system with the opioid receptor networks [F(2)(41)=43.53;intensity=128.7; R-amygdala beta=0.48; p-FDR<0.0001; R-putamen beta=0.3; p-FDR<0.0001; dorsal lateral prefrontal cortex beta=0.25; p-FDR=0.0002 and the posterior parietal cortex networks beta0.25; p-FDR=0.0002].

Conclusion: Painful DN treatment responders have better target engagement of opioid receptors systems compared to non-responders. Whilst further clinical validation in larger cohorts is warranted, our findings suggests that a functioning/intact descending pain inhibition network is crucial for a better pain response. Interventions targeted at this network could provide better pain relief in non-responders to neuropathic pain treatment.

O18. A novel data-driven machine learning approach to identify subtypes of painful diabetic neuropathy from resting-state functional magnetic resonance imaging

Kevin Teh [1], James McAllister[1], Aparna Anandhanarayanan[1], Gordon Sloan[2], Solomon Tesfaye[2], Dinesh Selvarajah[1]

[1]University of Sheffield, Sheffield, United Kingdom. [2]Sheffield teaching hospitals NHS Foundation Trust, Sheffield, United Kingdom

Aim: The traditional approach for studying the neurobiology of painful diabetic neuropathy (PDN) has followed a diagnostic/clinical framework through case-control studies. This approach has failed to deliver on hoped-for biomarkers. Our primary aim was to delineate the neurobiological heterogeneity in PDN by first defining the functional connectivity subtypes in patients then assessed the clinical significance with respect to prediction of clinical outcome with treatment.

Methods: 82 PDN subjects and 36 HV underwent detailed clinical and neurophysiological assessment and resting state functional MRI (RS-fMRI). Painful-DN subjects were divided into training (n=48) and testing (n=34) datasets. Painful-DN disease subtypes were identified via unsupervised and supervised machine learning (k-means algorithm) of the functional connectivity of key somatosensory/nociceptive brain regions. Responders and non-responders were defined as VAS<4 (n=23) and VAS>4 (n=11) respectively.

Results: RS-fMRI functional connectivity defines two clinically relevant PDN subtypes. The two subtypes were characterised by strong functional connectivity differences in the postcentral ($p<0.001$, 95%CI=0.22:0.65) and precentral ($p=0.002$, 95%CI=0.15:0.59) parietal cortex functional connectivity. The interhemispheric connectivity between homologous regions was also notable. Functional connectivity differences in the default mode network ($p=0.002$; 95%CI=-0.35:-0.08) was also identified. The performance of our unsupervised k-means model to predict treatment response was: accuracy=0.77, recall=0.83, precision=0.83 and an AUC=0.73.

Conclusion: We have identified neurobiological markers of clinically relevant subtypes of PDN using an unsupervised data-driven approach. The subtype whose functional connectivity differed most from healthy controls failed to respond to treatment. Our data-driven approach may constitute a generalizable solution to elucidate the clinical heterogeneity of PDN.

Day 2

17 / SEPTEMBER / 2022 / 08:30-09:45

Oral presentations (O19-O23) Epidemiology and natural history

Chairs: Anna Korei (Budapest, Hungary) and Christian Stevns Hansen (Herlev, Denmark)

O19. Autonomic and sensory neuropathy with multiple etiology in kidney transplanted patients

Tamás Várkonyi[1], Anna Vágvölgyi[1], Bernadett Borda[2], Andrea Orosz[3], Mónika Szűcs[4], Attila Nemes[1], György Lázár[2], István Baczkó[3], Péter Kempler[5], Csaba Lengyel[1]

[1]Department of Medicine, Uiniversity of Szeged, Szeged, Hungary. [2]Department of Surgery, University of Szeged, Szeged, Hungary. [3]Department of Pharmacology and Pharmacotherapy, University of Szeged, Szeged, Hungary. [4]Department of Medical Physics and Informatics, University of Szeged, Szeged, Hungary. [5]Department of Oncology and Internal Medicine, Semmelweis University, Budapest, Hungary

Aim: The present study aimed to assess the peripheral and autonomic neuronal functions in kidney transplanted (KTx) patients and to compare it to healthy controls.

Methods: The study involved 23 KTx patients, 8 of 23 patients had diabetes. The control group consisted of 19 individuals. All KTx patients and controls underwent an ECG, 5 standard Ewing-tests and a neuronal testing with Neurometer, Neuropad-test, Tiptherm, Monofilament and Rydel-Seiffer tuning folk.

Results: The heart rate response to deep breathing (controls vs. KTx patients: 21.21±6.93 vs. 16.7±5.89, p=0.045), the heart rate response to standing up (30/15 ratio controls vs. KTx patients: 1.20±0.15 vs. 1.07±0.16, p=0.007), and the systolic blood pressure response to standing up (controls vs. KTx patients: 4.63±6.07 vs. 12.26±13.66, p=0.022) were impaired in the KTx patients.

At the median and the peroneal nerves, the sensory testing revealed increased current perception thresholds (CPT) compared to controls at all tested frequencies. A correlation was found between the heart rate response to deep breathing and the eGFR (p=0.007, r=0.549), and between creatinine level and the Valsalva-ratio in the KTx group (p=0.04, r=-0.432). The glucose correlated with the CPT value of the peroneal nerve at 5 Hz stimulation (p=0.025, r=0.46).

Conclusion: Cardiovascular autonomic dysfunction and peripheral sensory neuropathy were detected in KTx patients compared to the controls. The renal impairment and the higher glucose levels correlated with some dysfunctions of the nervous system. Our observations prove the presence of neuropathy in KTx patients with multiple etiology

O20. Clinical phenotypes of neuropathic symptoms in type 2 diabetic patients: A multicenter study

Yu Ji Kim[1], *Tae Sun Park*[1], Heung Yong Jin[1], Kynung Ae Lee[1], Dong Sun Kim[2], Kyu Jeung Ahn[3], Jong Chul Won[4]

[1]Department of Internal Medicine, Division of Endocrinology and Metabolism, Medical School, Research Institute of Clinical Medicine of Jeonbuk National University - Biomedical Research Institute of Jeonbuk National University Hospital, Jeonju, Korea, Republic of. [2]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea, Republic of. [3]Department of Endocrinology and Metabolism, Kyung Hee University School of Medicine, Seoul, Korea, Republic of. [4]Division of Endocrinology and Metabolism, Department of Internal Medicine, Cardiovascular and Metabolic Disease Center, Inje University Sanggye Paik Hospital, Inje University College of Medicine, Seoul, Korea, Republic of

Aim: Diabetic peripheral neuropathy (DPN) is the most common complication of diabetes and it is known that the symptoms that patients complain of are very diverse. The purpose of this study is to classify DPN patients by subjective symptoms and identify the relationship between intensities of patterns of symptoms and clustered group of patients with DPN.

Methods: The present multi-center study analyzed epidemiological data and sensory symptoms of 649 patients with DPN. Data acquisition included standard demographic questions and self-report questionnaires. Cluster analysis was used to identify subgroups of patients with characteristic symptom profiles. Furthermore, factor analysis was performed to investigate symptom patterns of clustered group of patients with DPN.

Results: Three clusters of patients with DPN were identified: severe symptoms with decreased quality of life (QOL) (cluster 1, n =119, 18.3%), predominantly insensate symptoms with relatively good QOL (cluster 2, n = 318, 49.0%), and moderate pain intensity and decreased QOL (cluster 3, n = 204, 31.4%). Patients in cluster 1 were characterized by higher levels of fasting blood glucose and longer duration of diabetes compared with clusters 2 and 3. The frequency of symptoms on each item of MNSI showed a similar distribution according to pain intensities along with the three clusters.

Conclusions: The present cluster and factor analyses support the hypothesis that diversity in sensory symptoms exists in patients with DPN. Heterogeneity in the patient with DPN should be taken into account for a more stratified or individualized treatment approach.

O21. Painful diabetic peripheral neuropathy in type 1 diabetes (T1D) in the Epidemiology of Diabetes Interventions and Complications (EDIC) study

Barbara Braffett[1], Laure El ghormli[1], James Albers[2], Eva Feldman[2], Rose Gubitosi-Klug[3], William Herman[2], Catherine Martin[2], Trevor Orchard[4], Bruce Perkins[5], Neil White[6], John Lachin[1], *Rodica Pop-Busui* [2]

[1]George Washington University, Rockville, MD, USA. [2]University of Michigan, Ann Arbor, USA. [3]Case Western Reserve University, Cleveland, USA. [4]University of Pittsburg, Pittsburg, USA. [5]University of Toronto, Toronto, Canada. [6]Washington University, St Louis, USA

Aims: We evaluated the prevalence, incidence and risk factors associated with painful diabetic peripheral neuropathy (DPN) in participants with T1D enrolled in the EDIC study, an observational follow-up of the Diabetes Control and Complications Trial.

Methods: Data were obtained from 1,401 participants followed for 26 years during EDIC. Painful DPN was defined as a positive response to specific neuropathic pain questions (Q2, Q6) of the Michigan Neuropathy Screening Instrument (MNSI) questionnaire, plus a MNSI examination score >2. Sustained painful DPN was defined as occurring on 2 or more consecutive annual visits. Kaplan-Meier estimates were used to describe the 26-year cumulative incidence of the first occurrence of any sustained painful DPN.

Results: Over the 26-year EDIC follow-up, 889 participants (63.5%) did not experience any painful DPN, while 512 (36.5%) experienced painful DPN at least once, of which 263 (18.8%) met the criteria for sustained painful DPN. After adjusting for covariates, participants with sustained painful DPN had significantly higher BMI, waist circumference, systolic blood pressure, heart rate, total and LDL cholesterol, triglycerides and HbA1c levels over time versus participants without any painful DPN ($p<0.0005$for all). Among the 1,348 participants without painful DPN at EDIC year 1, the 26-year cumulative incidence of sustained painful DPN was 18%.

Conclusion: In this large cohort of well-characterized T1D participants, the prevalence of neuropathic pain and DPN increased steadily over the 26-year follow-up. These data also suggest that differences in several cardiometabolic risk factors, in addition to glucose control, may contribute to differences in painful DPN risk.

O22. Is it depression? Depressive symptoms at baseline are associated with the onset of diabetic peripheral neuropathy within 10 years following T2DM diagnosis

Dulce Alarcon Yaquetto [1], Prashanth Vas[2], Kirsty Winkley-Bryant[1], Michael Edmonds[2], Khalida Ismail[1]

[1]King's College London, London, United Kingdom. [2]King's College Hospital, London, United Kingdom

Background: Diabetic peripheral neuropathy (DPN) is a common complication in patients with Type-2 diabetes (T2DM). Early identification of patients more at risk is needed to enhance preventive strategies and achieve better outcomes. It has been proposed that depression is not only a consequence of the burden of living with T2DM but a precedent and accelerator of its onset and complications.

Aim: To assess the association between baseline depressive symptoms at the time of T2DM diagnosis and greater risk of DN 10 years follow-up.

Methods: Cross-sectional analysis of the SOUth London Diabetes (SOUL-D) cohort that recruited newly diagnosed T2DM patients from South London between 2008-2011. In the 10-year follow-up, 339 participants were invited for their physical examination. DPN was measured by vibration perception threshold (VPT) using a neurothesiometer. A VPT of ≥25V was coded as neuropathy. Depressive symptoms were assessed by the PHQ-9 questionnaire with a cut-off of ≥10 indicating the presence of depression.

Results. The prevalence of DPN was 12.1% at follow-up. Patients with DPN were predominantly male, of older age at diagnosis and white (Table 1). In fully adjusted models, baseline presence of depressive symptoms increased the odds of DN 3-fold (Figure 1).

Conclusions. People with depressive symptoms have a greater risk to develop diabetic neuropathy 10 years after the first T2DM diagnosis. Future models which consider depression and diabetes development in parallel are proposed, though epidemiological data suggests depression precedes the metabolic disorder.

Table 1. Characteristic of study sample

	No-DN n=283	DN n=41	P value
Gender (Male) (%)	53.63%	75.61%	<0.001
Age (years)	54.51±10.17	60.05±9.30	0.0011
Ethnicity (White) (%)	47.35%	78.05%	<0.001
HbA1c (%)	6.95±6.96	6.99±1.52	0.88
BMI (kg/m²)	31.82±6.39	33.39±5.22	0.13
Depressive symptoms (Yes) (%)	13.67%	24.39%	0.07
Values are mean±SD or %. P values from two tailed t test or χ^2			

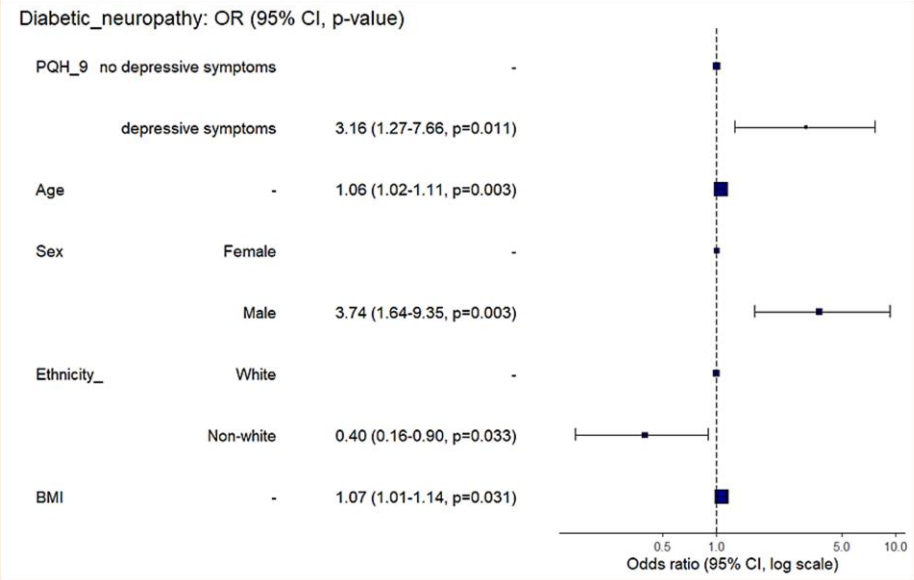


Figure 1. Multivariate odds ratios for depressive symptoms and diabetic neuropathy in T2DM patients

O23. Determining the Sequence of Microvascular Complications: Results of Multistate Markov Modelling in the Diabetes Control and Complications Trial (DCCT)

Leif Erik Lovblom [1,2], Laurent Briollais[1,2], George Tomlinson[3,4], Bruce A. Perkins[1,5,6]

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Aim: Screening for neuropathy is complex and underperformed in practice. If neuropathy rarely occurs first, screening for it could be delayed until retinopathy or nephropathy are documented. To address this, we aimed to definitively determine the sequence of microvascular complications in the natural history of type 1 diabetes (T1D).

Methods: Using data available from the public NIDDK Repository (1983-2012), independent of the DCCT/EDIC research group, we performed a multistate analysis using biostatistics techniques for complex trivariate processes of the 1441 participants with T1D. Retinopathy ('Eye', E), nephropathy ('Kidney', K), and neuropathy ('Nerve', N) were each screened repeatedly and defined by the early-stage phenotypes (Figure 1). Our model accounted for intermittent ascertainment and differing screening schedules.

Results: At baseline, participants had mean age 27±7 years and duration 6±4 years. Markov model simulations started in the absence of complications (Ø). Eye was the most common initial complication (49%), followed by nerve (28%), and kidney (22%). Median time to first complication was 5.3 years. 4% had no complications through follow-up.

Conclusions: While retinopathy is conclusively most common, the high frequency of other initial complications reinforces the current practice of unselected early screening for all three, including neuropathy.

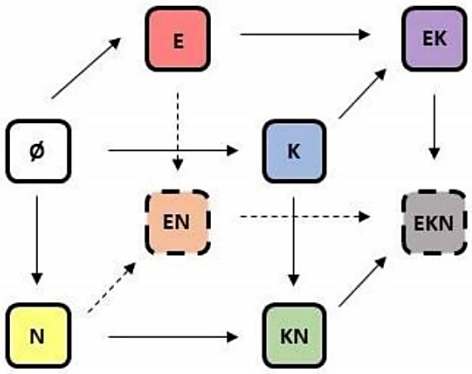

Figure 1. Markov state space of the multistate model. States Ø, E, K, and N defined in text. EK represents eye and kidney complications, EN eye and nerve, KN kidney and nerve, and EKN all 3. The Diabetes Control and Complications Trial (DCCT) and its follow-up the Epidemiology of Diabetes Interventions and Complications (EDIC) study were conducted by the DCCT/EDIC Research Group and supported by National Institute of Health grants and contracts and by the General Clinical Research Center Program, NCRR. The data [and samples] from the DCCT/EDIC study were supplied by the NIDDK Central Repository. This manuscript was not prepared under the auspices of the DCCT/EDIC study and does not represent analyses or conclusions of the DCCT/EDIC study group, the NIDDK Central Repository, or the NIH.

17 / SEPTEMBER / 2022 / 11:30-12:30

Oral presentations (O24-O27) Small fiber and painful neuropathy

Chairs: Dinesh Selvarajah (Sheffield, United Kingdom) and Tae Sun Park (Seoul, Republic of Korea)

O24. The LDI_{FLARE} method predicts the development of incipient diabetes polyneuropathy (DPN) – results of the 5-year longitudinal Ipswich NeuroDiab study

Sanjeev Sharma, Jenna Cross, Gerry Rayman

Ipswich Hospital (ESNEFT), Ipswich, United Kingdom

Aims: In this longitudinal 5-year study, we evaluated the LDI_{FLARE} – a sensitive method for small fibre function - to predict the development of DPN.

Methods: From the cohort of 160 diabetes subjects, 58 without DPN at onset and completed 5 years of follow-up were studied. Incident DPN was defined as progression to a Neurology Disability Sore (NDS) of ≥3. All subjects underwent comprehensive neurological review. We used duration-dependent receiver operating characteristic (ROC) curves to calculate the predictive validity of the baseline LDI_{FLARE} for the development of DPN.

Results: 34 subjects had Type-1 and 24 Type-2 diabetes; 35 females. Mean age(±SD) was 47.1±8.8 years. Mean follow up time was 5.4 years. Of these, 24 (10 T1Dm & 14 T2DM) progressed to a NDS of ≥3 (41%; 7.7 events/100 subject-years). There was a strong correlation with older age, longer duration of diabetes, raised HbA1c and raised triglycerides significance: $p<0.05$). The linear rate of fall of LDI_{FLARE} in newly diagnosed DPN was 0.16 cm2/yr for T1DM and 0.22cm2/yr for T2DM. The area under the ROC curve for LDIFLARE ranged 0.66 - 0.75. The optimal diagnostic threshold for a baseline LDI_{FLARE} of 5.05cm2 was associated with 71% sensitivity, 74% specificity, and a hazard ratio of 3.73 (95%CI 2.14-6.73; $P < 0.01$) for new-onset DPN.

Conclusions: We conclude that the LDI_{FLARE} method with a cut-off of 5.05 cm2 showed good predictive validity for identifying risk of developing DPN. We suggest that the LDIFLARE method may be preferred over conventional large fibre methods in predicting the later development of clinical DPN.

O25. Three-years follow up of retinal neurodegeneration and neuropathic characteristics in paediatric type 1 diabetic patients

Marika Menduni[1], Fabiana Picconi[1], Maria Cristina Parravano[2], Benedetta Russo[1], Alessio Maiorino[1], Laura Chioma[3], Dorina Ylli[4], Stefano Cianfarani[3], Patrizia Ippolita Patera[3], Simona Frontoni[1]

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Aim. The aim of our study is to evaluate the 3-year progression of neuroretinal alteration, the association between these early alterations and diabetic neuropathy (DN) and the role of glycemic variability (GV) and lipids on these changes, in pediatric T1DM subjects.

Methods. Twenty-five patients with T1DM, using CGM and CSII, without complication, and eighteen controls (C) were followed for three years. All subjects underwent an Optical Coherence Tomography, with analysis of neuroretinal layers. In T1DM, metabolic parameters, GV indexes, peripheral (MNSI, thermal threshold and vibration perception threshold-VPT) and autonomic assessment (using CARTs) were investigated. All data were collected at baseline and every 12 months.

Results. During the follow-up, RNFL, OPL and IRT were significantly thinner in T1DM versus C and a progressive reduction in OPL was observed in T1DM ($p<0.05$). In T1DM patients, negative correlations were observed between GV and these neuroretinal layers and between triglycerides and IRT. Among neuropathic characteristics, a negative correlation between the systolic blood pressure fall and OPL and a positive correlation between the VPT and RNFL were observed. Moreover, there was a positive correlation between LBGI and VPT and between MAG and MNSI.

Conclusion. Very early neuroretinal alterations are already present in pediatric T1DM patients without complications, and there is a possible association between these variations and early signs of peripheral and autonomic DN. These data corroborate the hypothesis that RN is an early sign of DN and GV and TG should be efficaciously addressed in the early stage of T1DM.

Correlations between neuroretinal layers and glycemic variability or lipid profile			
Neuroretinal Layer	**Parameter**	**r**	**p Value**
Retinal Nerve Fiber layer (RNFL)	Continuous overall net glycemic action-1h (CONGA 1h)	-0.4	0.05
Outer Plexiform Layer (OPL)	Mean absolute glucose (MAG)	-0.5	0.04
Inner Retinal Thickness (IRT)	Lability Index (LI)	-0.6	0.01
Inner Retinal Thickness (IRT)	Triglycerides	-0.5	<0.01
Correlations between neuroretinal layers and neuropathic characteristics			
Neuroretinal Layer	**Neuropathic parameter**	**r**	**p Value**
Outer Plexiform Layer (OPL)	Delta systolic blood pressure (Orthostatic Hypotension test)	-0.9	0.04
Retinal Nerve Fiber layer (RNFL)	Vibration Perception threshold (VPT)	0.2	0.05
Correlations between neuropathic characteristics and glycemic variability			
Neuropathic parameter	**GV parameter**	**r**	**p Value**
Vibration Perception threshold (VPT)	Low blood glucose index (LBGI)	0.7	0.01
Michigan Neuropathy Screening Instrument (MNSI)	Mean absolute glucose (MAG)	0.7	0.02

O26. Spinal disinhibition: evidence for a hyperpathia phenotype in painful diabetic neuropathy

Anne Marshall [1,2], Alise Kalteniece[2], Maryam Ferdousi[2], Shazli Azmi[2], Edward Jude[3], Clare Adamson[4], Luca D'Onofrio[5], Shaishav Dhage[6], Handrean Soren[2], Corinne Lee-Kubli[7], Shaheen Hamdy[2], Uazman Alam[1], Rayaz Malik[8], Nigel Calcutt[9], *Andrew Marshall*[1,2]

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Aims: Loss of function is the dominant sensory phenotype in painful diabetic polyneuropathy (pDPN). The mechanisms that underlie pain generation in the context of this reduced afferent input remain uncertain. Spinal disinhibition, whereby a loss of spinal inhibition leads to increased ascending nociceptive drive (through amplification or lack of suppression of peripheral signals) is a putative mechanism. Our previous published data demonstrates that in pDPN there is impaired Hoffmann-reflex rate dependent depression (HRDD), a biomarker of spinal disinhibition. Here we aimed to determine whether impaired HRDD is associated with a mechanistically appropriate and distinct pain phenotype in patients with pDPN.

Methods: In this cross-sectional observational study 93 patients with diabetic neuropathy underwent detailed clinical, neuropathy and sensory phenotyping, including DFNS quantitative sensory testing. Tibial nerve HRDD was performed using trains of stimuli at 1, 2 and 3Hz.

Results: Compared to patients with painless diabetic neuropathy, patients with pDPN had impaired HRDD at 1, 2 and 3Hz (p=<0.001). Patients with pDPN exhibited an overall loss of function profile on quantitative sensory testing. However, increasing impairment of HRDD and hence greater spinal disinhibition, was further associated with greater mechanical pain sensitivity, relative heat and cold hyperalgesia and higher ratings of spontaneous burning pain.

Conclusions: These findings support the hypothesis that spinal disinhibition is an important centrally mediated pain amplification mechanism in pDPN. Abnormal HRDD is associated with a distinct phenotype arguably akin to hyperpathia, with combined loss and relative gain of function leading to increasing nociceptive drive.

O27. Thalamic neuronal and mitochondrial function in painful and painless diabetic peripheral neuropathy: a multimodal magnetic resonance spectroscopy study

Gordon Sloan [1], Adriana Anton[2], Iain Wilkinson[2], Dinesh Selvarajah[2], Solomon Tesfaye[1]

[1]Sheffield Teaching Hospitals, Sheffield, United Kingdom. [2]University of Sheffield, Sheffield, United Kingdom

Aim: Our group has previously demonstrated abnormal proton Magnetic Resonance Spectroscopy (1H-MRS) metabolite ratios in the thalamus in patients with Painless-Diabetic Peripheral Neuropathy (DPN), whereas these ratios are preserved in Painful-DPN. We hypothesised that mitochondrial dysfunction, as assessed using 31-Phosphorus MRS (31P-MRS), will be evident in the thalamus in Painless- but not Painful-DPN.

Methods: 38 patients with type 2 diabetes [9 No-DPN, 11 Painless-DPN and 18 Painful-DPN] and 11 healthy volunteers (HV) underwent detailed clinical and neurophysiological assessments and 1H/31P-MRS of the brain at 3 Tesla to assess neurometabolites in the left thalamus. We calculated the N-acetyl aspartate to choline (NAA:Cho) and inorganic phosphate (Pi) to ATP (Pi:ATP) ratios.

Results: There was a significant group effect in both metabolite ratios: NAA:Cho (ANOVA, p=0.013) and Pi:ATP (p=0.021). The NAA:Cho was the lowest in Painless-DPN, reaching significance compared with HV (p=0.001) and Painful-DPN (p=0.019). Additionally, the Pi:ATP was significantly higher in Painless-DPN compared with HV (p=0.013) and Painful-DPN (p=0.008). There was also a significant correlation between the NAA:Cho and Pi:PCr (Pearson's r -0.336, p=0.034).

Conclusion: This is the first study to perform multimodal cerebral 1H- and 31P-MRS in human DPN. We have demonstrated abnormal thalamic 1H- and 31P-MRS ratios in Painless- but not Painful-DPN, suggesting mitochondrial dysfunction may underlie thalamic neuronal dysfunction in Painless-DPN. However, in Painful-DPN there is preservation of thalamic mitochondrial and neuronal function. This study adds further evidence for the thalamus as a potential target for therapeutic intervention in Painful-DPN.

Day 3

18 / SEPTEMBER / 2022 / 08:30-09:30

Oral presentations (O28-O31) Autonomic neuropathy and treatment

Chairs: Tryantafyllos Didangelos (Thessaloniki, Greece) and Eirik Søfteland (Bergen, Norway)

O28. Association of microangiopathic complications and cardiac autonomic neuropathy with cardiac structure and function in asymptomatic patients with type 2 diabetes

Paul Valensi[1], Minh Tuan Nguyen[1], Sara Pinto[1], Patricia Poignard[2]

[1]Unit of Endocrinology-Diabetology-Nutrition, AP-HP, Jean Verdier Hospital, Paris Nord University, Bondy, France. [2]Department of functional explorations. Jean Verdier hospital, Bondy, France

Aim: Diabetic retinopathy and nephropathy have been associated with echocardiographic alterations. The pathophysiology of diabetic cardiomyopathy is plurifactorial. We aimed to examine the association of microangiopathic complications (µApC) and cardiac autonomic neuropathy (CAN) with echocardiographic alterations in patients with type 2 diabetes (T2D).

Methods: We included 699 T2D patients, free of cardiac history and symptom but with other cardiovascular risk factors. They were separated in 4 groups according to the number of µApC among retinopathy, nephropathy and peripheral neuropathy (G0 to G3). An echocardiography was performed, silent myocardial ischemia (SMI, stress myocardial scintigraphy) and CAN (standard tests) were assessed, NT-proBNP was measured.

Results: A higher number of µApC was associated with male gender, age, diabetes duration, hypertension, SMI and CAN ($p<0.01$ for all). Left ventricle systolic dysfunction, dilatation, hypokinesia and hypertrophy were detected in 3.9%, 8.4%, 7.6% and 34.1% of the population, respectively. Hypokinesia was significantly associated with every µApC and CAN, and hypertrophy with retinopathy and nephropathy; the prevalence of hypokinesia and hypertrophy and NT-proBNP levels increased from G0 to G3 ($p=0.04$ to <0.0001). In models including gender, diabetes duration, hypertension, SMI, µApC number and CAN, hypertrophy and NT-proBNP were significantly associated with µApC number and there was a trend towards an association of hypokinesia with CAN ($p=0.07$).

Conclusion: The associations of µApC including neuropathy and the cumulative µApC number with left ventricle structural and functional alterations, independent from confounding factors including SMI, stand for a microvascular contribution to diabetic cardiomyopathy, with a potential role of CAN in hypokinesia.

O29. The PanGut-study: Evoked potentials following rectal balloon distention, a new way of diagnosing diabetic autonomic neuropathy in the gut?

Sondre Meling[1,2], Erling Tjora[2,3], Heike Eichele[4], Rasmus Bach Nedergaard[5,6], Niels Ejskjær[7,8], Eirik Søfteland[2,9]

[1]Department of Medicine, Stavanger University Hospital, Stavanger, Norway. [2]Department of Clinical Science, University of Bergen, Bergen, Norway. [3]Department of Pediatrics and Adolescent Medicine, Haukeland University Hospital, Bergen, Norway. [4]Department of Biological and Medical Psychology, Faculty of Psychology, University of Bergen, Bergen, Norway. [5]Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg University Hospital, Aalborg, Denmark. [6]Department of Clinical Medicine, Aalborg University, Aalborg, Denmark. [7]Steno Diabetes Center North Jutland, Aalborg, Denmark. [8]Department of Clinical Medicine and Endocrinology, Aalborg University Hospital, Aalborg, Denmark. [9]Department of Clinical Medicine, University of Bergen, Bergen, Norway

Aim: To compare established tests for diabetic neuropathy with evoked potentials (EP), following rapid rectal balloon distention, a novel test investigating the gastrointestinal autonomic nerves.

Method: 21 participants with longstanding type 2 diabetes, 15 with prediabetes or untreated type 2 diabetes diagnosis within one year, and 30 healthy controls, all without known autonomic neuropathy, were included. Tests included cardiovascular reflex tests, orthostatic blood pressure and electrical skin conductance assessment, using Sudoscan. Sural nerve test and cutaneous sensitivity to von Frey monofilament were performed to assess large nerve fibre function. EP were measured following rectal balloon distention at earliest sensation (VAS1) and threshold of unpleasant sensation (VAS5).

Results: No between-group differences in terms of nerve function tests or EP measures were found. The pressure needed to reach VAS1 was higher in people with diabetes and prediabetes (combined 0.037+0.013 bar) vs. controls (0.030+0.009 bar), p=0.02. Participants with moderate risk of cardiovascular autonomic neuropathy (CAN) vs. low risk, according to Sudoscan, also needed higher pressure (0.039+0.012 vs 0.030+0.011), p=0.003. Several correlations between EP amplitude and velocity, parameters of cardiovascular reflex and sural nerve tests were detected.

Conclusions: We did not find increased prevalence of neuropathy in diabetes or prediabetes compared to controls. Reduced rectal sensitivity was associated with diabetes and prediabetes, and an elevated risk of CAN, possibly implicating small nerve fibre dysfunction. We conclude that central neuronal signal processing is affected in parallel with peripheral neuronal function and find EP a promising research tool evaluating gut autonomic neuropathy.

O30. Sodium Glucose Cotransporter-2 Inhibitor Protects against Diabetic Neuropathy and Nephropathy in Modestly Controlled Type 2 Diabetes: Follow-up Study

Fukashi Ishibashi[1], Aiko Kosaka[1], *Mitra Tavakoli*[2]

[1]Ishibashi Clinic, Hiroshima, Japan. [2]University of Exeter, Exeter, United Kingdom

Aim: This three-year follow-up study aimed to elucidate whether sodium-glucose cotransporter-2 inhibitors (SGLT2is) have any protection against diabetic neuropathy and nephropathy in patients with type 2 diabetes via reducing variability in glycemia and extraglycemic factors or their averages.

Methods: Two type 2 diabetic cohorts of 40 and 73 patients treated with or without SGLT2i along with 60 control subjects were recruited. Two diabetic cohorts matched for HbA1c levels and oral hypoglycemic agents other than SGLT2is underwent glycemic control with or without SGLT2is more than two years. The urinary albumin to creatinine ratio (ACR), estimated glomerular filtration rate (eGFR) and neuropathy outcome measures and mean Z-score of 8 neurophysiological tests were determined at the baseline and endpoint. Glycemic variability, evaluated by the coefficient of variation of monthly measured HbA1c levels and casual postprandial plasma glucose (CPPG).

Results: The glycemic variability and variability of some extraglycemic factors in SGLT2i cohort were smaller than those in non-SGLT2i cohort. However, only smaller coefficient of variation of HbA1c improved some neuropathy outcome measures, and ameliorated eGFR decline. SGLT2i improved the Z-score of neurophysiological tests. The optimized changes in the blood pressure, HDL-cholesterol and uric acid by SGLT2i led to neurological and renal protection. SGLT2i decreased the prevalence of nephropathy significantly and the prevalence of neuropathy insignificantly.

Conclusion: Over 3 years period, SGLT2i significantly improved some neuropathy outcome measures, mean Z-score of 8 neurophysiological tests, and attenuated nephropathy in modestly controlled type 2 diabetes by reducing glycaemic variability and mean nonglycemic factors of diabetic microvascular complication.

O31. Effects of a cardiac rehabilitation programme on heart rate response to exercise and on aerobic performance in patients with newly detected glycemic disorders

Kamel Abdennbi[1], Minh Tuan Nguyen[2], Guy Amah[1], Sylvie Gagey[1], Nérimaine Chaib[1], Chabnam Guiti[1], Marie Sylva[1], *Paul Valensi*[2]

[1]Center of Cardiac rehabilitation, Léopold Bellan hospital, Paris, France. [2]Unit of Endocrinology-Diabetology-Nutrition, AP-HP, Jean Verdier Hospital, Paris Nord University, Bondy, France

Aim: Heart rate (HR) response to exercise is modulated by autonomic nervous system activity and is often impaired in diabetes. We aimed to analyse the changes in HR response and aerobic performance during a stress test after a one-month ambulatory cardiac rehabilitation programme in patients with newly detected glycemic disorders (NDGD) and in normoglycemic patients.

Methods: We included 463 patients without known diabetes, of which 75% had coronary disease. Findrisk score was calculated and an OGTT was performed at admission in the programme; artery stiffness was measured by carotid-to-femoral pulse wave velocity (PWV), and a stress test was performed at admission and the end of the programme.

Results: Based on OGTT, 189 patients had NDGD: diabetes (n=42) or prediabetes (n=147). During the stress test, HR at rest, maximal HR (HRmax), the percentage of HR reserve (%HRreserve) and VO2 max did not differ significantly between NDGD and normoglycemic patients. After the programme, in both groups, HRmax, %HRreserve and VO2 max increased ($p<0.05$ to <0.001), PWV decreased slightly. VO2max before and after the programme correlated negatively with Findrisk ($p<0.0001$) and glycemia at fasting and after OGTT ($p=0.05$ to <0.0001). Before the programme, VO2max correlated negatively with PWV ($p<0.0001$); after the programme, VO2max and its change (after-before) correlated negatively with PWV ($p<0.0001$ and $p=0.003$).

Conclusions: In patients with NDGD, HR response during a stress test is improved after the rehabilitation programme. This improvement in autonomic activity occurs despite a limitation of aerobic performance improvement related to mild hyperglycemia and artery stiffness.

POSTER ABSTRACTS

Day 2

17 September 13:30-14:30
Poster presentations (P2-P11) Young investigators award for the best poster presentation (Epidemiology, risk factors and diagnosis)
Chairs: Tamas Varkonyi (Szeged, Hungary) and Sondre Meling (Stavanger, Norway)

P2. Non-Alcoholic Fatty Liver Disease Is not Related to the Prevalence of Diabetic Polyneuropathy in Diabetes

Carla Greco, Stefano Boni, Silvia Coluccia, Massimiliano Colzani, Daniele Santi, Manuela Simoni

Unit of Endocrinology, Department Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy

Aim: Nonalcoholic fatty liver disease (NAFLD) has been suggested as independent predictor for kidney disease and proliferative retinopathy in patients with type 2 diabetes (T2D), while the association with diabetic polyneuropathy (DPN) is debated. The aim of this study is to evaluate the association between DPN and predictive tools and ultrasonography diagnosis of NAFLD.

Methods: Forty-two diabetic patients (mean age 57.83 ± 11.47 years, duration 9.44 ± 8.92 years, HbA1c 59.19 ± 13.85 mmol/mol, 27 males, 93% T2DM), underwent clinical evaluation of DPN by Michigan Neuropathy Screening Instrument (MNSI), Michigan Diabetic Neuropathy Score (MDNS) and Diabetic Neuropathy Index (DNI). NAFLD was evaluated by predictive tools Fatty Liver Index (FLI) and Hepatic Steatosis Index (HIS), and confirmed by liver ultrasonography.

Results: DPN was present in 22 (52.4%) participants. DPN patients were older (p=0.04) and characterized by higher prevalence of impaired urinary albumin excretion (p=0.035), hypertension (p=0.011) and dyslipidemia (p=0.041). High-risk FLI and HIS scores were detected in 81% and 64.3% of subjects, while ultrasonography NAFLD was present in 31 out of 36 (85.7%%) patients (20 with mild and 11 with moderate-severe grade), resulting more frequent in females than males (93.3% versus 63.0%, p=0.032).

No significant difference was found in DPN prevalence in patients with NAFLD than those without (54.8 versus 45.2 %, p=0.338), also considering only high-grade steatosis. No association was identified between DPN and non-invasive predictive tools of NAFLD.

Conclusion: Although in a small sample of diabetic subjects, liver steatosis is not independently associated with clinical diagnosis of DPN.

P3. Particularities of a Roma population with type 2 diabetes mellitus, obesity and peripheral neuropathy

Andrada Cosoreanu [1,2], Emilia Rusu[1,2], Gabriela Radulian[1,2]

[1]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania.
[2]"Nicolae Malaxa" Clinical Hospital, Bucharest, Romania

Aim: Undoubtedly, the prevalence of obesity in patients with T2DM complicated by peripheral neuropathy is significantly high. However, data among the Roma population is still scarce. This paper's aim is to emphasize the particularities among this population.

Method: The study comprised 114 patients, aged between 39 and 86 years old, of which 53% (n=61) were women. All patients were admitted in the Diabetes, Nutrition, Metabolic Diseases Department from "Nicolae Malaxa" Clinical Hospital, Bucharest and agreed on signing informed consent.

Results: The majority had class 2 obesity, with a mean BMI of 36.64 kg/m2. The number of patients was higher in the age group 50-59 years (n=49; 42.98%). General characteristics include the following mean values: age of 58.32 years, diabetes duration of 8.28 years, abdominal circumference of 119.82 cm, A1c of 9.57%, glycemia of 247.70 mg/dl and LDL-cholesterol of 128.79 mg/dl. 55 patients (48.24%) were active smokers, while 43 (37.71%) were alcohol consumers.

PVD's prevalence was 12.28% (n=14), more frequent in men (n=12),

with 1 patient suffering from LEA. Concerning microvascular complications, 31 (27.19%) had CAN, 54 (47.36%) DR and a great proportion associated CKD (n=60; 52.63%), with mean values of eGFR of 70.68 ml/min and UACR 44.35 mg/g.

Conclusion: The studied population associated a high duration of diabetes, A1c level, BMI, modified lipid panel and a predominance of smoking and alcohol consumption. The prevalence of complications was significant, highlighting the need of a preventive medical care and early diagnosis to reduce long term negative outcomes.

P4. The presence of chronic complications in prediabetes

Claudia Sivu, Ion-Vlad Vinereanu, Alexandru Nechita, Vasilica Enache, Florina Ciobanu, Gabriela Radulian

Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Aims: To assess the occurrence and prevalence of chronic microvascular complications of diabetes, in adults with prediabetes.

Methods: We evaluated 32 patients with prediabetes, which presented in our clinic. Trial design: cross sectional. Statistical data were analysed using IBM SPSS.

Results: Out of N=32 patients with prediabetes, 20 (62.5%) were women and 12 (37.5%) men, with a mean age of 62.06±8.996 years. BMI variated between 30.37±4.82 kg/m^2. The mean glycated haemoglobin values were 5.84 ± 0.33% with fasting blood glucose (FBG) of 112.78±7.63 mg/dl. Regarding estimated GFR, mean value was 91.22±14.75 ml/min/1.73m^2. Mean cholesterol value was 218.64 ± 64.77 mg/dl with LDL cholesterol of 129.14±49.03 mg/dl. The ankle-brachial index (ABI) was 1.07±0.89 on the right and 1.06±0.12 on the left side. FBG negatively correlates with ABI in the studied population (p=0.2). We found a significant correlation between the value of FBG and body weight (p=0.01). Patients with neuropathy tended to have higher creatinine and lower haemoglobin levels. There were statistically significant differences in the age distribution of patients and the outcome of Ewing score (p=0.029).

Conclusions: based on our findings, factors including age, creatinine or haemoglobin value did have an impact on the value of ABI, Ewing test score or the presence of diabetic peripheral polyneuropathy. A much larger population sample is needed in order to examine these correlations furthermore.

P5. Predicting neuropathy using routine eye and kidney test results: An application of novel statistical methods in the Diabetes Control and Complications Trial (DCCT)

Leif Erik Lovblom [1,2], Laurent Briollais[1,2], George Tomlinson[3,4], Bruce A. Perkins[1,5]

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Aim: Aims: Despite recent advances, neuropathy screening is not consistently performed in clinical practice. We aimed to determine if diabetic neuropathy risk could be predicted using routine eye and kidney screening outcomes in type 1 diabetes.

Methods: We used 28-year data from the DCCT/EDIC study, available via the NIH public repository. Due to the complexities involved in studying multiple simultaneous longitudinal outcomes, our objective has not been traditionally studied and we used and developed novel statistical methods called joint models for this purpose. Retinopathy was measured using the Early Treatment Diabetic Retinopathy Study Research (ETDRS) Group 23-point scale, and nephropathy was measured albumin excretion rate (AER) and eGFR. During certain parts of the study, neuropathy was not measured as frequently as the other complications; we therefore explored the late-stage event- time outcome of serious foot ulcer or amputation.

Results: After mutual adjustment, a 1-unit increase in the current value of AER (in mg/dl on the log-scale) was associated with a hazard ratio (HR) for 1.25 for late-stage neuropathy, and a 3-step increase in the current value of the ETDRS-scale was associated with a HR of 1.23. In addition to these HR estimates, strong predictive roles of AER, eGFR, and ETDRS for late-stage neuropathy were observed (Figure 1).

Conclusions: The dynamic predictions illustrated the proof-of-concept that routinely conducted eye and kidney screening outcomes can predict future risk of late-stage neuropathy. Future work will determine how to implement these tests in prediction of late-stage, as well as early-stage, neuropathy.

P6. Genetic factors that increase the risk of diabetic neuropathy

Dóra Tordai[1], Noémi Hajdú[1], Orsolya Erzsébet Vági[1], Miklós Kempler[2], Magdolna Békeffy[1], Anna Erzsébet Körei[1], Ildikó Istenes[1], Viktor Horváth[1], Péter Kempler[1], Zsuzsanna Putz[1]

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Aim: This study was undertaken to perform whole exom sequencing in patients with type 2 diabetes with/without neuropathy in order to identify genetic variants that may increase the risk of developing neuropathy.

Methods: For this study, 25 patients with type 2 diabetes with neuropathy and 24 without underwent detailed neurological assessment as well as whole exom sequencing. Cardiovascular autonomic function was examined by standard cardiovascular reflex tests, heart rate variability was characterized by the triangle index. Sensory nerve function was assessed using Neurometer (current perception threshold-CPT), Q-Sense devices. Symptoms were graded using the neuropathy total symptom score (NTSS6).

Results:

SNP	chr	pos	OR	p value
rs2032930	16	11350573	35,84802	0,000345
rs2032931	16	11350612	35,84802	0,000345
rs604349	1	1,09E+08	30,03101	0,000668

		SNP	Ref. Heterozygota		Var. Homozygota		p value
			mean	SD	mean	SD	
CPT N. medianus Hz	2000	rs604349	448,4	61,52	364,21	91,69	0,04918653
250 Hz		rs2032930	175,72	49,78	124,75	47,82	0,00355749
		rs2032931	175,72	49,78	124,75	47,82	0,00355749
		rs604349	180	14,27	132,86	53,46	0,01809446
5 Hz		rs2032930	98,1	42,28	74,64	32,57	0,0428283
		rs604349	122,4	28,37	78,74	28,51	0,00543309
CPT N. peroneus Hz	5	rs2032930	238,4	270,57	169,81	182,23	0,037662
		rs2032931	238,4	270,57	169,81	182,23	0,037662
Beat to beat		rs2032930	8,55	5,82	12,25	6,65	0,02260554
		rs2032931	8,55	5,82	12,25	6,65	0,02260554
NTSS6		rs2032930	1,27	0,47	1,67	0,48	0,02300515
		rs2032931	1,27	0,47	1,67	0,48	0,02300515
Q-sense warm		rs604349	39,27	4,24	35,82	2,59	0,04194715

Conclusion: We have successfully identified genetic variants that may increase the risk of developing neuropathy in type 2 diabetic patients.

P7. Genetic factors that reduce the risk of diabetic neuropathy

Noémi Hajdú [1], Dóra Tordai[1], Orsolya Erzsébet Vági[1], Miklós Kempler[2], Magdolna Békeffy[1], Anna Erzsébet Körei[1], Ildikó Istenes[1], Viktor Horváth[1], Péter Kempler[1], Zsuzsanna Putz[1]

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Aim: The present study was undertaken to perform whole exom sequencing in patients with type 2 diabetes with and without neuropathy in order to identify genetic variants that may decrease the risk of developing neuropathy.

Methods: For this study, 25 patients with type 2 diabetes with neuropathy and 24 without underwent detailed neurological assessment as well as whole exom sequencing. Cardiovascular autonomic function was examined by standard cardiovascular reflex tests, and heart rate variability was characterized by the triangle index. Sensory nerve function was assessed using Neurometer (for current perception threshold - CPT) and Q-Sense devices. Symptoms were graded using the neuropathy total symptom score (NTSS6).

Results:

SNP	chr	pos	OR	p value
rs917778	9	1,26E+08	0,032883	0,000638
rs2234753	9	1,34E+08	0,03935	0,001215

	SNP	Ref. Heterozygota		Var. Homozygota		p value
		mean	SD	mean	SD	
Q-sense cold	rs917778	30,15	1,15	28,73	3,05	0,01
CPT Nervus medianus 2000 Hz	rs2234753	333,22	47,20	376,5	92,79	0,02
Beat to beat	rs2234753	13,44	6,79	10,21	6,32	0,04
NTSS.6	rs2234753	1,83	0,38	1,39	0,49	0,003

Conclusion: We have successfully identified genetic variants that may decrease the risk of developing neuropathy in type 2 diabetic patients.

P8. Plasma levels of vitamin B12 and Neurofilament light chain in adolescents with type 1 diabetes with and without neuropathy

Mathilde Thrysøe Jespersen[1], Tina Parkner[2], Hatice Tankisi[3], Astrid Juhl Terkelsen[1,4], Jens Randel Nyengaard[5,6], Esben Thyssen Vestergaard[7,8], Kurt Kristensen[8], Vinni Faber Rasmussen[4,7]

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Aim: To investigate plasma levels of vitamin B12 and Neurofilament light chain (NfL) in adolescents with type 1 diabetes (T1D) with and without neuropathy. We hypothesize that patients with neuropathy have signs of B12 deficiency and increased NfL-levels.

Methods: Sixty adolescents (15-18 years, diabetes duration >5 years) with T1D and 23 control subjects were included. Based on results from nerve conduction studies (NCS), the patients were divided in two groups: with (DN+) and without (DN-) diabetic neuropathy. Plasma levels of vitamin B12 (B12), vitamin B12-TC-bound (holoTC) and NfL were determined by immunoassays, while plasma methylmalonate (MMA) was analyzed by mass spectrometry.

Results: Twenty-three of the adolescents with T1D had abnormal NCS (DN+, n=23), and 37 had normal NCS (DN-, n=37). There were no significant differences in B12 parameters between DN- and DN+ (B12 p=0.07; holoTC p=0.14; MMA p=0.3). Comparing DN+ with control subjects showed no difference in MMA-levels (MMA median: 0.12 vs. 0.15 µmol/l, p=0.6), but higher B12- and holoTC-levels in DN+ (B12 p=0.01; holoTC p=0.04). No significant differences in NfL levels between the groups were found (NfL median(range): DN+: 5.13 (2.12-13.24) ng/l; DN-: 5.85 (2.35-14.31) ng/l; control subjects: 5.24 (3.07-8.00) ng/l), p=0.4).

Conclusions: This study found similar plasma levels of B12 parameters and NfL in adolescents with and without diabetic neuropathy, suggesting that reduced B12 level is not contributing as cause of occurrence of neuropathy in adolescents with T1D. Furthermore, NfL is not a relevant biomarker of large nerve fiber damage in this subpopulation.

P9. Small nerve fibre pathology in people with obesity at high risk of non-alcoholic fatty liver disease (NAFLD): preliminary baseline

David Riley[1,2], *Azlinda Hamid* [1,2], Leandros Rapteas[1,2], Anne Marshall[1,2], Jamie Burgess[1,2], Ioannis Petropolous[3], Rayaz Malik[3], Theresa Hydes[1,2], Dan Cuthbertson[1,2], Uazman Alam[1,2]

[1]University of Liverpool, Liverpool, United Kingdom. [2]Liverpool University Hospital NHS Foundation Trust, Liverpool, United Kingdom. [3]Weill Cornell Medicine, Doha, Qatar

Aim:NAFLD is associated with microvascular complications. We aim to identify whether young adults with obesity at high risk for NAFLD have evidence of significant small fibre pathology.

Methods: CALIBRATE is a randomised, controlled trial assessing long-term changes in liver fat and neuropathy status with a 12 week low calorie diet (800 Kcal/day). Participants with obesity and a high risk of NAFLD (HR-NAFLD), based on a fatty liver index (FLI) >60, were compared to age/sex-matched healthy-volunteers. Baseline assessments included metabolic profiling, MRI liver scans, neuropathy symptom profile (NSP), McGill visual analogue scale (VAS), neuropathy disability score (NDS), and corneal confocal microscopy (CCM) evaluating corneal nerve fibre length (CNFL), density (CNFD) and branch density (CNBD).

Results: People with obesity at HR-NAFLD (FLI: mean 92.38±1.5) had poorer metabolic health, higher BMI (37kg/m2 vs 27kg/m2), higher systolic and diastolic blood pressure, waist circumference, triglyceride and cholesterol ($p<0.05$) with no difference in HbA1c, LDL and HDL compared to controls. HR-NAFLD demonstrated significant evidence of small nerve fibre pathology with greater neuropathic symptoms (NSP; $p<0.05$), and objective small fibre loss with a reduction in CNFL and CNFD ($p<0.05$). There was a non-significant reduction in CNBD ($p=0.056$). There was no significant difference in pain between the groups

Conclusion: Small nerve fibre pathology is present in people with obesity at high risk for NAFLD. We shall explore to what extent reversal of this metabolic dysfunction and reduction in liver fat with weight loss enhances small nerve fibre regeneration.

	Controls (n=13)	HR-NAFLD (n=13)	P-value
Demographics			
Age, yrs, Mean (±SEM)	47 (±0.9)	47 (±2.2)	
Sex, Male/Female (%)	46/54	38/62	
Anthropometric			
BMI, kg/m^2, Mean (±SEM)	26.9 (±1.1)	37.4 (±1.3)	**<0.001**
Waist circumference, cm, Mean (±SEM)	93 (±4.9)	116 (±2.3)	**0.001**
Systolic blood pressure, mmHg, Mean (±SEM)	128 (±3.3)	149 (±5.8)	**0.005**
Diastolic blood pressure, mmHg, Mean (±SEM)	73 (±1.7)	88 (±3.1)	**0.001**
Biochemistry			
HbA1c, mmol/mol, Mean (±SEM)	38 (±0.7)	37 (±1.3)	0.390
Total Cholesterol, mmol/L, Mean (±SEM)	5.1 (±0.2)	5.9 (±0.3)	**0.045**
LDL, mmol/L, Mean (±SEM)	3.0 (±0.2)	3.3 (±0.3)	0.100
HDL, mmol/L, Mean (±SEM)	1.5 (±0.1)	1.2 (±0.1)	0.133
Triglycerides, mmol/L, Mean (±SEM)	1.4 (±0.2)	2.3 (±0.3)	**0.021**
Neuropathy Assessments			
Neuropathy Symptom Profile, (-/38), Mean (±SEM)	0.31 (±0.2)	2.92 (±1.1)	**0.039**
Neuropathy Disability Score, (-/10), Mean (±SEM)	0.15 (±0.1)	0.15 (±0.1)	1.000
Visual Analogue Scale (-/10)	0.62 (±0.6)	1.55 (±0.8)	0.344
Corneal Confocal Microscopy			
CNFD, mm/mm^2, Mean (±SEM)	35.8 (±1.8)	27.3 (±2.1)	**0.005**
CNFL, mm/mm^2, Mean (±SEM)	20.5 (±0.5)	15.9 (±1.1)	**0.002**
CNBD, no./mm^2, Mean (±SEM)	50.0 (±3.5)	37.2 (±5.3)	0.056

P10. A New Diagnostic Method to Assess Small Fiber Neuropathies at Early Stages – An Experimental study investigating perception threshold stability

Mette Krabsmark Borbjerg [1], Elin Antonsson[2], Johan Roeikjer[1,3], Niels Ejskjaer[1,4], Carsten Dahl Moerch[5,3]

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Aim: Previous research has proven that epidermal- and transcutaneous stimulation can investigate the function of large and small nerve fibers individually using different electrodes. This study aimed to determine the stability of the perception thresholds when using such electrodes. This assessment is valuable for future research investigating small and large nerve fiber function separately using the technique over an extended period.

Methods: Twenty healthy volunteers participated in the study. The perception threshold of large nerve fibers, using a patch and small nerve fibers using a pin electrode was estimated 30 times during a period of 60 minutes. A threshold was established every other minute, alternating between the two electrodes. The stimulus duration was 1 ms and the interstimulus interval was 1.5-2.5 seconds. Linear regressions of the perception threshold as a function of time were performed. The slopes were used as an estimate of habituation and were compared between the electrodes.

Results: There was a significant difference in slope between the pin electrode (Mean: 0.023 [0.014; 0.031] mA/trial) and patch electrode (Mean: 0.011 [0.003; 0.020] mA/trial) (p=0.027, paired t-test), representing small and large fiber respectivly.

Conclusion: Both small and large fibers showed significant perception threshold increases over an hour. The higher slope of the pin electrode indicated that the small sensory nerve fibers are more prone to habituation than the large sensory nerve fibers.

P11. Perception threshold tracking: A novel method for assessing the function of large and small nerve fibers in diabetic peripheral neuropathy

Johan Røikjer[1,2], Suganthiya S Croosu[3], Jens B Frøkjær[3,4], Tine M Hansen[3,4], Niels Ejskjaer[1,4], Carsten D Mørch[2,5,6]

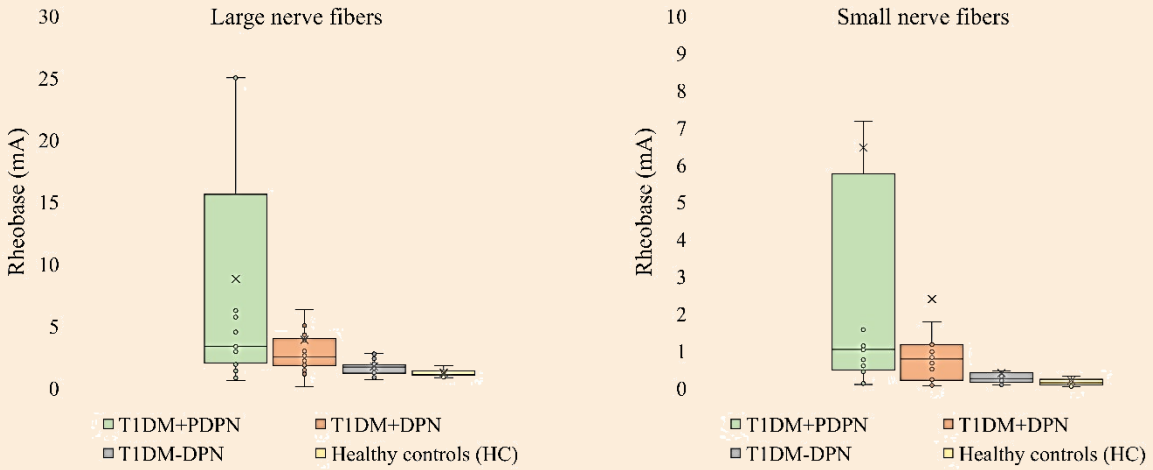
[1]Steno Diabetes Center North Denmark, Aalborg, Denmark. [2]Facullthy of Health Science and Technology, Aalborg University, Aalborg, Denmark. [3]Department of Radiology, Aalborg University Hospital, Aalborg, Denmark. [4]Department of Clinical Medicine, Aalborg University, Aalborg, Denmark. [5]Center for Sensory-Motor Interaction (SMI), Aalborg University, Aalborg, Denmark. [6]Center for Neuroplasticity and Pain (CNAP), Aalborg University Hospital, Aalborg, Denmark

Aim: Small nerve fibers are important when searching for early signs of diabetic peripheral neuropathy (DPN). The current methods for assessment are limited to examination of the extent of structural damage whereas this study aims to assess nerve function.

Methods: We utilized a novel perception threshold tracking technique to selectively assess the function of large and small nerve fibers in four age- and sex-matched groups of 20 participants with type 1 diabetes (T1DM) and: painful DPN (T1DM+PDPN), painless DPN (T1DM+DPN), no DPN or pain (T1DM-DPN), and 20 healthy controls (HC). Nerve fiber function was assessed using weak electrical currents with varying intensity by two different skin electrodes activating large- and small fibers, respectively. Nerve fiber activation was indicated by participants pressing a button. The minimal current needed to activate the nerve fibers were analyzed as the rheobase.

Results: The rheobase was highest for T1DM+PDPN (large/small fiber): 3.94 mA [IQR 1.99-25.0] and 1.09 mA [0.52-25.0], followed by T1DM+DPN: 2.49 mA [1.74-4.09] and 0.78 mA [0.19-1.17], T1DM-DPN: 1.68 mA [1.16-1.89] and 0.25 mA [0.14-0.45], and HC: 1.09 mA [1.02-1.36] and 0.14 mA [0.08-0.24]. There was a significant difference in rheobase between all groups and fibre-types (all $p<0.05$), apart from between large fibres of T1DM+PDPN versus T1DM+DPN and T1DM-DPN versus HC and the rheobase of the small fibres between T1DM-DPN versus HC and T1DM+DPN versus T1DM-DPN.

Conclusion: Perception threshold tracking reveals differences in large- and small nerve fiber function between groups with and without T1DM and pain.



17 / SEPTEMBER / 2022 / 13:30-14:30

Poster presentations (P12-P22) Young investigators award for the best poster presentation (Small fiber, autonomic neuropathy and treatment)

Chairs: Prash Vas (London, United Kingdom) and Ioannis Nikolaos Petropoulos (Doha, Katar)

P12. Subclinical corneal nerve loss in obese children and adolescents

Hoda Gad[1], Hajar Dauleh[2], Shiga Chirayath[2], Basma Haris[2], Houda Afyouni[2], Goran Petrovski[2], Saira Shehzad[2], Amel Khalifa[2], Fawziya Al-Khalaf[2], Parul Singh[2], Souhaila AlKodor[2], Mohamed A. Hendaus[2], Einas Elgassim[1], Ioannis N. Petropoulos[1], Georgios Ponirakis[1], Khalid Hussain[2], Rayaz A. Malik[1,3]

[1]Weill Cornell Medicine-Qatar, Doha, Qatar. [2]Sidra Medicine, Doha, Qatar. [3]Institute of Cardiovascular Medicine, University of Manchester, Manchester, United Kingdom

Aim: Corneal confocal microscopy (CCM) has identified small fiber neuropathy in obese adults. Corneal nerve morphology was quantified in obese children compared to age-matched healthy controls.

Method: Sixteen obese children and adolescents (age 14.0 ± 2 years, BMI 44.6±5.26 kg/m2) and 11 healthy controls underwent CCM to quantify corneal nerve fiber density (CNFD) (no./mm2), corneal nerve branch density (CNBD) (no./mm2) and corneal nerve fiber length (CNFL) (mm/mm2) and assessment of vibration perception threshold (VPT).

Results: Obese children with a significantly high body fat % (41.47±9.07, target range 10-19%) had normal VPT (3.17±1.04). CNFD (27.14±6.32 vs. 31.79±7.7, P=0.098) and CNFL (17.03±±2.09 vs. 18.37±2.71, P=0.159) did not differ, but CNBD (35.08±13.3 vs. 45.41±10.25, P=0.032) was significantly lower in obese children compared to controls. There was no significant correlation between CNFD (r=-0.086, P=0.752, r=-0.017, P=0.949), CNBD (r=-0.113, P=0.678, r=-0.369, P=0.160), and CNFL (r=-0.023, P=0.933, r=-0.193, P=0.160) with percent body fat and BMI, respectively.

Conclusion: Corneal confocal microscopy identifies early sub-clinical corneal nerve loss characterized by reduced branches in obese children and adolescents.

P13. People with type 1 diabetes mellitus and significant small nerve fibre loss have greater loss of grey matter volume in brain regions associated with pain and cognition

Jamie Burgess, Jonathan Lim, Christophe De Bezenac, Anne Marshall, David Riley, Cheong Ooi, Daniel Cuthbertson, Simon S Keller, Uazman Alam

University of Liverpool, Liverpool, United Kingdom

Aim: There is increasing data on structural central nervous system (CNS) alterations in people with type 1 diabetes (T1D). To identify grey matter volume alterations in an unselected cohort with T1D compared to healthy volunteers (HV) who have undergone comprehensive neuropathy phenotyping.

Methods: Neuropathy status of 20 participants (10 HV and 10 people with T1D) were undertaken using the McGill-visual analogue score (VAS), neuropathy symptom profile (NSP), neuropathy disability score (NDS), vibration perception threshold (VPT), sural nerve conduction velocity (SNCV), amplitude (SNAP) and corneal confocal microscopy. All participants underwent brain magnetic resonance imaging (3T) with a standard research protocol for volumetric analysis.

Results: T1D had a duration of diabetes of 18.8±13.5 years with a higher HbA1c. T1D reported more signs/symptoms and quantitative measures of neuropathy as indicated by higher NSP, NDS, VAS, VPT, SNAP and SNCV. There was significant small fibre loss with lower corneal nerve fibre length (CNFL) and branch density (CNBD) (both $p<0.05$). There were significant reductions in volume identified in areas implicated in neuropathic pain such as the amygdala and nucleus accumbens (both $p<0.05$). Reductions in volume are also identified in regions with a role in cognition and memory such as the hippocampus, parahippocampus and superior temporal gyrus (all $p<0.05$).

Conclusion: Reductions in grey matter volume are present in the amygdala and nucleus accumbens are associated with pain modulation in people with T1D and significant small nerve fibre deficits. Future research should focus on whether early neuropathy correlates with or precedes alterations in the CNS.

Table 1: Demographic, anthropometric, biochemical and neuropathy summary of participants

Variable	People with Diabetes[1]	Healthy Volunteers[1]	p-value[2]
Age (years)	36±10	37±11	0.9
Sex M/F (%)	40/60	50/50	>0.9
Systolic Blood Pressure (mmHg)	129±10	119±11	0.060
Diastolic Blood Pressure (mmHg	85±7	76±11	0.065
Heart Rate (bpm)	82±12	64±10	0.003
BMI (kg/m^2)	28±7	28.2±5	0.9
HbA1c (mmol/mol)	79±18	37±6	<0.001
Cholesterol (mmol/L)	4.85±0.86	4.87±0.28	>0.9
Triglycerides (mmol/L)	1.8±1.4	1.3±0.9	0.4
Neuropathy Symptom Profile (-/38)	9±8	0	0.007
McGill Visual Analogue Pain Score (-/10)	4±3	0	<0.001
Neuropathy Disability Score (-/10)	4±3	0	0.014
Vibration Perception Threshold (volts)	19±11	6±3	0.005
Cold Perception Threshold (°C)	21±10	28±2	0.09
Warm Perception Threshold (°C)	40.7±4.6	35.2±1.9	0.007
Cold-Induced Pain Threshold (°C)	8±9	18±5	0.011
Heat-Induced Pain Threshold (°C)	47.3±4	41.6±3.1	0.004
Chirality R/L (%)	90/10	90/10	0.6
Sural Amplitude (μV)	6.3±3.6	9.6±2.7	0.031
Sural Velocity (m/s)	42±10	53±4	0.009
Corneal Nerve Fibre Length – Automated (mm/mm²)	7.9±5.3	12.6±2	0.046
Corneal Nerve Fibre Density – Automated (number/mm^2)	15±11	23±2	0.11
Corneal Nerve Fibre Branch Density – Automated (number/mm^2)	13±10	24±5	0.012

[1] Mean ± SD
[2] t-test; Chi-squared test

P14. Equivalent neuropathic deficits, differing pain. A study of small fibre pathology and sensory phenotypes in patients with diabetic neuropathy and fibromyalgia syndrome

Leandros Rapteas [1], Anne Marshall[1,2], Jamie Burgess[1], David Riley[1], Alise Kalteniece[2], Maryam Ferdousi[2], Shazli Azmi[2], Rayaz Malik[3], Nigel Calcutt[4], Andrew Marshall[1,2], Uazman Alam[1]

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Aim: There is a high prevalence of small fibre neuropathy in patients with diabetes. Increasing evidence also implicates small fibre pathology in the generation of pain in fibromyalgia (FMS). Previous data suggests significant sensory overlap is observed between these two conditions, including neuropathic pain descriptors. To investigate the relationship between small fibre pathology, central pain mechanisms, and pain phenotype we undertook a cross-sectional study in patients with diabetic neuropathy (DPN) or FMS.

Methods: Participants with type 1 or type 2 diabetes (n=26) and FMS (n=27) underwent assessment of anthropomorphic, biochemical, and reported pain parameters. Structural and functional measures of small fibre dysfunction were quantified using corneal confocal microscopy, evaluating corneal nerve fibre length (CNFL), density (CNFD) and branch density (CNBD) along with quantitative sensory testing. Diffuse noxious inhibitory control was assessed using conditioned pain modulation (CPM).

Results: Patients with DPN were older with longer duration of respective disease than FMS. BMI, triglycerides, blood pressure and, interestingly, CNFD, CNFL and CNBD were comparable between the two groups. Patients with DPN displayed a loss-of-function phenotype across QST parameters. In contrast, patients with FMS demonstrated a gain-in-function in mechanical and thermal pain. Compared to DPN, patients with FMS showed impairment of CPM.

Conclusions: Despite showing an equivalent degree of small fibre pathology patients with DPN and FMS display markedly different sensory profiles. This disconnects between small fibre neuropathy and pain phenotypes may result from differences in central pain processing mechanisms or dysfunction of specific small fibre subtypes.

	FMS (n=27)	**DPN (n=26)**	**p-value**
Gender (F/M)	25/2	12/14	
Mean ± SD			
Age (years)	45.2 ± 14.1	57.9 ± 9.6	0.003
Duration of disease (years)	6.8 ± 4.9	16.2 ± 11.9	<0.001
BMI (Kg/m^2)	28.3 ± 9.9	29.2 ± 4.4	NS
Triglycerides (mmol/l)	1.62 ± 0.83	1.56 ± 1.09	NS
Systolic blood pressure (mmHg)	128 ± 20	125 ± 17	NS
Diastolic blood pressure (mmHg)	77 ± 12	72 ± 7	NS
CNFD (number of major nerves/mm^2) (5th centile reference value 18.8)	25.1 ± 5.8	22.5 ± 7.3	NS
CNFL (length of nerves/mm^2) (5th centile reference value 13.6)	14.9 ± 3.1	16.3 ± 5.5	NS
CNBD (number of nerve branches/mm^2) (5th centile reference value 18.8)	34.3 ± 13.6	43.6 ± 22.0	NS
Median (interquartile range)			
VAS (current pain score 0-100)	76.2 (62.6 – 88.8)	14 (4 – 34)	<0.001
QST testing site	**Hand**	**Foot**	
Mean ± SD			
CDT (z-score)	-0.31 ± 1.19	-1.08 ± 1.42	
WDT (z-score)	-0.32 ± 1.22	-0.92 ± 1.22	
TSL (z-score)	-0.25 ± 1.25	-0.92 ± 1.22	
MDT (z-score)	-0.70 ± 2.04	-1.44 ± 1.62	
PPT (z-score)	2.82 ± 4.54	0.28 ± 1.10	
Median (interquartile range)			
CPT (z-score)	0.93 (-0.36-1.39)	-0.98 (-1.02-0.05)	
HPT (z-score)	0.49 (-0.76-1.34)	-1.29 (-1.58—1.17)	
MPS (z-score)	1.23 (0.11-2.60)	-1.17 (-3.07-0.78)	
WUR (z-score)	0.14 (-0.37-1.22)	-0.10 (-0.91-0.72)	
VDT (z-score)	0.56 (0.41-0.62)	-0.29 (-2.91-0.83)	
DMA	0 (0-0.52)	0 (0-0)	
PHS	0 (0-0)	0 (0-0)	
CPM	0.37 (0-1.08)	3.33 (-1-13.67)	

P15. Early corneal nerve fiber regeneration with the weekly GLP-1 agonist semaglutide

Hoda Gad[1], Einas Elgassim[1], Adnan Khan[1], Ioannis N. Petropoulos[1], Georgios Ponirakis[1], Rayaz A. Malik[1,2]

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Aim: Glucagon-like peptide-1 receptor (GLP-1R) agonists may have a beneficial effect on the central and peripheral nervous system. Corneal Confocal Microscopy (CCM) has been used to show early nerve fiber regeneration in patients with diabetes and obesity.

Methods: Nine obese subjects (3 diabetic, 6 non-diabetic) who received Semaglutide 1.0mg weekly underwent CCM to quantify corneal nerve fiber density (CNFD), branch density (CNBD) and length (CNFL), assessment of sudomotor function using Sudoscan and vibration perception threshold (VPT) at baseline and after 6 months.

Results: In obese non-diabetic patients (103.4±11.19 kgs), weight was reduced (P=0.046) after 3 months, but there was no change in HbA1c (P=0.999), CNFD (P=0.500), CNBD (P=0.539), CNFL (P=0.146), sudomotor function or VPT after 6 months. In obese diabetic patients, after 3 months, weight (127.66±38.78 vs. 119.36±40.07, P=0.037) and HbA1c (7.56±1.4 vs. 6.7±1.21, P=0.043) improved significantly. There was no change in CNFD (P=0.893), CNBD increased non-significantly (36.45±8.1 vs. 47.56±20.8, P=0.282), whilst CNFL (16.25±3.6 vs. 20.38± 4.74, P=0.037) improved significantly at 6 months, with no change in VPT (P=0.225) or sudomotor function (P=0.678) at 6 months.

Conclusion: Corneal confocal microscopy identifies early corneal nerve regeneration after 6 months of Semaglutide treatment in obese patients with diabetes.

P16. Determinants of orthostatic hypotension in type 2 diabetes: is still cardiac autonomic neuropathy the main factor?

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Aim: Orthostatic hypotension (OH) is both a sign of cardiovascular autonomic neuropathy (CAN) and a common multifactorial condition in middle-aged adults. This study aimed to identify the determinants of OH in a well-characterized population with type 2 diabetes (T2D).

Method: In 208 participants with T2D (age 63.2±8.6, duration 11.7±9.1 years, 130 men), without severe comorbidities, we performed three heart rate based cardiovascular reflex tests (HR-CARTs), OH test and assessed diabetic polyneuropathy (DPN), clinical history and variables. We defined OH as a systolic blood pressure (BP) fall ≥20 and ≥30 mmHg in presence of supine BP <140 and ≥140 mmHg, respectively, and early and confirmed CAN in presence of 1 and 2 abnormal HR-CARTs. We used multivariate logistic regression analysis.

Results: We found OH in 25, confirmed CAN in 16 and overall CAN (early and confirmed) in 45 patients. OH was associated with lower HR-CARTs (P=0.0117, P=0.0134, P=0.0167), higher neuropathic signs (P=0.0037) and symptoms scores (P=0.0003), higher HbA1c (P=0.0039), with the presence of CAN (P<0.0001), confirmed CAN (P=0.0011), DPN (P=0.0007), retinopathy (P=0.0245), and peripheral vascular disease (P=0.0028), with the absence of hypertension (P=0.0002) and the lack of physical activity (P=0.0212). OH was not associated with the use of interfering drugs (i.e., diuretics, nitrates, alpha-lytic and sympatholytic agents) and beta-blockers. Table shows the results of multiple logistic regression analysis.

Conclusions: CAN is the main determinant of OH in this T2D population, but comorbidities and physical activity contribute to OH variance, while medications do not seem to play a significant role.

Table. Multivariate logistic regression analysis with OH as the dependent variable. Each variable was singularly included with age, sex, diabetes duration, and BMI in the model 1, with CAN in addition in the model 2, while the model 3 included CAN, physical activity, hypertension, and interfering drugs.

	Model 1				Model 2				Model 3			
Variables	Odds ratio	95% CI	R^2	P	Odds ratio	95% CI	R^2	P	Odds ratio	95% CI	R^2	P
CAN (yes)	7.85	2.9-21.0	0.143	**<0.0001**	-	-	-	-	5.88	2.05-16.9	0.238	**0.0010**
HbA1c (%)	1.41	1.08-1.84	0.090	**0.0115**	1.28	0.96-1.70	0.186	0.0908	-	-	-	-
Physical activity (yes)	0.18	0.05-0.67	0.097	**0.0101**	0.23	0.06-0.86	0.178	**0.0291**	0.16	0.04-0.66	0.238	**0.0114**
Hypertension (yes)	0.24	0.09-0.66	0.078	**0.0056**	0.26	0.09-0.73	0.186	**0.0111**	0.22	0.07-0.68	0.238	**0.0090**
Retinopathy (yes)	3.39	1.12-10.3	0.063	**0.0311**	2.68	2.08-16.5	0.141	0.1024	-	-	-	-
Peripheral vascular disease (yes)	4.00	1.49-10.8	0.075	**0.0060**	2.53	0.88-7.23	0.150	0.0839	-	-	-	-
Cardiovascular disease (yes)	2.87	1.06-7.82	0.052	**0.0390**	2.39	0.84-6.83	0.152	0.1025	-	-	-	-
Interfering drugs (yes)	0.70	0.26-1.88	0.032	0.1482	0.66	0.23-1.87	0.148	0.4289	0.55	0.17-1.84	0.238	0.3329

P17. Clinical characteristics in diabetic gastroparesis – the DIAGAS study

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Aim: Autonomic neuropathy is more common in patients with diabetic gastroparesis, however the association is imperfect and variable. Hence, we aimed to identify other clinical parameters that are associated with high probability of delayed gastric emptying in a population of patients with diabetes with symptoms indicating gastroparesis.

Methods: In a cross-sectional study, we examined patients referred to a University Hospital clinic with symptoms of diabetic gastroparesis with gastric emptying scintigraphy (4h), blood samples and cardiac autonomic function tests.

Results: We included 59 patients (82%) with type 1 and 13 (18%) with type 2 diabetes. Delayed gastric emptying was more common in the type 1 diabetes group (47%) compared to the type 2 diabetes group (8%), OR=10.45 (95% CI: 1.27, 85.7). Most patients had one (25%) or more (47%) known diabetic complications at the time of referral, most common were retinopathy (56%) and peripheral neuropathy (47%). Patients with delayed gastric emptying were generally younger (mean age 41.7 (SD 11.5)) than patients with normal gastric emptying (mean age 50.9 (SD 11.9)), p=0.002. We found a negative correlation between age and gastric emptying (r=-0.331, p=0.005). Diabetes patients with gastroparesis had signs of impaired cardiac autonomic function compared to diabetes patients with normal gastric emptying. BMI was negatively correlated to gastric emptying time (r=-0.359, p=0.003).

Conclusion: In addition to impaired autonomic function, patients with diabetic gastroparesis were younger and had lower BMI, and peripheral neuropathy or retinopathy compared to those with normal gastric emptying. Gastroparesis was more common in type 1 diabetes.

P18. Glycemic variability is associated with diastolic dysfunction in patients with type 2 diabetes

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Aim: Diastolic dysfunction is one of signs of heart failure and could be associated with autonomic neuropathy. Glycemic variability could be one of the reasons predisposing to heart failure in subjects with diabetes. We examined the relationship between glycemic variability and diastolic dysfunction in patients with type 2 diabetes mellitus without coronary artery disease.

Methods: Seventy-eight patients with heart failure with preserved left ventricular ejection fraction and type 2 diabetes mellitus were examined. Diastolic function was assessed by echocardiography, glycemic variability was evaluated by continuous glucose monitoring. According to the glycemic variability all studied patients were divided into two groups: group I - SD> 2 (high glycemic variability), n = 40; group II - SD ≤ 1.9 (normal glycemic variability), n = 38.

Results: Group I were older (49 (9) vs 46 (5); p<0.05 (the results of the study are presented as mean (SD)" or absolute number (%)), with a longer duration of DM (10 (9.5) vs 6 (5.5); p<0.01). In group I compared to group II there were more patients with grade 2 of diastolic dysfunction (25 (62.5%) vs 10 (26.3), p<0.05). Patients in group I had more severe diastolic dysfunction. In group I patients insulin and sulfonylureas were used more often (11 (27.5%) vs 0 p = 0.0001; 25 (62.5%) vs 10 (26.3%); p<0.01, resepctively); patients of group II were more often treated with iSGLT2 (2 (5%) vs 13 (34.21%); p<0.01).

Conclusions: Increased glycemic variability is associated with diastolic dysfunction and in patients with type 2 diabetes

P19. Meal-induced gallbladder emptying in diabetic, prediabetic, and control patients – preliminary results from the PanGut-study

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Aim: Autonomic neuropathy is a known complication of diabetes mellitus (DM) and leads to an increased disease burden. Gallbladder dysfunction has been observed in DM and is hypothesized to be a manifestation of gastrointestinal autonomic neuropathy. We aimed to evaluate gallbladder emptying in patients with type 2 DM compared to patients with prediabetes and healthy controls (HC).

Methods: Forty-one matched subjects have been included in this ongoing cross-sectional study (17 with DM, 11 with prediabetes, and 13 HCs). Gallbladder volumes were calculated from 3D ultrasound imaging collected at predefined intervals before and after consuming a high-fat nutritional drink. Fasting volumes and the smallest postprandial volumes were used to calculate the gallbladder ejection fraction (EF). Time from nutritional drink consumption to gallbladder emptying was also recorded.

Results: Table 1 shows the patient characteristics. The median maximum fasting gallbladder volume was significantly higher in the DM group compared to HCs (34.6 mL vs. 27.4 mL, p=0.022). There were no significant differences in smallest postprandial volume between groups. Similarly, mean EF did not differ significantly between groups (58% in HC, 54% in prediabetes patients, 63% in DM). We found a trend towards faster gallbladder emptying in HC comparted to DM (median time 20 min vs. 40 min, respectively, p=0.094).

Conclusion: Our preliminary results suggest differences in gallbladder function in type 2 DM patients compared to HC. This could be related to gastrointestinal autonomic neuropathy in DM patients. Thus, gallbladder ultrasonography may have a role as a non-invasive tool for evaluating gastrointestinal autonomic function.

Table 1: Patient characteristics

	Diabetes	Prediabetes	Controls	*p*
n	17	11	13	
Sex, % females	47	55	54	0.95
Age, mean (SD)	69.4 (7.4)	69.1 (6.3)	69.5 (7.1)	0.95
BMI, mean (SD)	26.5 (4.2)	26.4 (4.5)	25.6 (4.8)	0.68
Smokers, % current/former	12/41	9/0	8/46	0.23
Alcohol consumption, % high	12	0	8	0.41

P20. Effectiveness of Treatment with Vitamins B12 and D in Patients with Diabetic Peripheral Neuropathy by Sudoscan

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Aim: Diabetic peripheral neuropathy (DPN) is the most common cause of neuropathy worldwide; its prevalence increases with diabetes duration (DD). About 60%-70% diabetic patients will eventually develop DPN. Vitamin B12/D (VitB12/D) deficiency is a global public health problem. Around 29.66% of diabetic patients have confirmed B12 insufficiency. Patients on Metformin have statistically lower values of B12 (P = 0.01). Vitamin D deficiency is considered to be a contributing factor to the development of type 2 diabetes(T2DM). Our aim was to study the effect of VitB12/D therapy in patient with T2DM and DPN.

Methods: Totally 52 patients were studied (27 males/33 females, mean age 51±5yrs, DD - 5-10 years, HbA1c at entry - 8,3±1,5%). Before initiating treatment with VitB12/D below tests were performed and following results were obtained: Vitamin B12 (150±20pg/mL [n - 200-835 pg/mL]),Vitamin D (15±25 ng/m [n - 30-100ng/ml]); all neurological tests (10-g monofilament test, tip-term/temperature test, vibration test 128-Hz tuning fork, prick tests) were positive, and neurological examination with Sudoscan (a non–invasive method for the assessment of the small fiber function) revealed presence of mild small fiber neuropathy. Treatment with oral VitB12/D was initiated in all the patients.

Results: At month 3 post treatment initiation all tests were repeated. In 88% of patients VitB12/D levels were within the normal range; results of monofilament, tip-term/temperature test and Sudoscan examination improved in 41 patients (78,5%).

Conclusions: This study shows that 3-month treatment with VitB12/D improves condition of peripheral nerve fibers. Observations will continue.

P21. Study Protocol for Neuromuscular Electrical Stimulation For The Treatment Of Diabetic Peripheral Neuropathy: A Multi-centre, Double-blinded, Randomised Controlled Trial

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Aim: Diabetic peripheral neuropathy (DPN) has a lifetime prevalence of over 50% among people with diabetes. Lower limb symptoms range from numbness to unsteadiness and pain. Sequelae include foot ulceration and Charcot's neuroarthropathy, which are risk factors for amputation and mortality. Neuromuscular electrical stimulation (NMES) is a potential nonpharmacological treatment for DPN. By depolarising neurons and evoking muscle contraction it may improve peripheral nerve conductivity. The aim is to assess the clinical efficacy of a NMES device in patients with DPN.

Methods: This is a multi-centre, double-blind, randomised controlled trial for adults with DPN randomised to either best medical therapy (BMT) and a sham device (control) or BMT and a NMES device (intervention). A positive nerve conduction study (NCS) and a Michigan Neuropathy Screening Instrument score of ≥7 will confirm DPN. The primary outcome measure is any improvement in nerve conductivity of the sural, common peroneal, tibial and superficial peroneal nerves measured using a NCS at 6-months. Patient and public involvement has informed the methods.

Results: Based on a meta-analysis, the control group are expected to have a mean 0.165m/s (standard deviation 10.0) decrease in common peroneal nerve conductivity at 6-months. A pilot study demonstrated a mean 11.8m/s increase, therefore, a conservative estimate for the intervention group is a mean 5.9m/s increase. At 90% power and a 5% significance level, 190 participants are needed to detect a moderate effect size between groups, with 10% attrition at 6-months.

Conclusions: The trial is ongoing; therefore, conclusions cannot be drawn yet.

P22. Effects of progressive resistance training in individuals with type 2 diabetes and severe motor dysfunction following diabetic polyneuropathy

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Background: It remains to be studied whether individuals with type 2 diabetes (DM2) and severe diabetic polyneuropathy (DPN) including substantial muscle weakness benefit from progressive resistance training (PRT).

Aim: To assess if PRT can precipitate increased lower-body muscle strength and lead to improved quality and hypertrophy of striated muscles in individuals with DM2 and severe DPN.

Methods: Individuals with DM2 and DPN with muscle strength less than 60% of expected of distal muscle groups (ankle extensors and flexors) were included. Participants underwent 12-weeks of supervised PRT following a run-in period (RP) of 12-weeks without any intervention. Primary outcomes were isokinetic muscle strength (peak torque) of knee and ankle extensors and flexors. Secondary outcomes included muscle volume, muscle quality (muscle strength/muscle volume) and MRI assessment of muscle fat-infiltration. Results are presented as median-values of pooled data from proximal (knee extensors and flexors) and distal muscle groups (ankle extensors and flexors).

Results: Six male individuals (age, 69 years) with DM2 and severe DPN were included. Muscle strength (+6%, p=0.03) and lean muscle mass (+6%, p=0.04) increased at the upper-leg following PRT. Fat-infiltration increased at the upper (+6%, p=0.03) and lower-leg (+7%, p=0.03) in the RP. No change in fat-infiltration was observed following PRT. Muscle quality did not change significantly throughout neither the RP nor PRT.

Conclusion: Progressive resistance training may precipitate hypertrophy and improve muscle strength of thigh muscles, and delay progression of muscle fat infiltration of the lower-body in individuals with type 2 diabetes and severe diabetic polyneuropathy.

Day 3

18 / SEPTEMBER / 2022 / 11:20-12:20

Poster presentations (P23-P34) Pathogenesis, epidemiology and diagnosis

Chairs: Mitra Tavakoli (Exeter, United Kingdom) and Luca D'Onofrio (Rome, Italy)

P23. Abstract Withdrawn.

P24. Clinical characteristics of diabetic peripheral neuropathy in type 2 diabetes: results of a national health insurance service, 2012-2017

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Aim: To determine the prevalence and clinical characteristics of diabetic peripheral neuropathy in patients with type 2 diabetes in Korea.

Methods: From the target population a representative sample cohort of 1,422,492 participants was randomly selected, comprising 3% of the total eligible Korean population in 2012, and followed until 2017. Strata were constructed by age group, sex, eligibility status and income level. During the follow-up period, the cohort was refreshed annually by adding a representative sample of newborns. Data source: NHIS: National Health Insurance Service. Definition of diabetic peripheral neuropathy (DPN)

Results: From 2012 to 2017, the prevalence of DPN in diabetic patients was 27.0%- 24.0%. DPN medication was administered in 59.3% to 57.8% of DPN patients. Drug therapy was prescribed for up to 82% mono therapy, dual combination treatment for up to 15%, and triple combination treatment for up to 3%. Prescribed medications for DPN from 2012 to 2017 were α-lipoic acid (60.8% to 58.8%), anticonvulsant drugs (26.1% to 27.4%), tricyclic antidepressants (10.4% to 8.1%), serotonin-norepinephrine reuptake inhibitors (1.6% to 3.4%), γ-linoleic acid (2.1% to 2.3%).

Persistency for pharmacological treatment of DPN was 34.2%- 35.7%, and the rate of persistency was increasing over time.

Conclusions: The prevalence of DPN patients is about a quarter of those with diabetes, and medication is about 60 percent, and most medications are administered with mono therapy.

P25. The co-existence of peripheral and autonomic neuropathy in type 1 diabetes with and without pain

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Aims: To investigate the co-existence of diabetic peripheral neuropathy (DPN), painful diabetic peripheral neuropathy (PDPN), and cardiac autonomic neuropathy (CAN) and to establish a model to predict CAN based on peripheral measurements.

Methods: 80 participants (20 type 1 diabetes (T1DM) +PDPN, 20 T1DM+DPN, 20 T1DM-DPN (without DPN), and 20 healthy controls (HC)) underwent quantitative sensory testing, cardiac autonomic reflex tests (CARTs), and conventional nerve conduction. CAN was defined as ≥ 2 abnormal CARTs. After the initial analysis, the participants with diabetes were re-grouped based on the presence or absence of small (SFN) and large fibre neuropathy (LFN), respectively. A prediction-model for CAN was made using logistic regression with backward elimination.

Results: CAN was most prevalent in T1DM+PDPN (50%), followed by T1DM+DPN (25%) and T1DM-DPN and HC (0%). The differences in prevalence of CAN between T1DM+PDPN and T1DM-DPN/HC were significant ($p<0.001$). When re-grouping, 58% had CAN in the SFN group and 55% in the LFN group, while no participants without either SFN or LFN had CAN. The prediction-model had a sensitivity of 64%, a specificity of 67%, a positive predictive value of 30%, and a negative predictive value of 90%.

Conclusion: This study suggests that CAN only co-exists with concomitant DPN.

P26. Inflammatory markers are associated with prevalent cardiac autonomic neuropathy 10 years after diagnosis with type 2 diabetes: Observation from the multi-ethnic SOUth London Diabetes (SOUL-D) study

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Aim: Factors influencing the development of cardiac autonomic neuropathy (CAN) in people with diabetes remain poorly understood. Previous studies struggled with limitations in terms of lack of ethnic diversity, and different duration of diabetes diagnosis.

Methods: Cross-sectional analysis of the SOUth London Diabetes (SOUL-D) cohort that recruited newly diagnosed T2DM individuals from South London between 2008-2011. In the 10-year follow-up, a subgroup underwent CAN testing using the Vagus® device. Presence of CAN was considered 'borderline' if 1 of the testing measures was abnormal, while ≥2 abnormalities were considered to 'confirm' the diagnosis.

Results: Of the 91 participants (47% male) aged 55.05±9.58 years at baseline, 52 (55%) had no evidence, while 21 (22%) and 20 (23%) had borderline and confirmed CAN respectively at 10-years. Presence of confirmed CAN was associated with higher baseline white cell count (p=0.0017) and interlukin-10 (p=0.0023). At 10-years, in addition to the expected association with a higher HbA1C, a higher level of neutrophils (p=0.03), lymphocytes (p=0.023), triglycerides (p=0.023) and alanine aminotransferase (p=0.0059) were noted in confirmed CAN. There was no significant baseline to 10-year change in vibration perception thresholds (VPT) except in the confirmed CAN group. No association with ethnicity, gender or depressive symptoms were noted. Interestingly, only 9 (10%) individuals for the whole cohort increased their VPT≥25 volts.

Conclusion: Presence of inflammatory biomarkers was associated with prevalent confirmed CAN in our cohort. Close monitoring of plasma inflammatory biomarkers at the time of diagnosis may identify individuals at greatest risk for developing CAN.

P27. Inflammatory Markers and Cardiovascular Autonomic Neuropathy in Type 1 Diabetes

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Background and aims: Cardiovascular autonomic neuropathy (CAN) is a prevalent serious complication in individuals with type 1 diabetes (T1D). Low-grade inflammation has emerged as a potential mechanism in the development of neuropathy from both experimental and clinical studies. We aimed to assess the role of chronic inflammation in the pathogenesis of CAN in T1D.

Methods: We leveraged an ongoing randomized, placebo-controlled clinical trial targeting inflammation with salsalate in individuals with T1D, to measure a panel of 40 inflammatory markers analyzed on a Luminex xMAP instrument (Luminex Corporation, Austin, TX) (Figure) in baseline samples. Measures of CAN included standardized cardiovascular autonomic reflex tests (CARTs) (E/I, Valsalva, 30:15 ratios) and indices of heart rate variability (HRV). We used Spearman-rank to assess the correlations between inflammatory markers and CAN measures, and linear regression to adjust for age and hemoglobin A1c.

Results: The Figure displays the correlation between biomarkers and CAN measures in 58 T1D participants (mean age 51 ± 13 years, mean diabetes duration 31 ± 15 years, and HbA1c 8.4 ± 1.8%). Amongst all biomarkers, we noted a singular negative correlation between soluble urokinase plasminogen activator receptor (suPAR) and measures of CAN, which remained significant in multivariable analysis (E/I ratio p=0.005, Valsalva p=0.037, RFA p=0.019, LFA p=0.023).

Conclusion: Amongst a large panel of inflammatory markers, we found suPAR to have a notable association with CAN. suPAR is an immune-mediated signalling glycoprotein which levels are strong predictors of risk in patients with diabetes, which role in CAN warrants further exploration

P28. The Effect of Statins on Peripheral Neuropathy in Diabetic Patients

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Aim: Peripheral neuropathy has many causes. Hyperlipidaemia has been associated with neuropathy. However, acute peripheral neuropathy has been reported in patients treated with statins. Although, there are studies suggesting that statins may improve neuropathy. We aimed to assess the effect of statin treatment on neuropathy in patients with diabetes mellitus.

Methods: 41 non-statin treated (age: 42.83±18.75) and 112 statin treated patients with diabetes (age; 60.45±10.28) were recruited. All participants underwent the assessments of HbA1C, lipid profile and neuropathy assessments which included the vibration perception threshold (VPT), cold and (CPT), warm perception threshold (WPT), the sural nerve conduction velocity (SNCV) and corneal confocal microscopy (CCM). Corneal nerve fibre density (CNFD), corneal nerve branch density (CNBD) and corneal nerve fibre length (CNFL) were quantified using CCM.

Results: There was no significant difference in duration of diabetes(years) (17.15±1.54 vs. 18.45±1.20, P=0.5) and HbA1C(%) (65.66±2.44 vs. 63.68±1.48, P=0.4) in non-statin treated compared with statin treated patients. CNFD(no./mm2) (25.62±1.41 vs. 25.37±0.7,P=0.8), CNBD(no./mm2) (56.98±6.5 vs. 57.819±3.6,P=0.2), CNFL(mm/mm2) (20.15±1.2 vs. 20.12±0.66,P=0.8), VPT(V) (13.12±1.7 vs. 15.59±0.98,P=0.2), CPT(C0) (24.54±1.005 vs. 24.66±0.57,P=0.8), WPT(C0) (40.75±0.65 vs.40.78±0.32,P=0.9) and SNCV(ms) (43.13±1.23 vs. 44.72±0.69,P=0.2) did not differ significantly between non-statin treated compared to statin treated patients after adjusting for age.

Conclusion; There is no significant difference in small or large nerve fibre damage in statin treated compared to non-statin treated patients.

P29. Determinants of prolonged sensory neuropathy after severe COVID-19 infection

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Aim: Determine predictors of sensory neuropathy in severe COVID-19 infection.

Methods: Patients hospitalized with severe SARS-CoV-2 underwent vibration (VPT), cold (CPT), warm perception (WPT), and heat induced pain (HIP) threshold testing on the foot using NerveCheck Master at baseline and 1 year.

Results: 35 subjects with severe COVID-19 aged 69.7±12.9 with hypertension (43%), diabetes (17%), obesity (9%), elevated procalcitonin (17%), and long-COVID (34%) were studied. 82% had abnormal HIP, 80% abnormal VPT and WPT, 51% abnormal CPT, 49% neuropathic pain. The percentage with abnormal VPT (-30%, P=0.01) and WPT (-36%, P<0.01) significantly reduced whilst neuropathic pain (-7%, P=0.68) and abnormal CPT (-17%, P=0.16) did not change. In patients with hypertension WPT (P=0.04) improved, whilst in those without hypertension both VPT (P=0.01) and WPT (P=0.02) improved. There was no improvement in any of the neuropathy assessments in those with diabetes, abnormal procalcitonin or long-COVID, whereas in those without diabetes, long-COVID, or normal procalcitonin levels VPT (P=0.03-0.01), WPT (P=0.01-0.001) and HIP (P=0.02-0.01) improved.

Conclusions: Sensory neuropathy in severe COVID-19 infection might be prolonged by hypertension, diabetes, severity of infection, and long COVID

P30. Diabetic neuropathy is a generalized phenomenon with significant impact on hand functional performance and quality of life

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Aims: Diabetic neuropathy (DPN) is usually considered to affect predominantly the lower limbs (LL-N), while the impact of upper limb neuropathy (UL-N) on hand functional performance and quality of life (QoL) has not been evaluated systematically. This study aims to investigate UL-N and the functional and psychosocial consequences in type 2 diabetes.

Methods: Individuals with type 2 diabetes (n=141) and an age- and sex-matched control group (n=73) underwent comprehensive assessment of neuropathy, hand functional performance and psychosocial status.

Results: Patients with diabetes showed similar sensory phenotype in hands and feet. The prevalence of UL-N was 30.5% in patients with diabetes and that of LL-N 49.6%, with 25.5% exhibiting both. UL-N correlated with the severity of LL-N, but not with duration of diabetes, glycaemia, age, or sex. Patients with UL-N showed reduced manual dexterity, but normal hand grip force. Additionally, there was a correlation between reduced dexterity and sensory deficits. Patients with combined UL-N and LL-N had reduced QoL compared to control subjects and patients with only LL-N.

Conclusions: This study points to a high prevalence of UL-N in type 2 diabetes. The sensory phenotype of patients with UL-N was similar to LL-N and was characterized by loss of sensory function. Our study demonstrated an association of UL-N with impaired manual dexterity and reduced QoL. Thus, upper limb sensorimotor functions should be assessed early in patients with diabetes.

P31. Retinal neurodegeneration as a marker of diabetic peripheral neuropathy and cognitive impairment in type 2 diabetes mellitus

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Aims: the aim of our study is to evaluate the relationship between the neuroretina alterations and both diabetic peripheral neuropathy (DPN) and mild cognitive impairment (MCI) in patients with type 2 diabetes mellitus (DM2).

Materials and methods: 56 DM2 patients (65-90 years), with a disease duration greater than 5 years, with mild diabetic retinopathy and without previous history of stroke or neurodegenerative diseases, were enrolled. DPN was investigated using the Michigan Diabetes Neuropathy Instruments (MNSI), vibration perception threshold (VPT) and thermal perception thresholds. We identified two groups: DPN+ and DPN-. Participants were also classified in MCI or controls, according to Montreal Cognitive Assessment Test (MoCA). All patients underwent retinal microperimetry measuring retinal sensitivity and average threshold macular sensitivity (ATMS), multifocal electroretinogram (mfERG) with Implicit Time (IT) evaluation and SD-optical coherence tomography (SD-OCT).

Results: In DPN+ ATMS and the GCL+IPL average thickness were significantly reduced in MCI versus C. IT of mfERG, was significantly increased in MCI versus C. In MCI patients of the DPN+, a positive correlation between VPT and a negative correlation between VPT and ATMS and between VPT and the GCL+IPL average thickness were found.

Conclusion: Morphological and functional alterations of neuroretina are observed in DM2 patients affected by MCI and DPN. A significant relation between neuroretina dysfunction and peripheral neuropathy signs was also evident in MCI with DPN. These results allow to consider the retina as a window for the evolution of peripheral and central neuropathy in the patient with type 2 diabetes.

P32. The association between prevalent sensory neuropathy and age or diabetes duration in people cared for type 2 diabetes mellitus in an internal medicine outpatient clinic – a cross-sectional study

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Introduction: Given that sensory neuropathy affects one in ten non-diabetic people, it is likely that its routine screening methods in diabetic populations also detect non-diabetic, age-related sensory nerve dysfunction. We examined independent determinants of screen-detected sensory neuropathy in a diabetes outpatient practice.

Material and method: All type 2 diabetes patients cared for at our outpatient clinic were included. Sensory neuropathy was screened using standard methods (tuning fork, monofilament test, standard set of questions). Parameters independently related to test positivity for each method were examined by hierarchical logistic regression.

Results: A total of n=479 patients (51% female) were included; mean age was 62.4±14.3 (SD) years, diabetes duration 10.2±9.9 years, and HbA1c 7.7±1.8%. In multivariate models, older age (tuning fork: OR:1.067; 95%CI: 1.042-1.093; monofilament: OR: 1.026, 95%CI: 1.004-1.048; question set: OR: 1.033, 95%CI: 1.01-1.056) but not diabetes duration was independently associated with screen detected sensory neuropathy. While the other independent determinants of sensory neuropathy based on the tuning fork test were body height, smoking, and anamnestic myocardial infarction, neuropathy diagnosed by the other 2 methods showed independent associations with hypertension and measures of renal impairment.

Summary: According to our results, commonly used tests to screen for peripheral nerve damage detect abnormalities that are more closely related to age than to the duration of diabetes in an aging type 2 diabetes population. Further prospective studies using different screening tests in the general population are required to better differentiate diabetic and non-diabetic (age-related) neuropathy.

P33. Multiple musculoskeletal complications as a consequence of diabetic polyneuropathy in one patient - a case report

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Chronic complications of diabetes mellitus rarely recall thoughts of musculoskeletal disorders. However, they are prevalent and may lead to impaired quality of life and disability.

The diabetes of our 75-year-old patient has been known for 26 years. Two years ago, he was admitted to hospital because of weight loss and progredient weakness and wasting of the proximal lower extremity muscles. His severe distal symmetrical diabetic polyneuropathy supported the hypothesis of diabetic amyotrophy. Other aetiologies (malignancies, autoimmune disorders) were excluded. Pathogenetically-oriented treatment for diabetic neuropathy and regular physical exercise were implemented.

One year after, the patient presented with a dry gangrene of the right hallux. The X-ray depicted osteolytic lesions typical for neuropathic osteoarthropathy. Meanwhile, he experienced weight gain and improving lower limb muscle strength.

Last summer, the patient complained of flexion deformity and waxy thickening of the dorsal aspect of his fingers. Limited joint mobility of the metacarpophalangeal and interphalangeal joints could be proven by the Prayer's sign and tabletop sign. Hand imaging studies did not show any major abnormalities. On neuropathy examinations, progression of hypaesthesia of the upper extremities could be demonstrated and the diagnosis of diabetic cheiroarthopathy was made. To maintain hand function, physical therapy was suggested.

Beyond osteoneuroarthropathy, musculoskeletal complications of our patient comprise diabetic cheiroarthropathy and amyotrophy. These manifestations show associations with diabetic polyneuropathy and other microvascular complications. We should be aware of these manifestations in diabetic patients with polyneuropathy and patients with musculoskeletal complaints should be screened and treated for diabetic neuropathy as well.

P34. Assessing diabetes polyneuropathy using a 5.07/10g Semmes-Weinstein monofilament

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Aim: Despite earlier studies demonstrating poor diagnostic accuracy, monofilament tests are widely used and advocated for in guidelines for diagnosing diabetes polyneuropathy. We aimed to determine the diagnostic accuracy of the standard 10g Semmes-Weinstein monofilament examination (SWME) in patients with diabetes referred to a polyneuropathy assessment.

Methods: We included patients with diabetes, referred to neurological outpatient clinics at five Norwegian University hospitals for polyneuropathy assessment. All patients were investigated with a 5.07/10g SWME in concordance with the Norwegian guidelines. In addition, subjects underwent neurological examination and thorough nerve conduction studies. The Toronto consensus criteria (Tesfaye grading scale) for diagnosing diabetes polyneuropathy served as the reference standard.

Results: In total, 305 patients were included. Sample prevalence of diabetes polyneuropathy was 66%. Compared to nerve conduction measurements, the SWME demonstrated low sensitivity, but relatively high specificity. The positive predictive value and likelihood ratio were acceptable, while the negative predictive value and likelihood ratio were poor.

Conclusions: A positive SWME may help rule in diabetes polyneuropathy. However, very low sensitivity erodes the clinical usefulness, leading to a high false negative rate and greatly reducing the test's impact on post-test probability of disease, regardless of test result. In addition, tests that are able to rule out disease may be more appropriate for outpatient clinics that assess patients with suspected diabetes polyneuropathy, especially when results are likely to impact further examination and treatment. We conclude that the standard 5.07/10g SWME is not suited to assess diabetes polyneuropathy in patients referred to a polyneuropathy assessment.

Day 3

18 / SEPTEMBER / 2022 / 11:20-12:20

Poster presentations (P35-P45) Autonomic neuropathy and treatment
Chairs Sanjeev Sharma (Ipswich) and Aleksandra Araszkiewicz (Poznan, Poland)

P1. Prevalence and risk factors for diabetic peripheral neuropathy, neuropathic pain and foot ulceration in the Arabian Gulf Region

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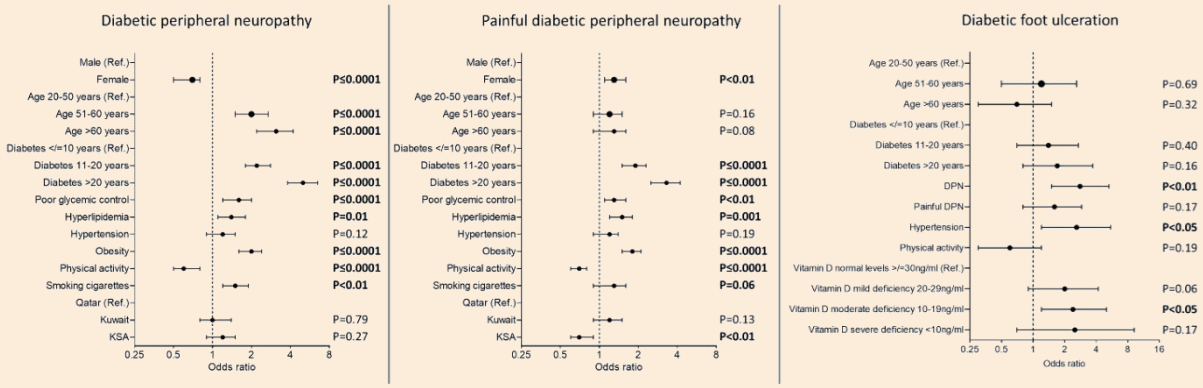
Aim: This study determined the prevalence and risk factors for diabetic peripheral neuropathy (DPN), painful DPN and diabetic foot ulceration (DFU) in patients with type 2 diabetes (T2D) in secondary health care (SHC) in Qatar, Kuwait and Kingdom of Saudi Arabia.

Methods: Adults 18-85 years old with T2D were randomly enrolled from SHC and underwent clinical, metabolic, DPN using vibration perception threshold (VPT) and DN4 questionnaire, and DFU assessments.

Results: 3,021 subjects were recruited between June 2017 and May 2019. The prevalence of DPN was 33.3% of whom 52.2% were at risk of DFU and 53.6% were undiagnosed. The prevalence of painful DPN was 43.3%, of whom 54.3% were undiagnosed. DFU was present in 2.9%. The adjusted odds ratios (AOR) for DPN and painful DPN were higher with increasing diabetes duration, obesity, poor glycemic control, hyperlipidemia, and lower with greater physical activity. The AOR for DFU was higher with the presence of DPN, severe loss of vibration perception, hypertension, and vitamin D deficiency.

Conclusions: This is the largest study to date from the Middle East showing a high prevalence of undiagnosed DPN, painful DPN and those at risk of DFU in patients with T2D and identifies their respective risk factors.



P35. Predictors of erectile dysfunction in type 2 diabetes in secondary care in Qatar

Georgios Ponirakis [1], Tarik Elhadd[2], Subitha Chinnaiyan[2], Zeinab Dabbous[2], Mashhood Siddiqui[2], Hamad Al-muhannadi[1], Ioannis Petropoulos[1], Adnan Khan[1], Khaled A. E. Ashawesh[3], Khaled M. O Dukhan[3], Ziyad R. Mahfoud[1], Rayaz A. Malik[1]

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Aim: This study determined the predictors for erectile dysfunction (ED) in patients with type 2 diabetes (T2D) in secondary health care (SHC) in Qatar.

Methods: Adults 18-85 years old with T2D were randomly enrolled from SHC and underwent assessments of clinical, metabolic, diabetic peripheral neuropathy (DPN) and painful DPN (pDPN) using DN4 questionnaire, and the International Index of Erectile Function (IIEF-5) questionnaire.

Results: 67 subjects aged 49±8.5 with 7.2 years of T2D were studied. The prevalence of ED was 37.3% (25/67) of which 64% was mild, 20% was moderate and 16%. Subjects with ED had a significantly higher prevalence of DPN (28% vs 2.4%, P<0.01) and pDPN (40% vs 14.3%, P=0.01) compared to those without ED.

The odds of ED was 15.9 (95%CI: 1.8-139.3, P=0.01) times higher with DPN and 4 (95%CI: 1.2-13, P=0.02) times higher with pDPN. The prevalence of poor glycemic control (25% vs 21.4%, P=0.89), obesity (48% vs 31%, P=0.34), smoking cigarettes (36% vs 23.8%, P=0.26) and physical activity (36% vs 47.6%, P=0.19) did not differ between patients with and without ED. ED had no association with hypertension (P=0.47), retinopathy (P=0.76), and dyslipidaemia (P=0.89).

Conclusions: Erectile dysfunction is strongly associated with DPN and pDPN, and its prevalence might increase with DPN risk factors.

P36. Influence of body composition on cardiovascular autonomic neuropathy in patients with type 2 diabetes mellitus

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Aims: Cardiovascular autonomic neuropathy (CAN) is a common but often overlooked complication of diabetes. In this study we investigated the influence of visceral adipose tissue (VAT) on CAN in patients with type 2 diabetes mellitus (T2DM). We also tried to see if there was a correlation between CAN and bone mineral density (BMD) in patients with T2DM.

Methods: We evaluated 241 patients with T2DM by doing DXA whole body, Ewing tests and an evaluation of sweat gland function. Study design was cross sectional and statistic data were analysed using IBMSPSS.

Results: Out of 241 patients with T2DM, 51,9% (n= 125) were female and 48,1% (n=116) were male, with a mean age of 59,66 ± 8,04 years. The prevalence of CAN in the study group was 68% (n=164). The mean VAT mass was 966,7±285,3 grams. The VAT mass and total body fat percentage showed positive correlations with presence of CAN ($p<0.05$). There was no statistically significant difference between BMD and presence of CAN in our group (p=0,14).

The mean QTc interval was 459±61,4 milliseconds in CAN – group and 461±64,6 milliseconds in CAN+ group without statistical significance (p=0,27). We also found strong statistical correlations between the Ewing score and the CAN score obtained by the sweating test (p<0,00001).

Conclusion: The results of this study suggest that visceral adiposity contributes to an autonomic imbalance as demonstrated by the cardiovascular reflex test. The QTc interval alone is not enough to diagnose CAN and more advanced diagnostic methods are needed.

P37. Clinical Characteristics of Diabetic Cardiovascular Autonomic Neuropathy in Republic of Korea

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Objectives: To investigate the prevalence and clinical characteristics of cardiovascular autonomic neuropathy (CAN) in Korean patients with DM, multi-center based study was performed.

Methods: Data of 884 diabetic patients undergoing CAN assessment was collected retrospectively from 8 hospitals in Korea. Patients' biodata were recorded, and electrocardiography (ECG) and cardiovascular autonomic function tests were performed to aid the diagnosis of CAN.

The final CAN diagnosis was based on the ECG-QTc interval or Ewing's test in which five cardiovascular autonomic reflex tests(CARTs) were evaluated through deep-breathing, lying-to-standing, sustained handgrip test and Valsalva tests.

Results: Out of 884 patients (Type 1 DM; 17, Type 2 DM; 867), the mean age of the patients was 59.6 years old and the mean duration of diabetes was 13.2 years. Patients were divided into two groups; "without CAN" (Non-CAN) and "with CAN" (CAN). The prevalence of CAN was 88% (778). The patients with CAN were older (62.38 vs 56.77; $P < 0.0001$), had longer diabetes duration (13.69 vs. 12.65; $P = 0.0161$), higher creatinine (1.05 vs 0.81; $P = 0.0472$), higher urine albumin (117.70 vs 45.99; $P=0.0216$) and higher ECG-QTc interval (431.16 vs 420.71; $P<0.0001$), compared to patients without CAN. On multiple logistic regression analysis, duration of diabetes (OR; 1.073, $P = 0.0161$), older age (OR; 1.053, $P < 0.0001$), and higher Cr (OR; 2.288, $P = 0.0281$) were risk factors for CAN.

Conclusions: CAN is common complication, and its' factors are duration of diabetes, age, and nephropathy in Korean patients with DM.

P38. Role of the Nerve Check Master to identify diabetic patients with cardiac autonomic neuropathy

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Aim: The association between diabetic peripheral neuropathy (DPN) and cardiac autonomic neuropathy (CAN) is not consistent across the literature. This study aimed to examine the relation between DPN as detected by two different methods and CAN in patients with diabetes.

Methods: We included 76 T1D adults and 65 T2D patients (means: age 39 and 59 yrs; diabetes duration 13.5 and 11.4 yrs, HbA1c 8.0% and 7.8%, respectively). DPN was defined according to Michigan neuropathy screening instrument (MNSI) and Nerve Check Master (NCM) (≥2 abnormal tests out of 4). CAN was assessed by analysing heart rate variations during standard tests (Valsalva, deep-breathing, lying-to-standing) and postural hypotension and considered to be present if ≥2 abnormal tests.

Results: According to MNSI and NCM, DPN prevalence was respectively 26.3% and 61.8% in T1Ds, 35.4% and 70.8% in T2Ds. CAN prevalence was 22.4% and 41.4% in T1Ds and T2Ds, respectively. When considering DPN as detected by NCM, CAN prevalence was markedly higher among DPN+ compared to DPN- patients among T1Ds (34% vs 3.4%, p=0.0002) but not among T2Ds (45% vs 33.3%, NS). DPN as detected by MNSI was not associated with CAN neither in T1Ds nor in T2Ds.

Conclusions: Among T1Ds, the presence of DPN on NCM, which accounts for both small and large fibers impairment, allows to identify all but one patients with CAN while DPN absence rules out CAN. MNSI is inappropriate to detect patients with CAN. In T2D the weak DPN-CAN association is consistent with the plurifactorial pathophysiology of CAN.

P39. Predicting diabetic cardiac autonomic neuropathy using advanced machine learning algorithms in type 2 diabetes patients

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Aim: Diabetic cardiac autonomic neuropathy (DCAN) is a very common complication in patients with diabetes mellitus (DM), and early detection or prediction of DCAN is important for preventing sudden death and cardiovascular complications. Our aim is to delineate whether machine learning (ML) techniques are useful for predicting DCAN in type 2 DM patients.

Methods: Nine hundred fifty-nine DM patients were classified into two groups DCAN (-) and DCAN (+) based on Ewing method tests by machine (DiCAN) and EKG QTc of suspected DCAN patients. Prediction models were computed with clinical risk factors (27 measures) based on electric health records and examination results. Four machine learning methods, Extreme Gradient Boost (XGBoost), support vector machine (SVM), and random forest (RF), Decision Tree (DT) were used for analysis of parameters which affect the DCAN prediction. We compare the accuracy, sensitivity, and specificity of each method by using K-fold cross validation.

Results: The best results were achieved with XGBoost model followed by RF model. However, XGBoost showed the best accuracy, specificity, and sensitivity. The important features for prediction of DCAN were upright HR, upright LF, EKGQTc, age, and DM duration.

Conclusions: In conclusion, ML techniques, especially XGBoost, can predict DCAN in DM patients effectively, and spectral analysis parameters of Ewing methods and clinical risk factors are important for identifying DCAN. Further replication of ML tools in a real-world context will facilitate implementation in the clinic.

P40. The Composite Autonomic Symptom Score 31 (COMPASS 31) in a Norwegian population of longstanding type 2 diabetes, early diabetes, and healthy controls. A part of the PanGut study.

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Aims: To use the Composite Autonomic Symptom Score 31 (COMPASS 31) in a Norwegian population of people with longstanding diabetes, early diabetes, and healthy controls, and to compare the score to established tests for diabetic autonomic neuropathy, peripheral polyneuropathy, and to a novel test examining gastrointestinal autonomic function.

Methods: 21 participants with longstanding type 2 diabetes, 15 with early type 2 diabetes, and 30 healthy controls were included. The Danish version of COMPASS 31 was translated to Norwegian language using forward/backward translation. Tests performed were cardiovascular autonomic reflex tests (CARTs), electrical skin conductance, sural nerve electrophysiology and the monofilament test. Evoked potentials were measured following rectal balloon distention at earliest sensation and threshold of unpleasant sensation.

Results: Participants with longstanding diabetes scored higher, 20.2+13.4, than people with early diabetes, 10.4+10.8, and healthy controls, 12.7+13.0, p= 0.03 and 0.04, respectively. Women scored higher, 18.9+15.2, than men, 9.4+7.8, p=0.01. In CARTs, people with borderline cardiac autonomic neuropathy (CAN), scored higher, 18.9+11.0, than people with no CAN, 12.7+12.1, p=0.07. Participants with possible neuropathy on monofilament test scored higher, 25.4+15.3, than those with normal sensation, 13.9+12.2, p=0.01.

Conclusions: We successfully used the COMPASS31 in a Norwegian population. Participants with longstanding diabetes reported more symptoms of autonomic neuropathy than people with early diabetes and healthy controls. These findings could be associated with diabetes medication. Women reported more symptoms than men. We found correlation between increased symptom burden and borderline CAN on CARTs, and correlation related to possible neuropathy on monofilament test.

P41. Renal Hemodynamic Dysfunction and Neuropathy in Longstanding Type 1 Diabetes: Results from the Canadian Study of Longevity in Type 1 Diabetes

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Aim: Renal hemodynamic function is partially regulated by the autonomic nervous system. We aimed to determine the relationship between renal hemodynamic function and neuropathy measures in adults with ≥50-years of type 1 diabetes (T1D) compared to nondiabetic controls.

Methods: Glomerular filtration rate (GFR, inulin), effective renal plasma flow (ERPF, p-aminohippurate), modified Toronto Clinical Neuropathy Score (mTCNS), corneal confocal microscopy, nerve conduction, and heart rate variability (autonomic function) were measured; afferent (RA) and efferent (RE) arteriolar resistances were estimated using the Gomez equations in 74 participants with T1D and in 75 controls. DKD non-resistors were defined by eGFRMDRD<60ml/min/1.73m2 or 24-hour urine albumin excretion >30mg/day. DKD non-resistors were compared to DKD resistors using ANCOVA with age, sex, HbA1c and LDL as covariate. Linear regression was applied to examine the relationships between renal function (dependent variable) and neuropathy measures (independent variable), adjusted for age, sex, HbA1c, systolic blood pressure, LDL, and 24 hour albumin to creatinine excretion ratio.

Results: Greater mTCNS associated with lower renal blood flow (b±SE:-9.29±4.20, p=0.03) and greater RE (b±SE:32.97±15.43, p=0.04) in participants with T1D, but not in controls. DKD non-resistors had a greater mTCNS and worse measures of corneal nerve morphology compared to those without DKD. Renal hemodynamic parameters did not associate with autonomic nerve function.

Conclusions: Although peripheral neurological dysfunction in the presence of diabetes may be related to impaired renal blood flow resulting in ischemic injury in patients with T1D, early autonomic dysfunction does not appear to be a cause.

P42. Early witnesses of sympathetic activation during hypopneic episodes induced by the slow breathing test in obese or diabetic patients with obstructive sleep apnoea syndrome (OSAS)

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Aim: In patients with OSAS, blood pressure decreases during apneas and increases abruptly after apneas due to sympathetic activation. We previously showed that a brief period of slow breathing (SLB) can trigger hypopneic events. This study aimed to assess the earliest changes in hemodynamic parameters occurring during hypopneic events induced by SLB.

Methods: In 110 obese or diabetic patients diagnosed with moderate/severe OSAS based on nocturnal polygraphy, we continuously monitored respiration, SaO2, heart rate (HR), peripheral blood flow (photoplethysmography, PPG), diastole duration (from PPG recordings) and arterial stiffness (derived from PPG) during spontaneous respiration (5minutes), 5-min of SLB (6 cycles/min) and 5-min follow-up under spontaneous breathing.

Results: During the SLB, HR difference between breathing-in and breathing-out was 2.7±4.9 bpm during the first minute and slightly decreased during the sixth minute; diastole duration expressed as percentage of cardiac cycle (DD%) increased from 41.7±3.6% to 47.4±3.6% during breathing-in ($p<0.0001$) and did not change during breathing-out. During hypopneic events occurring after SLB, compared to before hypopnea, SaO2 (mean: -3%), HR (-5 bpm), DD% (50.8±10.7% vs 66.8±12.9%), blood flow (-30%) and arterial stiffness index (-1 m/s) decreased significantly ($p<0.0001$ for all).

Conclusion: In obese/diabetic patients with OSAS, HR variations are depressed, diastole duration increases after SLB probably through a reduction of sympathetic activity. During hypopneas, diastole shortening despite HR slowing and peripheral vasoconstriction are the earliest witnesses of sympathetic activation while arterial stiffness decrease is likely to result from transient blood pressure lowering

P43. Life threatening recurring hypoglycemic episodes in a type-1 diabetic patient with severe autonomic neuropathy and chronic malabsorption

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Autonomic neuropathy has several detrimental effects on glycemic control even in patients with multiple morbidity. The 45-year-old male type-1 diabetic patient was an alcoholic consumer with chronic pancreatitis by his previous history. He was admitted to the neurology clinic due to severe recurrent convulsions and transient unconsciousness after breakfast and dinner. The CGMS on 6 consecutive days detected a regularly recurrent trend of postprandial hypoglycemia after all breakfasts and most of the dinners explaining the etiology of the unconsciousness. All of the hypoglycemic epidoses were followed by hyperglycemic intervals in accordance with the Somogyi phenomenon. The cardiovascular reflex tests revealed very severe autonomic neuropathy (AN) at admission (heart rate response to breathing: 4/min, Valsalva ratio:1.015, 30/15 ratio: 1.012, orthostatic systolic blood pressure fall: 16 mm Hg, diastolic blood pressure elevation at handgrip: 7 mm Hg, AN score: 8). The peripheral sensory function assessed with a Neurometer was normal despite of the established severe autonomic disorder. The half time of the scintigraphic gastric emptying (HTE) of radioiodine labelled test meal revealed an extremely slow gastric motility (HTE: 487.6 min, normal range: ≤ 67.6 min). The impaired carbohydrate absorption due to chronic pancreatitis, the abnormal counterregulatory response and unawareness as well as the extremely slow gastric emptying caused by severe autonomic neuropathy leads to life-threatening hypoglycemic attacks imitating epilepsy.

P44. Venesection Improves Small Fiber Nerve Function in Diabetics with Elevated Ferritin

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The effect of iron overload on the nervous system has been studied and there are multiple reports correlating with Friedrich's ataxia and a few with parkinsonism. The effects on the peripheral nervous system have been described and show causality of small fiber neuropathy (by histopathology examination). The effects on large fibers give a picture similar to diabetic neuropathy. Electrochemical Skin Conductance (Sudoscan) provides a non-invasive method for assessment of small fiber function

Aim: to assess whether the reduction of iron overload in diabetics with hemochromatosis by venesection affects small fiber neuropathy

Method: We searched our records for patients with elevated ferritin who had Sudoscan repeated before and after venesection. We then compared the ferritin reduction with Sudoscan results and with liver enzymes using the Student's T-Test

Results: 8 patients (6/8 M/F) were identified with full datasets. Ferritin reduction by venesection significantly improved small nerve function by Sudoscan Feet Conductance increased by an average of 10.5 uS ($P<0.005$) Hands increased by an average of 4.5 uS ($P<0.005$) and decreased liver enzymes ALT decreased an average of 20 IU($P<0.05$), AST decreased average 8.3 IU ($P<0.005$).

Conclusion: Iron overload may be an aggravating, easily correctable factor in patients with small fiber diabetic neuropathy.

P45. Efficacy and Safety of the combination of Superoxide Dismutase, Alpha Lipoic Acid, Vitamin B12, B1, B2, B6, E, Mg, Zn and a fatty acid for 6 months in patients with diabetic neuropathy

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To investigate the efficacy of Superoxide Dismutase, Palmitoyethanolamide, Alpha Lipoic Acid, vitamins B6, B1, B12, E, Nicotinamide and minerals (Mg, Zn) in one tablet in Diabetic Neuropathy (DN).

In this pilot study, 61 patients with Diabetes Mellitus Type 2 (DMT2, 31 women), with mean duration of DM 17.5 years and mean age 63 years were randomly assigned, either to receive the combination of ten elements (2 tablets/24h) in the active group (n=30), or the placebo (n=31) for 6 months. We used Michigan Neuropathy Screening Instrument Questionnaire and Examination (MNSIQ, MNSIE), measured vibration perception threshold (VPT) and Cardiovascular Autonomic Reflex Tests (CARTs). Nerve function was assessed by DPN Check [sural nerve conduction velocity (SNCV), amplitude (SNAP)]. Sudomotor function was assessed with SUDOSCAN that measures electrochemical skin conductance (ESCH, ESCF). Pain (PS) questionnaire was administered, also.

Changes in B12 levels, VPT, MNSIE and pain from baseline to follow up differed significantly between the two groups (p<0,001, 0,025, 0,012, <0,001 respectively). Measurements from CARTs, SNAP, ESCH did not change significantly in both groups. B12 levels, pain, MNSQ, SNCV, VPT and ESCF significantly improved in active group (222.1 vs 576.3 pg/ml, p<0.001, 19.2 vs 13.9, p<0.001, 6.1 vs 5.9, p=0.017, 28.8 vs 30.41, p=0.001, 32.1 vs 26.7, p=0.001, 76.5 vs 73.10, p=0.023 respectively), whereas in placebo the aforementioned parameters remained unchanged. The combination of the ten elements in one tablet for 6 months at a daily dose of two tablets in patients with DMT2 improved pain and Vit B12 levels.

GENERAL INFORMATION

About Bergen



“The Gateway to the Fjords”

Bergen is Norway’s second largest city with the facilities of a large city and the charm and atmosphere of a small city. Old wooden houses and narrow cobbled streets meets urban, modern character.

The UNESCO World Heritage site Bryggen, “The Hanseatic Wharf”, is the most obvious remnant from the time Bergen used to be the centre of trade between Norway and the rest of Europe. It still looks the same as it did when the town was in its infancy.

Today, the wharf houses a museum, shops, galleries, and restaurants, and is a focal point for both locals and visitors.

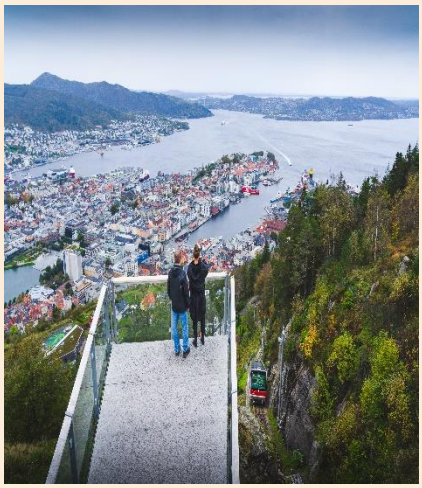
Just a stone’s throw away from Bryggen is the lively Fish Market which has been providing the locals with freshly caught treasures from the sea since 1276.

One of the cool things about Bergen is that you don’t necessarily need to visit a museum or gallery to experience great art. This is where old meets new. All over the city, you can admire dense collections of spray-painted glory thanks to world-class street artists from near and far. Skostredet, perhaps Bergen’s most charming restaurant street, is an ideal starting point for a self-guided street art safari.

Bergen is known as the "City of the Seven Mountains". These mountains surround the city and offer great hiking opportunities.

By far the most easily accessible is Mount Fløien 320 metres above sea level. It is connected to the city centre by Fløibanen Funicular, a six-minute ride.

The highest mountain is Ulriken, 643 metres above sea level. You can easily reach the top, thanks to the Ulriken cable car.



About the venue

Hotel Norge by Scandic

Our venue for the 32nd Neurodiab Conference is Hotel Norge by Scandic, located in the heart of Bergen. For further information regarding the hotel, please check out the landing page Accommodation.

Our 3-day conference will take place in their main Ballroom, situated on their ground floor, just past the main entrance of the hotel.

The spacious conference room Ballroom, approx. 280 square meters, with a capacity for up to 250 delegates, is ready to welcome you to interesting, inspiring presentations and talks.

Everything is set to create unforgettable and successful meetings together with CIC's professional production and technical team.

Mingling, coffee breaks and our tapas-lunches will take place in the Foyer just outside the Ballroom in addition to the sponsorship exhibitors.

Poster Sessions will be conducted in the hotel's Studio rooms 1-2-3, just upstairs from the main hall.

Accommodation

Hotel Norge by Scandic

Address: Ole Bulls Plass 4, 5012 Bergen

Hotel Norge has been an icon and one of Bergen's most prominent hotels ever since it first opened in 1885. The hotel was completely renovated a couple of years ago and now appears as a modern and lively meeting place.

Hotel Norge is situated in the heart of the city, at the end of Torgallmenningen Square and right next to Byparken. You are within easy reach of everything Bergen has to offer. You are just a short walk from the buzz of the city, with its great shopping and cafés, museums, galleries and the most popular attractions such as Fløibanen funicular, the Fishmarket, Bryggen and the Hanseatic area.

The hotel can offer 415 new and elegant rooms with high standard of quality in a contemporary style.

Scandic Neptun Hotel

Address: Valkendorfsgaten 8, 5012 Bergen

Scandic Neptun has always been an arena for art and cultural events. It offers one of Bergen’s largest collections of almost 750 artworks.

The hotel is centrally located, only 2 minutes from Torgallmenningen Square and within walking distance of the most popular attractions such as Fløibanen Funicular, the Fishmarket, Bryggen and the Hanseatic area.

Scandic Neptun can offer 270 rooms in total with all facilities.

Walking distance to Hotel Norge by Scandic is approximately 10 minutes.

Reservation and cancellation conditions both hotels:

- Check-in from 15:00, check out latest at 12:00 noon.
- Cancellations from August 15th, will be refunded 50%.
- Cancellations from September 1st, no refund.
- All cancellations/changes must be in writing, forwarded to neurodiab@cic.no.
- In the event of government-imposed band from September 1st, on carrying out the conference due to the covid situation, you will be refunded 90% av the accommodation costs.
  Make sure you have your insurance policy updated and covered.

Posters Presentations

All posters are presented at special, formal Poster Discussion Sessions which will be held on Saturday 13.30-14.30 and Sunday 11.20-12.20. Opportunity is available for the posters to be displayed from Thursday 17:00 onwards. The poster sessions offer an excellent opportunity for scientific discussions. During the Poster Presentation Sessions, the presenting author must be present or make arrangements for somebody with knowledge of the displayed work to be present at the poster. An average of 3 minutes will allow for each author to present his/her poster, followed by open discussion of 2 minutes (depending on the number of abstracts in the poster session).

Posters must be on display throughout the whole duration of the Meeting.

Preparation

Please have your poster prepared in advance; the poster boards' surface will be fabric.

All Posters must be on display from 16-18 September 2022.

Poster mode: PORTRAIT A0 (85 cm X 118 cm)

The Title, the Author(s) and the Place(s) of work should be positioned at the top of the poster. Each presentation should include a brief explanation of the Aims, Methods, Results and Conclusions. Please do include any relevant disclosure information on your poster. All text, tables, and drawings should be large enough to be seen at a distance of 2 m. Drawings may be originals or photographs, provided they are of appropriate size. Data should be in the form of tables and/or figures.
Only English language may be used.
No branding / advertising is allowed.

Mounting of Posters

Posters can be mounted from 17:00 Hrs. on Thursday, 15 September 2022.

Posters must be kept on display until 14:30 Hrs. on Sunday, 18 September 2022.

Posters are best attached using Velcro. We will supply the Velcro. Please find the details concerning the location of your poster upon arrival in Bergen. Posters are placed by the author (or person entrusted by the author) according to the assigned poster numbers, the poster rooms can be found on the 2nd floor, “Studio 1, 2 and 3”.

There will not be any Poster Printing Services offered via Neurodiab.

Posters that have not been taken down by the author(s) will be removed and disposed of by the organisation. Neurodiab and the Local Organisers are NOT liable for any loss or damage that may occur to the Posters at the Poster Help Desk or on the Poster Boards.

Registrations desk

CIC Event Congress

neurodiab@cic.no

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Opening hours during the conference

Day 1 (15 SEP): 17:00 – 20:00 Neurodiab Hospitality Desk open for Registration
Day 2 (16 SEP): 07:30 – 17:00 Neurodiab Hospitality Desk open for Registration
Day 3 (17 SEP): 08:00 – 18:00 Neurodiab Hospitality Desk open
Day 4 (18 SEP): 08:00 – 14:00 Neurodiab Hospitality Desk open

Practical Information

Currency

The official currency in Norway is Norwegian Kroner (NOK).

1 NOK = 0.10 EURO

September 2022

Electricity

Norway uses 220 – 240 Volt/ 50Mhz system and two-pin continental plugs, the same as most other European countries.

Conference language

The official language of the conference is English. No simultaneous translation will be provided.

Time zone

Norway is in the Central European Time zone (CET).

Public transport

All sorts of tickets can be bought at the Bergen Tourist Information next to Fisketorget in downtown Bergen. With the Bergen Card you get to travel with Bybanen and the busses in the region all for free.

Wi-Fi

Free Wi-Fi is available for all participants at the conference venue and the two hotels when you log into to the guest Wi-Fi .

In case of emergency

110 Fire department

112 Police

113 Ambulance

116 117 Emergency room

What's the weather like in Bergen in September?

Bergen is known for its “humidity” and we could possibly have a bit of rain. Daytime average temperature 14-16°C and nighttime average 10-12°C.

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CIC event congress is a professional event organiser and PCO (Professional Congress Organiser) with long standing expertise and experience for nearly 27 years. CIC's mission is to aim for excellence and to exceed expectations, and we do this with our team of professional and dedicated staff.

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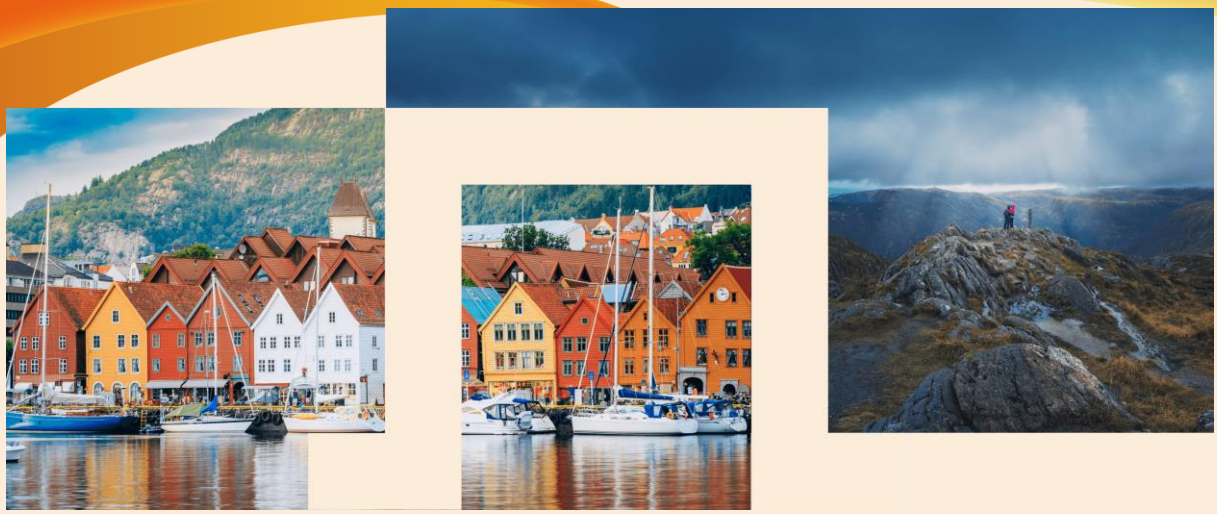

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