NEURODIAB

31ST ANNUAL MEETING OF THE DIABETIC NEUROPATHY STUDY GROUP OF THE EASD

27-30 AUGUST 2021

ARISTOTLE UNIVERSITY OF THESSALONIKI
RESEARCH DISSEMINATION RESULTS

UNDER THE AUSPICES OF:
DEAN AND SCHOOL OF MEDICINE OF THE ARISTOTLE UNIVERSITY OF THESSALONIKI
SHOOL OF MEDICINE OF THE ARISTOTLE UNIVERSITY OF THESSALONIKI

IN COLLABORATION WITH:
SOCIETY OF INTERNAL MEDICINE OF GREECE

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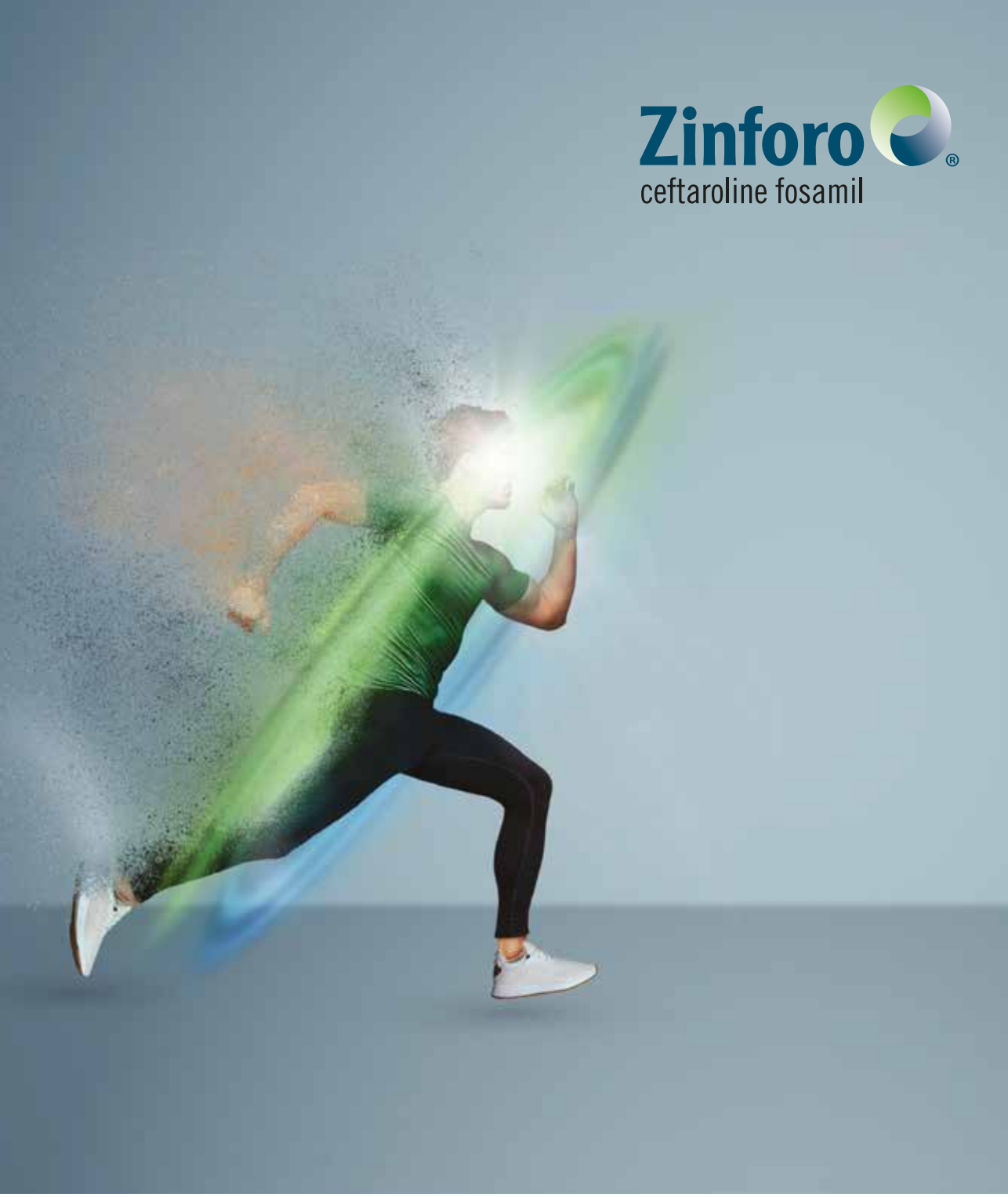
SCIENTIFIC PROGRAM | **ABSTRACT BOOK**



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Λεωφόρος Αθαλάσσας 26, 2018 Λευκωσία, Κύπρος,
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Για πλήρεις συνταγογραφικές πληροφορίες συμβουλευτείτε την Περίληψη Χαρακτηριστικών του Προϊόντος που διατίθεται από την εταιρεία.

Βοηθήστε να γίνουν τα φάρμακα πιο ασφαλή και Αναφέρετε ΟΛΕΣ τις ανεπιθύμητες ενέργειες για ΟΛΑ τα φάρμακα Συμπληρώνοντας την «ΚΙΤΡΙΝΗ ΚΑΡΤΑ»

PP-ZFO-GRC-0115-MAY21

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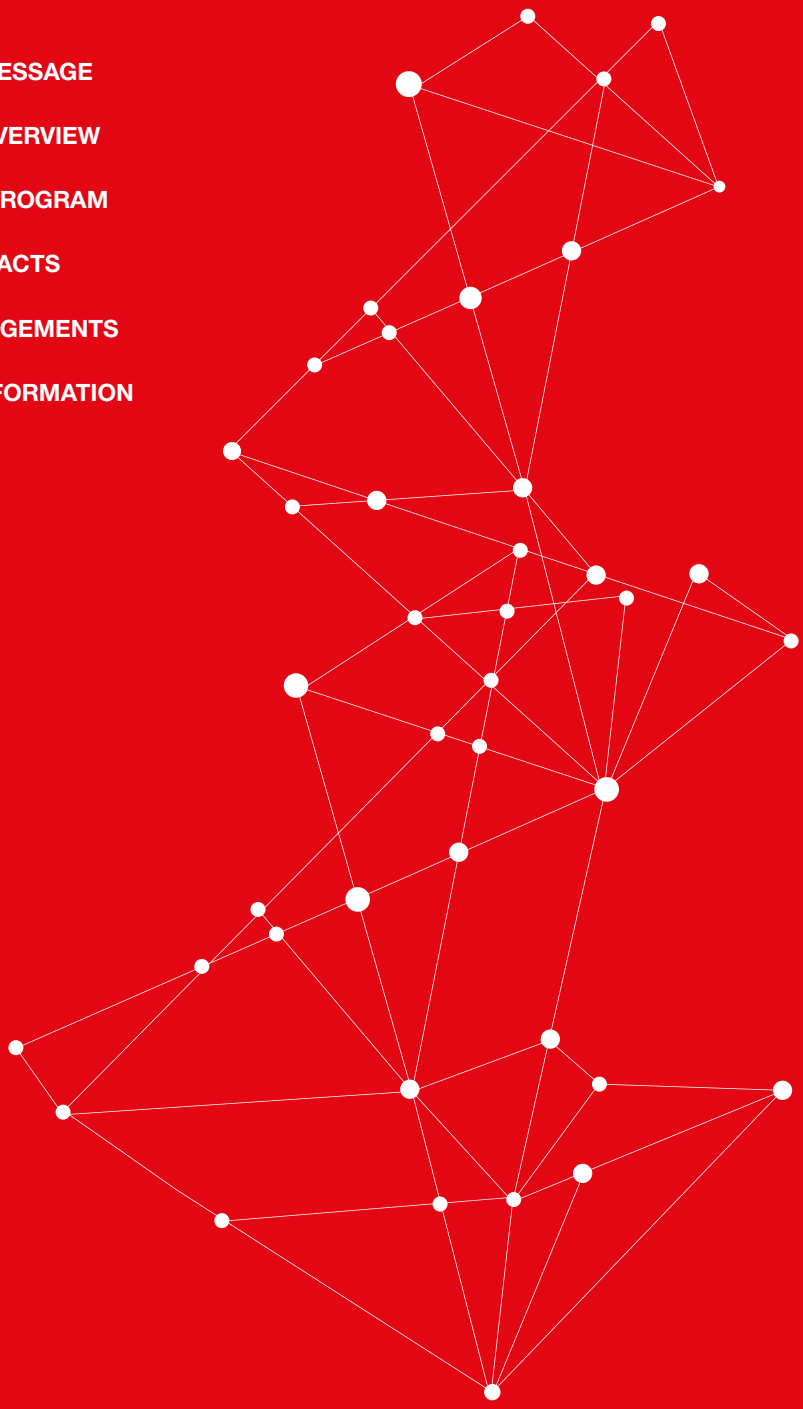

NEURODIAB 2021 COMMITTEE

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Executive Committee

Prof. Gerry Rayman

Dr. Tamas Varkonyi

Dr. Fabiana Picconi

Prof. Rodica Pop- Busui

Prof. Eirik Søfteland

WELCOME MESSAGE

31st ANNUAL MEETING
Of the Diabetic Neuropathy Study of the European Association for the Study of Diabetes

Dear Distinguished Colleagues and Friends

On behalf of the organizing committee, we have the great honor and the pleasure to invite you to participate at the 31st Annual Meeting of NEURODIAB, the diabetic Neuropathy Study Group of the European Association for the Study of Diabetes. The meeting will be held for the first time from 27th to 30th August 2021 in Thessaloniki, one of the most beautiful cities of Greece.

At present, we are preparing for **a hybrid virtual and an in-person meeting.** A final decision will be made later, depending on any travel restrictions imposed by the COVID-19 pandemic.

The congress NEURODIAB 2021 is considered the most important international annual event in the scientific field of Diabetic Neuropathy with presentations about all new research findings and outstanding lectures and symposia from distinguished and awarded speakers and researchers.

The venue of the congress is the Center for Dissemination of Research Results in the center of the city nearby Aristotle University of Thessaloniki. There are many spectacular sightseeing places, archaeological sites (Thessaloniki is nearby to Vergina the historical place where Alexander the Great was born, see at website https://www.discovergreece.com/macedonia/vergina), views, and many museums for visiting. The town is, also, near the mountain Olympus where the ancient Greek Gods lived.

We hope to join us and welcome all of you to Thessaloniki for an unforgettable 31st congress of NEURODIAB!

On behalf of the Organizing Committee
Local Chairman Prof. Triantafyllos Didangelos
Thessaloniki, Greece


wörwag
PHARMA

DAY 1 — FRIDAY 27-8-2021 / PROGRAM OVERVIEW

PRE-CONGRESS MEETING

09:00 – 09:30 **LECTURE**
Chair: **T. Didangelos** – Greece, **G. Kaiafa** – Greece
Diabetic neuropathy and nutritional supplements
Presenter: **P. Giannoulaki** – Greece

09:30 – 10:00 **LECTURE**
Chair: **L. Lanaras** - Greece
Autonomic nervous system function in Obesity and prediabetes
Presenter: **M. Bristianou** – Greece

10:00 – 10:30 **LECTURE**
Chair: **I. Migdalis** – Greece
Diabetic Charcot arthropathy
Presenter: **N. Papanas** – Greece

10:30 – 11:00 COFFEE BREAK

11:00 – 11:30 **LECTURE**
Chair: **A. Mavrogiannaki** - Greece
Diabetic Painful Neuropathy
Presenter: **I. Migdalis** – Greece

11:30 – 12:00 **LECTURE**
Chair: **A. Mitrakou** - Greece
Diabetic Autonomic Neuropathy and Hypoglycemia Unawareness
Presenter: **S. Bakatselos** – Greece

12:00 – 12:30 **LECTURE**
Chair: **S. Bakatselos** – Greece
Diabetic neuropathy and Central Nervous System Function
Presenter: **T. Tegos** - Greece

12:30 – 13:00 **LECTURE**
Chair: **T. Didangelos** – Greece, **Ch. Savopoulos** – Greece
Diabetic neuropathy and corneal confocal microscopy (CCM) as a biomarker from a clinical perspective
Presenter: **G. Ponirakis** – Qatar

13:00 – 14:00 BREAK

DAY 1 FRIDAY 27-8-2021 / PROGRAM OVERVIEW

CONGRESS NEURODIAB 2021

14:00 – 14:45	**Introductions** **P. Kempler** – Hungary, **T. Didangelos** – Greece **Opening Ceremony** Greetings
14:45 – 16:00	**ORAL SESSION 1:** Autonomic Neuropathy 1 Chairs: **S. Frontoni** – Italy, **I. Migdalis** – Greece
16:00 – 16:30	COFFEE BREAK
16:30 – 17:10	**INVITED LECTURE 1** Chairs: **N. Tentolouris** - Greece, **G. Rayman** - UK, **D. Selvarajah** - UK Diabetic skin pathophysiology: new insights from single cell transcriptomics Presenter: **A. Veves** - USA
17:10 – 18:25	**ORAL SESSION 2:** Diagnostics and interventions Chairs: **N. Tentolouris** - Greece, **G. Rayman** - UK, **D. Selvarajah** - UK

DAY 2 — SATURDAY 28-8-2021 / PROGRAM OVERVIEW

CONGRESS NEURODIAB 2021

08:30 – 09:10	**INVITED LECTURE 2** Chairs: **R. Pop-Busu**i - USA, **G. Ponirakis** - Qatar Relationship between lipids and diabetic neuropathy: a new potential therapeutic target? Presenter: **F. Picconi** - Italy
09:10 – 10:25	**ORAL SESSION 3:** From Mice to Men Chairs: **R. Pop-Busui** - USA, **G. Ponirakis** - Qatar
10:25 – 10:55	COFFEE BREAK
10:55 – 11:55	**SPONSORED SYMPOSIUM 1 by Impeto Medical** Chairs: **P. Kempler** - Hungary, **V. Spallone** - Italy Sudoscan theory and in vitro validation Presenter: **P. Brunswick** - France Clinical developments and applications of Sudoscan Presenter: **T. Didangelos** - Greece Application for early detection of diabetic foot complications in France Presenter: **R. Roussel** Questions and debates
11:55 – 12:35	**SPONSORED SYMPOSIUM 2 by UNI-PHARMA** Chair: **K. Kantartzis** - Germany Vitamin B12 supplementation in the management of neuropathy in type 2 diabetes: New evidence Presenter: **T. Didangelos** - Greece Q&A
12:35 – 13:35	LUNCH
13:35 – 14:50	**ORAL SESSION 4:** Autonomic Neuropathy 2 Chairs: **E. Søfteland** - Norway, **T. Tegos** - Greece
14:50 – 15:20	**CLINICAL PRIZE LECTURE – GORAN SUNDKVIST award** Chairs: **P. Kempler** - Hungary, **T. Didangelos** - Greece Diabetic neuropathy – lessons learned from contemporary cohorts Presenter: **K. Mizokami-Stout** - USA
15:20 – 15:50	COFFEE BREAK
15:50 – 17:05	**ORAL SESSION 5:** From Men to Mice Chairs: **C. S. Hansen** - Denmark, **N. Papanas** - Greece
17:05 – 17:45	**INVITED LECTURE 3** Chairs: **T. Varkonyi** - Hungary, **H. Andersen** - Denmark Metabolic neuropathy and its potential treatments Presenter: **B. Callaghan** - USA
18:00 – 19:00	**General Assembly**

DAY 3 SUNDAY 29-8-2021 / PROGRAM OVERVIEW

CONGRESS NEURODIAB 2021

08:30 – 09:45 **ORAL SESSION 6:** Central Mechanisms
Chairs: **S. Tesfaye** - UK, **F. Piccon**i - Italy

09:45 – 10:15 **PRE-CLINICAL PRIZE LECTURE - ANGELIKA BIERHAUS**
Chairs: **P. Kempler** - Hungary, **T. Didangelos** - Greece
Introduction
Presenter: **E. Feldman** - USA
NADPH Oxidase 5 Promotes Nerve Damage in Prediabetes and Diabetes
Presenter: **S. Eid** – USA

10:15 – 10:45 COFFEE BREAK

10:45 – 11:45 **ORAL SESSION 7:** Case Reports and Observation Studies
Chairs: **S. Sharma** - UK, **G. J. Bönhof** - Germany

11:45 – 12:45 **SPONSORED SYMPOSIUM 3 by Wörwag Pharma**
Screening, diagnosis and management of diabetic sensorimotor polyneuropathy (DSPN) in clinical practice: An International Consensus Statement
Chair: **D. Ziegler** - Germany
Introduction
Presenter: **D. Ziegler** - Germany
Implementation of screening for DSPN in clinical practice
Presenter: **P. Kempler** - Hungary
International guidelines for pharmacotherapy of DSPN and neuropathic pain
Presenter: **D. Ziegler** - Germany
Challenges in symptomatic treatment of painful DSPN
Presenter: **S. Tesfaye** - UK
Q&A

12:45 – 13:45 **LUNCH**

13:45 – 14:45 **ORAL SESSION 8:** Pathogenesis 3
Chairs: **M. Yorek** – USA, **R. Malik** – UK

14:45 – 15:25 **INVITED LECTURE 4**
Chair: **S. Tesfaye** - UK, **Ch. Savopoulos** - Greece
Management of Cardiovascular Autonomic Neuropathy with ACE Inhibitors
Presenter: **T. Didangelos** - Greece

DAY 4 MONDAY 30-8-2021 / PROGRAM OVERVIEW

CONGRESS NEURODIAB 2021

08:30 – 09:40 **INVITED LECTURE 5**
Chairs: **S. Tesfaye** - UK, **P. Valensi** - France
Diabetic painful neuropathy: patient stratification by symptom and sensory profiling
Presenter: **R. Baron** - Germany

09:40 – 10:40 **ORAL SESSION 9:** Autonomic Neuropathy 3
Chairs: **V. Spallone** - Italy, **C. Brock** - Denmark

10:40 – 10:45 CLOSING REMARKS - **P. Kempler** - Hungary, **T. Didangelos** - Greece

ΠΛΕΟΝ ΔΙΑΘΕΣΙΜΟ

Βοηθήστε τα άτομα με Σακχαρώδη Διαβήτη Τύπου 2

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Ozempic® - Εβδομαδιαίος αγωνιστής υποδοχέα GLP-1 που συνδυάζει ισχυρή αποτελεσματικότητα* στη μείωση της HbA1c και του σωματικού βάρους και καρδιαγγειακό‡ όφελος.[1-5,7,8,9]

ΙΣΧΥΡΟΣ ΓΛΥΚΑΙΜΙΚΟΣ ΕΛΕΓΧΟΣ[1-5,7,8,9*]

ΑΠΟΔΕΔΕΙΓΜΕΝΟ† ΚΑΡΔΙΑΓΓΕΙΑΚΟ ΟΦΕΛΟΣ[5‡]

ΙΣΧΥΡΗ ΚΑΙ ΣΥΝΕΠΗΣ ΑΠΩΛΕΙΑ ΒΑΡΟΥΣ[1-5,7,8,9*]

5% ΣΥΜΜΕΤΟΧΗ ΑΣΘΕΝΟΥΣ***

Για ενήλικες με σακχαρώδη διαβήτη τύπου 2 που υπερισχύει η αθηροσκληρωτική καρδιαγγειακή νόσος (ασθενείς με δείκτες υψηλού κινδύνου για ASCVD ή εγκατεστημένη ASCVD).†

Το Consensus Report των ADA/EASD 2019 συνιστά τη θεραπεία με αγωνιστή του υποδοχέα του GLP-1 με αποδεδειγμένο# καρδιαγγειακό όφελος[6]

Το Ozempic® (σεμαγλουτίδη) έχει ένδειξη για τη θεραπεία ενηλίκων με σακχαρώδη διαβήτη τύπου 2 που δεν ελέγχεται επαρκώς σε συνδυασμό με δίαιτα και άσκηση.

ΠΕΡΙΛΗΨΗ ΤΩΝ ΧΑΡΑΚΤΗΡΙΣΤΙΚΩΝ ΤΟΥ ΠΡΟΪΟΝΤΟΣ

Το φάρμακο αυτό τελεί υπό συμπληρωματική παρακολούθηση. Αυτό θα επιτρέψει το γρήγορο προσδιορισμό νέων πληροφοριών ασφάλειας. Ζητείται από τους επαγγελματίες υγείας να αναφέρουν οποιεσδήποτε πιθανολογούμενες ανεπιθύμητες ενέργειες. Βλ. παράγραφο «Ανεπιθύμητες ενέργειες» για τον τρόπο αναφοράς ανεπιθύμητων ενεργειών. **ΟΝΟΜΑΣΙΑ ΤΟΥ ΦΑΡΜΑΚΕΥΤΙΚΟΥ ΠΡΟΪΟΝΤΟΣ** Ozempic 0,25 mg, Ozempic 0,5 mg, Ozempic 1 mg ενέσιμο διάλυμα σε προγεμισμένη συσκευή τύπου πένας **ΠΟΙΟΤΙΚΗ ΚΑΙ ΠΟΣΟΤΙΚΗ ΣΥΝΘΕΣΗ** Ένα ml διαλύματος περιέχει 1,34 mg σεμαγλουτίδης*. Ozempic 0,25 mg: Μία προγεμισμένη συσκευή τύπου πένας περιέχει 2 mg σεμαγλουτίδης* σε 1,5 ml διαλύματος. Κάθε δόση περιέχει 0,25 mg σεμαγλουτίδης σε 0,19 ml διαλύματος. Ozempic 0,5 mg: Μία προγεμισμένη συσκευή τύπου πένας περιέχει 2 mg σεμαγλουτίδης* σε 1,5 ml διαλύματος. Κάθε δόση περιέχει 0,5 mg σεμαγλουτίδης σε 0,37 ml διαλύματος. Ozempic 1 mg: Μία προγεμισμένη συσκευή τύπου πένας περιέχει 4 mg σεμαγλουτίδης* σε 3,0 ml διαλύματος. Κάθε δόση περιέχει 1 mg σεμαγλουτίδης σε 0,74 ml διαλύματος. *ανάλογο της ανθρώπινης ορμόνης «γλυκαγονόμορφο πεπτίδιο-1 (GLP–1)» που παρασκευάζεται με χρήση της τεχνολογίας ανασυνδυασμένου DNA σε κύτταρα *Saccharomyces cerevisiae*. **Θεραπευτικές ενδείξεις** Το Ozempic ενδείκνυται για τη θεραπεία ενηλίκων με σακχαρώδη διαβήτη τύπου 2 που δεν ελέγχεται επαρκώς σε συνδυασμό με δίαιτα και άσκηση • ως μονοθεραπεία όταν η μετφορμίνη θεωρείται ακατάλληλη εξαιτίας δυσανεξίας ή αντενδείξεων • σε συνδυασμό με άλλα φαρμακευτικά προϊόντα για τη θεραπεία του διαβήτη. **Δοσολογία και τρόπος χορήγησης** Δοσολογία Η αρχική δόση είναι 0,25 mg σεμαγλουτίδης μία φορά εβδομαδιαίως. Μετά από 4 εβδομάδες, η δόση πρέπει να αυξάνεται στα 0,5 mg μία φορά εβδομαδιαίως. Μετά από τουλάχιστον 4 εβδομάδες με δόση 0,5 mg μία φορά εβδομαδιαίως, η δόση μπορεί να αυξηθεί σε 1 mg μία φορά εβδομαδιαίως προκειμένου να βελτιωθεί περαιτέρω ο γλυκαιμικός έλεγχος. Η σεμαγλουτίδη 0,25 mg δεν αποτελεί δόση συντήρησης. Εβδομαδιαίες δόσεις μεγαλύτερες του 1 mg δε συνιστώνται. Όταν το Ozempic προστίθεται σε υπάρχουσα αγωγή με μετφορμίνη ή/και θειαζολιδινεδιόνη ή σε αναστολέα 2 συμμεταφορέα νατρίου-γλυκόζης (SGLT2), η τρέχουσα δόση μετφορμίνης ή/και θειαζολιδινεδιόνης ή αναστολέα SGLT2 μπορεί να διατηρηθεί αμετάβλητη. Όταν το Ozempic προστίθεται σε υπάρχουσα αγωγή με σουλφονυλουρία ή ινσουλίνη, πρέπει να εξετάζεται το ενδεχόμενο μείωσης της δόσης της σουλφονυλουρίας ή της ινσουλίνης για τη μείωση του κινδύνου υπογλυκαιμίας. Δεν είναι αναγκαία η αυτοπαρακολούθηση των επιπέδων γλυκόζης στο αίμα για τη ρύθμιση της δόσης του Ozempic. Η αυτοπαρακολούθηση των επιπέδων γλυκόζης στο αίμα είναι απαραίτητη για τη ρύθμιση της δόσης της σουλφονυλουρίας και της ινσουλίνης, ειδικά όταν ξεκινά το Ozempic και μειώνεται η ινσουλίνη. Συνιστάται μια προσέγγιση σταδιακής μείωσης της ινσουλίνης. *Παράλειψη δόσης* Εάν παραλειφθεί μία δόση, αυτή πρέπει να χορηγείται το συντομότερο δυνατό και εντός 5 ημερών από την παράλειψη της δόσης. Εάν έχουν παρέλθει περισσότερες από 5 ημέρες, η δόση πρέπει να παραλείπεται αριστικά και η επόμενη δόση να χορηγείται κατά την προγραμματισμένη ημερομηνία. Σε κάθε περίπτωση, οι ασθενείς μπορούν έπειτα να συνεχίσουν το σύνηθες πρόγραμμα χορήγησης της μίας φοράς εβδομαδιαίως. *Ηλικιωμένοι* Δεν απαιτείται προσαρμογή της δόσης βάσει της ηλικίας. Η θεραπευτική εμπειρία σε ασθενείς ηλικίας ≥75 ετών είναι περιορισμένη. *Νεφρική δυσλειτουργία* Δεν απαιτείται προσαρμογή της δόσης σε ασθενείς με ήπια, μέτρια ή σοβαρή νεφρική δυσλειτουργία. Η εμπειρία με τη χρήση της σεμαγλουτίδης σε ασθενείς με σοβαρή νεφρική δυσλειτουργία είναι περιορισμένη. Η σεμαγλουτίδη δε συνιστάται για χρήση σε ασθενείς με νεφροπάθεια τελικού σταδίου. *Ηπατική δυσλειτουργία* Δεν απαιτείται προσαρμογή της δόσης σε ασθενείς με ηπατική δυσλειτουργία. Η εμπειρία με τη χρήση της σεμαγλουτίδης σε ασθενείς με σοβαρή ηπατική δυσλειτουργία είναι περιορισμένη. Πρέπει να επιδεικνύεται προσοχή κατά τη χορήγηση θεραπείας με σεμαγλουτίδη σε αυτούς τους ασθενείς. *Παιδιατρικός πληθυσμός* Η ασφάλεια και αποτελεσματικότητα της σεμαγλουτίδης σε παιδιά και εφήβους ηλικίας κάτω των 18 ετών δεν έχουν ακόμα τεκμηριωθεί. Δεν υπάρχουν διαθέσιμα δεδομένα. Τρόπος χορήγησης Το Ozempic χορηγείται μία φορά εβδομαδιαίως οποιαδήποτε ώρα της ημέρας, με ή χωρίς γεύματα. Το Ozempic χορηγείται υποδορίως με ένεση στην κοιλιά, τον μηρό ή το άνω μέρος του βραχίονα. Η θέση της ένεσης μπορεί να αλλάζει χωρίς προσαρμογή της δόσης. Το Ozempic δεν πρέπει να χορηγείται ενδοφλέβια ή ενδομυϊκά. Η ημέρα της εβδομαδιαίας χορήγησης μπορεί να αλλάζει, εάν είναι απαραίτητο, εφόσον το διάστημα που μεσολαβεί μεταξύ των δύο δόσεων είναι τουλάχιστον 3 ημέρες (>72 ώρες). Μετά την επιλογή νέας ημέρας χορήγησης, πρέπει να συνεχιστεί το πρόγραμμα χορήγησης της μίας φοράς εβδομαδιαίως. **Αντενδείξεις** Υπερευαισθησία στη δραστική ουσία ή σε κάποιο από τα έκδοχα. **Ειδικές προειδοποιήσεις και προφυλάξεις κατά τη χρήση** Η σεμαγλουτίδη δεν πρέπει να χρησιμοποιείται σε ασθενείς με σακχαρώδη διαβήτη τύπου 1 ή για τη θεραπεία της διαβητικής κετοξέωσης. Η σεμαγλουτίδη δεν είναι υποκατάστατο της ινσουλίνης. Έχει αναφερθεί διαβητική κετοξέωση σε ινσουλινοεξαρτώμενους ασθενείς που προχώρησαν σε ταχεία διακοπή ή μείωση της δόσης της ινσουλίνης κατά την έναρξη θεραπείας με αγωνιστή υποδοχέα GLP-1. Δεν υπάρχει εμπειρία σε ασθενείς με συμφορητική καρδιακή ανεπάρκεια κατηγορίας IV σύμφωνα με την ταξινόμηση κατά NYHA (New York Heart Association) και επομένως η σεμαγλουτίδη δε συνιστάται σε αυτούς τους ασθενείς. Επιδράσεις στο γαστρεντερικό Η χρήση αγωνιστών του υποδοχέα GLP–1 μπορεί να συσχετιστεί με ανεπιθύμητες ενέργειες στο γαστρεντερικό σύστημα. Αυτό πρέπει να λαμβάνεται υπόψη κατά τη χορήγηση θεραπείας σε ασθενείς με επηρεασμένη νεφρική λειτουργία καθώς η ναυτία, ο έμετος και η διάρροια μπορεί να προκαλέσουν αφυδάτωση, η οποία θα μπορούσε να προκαλέσει επιδείνωση της νεφρικής λειτουργίας. Οξεία παγκρεατίτιδα Έχει παρατηρηθεί οξεία παγκρεατίτιδα κατά τη χρήση αγωνιστών του υποδοχέα GLP–1. Οι ασθενείς πρέπει να ενημερώνονται για τα χαρακτηριστικά συμπτώματα της οξείας παγκρεατίτιδας. Εάν υπάρχει υποψία παγκρεατίτιδας, η σεμαγλουτίδη πρέπει να διακόπτεται. Εάν επιβεβαιωθεί, η θεραπεία με σεμαγλουτίδη δεν πρέπει να ξεκινήσει ξανά. Πρέπει να δίνεται προσοχή σε ασθενείς με ιστορικό παγκρεατίτιδας. Υπογλυκαιμία Οι ασθενείς που λαμβάνουν σεμαγλουτίδη σε συνδυασμό με σουλφονυλουρία ή με ινσουλίνη ενδέχεται να έχουν αυξημένο κίνδυνο υπογλυκαιμίας. Ο κίνδυνος της υπογλυκαιμίας μπορεί να ελαττωθεί με μείωση της δόσης της σουλφονυλουρίας ή της ινσουλίνης, κατά την έναρξη θεραπείας με σεμαγλουτίδη. Διαβητική αμφιβληστροειδοπάθεια Σε ασθενείς με διαβητική αμφιβληστροειδοπάθεια που λαμβάνουν θεραπεία με ινσουλίνη και σεμαγλουτίδη, έχει παρατηρηθεί αυξημένος κίνδυνος ανάπτυξης επιπλοκών διαβητικής αμφιβληστροειδοπάθειας. Πρέπει να επιδεικνύεται προσοχή κατά τη χρήση σεμαγλουτίδης σε ασθενείς με διαβητική αμφιβληστροειδοπάθεια που λαμβάνουν ινσουλίνη. Οι ασθενείς αυτοί πρέπει να παρακολουθούνται στενά και να λαμβάνουν θεραπεία σύμφωνα με τις κλινικές κατευθυντήριες οδηγίες. Η ταχεία βελτίωση του ελέγχου της γλυκόζης έχει συσχετιστεί με προσωρινή επιδείνωση της διαβητικής αμφιβληστροειδοπάθειας, όμως δεν μπορούν να αποκλειστούν άλλοι μηχανισμοί. Περιεκτικότητα σε νάτριο Το φάρμακο αυτό περιέχει λιγότερο από 1 mmol νατρίου (23 mg) ανά δόση, δηλαδή πρακτικά στερείται νατρίου. Ικανομαιμότητα Προκειμένου να βελτιωθεί η γνησιασμότητα των βιολογικών φαρμακευτικών προϊόντων, το όνομα και ο αριθμός παρτίδας του χορηγούμενου φαρμάκου πρέπει να καταγράφεται με σαφήνεια. **Γονιμότητα, κύηση και γαλουχία** Οι γυναίκες σε αναπαραγωγική ηλικία συνιστάται να χρησιμοποιούν αντισύλληψη κατά τη διάρκεια της θεραπείας με σεμαγλουτίδη. Η σεμαγλουτίδη δεν πρέπει να χρησιμοποιείται κατά τη διάρκεια της εγκυμοσύνης. Η θεραπεία με σεμαγλουτίδη πρέπει να διακόπτεται τουλάχιστον 2 μήνες πριν από μία προγραμματισμένη εγκυμοσύνη λόγω του μεγάλου χρόνου ημίσειας ζωής. Η σεμαγλουτίδη δεν πρέπει να χρησιμοποιείται κατά τη διάρκεια του θηλασμού. Η επίδραση της σεμαγλουτίδης στην ανθρώπινη γονιμότητα είναι άγνωστη. **Ανεπιθύμητες ενέργειες** Πολύ συχνές: Υπογλυκαιμία όταν χρησιμοποιείται με ινσουλίνη ή σουλφονυλουρία, ναυτία, διάρροια. Συχνές: Υπογλυκαιμία όταν χρησιμοποιείται με άλλα από του στόματος αντιδιαβητικά φάρμακα, μειωμένη όρεξη, ζάλη, επιπλοκές διαβητικής αμφιβληστροειδοπάθειας, έμετος, κοιλιακό άλγος, διάταση της κοιλίας, δυσκοιλιότητα, δυσπεψία, γαστρίτιδα, γαστροοισοφαγική παλινδρόμηση, ερυγή, μετεωρισμός, χολολιθίαση, κόπωση, αυξημένη λιπάση, αυξημένη αμυλάση, μείωση σωματικού βάρους. Όχι συχνές: Υπερευαισθησία, δυσγευσία, αυξημένος καρδιακός ρυθμός, οξεία παγκρεατίτιδα, αντιδράσεις της θέσης ένεσης. Σπάνιες: Αναφυλακτική αντίδραση. Μη γνωστές: Αγγειοοίδημα Αναφορά πιθανολογούμενων ανεπιθύμητων ενεργειών: Η αναφορά πιθανολογούμενων ανεπιθύμητων ενεργειών μετά από τη χορήγηση άδειας κυκλοφορίας του φαρμακευτικού προϊόντος είναι σημαντική. Επιτρέπει τη συνεχή παρακολούθηση της σχέσης οφέλους-κινδύνου του φαρμακευτικού προϊόντος. Ζητείται από τους επαγγελματίες υγείας να αναφέρουν οποιεσδήποτε πιθανολογούμενες ανεπιθύμητες ενέργειες: στον Εθνικό Οργανισμό Φαρμάκων (Μεσογείων 284, GR-15562 Χολαργός, Αθήνα, Τηλ: + 30 21 32040380/337, Φαξ: + 30 21 06549585, Ιστότοπος: http://www.eof.gr), για την Ελλάδα, ή στις Φαρμακευτικές Υπηρεσίες, Υπουργείο Υγείας, CY-1475 Λευκωσία, Τηλ: + 357 22608607, Φαξ: + 357 22608669, Ιστότοπος: www.moh.gov.cy/phs, για την Κύπρο. **ΚΑΤΟΧΟΣ ΤΗΣ ΑΔΕΙΑΣ ΚΥΚΛΟΦΟΡΙΑΣ** Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Δανία. **ΑΡΙΘΜΟΙ ΑΔΕΙΑΣ ΚΥΚΛΟΦΟΡΙΑΣ** EU/1/17/1251.002-006 **ΗΜΕΡΟΜΗΝΙΑ ΠΡΩΤΗΣ ΕΓΚΡΙΣΗΣ ΤΗΣ ΑΔΕΙΑΣ** 08 Φεβρουαρίου 2018. **ΗΜΕΡΟΜΗΝΙΑ ΑΝΑΘΕΩΡΗΣΗΣ ΤΟΥ ΚΕΙΜΕΝΟΥ** 03/2021. Λεπτομερείς πληροφορίες για το παρόν φαρμακευτικό προϊόν είναι διαθέσιμες στον δικτυακό τόπο του Ευρωπαϊκού Οργανισμού Φαρμάκων: http://www.ema.europa.eu. Περαιτέρω πληροφορίες περιλαμβάνονται στην πλήρη Περίληψη Χαρακτηριστικών του Προϊόντος. Διατίθεται με ιατρική συνταγή. Λ.Τ.: 124,31 €.

ADA=Αμερικανική Διαβητολογική Εταιρεία, EASD=Ευρωπαϊκή Εταιρεία για τη Μελέτη του Διαβήτη, GLP-1=γλυκαγονόμορφο πεπτίδιο-1.

*Τα αποτελέσματα αφορούν το Ozempic® σε όλες τις συγκριτικές μελέτες SUSTAIN, οι οποίες περιελάμβαναν εικονικό φάρμακο, τη σιταγλιπτίνη, τη ντουλαγλουτίδη, την εξενατίδη ER, την ινσουλίνη glargine U100, την καναγλιφλοζίνη και τη λιραγλουτίδη.[1,2,7,8]

**Με βάση το πρόσφατο Δελτίο Τιμών Φαρμάκων Ανθρωπίνης Χρήσης 02/2021 https://www.moh.gov.gr/articles/times-farmakwn/deltia-timwn/8483-epikairopoihsh-deltioy-timwn-farmakwn-anthrwpinhs-xrhshs-me-enswmatwsh-dialkithikwn-metabolwn.

†Στη μελέτη SUSTAIN 6, το Ozempic® μείωσε τον καρδιαγγειακό κίνδυνο (θάνατος από καρδιαγγειακό αίτια, μη θανατηφόρο έμφραγμα μυοκαρδίου ή μη θανατηφόρο εγκεφαλικό επεισόδιο), συγκριτικά με το εικονικό φάρμακο σε ασθενείς με διαβήτη τύπου 2 οι οποίοι διέτρεχαν υψηλό καρδιαγγειακό κίνδυνο, επιπροσθέτως της πρότυπης φροντίδας. Τα αποτελέσματα της μελέτης καρδιαγγειακής έκβασης SUSTAIN 6 του Ozempic® βρίσκονται στην παράγραφο 5.1 της Περίληψης Χαρακτηριστικών του Προϊόντος (Καρδιαγγειακή νόσος).

‡Σε ασθενείς με Σακχαρώδη Διαβήτη Τύπου 2 και υψηλό καρδιαγγειακό κίνδυνο.

#Αποδεδειγμένο καρδιαγγειακό όφελος σημαίνει ότι έχει επίσημη ένδειξη μείωσης καρδιαγγειακών επεισοδίων.

Βιβλιογραφία: 1. Ozempic®, Περίληψη Χαρακτηριστικών του Προϊόντος (03/2021). **2.** Pratley RE, Aroda VR, Lingvay I, et al; SUSTAIN 7 Investigators. Semaglutide versus dulaglutide once weekly in patients with type 2 diabetes (SUSTAIN 7): a randomised, open-label, phase 3b trial. Lancet Diabetes Endocrinol. 2018;6(4):275- 286. **3.** Ahmann et al. Diabetes Care. 2018; 41(2):258–66. **4.** Aroda VR et al. Lancet Diabetes Endocrinol 2017;5:355-66. **5.** Marso SP, Bain SC, Consoli A, et al; SUSTAIN-6 Investigators. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2016;375(19):1834-1844. **6.** Buse JB, Wexler DJ, Tsapas A, et al. 2019 update to: management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2020;43(2):487-493. **7.** Lingvay I, Catarig AM, Frias JP, et al. Efficacy and safety of once-weekly semaglutide versus daily canagliflozin as add-on to metformin in patients with type 2 diabetes (SUSTAIN 8): a double-blind, phase 3b, randomised controlled trial. Lancet Diabetes Endocrinol. 2019;7(10):834-844. **8.** Capehorn MS, Catarig AM, Furberg JK, et al. Efficacy and safety of once-weekly semaglutide 1.0 mg vs once-daily liraglutide 1.2 mg as add-on to 1-3 oral antidiabetic drugs in subjects with type 2 diabetes (SUSTAIN 10). Diabetes Metab. 2020;46(2): 100-109.

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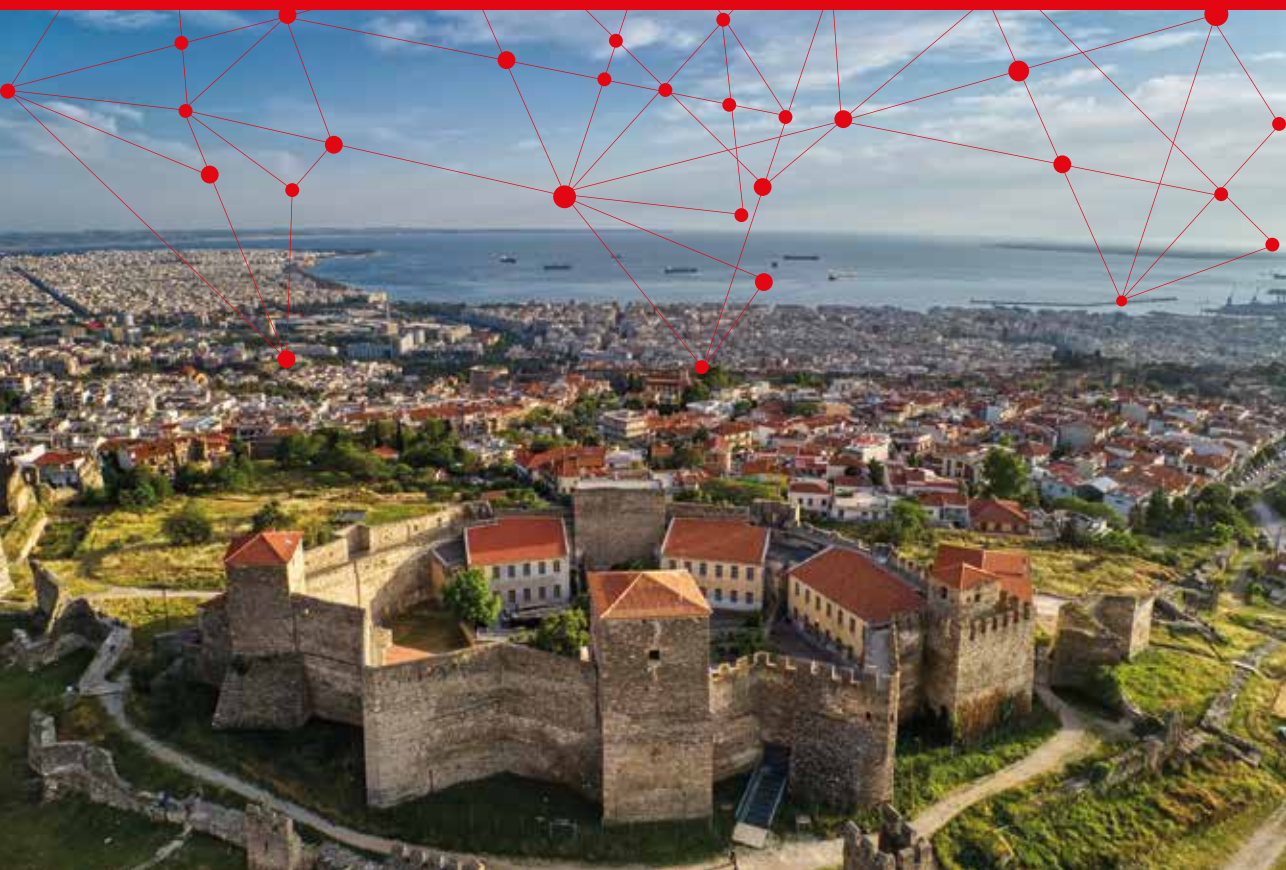
ONCE-WEEKLY OZEMPIC® semaglutide injection

CONGRESS NEURODIAB 2021

SCIENTIFIC PROGRAM

The old Byzantine Castle of Thessaloniki, Greece



DAY 1 FRIDAY 27 AUGUST 2021

PRE-CONGRESS MEETING

09:00 – 09:30 **LECTURE**
Chair: **T. Didangelos** – Greece, **G. Kaiafa** – Greece

Diabetic neuropathy and nutritional supplements
Presenter: **P. Giannoulaki** - Greece

09:30 – 10:00 **LECTURE**
Chair: **L. Lanaras** - Greece

Autonomic nervous system function in Obesity and prediabetes
Presenter: **M. Bristianou** - Greece

10:00 – 10:30 **LECTURE**
Chair: **I. Migdalis** - Greece

Diabetic Charcot arthropathy
Presenter: **N. Papanas** - Greece

10:30 – 11:00 COFFEE BREAK

11:00 – 11:30 **LECTURE**
Chair: **A. Mavrogiannaki** - Greece

Diabetic Painful Neuropathy
Presenter: **I. Migdalis** - Greece

11:30 – 12:00 **LECTURE**
Chair: **A. Mitrakou** - Greece

Diabetic Autonomic Neuropathy and Hypoglycemia Unawareness
Presenter: **S. Bakatselos** - Greece

12:00 - 12:30 **LECTURE**
Chair: **S. Bakatselos** - Greece

Diabetic neuropathy and Central Nervous System Function
Presenter: **T. Tegos** - Greece

12:30 – 13:00 **LECTURE**
Chair: **T. Didangelos** - Greece, **Ch. Savopoulos** - Greece

Diabetic neuropathy and corneal confocal microscopy (CCM)
as a biomarker from a clinical perspective
Presenter: **G. Ponirakis** - Qatar

13:00 – 14:00 BREAK

Online participation

DAY 1 FRIDAY 27 AUGUST 2021

CONGRESS NEURODIAB 2021

14:00 – 14:45 **Introductions**

P. Kempler – Hungary, **T. Didangelos** – Greece

Opening Ceremony

Greetings

A. Mavrogiannaki - President of the Hellenic Diabetes Association

S. Pagoni - President of EINAP, President of the Supreme Disciplinary of Panhellenic Medical Association

K. Anastasiadis - Head of the School of Medicine, Aristotle University of Thessaloniki

Th. Dardavesis - Dean of the School of Health Sciences, Aristotle University of Thessaloniki

K. Tsiaras - Greek Minister of Justice

P. Kempler - Neurodiab Chairman

14:45 – 16:00 **ORAL SESSION 1:** Autonomic Neuropathy 1

Chairs: **S. Frontoni** - Italy, **I. Migdalis** - Greece

OR.01 CARDIAC AUTONOMIC NEUROPATHY AND RISK OF CARDIOVASCULAR DISEASE EVENTS AND MORTALITY IN DIABETES: A META-ANALYSIS

Mahin Chowdhury - UK

OR.02 A SIMPLE AND ACCURATE METHOD TO ASSESS THE AUTONOMIC NERVOUS SYSTEM THROUGH SUDOMOTOR FUNCTION

Jean-Henri Calvet - France

OR.03 EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF DIABETIC CARDIOVASCULAR AUTONOMIC NEUROPATHY(CAN) IN KOREAN

Chong Hwa Kim - Korea

OR.04 SEXUAL DYSFUNCTION IN NORWEGIAN WOMEN WITH TYPE 1 DIABETES: ASSOCIATIONS WITH DISTRESS, DEPRESSION AND AUTONOMIC NEUROPATHY

Eirik Søfteland - Norway

OR.05 VALUE OF A SLOW BREATHING TEST AS A SCREENING TOOL AND A TEST OF SYMPATHETIC ACTIVATION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNOEA SYNDROME (OSAS)

Paul Valensi - France

DAY 1 FRIDAY 27 AUGUST 2021

CONGRESS NEURODIAB 2021

16:00 – 16:30 COFFEE BREAK

16:30 – 17:10 **INVITED LECTURE 1**
Chairs: **N. Tentolouris** - Greece, **G. Rayman** - UK, **D. Selvarajah** - UK

Diabetic skin pathophysiology: new insights from single cell transcriptomics
Presenter: **A. Veves** - USA

17:10 – 18:25 **ORAL SESSION 2:** Diagnostics and interventions
Chairs: **N. Tentolouris** - Greece, **G. Rayman** - UK, **D. Selvarajah** - UK

OR.06 ARTIFICIAL INTELLIGENCE UTILIZING CORNEAL CONFOCAL MICROSCOPY FOR THE DIAGNOSIS AND CLASSIFICATION OF PERIPHERAL NEUROPATHY IN DIABETES MELLITUS AND PREDIABETES
Frank Preston - UK

OR.07 MACHINE LEARNING TECHNIQUES FOR THE ANALYSIS OF TACTILE SENSITIVITY IN TYPE 1 DIABETES MELLITUS
Fabiana Picconi - Italy

OR.08 NERVE CHECK MASTER FOR SCREENING OF PERIPHERAL NEUROPATHY. DATA IN A POPULATION OF PATIENTS WITH TYPE 1 AND TYPE 2 DIABETES
Raffaele Galiero - Italy

OR.09 ULTRA-HIGH FIELD MR NEUROGRAPHY OF THE SCIATIC NERVE AT 7 TESLA DETECTS NERVE FIBER DAMAGE IN DIABETIC NEUROPATHY
Zoltan Kender - Germany

OR.10 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 2 MONTHS IN PATIENTS WITH DIABETIC NEUROPATHY
Eleni Karlafti - Greece

CONGRESS NEURODIAB 2021

PROGRAM DAY 2

The Rotunda of Galerius, Thessaloniki, Greece

DAY 2 SATURDAY 28 AUGUST 2021

CONGRESS NEURODIAB 2021

08:30 – 09:10 **INVITED LECTURE 2**
Chairs: **R. Pop-Busui** - USA, **G. Ponirakis** - Qatar

Relationship between lipids and diabetic neuropathy:
a new potential therapeutic target?
Presenter: **F. Picconi** - Italy

09:10 – 10:25 **ORAL SESSION 3:** From Mice to Men
Chairs: **R. Pop-Busui** - USA, **G. Ponirakis** - Qatar

OR.11 STIMULATING EFFECTS OF EXENDIN-4 ON AKT PHOSPHORYLATION, PROLIFERATION, MIGRATION, AND MYELINATION OF SCHWANN CELLS
Kazunori Sango - Japan

OR.12 ANGIOTENSIN II INDUCED PERICYTE MEDIATED VASOCONSTRICTION IN THE SPINAL CORD CAUSES DIABETIC NEUROPATHIC PAIN
Richard Hulse - UK

OR.13 LIVER FIBROSIS INDICES ARE RELATED TO DIABETIC PERIPHERAL NEUROPATHY IN INDIVIDUALS WITH TYPE 2 DIABETES
Tae Jung Oh - Korea

OR.14 TWO-YEAR PROGRESSION OF RETINAL NEURODEGENERATION IN PEDIATRIC PATIENTS WITH TYPE 1 DIABETES MELLITUS: THE ROLE OF GLYCEMIC VARIABILITY
Marika Menduni - Italy

OR.15 MODULATION OF PGC1A, NRF2 AND LONP1 BY SAROGLITAZAR ATTENUATES MITOCHONDRIAL DYSFUNCTION IN EXPERIMENTAL DIABETIC NEUROPATHY
Ashutosh Kumar - India

10:25 – 10:55 COFFEE BREAK

DAY 2 SATURDAY 28 AUGUST 2021

CONGRESS NEURODIAB 2021

10:55 – 11:55 **SPONSORED SYMPOSIUM 1 by Impeto Medical**
Chairs: **P. Kempler** - Hungary, **V. Spallone** - Italy

Sudoscan theory and in vitro validation
Presenter: **P. Brunswick** - France

Clinical developments and applications of Sudoscan
Presenter: **T. Didangelos** - Greece

Application for early detection of diabetic foot complications in France
Presenter: **R. Roussel**

Questions and debates

11:55 – 12:35 **SPONSORED SYMPOSIUM 2 by UNI-PHARMA**
Chair: **K. Kantartzis** - Germany

Vitamin B12 supplementation in the management of neuropathy in type 2 diabetes: New evidence
Presenter: **T. Didangelos** - Greece

Q&A

12:35 – 13:35 **LUNCH**

13:35 – 14:50 **ORAL SESSION 4:** Autonomic Neuropathy 2
Chairs: **E. Søfteland** - Norway, **T. Tegos** - Greece

OR.16 FIVE-YEAR CHANGE IN BODY COMPOSITION IE RELATED TO HEART RATE BUT NOT AUTONOMIC DYSFUNCTION IN THE WHITE HALL II STUDY
Christian Stevns Hansen - Denmark

OR.17 HEART RATE RESPONSE DURING A STRESS TEST AND EFFECTS OF A CARDIAC REHABILITATION PROGRAMME IN PATIENTS WITH KNOWN DIABETES AND WITH NEWLY-DETECTED GLYCEMIC DISORDERS
Paul Valensi - France

DAY 2 SATURDAY 28 AUGUST 2021

CONGRESS NEURODIAB 2021

OR.18. ASSOCIATION BETWEEN URINARY ENDOTHELIAL GROWTH FACTOR LEVELS AND INDICES OF CARDIOVASCULAR AUTONOMIC NEUROPATHY IN PATIENTS WITH TYPE 1 DIABETES
Yu Kuei Lin - USA

OR.19 CARDIOVASCULAR AUTONOMIC NEUROPATHY AND RISK OF HEART FAILURE IN PARTICIPANTS WITH TYPE 2 DIABETES ENROLLED IN DEVOTE TRIAL
Rodica Pop-Busui - USA

OR.20 LESIONS OF THE SMALL FIBERS OF THE AUTONOMIC NERVOUS SYSTEM AND GRADATION OF THE DIABETIC FOOT RISK IN PATIENTS WITH DIABETES
Jean-Henri Calvet - France

14:50 – 15:20 **CLINICAL PRIZE LECTURE – GORAN SUNDKVIST award**
Chairs: **P. Kempler** - Hungary, **T. Didangelos** - Greece

Diabetic neuropathy – lessons learned from contemporary cohorts
Presenter: **K. Mizokami-Stout** - USA

15:20 – 15:50 COFFEE BREAK

15:50 – 17:05 **ORAL SESSION 5:** From Men to Mice
Chairs: **C. S. Hansen** - Denmark, **N. Papanas** - Greece

OR.21 RISK FACTORS ASSOCIATED WITH PROGRESSION OF DIABETIC NEUROPATHY
Georgios Ponirakis - Qatar

OR.22 HIGH FAT DIET INDUCES MITOCHINDRIAL DYSFUNCTION IN THE PERIPHERAL NERVOUS SYSTEM
M. Sajic, AE Rumor, K.J. Smith, Eva Feldman - USA

OR.23 IMPACT OF CHOLESTEROL DYSREGULATION ON THE DEVELOPMENT OF PERIPHERAL NEUROPATHY
Ali Jaafar - France

DAY 2 SATURDAY 28 AUGUST 2021

CONGRESS NEURODIAB 2021

OR.24 FOLLOW UP OF PERIPHERAL POLYNEUROPATHY SIGNS AND SYMPTOMS IN SEVERELY OBESE PATIENTS FOLLOWING BARIATRIC SURGERY
Helena Schmid - Brazil

OR.25 OMEGA-3 POLYUNSATURATED FATTY ACIDS IN THE TREATMENT OF DIABETIC PERIPHERAL NEUROPATHY: IS THE SOURCE IMPORTANT?
Mark Yorek - USA

17:05 – 17:45 **INVITED LECTURE 3**
Chairs: **T. Varkonyi** - Hungary, **H. Andersen** - Denmark

Metabolic neuropathy and its potential treatments
Presenter: **B. Callaghan** - USA

18:00 – 19:00 **General Assembly**

CONGRESS NEURODIAB 2021

PROGRAM DAY 3

Fragment from the Arch of Galerius. Thessaloniki, Greece

DAY 3 SUNDAY 29 AUGUST 2021

CONGRESS NEURODIAB 2021

08:30 – 09:45 **ORAL SESSION 6:** Central Mechanisms
Chairs: **S. Tesfaye** - UK, **F. Piccon**i - Italy

OR.26 ALTERATIONS IN THE FUNCTIONAL BRAIN NETWOK IN TYPE 1 DIABETES
Suganthiya S. Croosu - Denmark

OR.27 DEEP LEARNING TREATMENT RESPONSE CLASSIFICATION OF DIABETIC PAINFUL NEUROPATHY
Kevin Teh - UK

OR.28 CLASSIFYING SENSORY PHENOTYPES IN PAINFUL DPN: MULTIMODAL MAGNETIC RESONANCE IMAGING AND A MACHINE LEARNING APPROACH
Dinesh Selvarajah - UK

OR.29 INCREASED FUNCTIONAL CONNECTIVITY OF THE THALAMUS TO THE PRIMARY SOMATOSENSORY CORTEX AND INSULAR CORTEX FOLLOWING TREATMENT WITHDRAWAL: A POTENTIAL BIOMARKER OF PAINFUL-DPN
Gordon Sloan - UK

OR.30 THALAMIC H1-MRS METABOLITE PARAMETERS ARE RELATED TO MOOD DISORDERS
Marni Greig - UK

09:45 – 10:15 **PRE-CLINICAL PRIZE LECTURE - ANGELIKA BIERHAUS**
Chairs: **P. Kempler** – Hungary, **T. Didangelos** - Greece

Introduction
E. Feldman - USA

NADPH Oxidase 5 Promotes Nerve Damage in Prediabetes and Diabetes
Presenter: **S. Eid** – USA

10:15 – 10:45 COFFEE BREAK

DAY 3 SUNDAY 29 AUGUST 2021

CONGRESS NEURODIAB 2021

10:45 – 11:45 **ORAL SESSION 7:** Case Reports and Observation Studies
Chairs: **S. Sharma** - UK, **G. J. Bönhof** - Germany

OR.31 SEVERE ATYPICAL AMYOTROPHY (RADICULOPLEXUS NEUROPATHY) IN A PATIENT WITH NEWLY DIAGNOSED TYPE 2 DIABETES AND COVID-19 INFECTION - A CASE REPORT
Anna Korei - Hungary

OR.32 PERIPHERAL NEUROPATHY AND COVID-19
Tamar Maghradze - Georgia

OR.33 INFLUENCE OF DIABETIC POLYNEUROPATHY ON THE SEVERITY OF SARS-COV-2 INFECTION
Claudia Sivu - Romania

OR.34 CEREBRAL AND PERIPHERAL MICROCIRCULATION IN TYPE 2 DIABETES MELLITUS AND OBESITY, INFLUENCE OF NEUROPATHY AND C-PEPTIDE LEVELS
Miklós Káplár - Hungary

11:45 – 12:45 **SPONSORED SYMPOSIUM 3** by **Wörwag Pharma Screening,** Screening, diagnosis and management of diabetic sensorimotor polyneuropathy (DSPN) in clinical practice: An International Consensus Statement
Chair: **D. Ziegler** - Germany

Introduction
Presenter: **D. Ziegler** - Germany

Implementation of screening for DSPN in clinical practice
Presenter: **P. Kempler** - Hungary

International guidelines for pharmacotherapy of DSPN and neuropathic pain
Presenter: **D. Ziegler** - Germany

Challenges in symptomatic treatment of painful DSPN
Presenter: **S. Tesfaye** - UK

Q&A

DAY 3 SUNDAY 29 AUGUST 2021

CONGRESS NEURODIAB 2021

12:45 – 13:45 **LUNCH**

13:45 – 14:45 **ORAL SESSION 8:** Pathogenesis 3
Chairs: **M. Yorek** - USA, **R. Malik** - UK

OR.35 PROGRESSION AND REGRESSION OF SMALL AND LARGE NERVE FIBER PATHOLOGY AND DYSFUNCTION IN RECENT-ONSET TYPE 1 AND TYPE 2 DIABETES: A 5-YEAR PROSPECTIVE STUDY
Gidon J. Bönhof - Germany

OR.36 EFFECTS OF PROGRESSIVE RESISTANCE TRAINING IN PATIENTS WITH TYPE 2 DIABETIC POLYNEUROPATHY; A RANDOMIZED SINGLE-BLINDED CONTROLLED TRIAL
Karolina S. Khan - Denmark

OR.37 THE EFFECTS OF 12-WEEKS PROGRESSIVE RESISTANCE TRAINING ON CUTANEOUS INNERVATION IN PATIENTS WITH DIABETIC POLYNEUROPATHY; A RANDOMIZED SINGLE-BLINDED CONTROLLED TRIAL
Karolina S. Khan - Denmark

OR.38 CHANGES OF THE PLASMA MRNA LEVELS OF SOME GENES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS
Yanina Saenko - Ukraine

14:45 – 15:25 **INVITED LECTURE 4**
Chair: **S. Tesfaye** - UK, **Ch. Savopoulos** - Greece

Management of Cardiovascular Autonomic Neuropathy with ACE Inhibitors
Presenter: **T. Didangelos** - Greece

CONGRESS NEURODIAB 2021

PROGRAM DAY 4

Early 20th century buildings in Thessaloniki, Greece

DAY 4 MONDAY 30 AUGUST 2021

CONGRESS NEURODIAB 2021

08:30 – 09:40 **INVITED LECTURE 5**
Chairs: **S. Tesfaye** - UK, **P. Valensi** - France

Diabetic painful neuropathy: patient stratification by symptom and sensory profiling
Presenter: **R. Baron** - Germany

09:40 – 10:40 **ORAL SESSION 9:** Autonomic Neuropathy 3
Chairs: **V. Spallone** - Italy, **C. Brock** - Denmark

OR.39 DOES THE DIAGNOSTIC VALUE OF THE QUESTIONNAIRE FOR AUTONOMIC SYMPTOMS COMPASS 31 DIFFER BETWEEN TYPE 1 AND TYPE DIABETES?
Ilenia D'Ippolito - Italy

OR.40 EVALUATION OF THE AUTONOMIC AND PERIPHERAL SENSORY NERVOUS SYSTEM FUNCTION IN YOUNG PATIENTS WITH TYPE 1 DIABETES AT THE TIME OF THE TRANSITION FROM PEDIATRIC TO ADULT-ORIENTED HEALTH CARE SYSTEM
Tamas Varkonyi - Hungary

OR.41 CHARACTERIZATION OF THE AUTONOMIC AND SENSORY FUNCTIONS IN PATIENTS WITH DIFFERENT DURATIONS OF TYPE 1 DIABETES
Tamas Varkonyi - Hungary

OR.42 CARDIOVASCULAR AUTONOMIC NEUROPATHY IN CONTEXT OF OTHER COMPLICATIONS OF TYPE 2 DIABETES MELLITUS
Andra-Elena Nica - Romania

10:40 – 10:45 CLOSING REMARKS - **P. Kempler** - Hungary, **T. Didangelos** - Greece

Στην αντιμετώπιση του διαβήτη τύπου 2[1]

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ADA=American Diabetes Association, ΚΔ=Καρδιαγγειακός/ή/ό, EASD=European Association for the Study of Diabetes.

Βιβλιογραφία: 1. JARDIANCE® Περίληψη Χαρακτηριστικών του Προϊόντος. 2. Zinman B, Wanner C, Lachin JM, et al; EMPAREG OUTCOME Investigators. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med. 2015;373(22):2117-2128. 3. Davies MJ, D'Alessio DA, Fradkin J, et al. Management of hyperglycaemia in type 2 diabetes, 2018: a consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 2018;61(12):2461-2498.

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CONGRESS NEURODIAB 2021

ORAL ABSTRACT DAY 1

Bath historic building at Thessaloniki, Greece

DAY 1 | FRIDAY 27 AUGUST 2021, ORAL ABSTRACT

14:45 – 16:00 | ORAL SESSION 1: Autonomic Neuropathy 1
Chairs: **S. Frontoni** - Italy, **I. Migdalis** - Greece

OR.01 CARDIAC AUTONOMIC NEUROPATHY AND RISK OF CARDIOVASCULAR DISEASE EVENTS AND MORTALITY IN DIABETES: A META-ANALYSIS

Mahin Chowdhury[1], Sarah Nevitt[2], Aikaterini Eleftheriadou[1], Prathap Kanagala[1], Hani Esa[1], Daniel Cuthbertson[1], Abd Tahrani[3], Uazman Alam[4]

[1]Department of Cardiovascular & Metabolic Medicine, University of Liverpool, UK
[2]Department of Biostatistics, University of Liverpool, UK
[3]Institute of Metabolism and Systems Research, University of Birmingham, UK
[4]Department of Cardiovascular & Metabolic Medicine, Institute of Life Course and Medical Sciences and Pain Research Institute, University of Liverpool and Liverpool University Hospital NHS Foundation Trust, Liverpool, UK

Objectives: Several studies have demonstrated that cardiac autonomic neuropathy (CAN) is a risk factor for major adverse cardiovascular events and mortality. We aimed to determine the prognostic association between CAN and major adverse cardiovascular events and mortality in people with diabetes through a systematic review and meta-analysis.

Methods: An electronic literature search was carried out systematically using MEDLINE, PubMed, Scopus, Cochrane and CINAHL databases. CAN was defined based on 1 (early/possible CAN) or ≥2 (definite CAN) positive autonomic function tests (AFT) as per the Toronto Consensus guidelines. Full-text English language publications in participants aged over 18 years old with CAN with cardiovascular events or mortality data were included. All articles were screened using a priori criteria as per PRISMA methodology. Methodological variables and risk of bias were assessed using RoBINS-1 and RoB 2 tools. A meta-analysis was conducted with a pre-determined cut-off for heterogeneity of I2>90%.

Results: Twenty-six articles fulfilled the inclusion criteria for quantitative synthesis. Of these, sixteen studies demonstrated a pooled relative risk (RR) of 3.16 (95%CI 2.42-4.13; P< 0.00001) was higher with possible/early CAN compared to definite CAN (RR: 2.84 (95%CI 1.84-4.38; P < 0.00001). However, risk of all-cause mortality was higher with definite CAN (RR: 3.88 (95%CI 2.51-6.00; P

Conclusions: There is a significant association between CAN and cardiovascular disease events and all-cause mortality. Future research should investigate pharmacological and non-pharmacological interventions in reducing the burden of CAN and its impact on hard cardiovascular endpoints.

OR.02 SIMPLE AND ACCURATE METHOD TO ASSESS THE AUTONOMIC NERVOUS SYSTEM THROUGH SUDOMOTOR FUNCTION

Philippe Brunswick[1], Marie-laure Névoret[2], Jean-Henri Calvet[2], Kamel Khalfallah[3]
[1]General Management, Impeto Medical
[2]Medical Department, Impeto Medical
[3]Development, Impeto Medical

Objectives: Peripheral neuropathies are assessed mostly using large fiber tests. Current clinical small fiber tests (e.g., pinprick, cold and heat perception) are subjective, operator-dependent, qualitative, and insufficiently used. The gold standard test for small fiber neuropathies, Epidermal Nerve Fiber Density measured from punch skin biopsies, is not appropriate for recurrent assessments nor recommended for patients with diabetes. The autonomic nervous system, mostly comprised of small fiber nerves, is not easily assessed today. Testing sudomotor function can evaluate autonomic neuropathies and small fiber neuropathies simultaneously and objectively.
Methods: The simplified principle of Sudoscan technology consists in imposing on human skin decreasing pulses of low direct current voltages and to collect the electrochemical response of the skin. Measurements are performed on glabrous skin surfaces where the eccrine sweat glands are the most numerous: on the palms of the hands and soles of the feet. No specific patient preparation (fasting or other) or medical personnel training is required for Sudoscan testing. To conduct the test, patients are required to place their hands and feet on the electrodes. They must then stand still for the approximately 2-minute duration of the test, in contact only with the electrodes.
Results: Normative ESC values in adults were defined in a population of over 1350 healthy subjects. Mean ESC for women or men at the hands or feet were not significantly different. There was no effect on ESC of body mass index or exercise status; a very small (and clinically insignificant) decrease with age; and a significant effect of race/ethnicity. The accuracy of the method, determined according to FDA guidelines (2 measurements performed on each of 3 devices, i.e., 6 Sudoscan tests per patient), demonstrated a coefficient of variation of feet or hands ESC of 4% in healthy subjects and 7% in patients with diabetes. Nine studies involving more than 1000 patients with diabetes showed sensitivities from 73 to 97% to detect peripheral neuropathy (DPN) with negative predictive values from 83 to 94% when Sudoscan was compared to reference symptom scores or usual clinical DPN tests.
Conclusion: More than 150 published clinical studies established that the Sudoscan technology is robust under a variety of clinical circumstances and for a wide range of populations; additionally, if the technology is used to monitor patients over time, the good reproducibility ensures that a change in ESC is a reliable marker of sudomotor function change and should prompt further investigation.

DAY 1 FRIDAY 27 AUGUST 2021, ORAL ABSTRACT

OR.03 EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF DIABETIC CARDIOVASCULAR AUTONOMIC NEUROPATHY(CAN) IN KOREAN

Chong Hwa Kim[1], Jae Hyuk Lee[2], Sangsoo Kim[3], Jong Cheol Won[4], Tae Sun Park[5]

[1]Division of Endocrinology and Metabolism, Department of Internal Medicine, Sejong General Hospital

[2]Division of Endocrinology and Metabolism, Department of Internal Medicine, Myunggi Hospital, Hanyang University

[3]Division of Endocrinology and Metabolism, Department of Internal Medicine, Busan National University Hospital

[4]Division of Endocrinology and Metabolism, Department of Internal Medicine, Sanggye Baik Hospital, Inje Medical School

[5]Division of Endocrinology and Metabolism, Department of Internal Medicine, Chonbuk National University Medical School

Objectives: Cardiovascular autonomic neuropathy (CAN) is often an underdiagnosed complication of diabetes mellitus (DM) and is associated with increased mortality and morbidity. The prevalence of CAN is approximately 31–73% in type 2 DM and the annual incidence has been reported to be 2%. To investigated the epidemiology and clinical characteristics of CAN in patients with Type 2 diabetic mellitus in Korea.

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 autonomic nervous system function tests performed to aid in the diagnosis of CAN. The final CAN diagnosis was based on the ECG-cQT interval and Ewing's test in which heart rate variation (HRV) values were evaluated through deep-breathing, lying-to-standing, sustained handgrip test and Valsalva tests. Their clinical, biochemical, and metabolic parameters were analyzed.

Results: Out of 884 patients (Type 1DM ;13, Type 2 DM;867), 510 were males and 371 were females. The mean age of the patients was 59.6 years 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) and Non-CAN was 12% (106).

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 patients without CAN. Nephropathy and hospitalization were common in CAN patients. On multiple logistic regression analysis, duration of diabetes [odds ratio (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 a common complication in type 2 DM with duration of diabetes, age, and nephropathy being its significant determinants

OR.04 SEXUAL DYSFUNCTION IN NORWEGIAN WOMEN WITH TYPE 1 DIABETES: ASSOCIATIONS WITH DISTRESS, DEPRESSION AND AUTONOMIC NEUROPATHY

Anne Haugstvedt[1], Ragnhild Strandberg[1], Roy Miodini Nilsen[1], Jannike Jørgensen[2], Jakob Haugstvedt[3], Rodica Pop-Busui[4], Mari Sørstrand Æsøy[5], Mari Clausen-Bekkelien[5], Eirik Søfteland[2]

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[5]Faculty of Medicine, University of Bergen, Norway

Objectives: To estimate the prevalence of female sexual dysfunction in women with type 1 diabetes (T1D) in Norway, and to investigate the association with diabetes complications, diabetes distress, psychosocial health and dysfunction of the autonomic nervous system.

Methods: 171 women with T1D and 60 matched non-diabetic controls completed the Female Sexual Function Index (FSFI), the Hospital Anxiety and Depression Scale (HADS), and the Problem Areas in Diabetes Scale (PAID-20). Logistic regression analyses were performed to examine associations between sexual dysfunction (FSFI≤ 26.55) and complications, distress and depression. Subsequently, thirty women with T1D (50% with sexual dysfunction) were further investigated in terms of sudomotor reflex (Sudoscan), cardiac autonomic reflex tests (CARTs), and orthostatic blood pressure.

Results: The prevalence of sexual dysfunction was 50.3% in women with T1D, compared to 35% in controls (adjusted odds ratio 1.78, 95% CI: 0.99-3.20, p value 0.052). There were strong and significant positive associations between sexual dysfunction and both diabetes distress and symptoms of depression. Sudomotor function in the feet was lower in cases with sexual dysfunction. Presence of definite or possible autonomic neuropathy was significantly higher in and all CARTs were trending towards impaired function in cases (Table 1). No differences in orthostatic blood pressure were detected.

Conclusion: Sexual dysfunction was higher in women with T1D than non-diabetic controls, and was associated with depression and diabetes distress. Further, we uncovered impairments of at least two branches of the autonomic nervous system, in line with a hypothesis involving autonomic neuropathy as a pathomechanism of sexual dysfunction in diabetes. There are still huge knowledge gaps in the field of sexual health in women with diabetes, and hence further studies are warranted.

DAY 1 FRIDAY 27 AUGUST 2021

Table 1: Autonomic function tests in T1D women with vs. without sexual dysfunction

Autonomic function tests	Cases	Controls	*p*-value
Sudoscan hands (µS)	70.5 (13.3)	73.1 (13.4)	0.60
Sudoscan feet (µS)	77.1 (13.5)	86.1 (5.6)	0.03
Resting heart rate (bpm)	77.1 (10.7)	65.9 (10.1)	0.01
30:15-ratio	1.18 (0.13)	1.32 (0.21)	0.03
E/I-ratio	1.26 (0.18)	1.40 (0.14)	0.03
Valsalva-ratio	1.66 (0.36)	1.87 (0.23)	0.08

OR.05 VALUE OF A SLOW BREATHING TEST AS A SCREENING TOOL AND A TEST OF SYMPATHETIC ACTIVATION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNOEA SYNDROME (OSAS)

Paul Valensi, Sofia Domanovic, Nada Younes, Ryma Fahmi, Sara Pinto
Unit of Endocrinology-Diabetology-Nutrition, Jean Verdier hospital, AP-HP, CRNH-IdF, Paris-Nord University, Bondy, France

Objectives: We previously showed that a brief period of slow breathing (SLB), by improving baro-chemoreflex interaction and oxygen saturation (SaO2), could acutely trigger OSAS-related respiratory abnormalities. Using a different device the present study aimed to confirm the screening value of SLB test for OSAS in a larger population and to investigate the acute cardiovascular changes occurring during induced apnoea-hypopnea events.
Methods: We included 121 patients with symptoms evocative of OSAS, including 18 treated by CPAP, 67% women/33% men, aged 49.5±15.2 yrs, 58% nondiabetic obese and 42% patients with type 2 diabetes, BMI 35.8±7.2 kg/m2. All patients underwent standard nocturnal polygraphy (NP) using Nox-T3 polygrapher (Resmed). With the same device we continuously monitored respiration, SaO2, heart rate (HR), peripheral blood flow (PPG, plethysmography) and diastole duration (from PPG recordings), during spontaneous respiration (5min), 5-min of SLB at 6 cycles/min and 5-min follow-up under spontaneous breathing. Artery stiffness was measured by the Cardio-Ankle Vascular Index.
Results: Considering the apnea-hypopnea index (AHI) measured by NP, the patients were separated in 3 groups: untreated patients with AHI < or ≥15 events/hour) (kappa coefficient=0.83), with good performances of SLB test: sensitivity 98%, specificity 83%, positive and negative predictive values 96% and 91%, respectively. In the 3 groups SaO2 was similar before apnea, decreased significantly (-3% in means) and similarly during apnea/hypopnea events post-SLB, and reaugmented similarly after these events. HR was similar before SLB, and increased after apnea/hypopnea events (+ 5.8±5.4 bpm, p
Conclusion: SLB, a short and simple test based upon analysis of cardio-respiratory reflex imbalance, can accurately detect obese and diabetic patients with moderate/severe OSAS. In these patients the greater diastole shortening after SLB is likely to result from stronger sympathetic activation, which seems to be prevented by CPAP, even if inappropriately used.

DAY 1 | FRIDAY 27 AUGUST 2021, ORAL ABSTRACT

17:10 – 18:25 | ORAL SESSION 2: Diagnostics and interventions
Chairs: **N. Tentolouris** - Greece, **G. Rayman** - UK, **D. Selvarajah** - UK

OR.06 ARTIFICIAL INTELLIGENCE UTILIZING CORNEAL CONFOCAL MICROSCOPY FOR THE DIAGNOSIS AND CLASSIFICATION OF PERIPHERAL NEUROPATHY IN DIABETES MELLITUS AND PREDIABETES

Frank Preston[1], Yanda Meng[1], Jamie Burgess[2], Maryam Ferdousi[3], Shazli Azmi[3], Ioannis Petropoulos[4], Stephen Kaye[1], Rayaz Malik[4], Yalin Zheng[1], Uazman Alam[5]
[1]Eye & Vision Sciences, University of Liverpool
[2]Institute of Cardiovascular and Metabolic Medicine, University of Liverpool
[3]Institute of Cardiovascular Science, University of Manchester and Manchester Diabetes Centre
[4]Research Division, Weill Cornell Qatar
[5]Cardiovascular & Metabolic Medicine, Institute of Life Course and Medical Sciences, University of Liverpool & Liverpool University NHS Hospital Foundation Trust

Objectives: Analysis of corneal confocal microscopy (CCM) images for the diagnosis of diabetic neuropathy has previously consisted of labour-intensive manual annotation or automated systems. We developed an AI-based deep learning algorithm (DLA) applying attribution methods for image classification to detect diabetic neuropathy, without the use of image segmentation.
Methods: The AI-based DLA was developed and refined to utilise convolutional neural networks with data augmentation to increase the algorithm's generalisability. The algorithm was trained using a high-end graphics processor for 300 epochs on 329 corneal nerve images (1 image/participant). Participants consisted of healthy-volunteer participants (HV), (n=90); patients with type 1 diabetes (n=88); and patients with type 2 diabetes or prediabetes (n=191). In total, there were 90 HV, 149 patients without neuropathy (No-PN), and 130 with neuropathy (PN+). After training, the algorithm was tested on 40 images (15 HV, 13 No-PN, 12 PN+). The attribution methods gradient-weighted class activation mapping (Grad-CAM) and Guided Grad-CAM displayed the areas within the image which had the greatest impact on the decision of the algorithm.
Results: The AI-based DLA, a modified residual neural network called ResNet-50, was developed and used to extract features from images and perform classification The results were as follows; HV: recall of 1.0 (95%CI: 1.0–1.0), precision of 0.88 (95%CI: 0.706–1.0), F1-score of 0.94 (95%CI: 0.828–1.0); No-PN: recall of 0.77 (95%CI: 0.50–1.0), precision of 0.77 (95%CI: 0.50–1.0), F1-score of 0.77 (95%CI: 0.533–0.917); PN+: recall of 0.75 (95%CI: 0.50–1.0), precision of 0.90 (95%CI: 0.70–1.0), F1-score of 0.82 (95%CI: 0.60–0.963). The features displayed by the attribution methods demonstrated a greater presence of corneal nerves for HV images, a reduction in the corneal nerves for No-PN and an absence of corneal nerves for PN+ images.
Conclusions: Our AI-based DLA demonstrated promising results in the classification of peripheral neuropathy (or lack of) and healthy individuals using a single corneal image. A large-scale multicentre validation study in a clinical population is required for its future utilisation in screening and diagnostic programmes in diabetes.

OR.07 MACHINE LEARNING TECHNIQUES FOR THE ANALYSIS OF TACTILE SENSITIVITY IN TYPE 1 DIABETES MELLITUS

Colleen P Ryan1, Fabiana Picconi[2], Alessandro Moscatelli[1], Alessio Pepe[3], Simone Ciotti[4], Benedetta Russo[2], Marika Menduni[2], Lacquaniti Francesco[1], Simona Frontoni[2]

[1]Department of Systems Medicine and Centre of Space Bio-medicine, Laboratory of Neuromotor Physiology, IRCCS Santa Lucia Foundation, University of Rome "Tor Vergata", Rome, Italy

[2]Unit of Endocrinology, Diabetes and Metabolism, S. Giovanni Calibita Fatebenefratelli Hospital, Department of Systems Medicine, University of Rome "Tor Vergata", Italy

[3]Unit of Neurology, S. Giovanni Calibita Fatebenefratelli Hospital, Rome, Italy

[4]Laboratory of Neuromotor Physiology, IRCCS Santa Lucia Foundation, Rome, Italy

Objectives: Tactile sensitivity (TS) is frequently altered in patients affected by diabetic peripheral neuropathy (DPN). We developed a novel test based on haptic technology to evaluate TS in type 1 diabetic patients (T1DM). We used different machine learning techniques with the aims of evaluating the relationship between TS and standard tests and predict the probability of DPN.

Methods: 40 consecutive T1DM patients (HbA1c < 9.5%) and 18 healthy control subjects (C) were enrolled. Patients underwent a neurological assessment including vibratory perception (VP) using biothesiometry and bilateral sensory motor nerve conduction studies (NCS) to upper and lower limbs. Patients were divided in 2 groups based on VP alterations (VP- and VP+). TS was evaluated using a haptic device that produced highly precise motion. The protocol was replicated with and without masking vibrations (MV). By means of Generalized Linear Mixed Models (GLMM), we tested the ability of the participants to discriminate motion speed in the two conditions. Principal Component Analysis (PCA) was performed on biothesiometer data. Linear Discriminant Analysis (LDA) was used to predict the probability of DPN at the NCS from the following variables: disease duration, TS, biothesiometer test, Michigan Score, age and gender.

Results: T1DM group was divided into 21 VP+ and 19 VP-. TS in upper limbs was significantly lower in VP+ as compared to the C without MV ($p < 0.001$) and significantly lower in VP- and in VP+ as compared to the C with MV ($p < 0.05$; $p < 0.001$ respectively). A positive significant linear relationship between TS with and without MV and conduction velocity ($p = 0.017$; $p = 0.01$ respectively) of sural and radial nerve were observed in T1DM patients. The first principal component (PC1) explained more than 80% of the variance. The LDA correctly assigned the patient with and without DPN in 87% of the cases. To evaluate the predictive power of the different tests, we ran the LDA by removing either biothesiometer PCs or TS. The results were compared by means of ROC curves; the Area Under the Curve (AUC) was similar in the complete model and in the model excluding biothesiometer PC, but it falls to 88% if TS is excluded from the analysis.

Conclusions: TS was already significantly lower in T1DM patients without VP alteration in lower limbs. A significant relationship between NCS and TS was also observed. Haptics could complement standard quantitative sensitivity tests and enhance DPN assessment.

DAY 1 FRIDAY 27 AUGUST 2021, ORAL ABSTRACT

OR.08 NERVE CHECK MASTER FOR SCREENING OF PERIPHERAL NEUROPATHY. DATA IN A POPULATION OF PATIENTS WITH TYPE 1 AND TYPE 2 DIABETES

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Objectives: Quantitative sensory testing (QST) is required for early detection of sensory neuropathy. Nerve Check Master (NCM) is a portable device designed to assess vibration (VPT), warm (WPT), cold (CPT), heat pain (HPT) perception thresholds. Previous studies have suggested that NCM offers good accuracy to diagnose diabetic peripheral neuropathy (DPN). The present study aimed to test the diagnostic validity of NCM in patients with type 1 (T1D) or type 2 diabetes (T2D) as compared to healthy subjects (HC), included both in France and in Italy.

Methods: We included 76 T1D adults (aged 35 years, median; diabetes duration 13.5 years, mean HbA1c 8.0%), 56 T2D subjects (aged 60 years; diabetes duration 12.6 years, mean HbA1c 7.6%) and 43 HC (aged 53 years; HbA1c 5.7%, median), who underwent QST assessment with NCM. DPN was defined according to the Michigan Neuropathy Screening Instrument (MNSI). NCM measurements were considered in favor of DPN if 3 of the 4 tests were abnormal.

Results: Among T1D patients, the prevalence of DPN was 26% and 38% according to MNSI and NCM, respectively, while it was 35% and 48% among T2D patients. In T1D patients, compared to MNSI, NCM offered sensitivity 65%, specificity 71%, positive (PPV) and negative predictive values (NPV) 45% and 85% respectively. In T2D patients, NCM offered sensitivity 65%, specificity 61%, PPV 48% and NPV 76%. The rates of abnormal tests were the highest for VPT and HPT: 67% and 58% in T1Ds, and 83% and 66% in T2Ds. Among patients with abnormal MNSI, 90% and 70% of T1Ds and 95% and 80% of T2Ds had abnormal VPT and HPT, respectively. Among patients with negative MNSI, VPT and HPT were abnormal in 59% and 53% of T1Ds and in 72% and 55% of T2Ds. Among the 43 HCs, all were negative at MNSI and 38 negative subjects at NCM. All of 5 positive HC were positive both at VPT and HPT.

Conclusions: These data suggest that both in T1D and T2D subjects, NCM may be used as a screening tool to assess DPN. Considering the cut-off of 3 abnormal tests, NCM shows a good accuracy compared to MNSI. By evaluating both small and large fiber impairment, NCM may detect more patients with DPN than MNSI. In our T2D population the prevalence of DPN was slightly higher than in T1D population.

OR.09 ULTRA-HIGH FIELD MR NEUROGRAPHY OF THE SCIATIC NERVE AT 7 TESLA DETECTS NERVE FIBER DAMAGE IN DIABETIC NEUROPATHY

Zoltan Kender[1,3], Felix T. Kurz[2], Christoph Mooshage[2], Daniel Paech[4], Regula Gnirs[4], Julia Szendroedi[1,3], Peter Nawroth[1,3,5], Martin Bendszus[2], Stefan Kopf[1,3], Johann M. E. Jende[2]

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Objectives: Studies on magnetic resonance neurography (MRN) found proximal sciatic nerve lesions in patients with diabetic neuropathy (DPN). The aim of this pilot study was to explore the feasibility and efficacy of high resolution 7 Tesla MRN for the detection of nerve fiber lesions of functional relevance in patients with type 2 diabetes.

Methods: Twelve patients with type 2 diabetes (6 without DPN and 6 with DPN), as well as 9 healthy controls (HC) were enrolled, undergoing clinical and electrophysiological assessments for DPN and high resolution MRN at 7 Tesla. Nerve fascicles of the sciatic nerve were identified at 0.145 x 0.145 x 3.0 mm resolution.

Results: T2-weighted (T2w)-hyper and- hypointense lesions could be identified. The hyper- and hypointense lesion load (median percentage of lesions/healthy nerve tissue) was significantly higher in patients with type 2 diabetes compared to healthy controls (10.7 vs. 24.8 % and 2,55 vs. 6.82 %, respectively; $p<0.001$ and $p=0.02$). There was a positive correlation between T2w hyperintense and hypointense lesions ($r=0.73$, $p<0.001$). The hypointense lesion load correlated with clinical neuropathy scores (neuropathy deficit score, $r=0.55$, $p=0.009$, and neuropathy symptom score, $r=0.45$, $p=0.04$) and HbA1c ($r=0.55$, $p=0.01$), while the hyperintense lesion load was correlated with electrophysiological parameters such as peroneal and tibial NCV ($r=-0.55$, $p=0.01$ and $r=-0.56$, $p=0.01$, respectively) and distal motor latency ($r=0.61$, $p=0.004$ and $r=0.75$, $p<0.001$).

Conclusion: This study is the first to assess both feasibility and efficacy of high resolution MRN at 7 Tesla for the identification of fascicular damage to the sciatic nerve in patients with type 2 diabetes. 7 Tesla MRN appears to be an objective method for the detection of neuropathic deficits in diabetic neuropathy.

DAY 1 FRIDAY 27 AUGUST 2021, ORAL ABSTRACT

OR.10 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 2 MONTHS IN PATIENTS WITH DIABETIC NEUROPATHY

Eleni Karlafti[1], Evangelia Kotzakioulafi[1], Zisis Kontoninas[1], Parthena Giannoulaki[2], Konstantinos Kantartzis [3,4,5], Christos Savopoulos[1], Triantafyllos Didangelos[1]

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Aim: To investigate the efficacy of Superoxide Dismutase (SOD, 70 UI), Palmitoyethanolamide (PEA, 300 mg) Alpha Lipoic Acid (ALA, 300 mg), vitamins B6 (1.5 mg), B1 (1.1 mg), B12 (2.5 mcg), E (7.5 mg), Nicotinamide (9 mg) and minerals (Mg 30 mg, Zn 2,5 mg) in one tablet in Diabetic Neuropathy (DN).

Patients – methods: In this pilot study, 29 patients with Diabetes Mellitus Type 2 (DMT2, 15 women), with mean duration of DM 16.9 years and mean age 61.8 years were randomly assigned, either to receive the combination of ten elements (2 tablets/24h) in the active group, (n=15), or the placebo (n=14) for 2 months. We used Michigan Neuropathy Screening Instrument Questionnaire and Examination (MNSIQ and MNSIE), measured vibration perception threshold (BIO) and Cardiovascular Autonomic Reflex Tests (CARTs). Nerve function was assessed by DPN Check [sural nerve conduction velocity (SNCV) and amplitude (SNAP)]. Sudomotor function was assessed with SUDOSCAN that measures electrochemical skin conductance in hands and feet (ESCH and ESCF). Pain (PS) questionnaire was administered, also. All patients received metformin for at least 4 years.

Results: At follow-up, BIO, MNSIQ, MNSIE, Measurements from CARTs, SNCV, SNAP, ESCH and ESCF did not change significantly in both groups. B12 levels and pain had significantly improved in active group (235.6 vs 464.9 pg/ ml, $p<0.001$, and 17.9 vs 16.9, $p<0.008$ respectively), whereas in placebo B12 levels and pain did not change (220.2 vs 236.6 pg/ ml, p, 0.274, and 22.5 vs 22.9, p, 0.166 respectively).

Conclusions: The combination of the ten elements in one tablet for 2 months at a daily dose of two tablets in patients with DMT2 improved pain and Vit b12 levels.

CONGRESS NEURODIAB 2021

ORAL ABSTRACT DAY 2

The sculpture Umbrellas by George Zongolopoulos

DAY 2 | SATURDAY 28 AUGUST 2021, ORAL ABSTRACT

09:10 – 10:25 | ORAL SESSION 3: From Mice to Men
Chairs: **R. Pop-Busui** - USA, **G. Ponirakis** - Qatar

OR.11 STIMULATING EFFECTS OF EXENDIN-4 ON AKT PHOSPHORYLATION, PROLIFERATION, MIGRATION, AND MYELINATION OF SCHWANN CELLS

Kazunori Sango, Shizuka Takaku, Masami Tsukamoto, Naoko Niimi, Hideji Yako
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Objectives: The beneficial effects of a glucagon-like peptide-1 receptor (GLP-1R) agonist exendin-4 (Ex-4) on functional repair after sciatic nerve injury and amelioration of diabetic peripheral neuropathy (DPN) have been documented; however, the underlying mechanisms remain unknown and therefore define the aim of this study.
Methods: 1) GLP-1R mRNA/protein expression in IFRS1 immortalized rat Schwann cells was confirmed by RT-PCR, western blotting, and immunocytochemistry. 2) The effects of 100 nM Ex-4 on phosphorylation of a serine/threonine kinase AKT in IFRS1 cells and the coculture system of primary cultured adult rat DRG neurons and IFRS1 cells were investigated by western blotting. 3) The effects of 10 nM and 100 nM Ex-4 on survival/proliferation and migration of IFRS1 and 1970C3 immortalized mouse Schwann cells were investigated by MTS and scratch wound assays. 4) The effects of 100 nM Ex-4 on myelination in the DRG neuron-IFRS1 coculture system were investigated by immunocytochemistry and western blotting.
Results: 1) GLP-1R mRNA/protein was detected in IFRS1 cells. 2) Ex-4 significantly upregulated the expression of phosphorylated AKT in IFRS1 and cocultured cells. 3) Ex-4 dose-dependently promoted survival/proliferation and migration of IFRS1and 1970C3 cells, and these Ex-4 effects were attenuated by co-treatment with 25 uM phosphatidyl inositol-3'-phosphate-kinase (PI3K) inhibitor LY294002. 4) Ex-4 significantly increased the average number of IFRS1 cells attached to a neurite growing from DRG neurons and upregulated the expression of myelin protein zero and peripheral myelin protein 22 at 21 days of coculture.
Conclusions: Ex-4 appears to accelerate Schwann cell survival/proliferation and myelination via activating PI3K-AKT signaling pathway. To strengthen our hypothesis, we plan to manipulate GLP-1R and AKT genes in IFRS1, 1970C3 and other Schwann cells. The findings in this study imply the potential efficacy of Ex-4 toward DPN and other peripheral nerve lesions.

OR.12 ANGIOTENSIN II INDUCED PERICYTE MEDIATED VASOCONSTRICTION IN THE SPINAL CORD CAUSES DIABETIC NEUROPATHIC PAIN

Lydia Hardowar[1], Marlene Da Vitoria Lobo[2], Philip McTernan[1], David Bates[2], Richard Hulse[1]

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Objectives: Vascular degeneration is a key factor in the development of neurological disease. Recent evidence implies that reduced blood perfusion in the spinal cord greatly influences pain perception, in particular diabetic neuropathic pain. Pericytes, abluminally positioned on small capillaries, demonstrate contractile abilities within cerebral tissue to modulate blood perfusion of nervous tissues. Furthermore, pericyte mediated vasoconstriction is implicated in neuropathology. Our current work explores how pericyte contractility is driven by angiotensin II type 1 (ATR1) receptor in the spinal cord and how this is associated with vascular disruption in diabetic neuropathic pain.

Methods: All Experiments were designed in accordance with UK Home Office legislation, Animals (Scientific Procedures) Act 1986. Type 1 diabetes was induced in female DBA2J mice (~20g) (n=6/group). Streptozotocin (intraperitoneal 50mg/kg) was administered on 5 consecutive days. Animals body weight and blood glucose level was measured (hyperglycaemia>15mmol/l). 8 weeks following streptozotocin administration, animals were terminally anaesthetised (intraperitoneal 60mg/kg Sodium Pentobarbital) and cardiac perfused with 4% paraformaldehyde. Lumbar spinal cords were extracted and processed (40μM thick sections) for confocal microscopy to identify the endothelium (CD31), pericytes (NG2, PDGFRβ) and ATR1. Intravital confocal and laser speckle imaging were performed on terminally anaesthetised male C57.bl6 mice and were treated with either vehicle or 100nM angiotensin II topically to the spinal cord to allow measurement of blood flow dynamics. C57.bl6 male mice were intrathecally injected (i.t.) with vehicle (PBS) or angiotensin II (I.t. 100nM) in combination with either vehicle (Intraperitoneal PBS) or angiotensin type receptor 1 inhibitor, Losartan (Intraperitoneal 20mg/kg). Lumbar SC tissue were paraformaldehyde (PFA) fixed and the dorsal horn imaged for endothelial cell (CD31) and pericytes (NG2) immunofluorescent stained markers.

Results: In a rodent model of diabetic neuropathic pain there was a reduction in vessel diameter in the spinal cord versus age-matched controls ($p<0.01$). Furthermore, following intrathecal angiotensin II treatment, increased proportions of constricted vessels were associated with NG2 labelled pericytes (*PAngiotensin II led to thermal and mechanical hypersensitivity when compared to vehicle treated group (*$P<0.0037$).

Conclusions: ATR1 mediated pericyte vasocontractility induces pain hypersensitivity and is implicated in the development of diabetic neuropathic pain.

DAY 2 SATURDAY 28 AUGUST 2021, ORAL ABSTRACT

OR.13 LIVER FIBROSIS INDICES ARE RELATED TO DIABETIC PERIPHERAL NEUROPATHY IN INDIVIDUALS WITH TYPE 2 DIABETES

Tae Jung Oh[1], Kyuho Kim[1], Hyen Chung Cho[1], Yun Kyung Lee[1], Chang Ho Ahn[1], Bo Kyung Koo[2], Jae Hoon Moom[1], Sung Hee Choi[1], Hak Chul Jang[1]
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Objectives: Non-alcoholic fatty liver disease (NAFLD) and liver fibrosis are associated with an increased risk of diabetic retinopathy or nephropathy in individuals with type 2 diabetes. However, the association between NAFLD or liver fibrosis and diabetic peripheral neuropathy (DPN), another important microvascular complication, has not been well studied. We aimed to investigate the association of NAFLD or liver fibrosis and DPN in individuals with type 2 diabetes.
Methods: This cross-sectional study analysed 264 individuals with type 2 diabetes. DPN was diagnosed when a Michigan Neuropathy Screening Instrument - Physical Examination score was ≥ 2.5. NAFLD liver fat score, NAFLD fibrosis score, and Fibrosis-4 (FIB-4) index were calculated. The association of NAFLD liver fat score, NAFLD fibrosis score, and FIB-4 index with the presence of DPN were analysed using logistic regression models. Serum levels of fetuin-A, a hepatokine were measured by ELISA in individuals with high NAFLD liver fat score.
Results: NAFLD liver fat score was comparable between individuals with DPN and those without DPN. However, NAFLD fibrosis score and FIB-4 index were significantly higher in individuals with DPN than in those without DPN (-0.75 ± 1.14 vs -1.11 ± 1.08, p = 0.010, and 1.58 ± 0.79 vs 1.34 ± 0.59, p = 0.009, respectively). Logistic regression analyses showed that NAFLD fibrosis score and FIB-4 index were associated with DPN after adjustment for covariates (OR 1.474 [95% CI 1.055, 2.058], and OR 1.961 [95% CI 1.209, 3.183], respectively). In the subgroup analysis, this association was only significant in group with high NAFLD liver fat score (> -0.640). Serum fetuin-A level was decreased in individuals with abnormal vibration perception or 10-g monofilament test and it discriminated these abnormalities.
Conclusions: NAFLD fibrosis score and FIB-4 index were associated with the presence of DPN in individuals with type 2 diabetes and suspected NAFLD. The present study suggests that liver fibrosis might be associated with DPN in individuals with type 2 diabetes.

OR.14 TWO-YEAR PROGRESSION OF RETINAL NEURODEGENERATION IN PEDIATRIC PATIENTS WITH TYPE 1 DIABETES MELLITUS: THE ROLE OF GLYCEMIC VARIABILITY

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

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Objective: Retinal neurodegeneration (RN) is an early marker of diabetic retinopathy (DR), which precedes vascular damage. Few data are available on the impact and predictive role of metabolic control and daily glycemic variability (GV) on early RN signs in the pediatric population with type 1 diabetes mellitus (T1DM).

The aim of our study is to evaluate for two years the structural alteration of neuroretina and the predictive role of GV on RN in pediatric T1DM subjects without any complications.

Methods: 25 T1DM patients (ages 10-20 years), using Continuous Glucose Monitoring (CGM) and treated with Continuous subcutaneous insulin infusion, without any complication, and 18 healthy control subjects (C), comparable in age and gender, were enrolled and followed for 2 years. All subjects underwent an Optical Coherence Tomography, with analysis of all macular neuroretinal layers measuring mean of subfoveal, inner and outer quadrants. In T1DM patients, metabolic parameters, GV indexes and standardized CGM metrics were calculated. All the data were collected at baseline (V0) and after 12 (V1) e 24 months (V2).

Results: At V1 and V2, the Outer Plexiform Layer (OPL) was significantly thinner in the inner quadrants (152.8 ± 9.4 vs. 163.9 ± 12.8, $p < 0.01$) (150.3 ± 9.5 vs 163.5 ± 12.8, $p < 0.01$) and in the whole quadrants (257.1 ± 12.6 μm vs. 286.4 ± 66.5 μm, $p = 0.05$), (254.3 ± 10.2 vs. 289.6 ± 67,6, $p = 0.05$) in T1DM versus C. At V2, the Inner Retinal Thickness (IRT) was significantly thinner (1201.3 ± 40.5 vs. 1244.1 ± 61.6, $p = 0.04$) in T1DM versus C. In the T1DM, a progressive reduction in IRT was observed after the two-year follow-up ($p<0.05$).

In T1DM patients, a negative correlation between Mean Absolute Glucose (MAG) and inner OPL ($r=-0.53$, $p=0.04$) at V2 and between the IRT delta thickness (V2-V1) and Lability Index ($r=-0.64$, $p=0.01$) and MAG ($r=-0.61$, $p=0.02$) were observed. Among metabolic parameters, a negative correlation between triglycerides levels and the IRT delta thickness (V2-V1) ($r=-0.67$, p Triglycerides variation alone explains the 48% of the IRT delta thickness ($R2 = 48.2\%$).

Conclusion: Very early morphological alterations of neuroretina are already present in pediatric T1DM patients without both vascular retinopathy and neuropathy, supporting the hypothesis that RN occurs early in the course of diabetes. GV and triglycerides seems to play a predictive role in the morphological abnormalities of neurosensory retina in T1DM pediatric population.

DAY 2 SATURDAY 28 AUGUST 2021, ORAL ABSTRACT

OR.15 MODULATION OF PGC1A, NRF2 AND LONP1 BY SAROGLITAZAR ATTENUATES MITOCHONDRIAL DYSFUNCTION IN EXPERIMENTAL DIABETIC NEUROPATHY

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Objective: Altered mitochondriogenesis and protein quality control mechanisms have surfaced as central mechanisms involved in mitochondrial dysfunction which can compromise nerve functioning due to bioenergetic failure of nerves and may lead to diabetic neuropathy. This study assessed the effects of Saroglitazar, a dual PPAR α/γ agonist in experimental diabetic neuropathy and if it has any role on modulation of mitochondrial function.

Methods: Functional and behavioral studies were performed in rats. Mechanistic studies were performed in isolated dorsal root ganglions (DRG) of diabetic rats to confirm the neuro-protective mechanisms of Saroglitazar. This study utilized Saroglitazar (2 and 4 mg/kg) in a reversal paradigm for 2 weeks post 6 weeks of diabetes induction using streptozotocin (55 mg/kg)

Results: Saroglitazar treatment improved MNCV (62.4±1.2 Vs 43.4±2.1 m/s, p

Conclusion: Saroglitazar improved neuro-behavior, nerve function and sensorimotor alteration in diabetic rats. Treatment was also able to improve mitochondrial function and mitochondrial quality control by activation of PGC-1α-NRF 2-LONP1 axis. With these results, we conclude, Saroglitazar may be a promising drug to treat DN.

13:35 – 14:50 | ORAL SESSION 4: Autonomic Neuropathy 2
Chairs: **E. Søfteland** - Norway, **T. Tegos** - Greece

OR.16 FIVE-YEAR CHANGE IN BODY COMPOSITION IE RELATED TO HEART RATE BUT NOT AUTONOMIC DYSFUNCTION IN THE WHITE HALL II STUDY

Christian Stevns Hansen[1], Gregers S Andersen[2], Marek Malik[3], Daniel R Witte[4], Eric J Brunner[5], Adam G Tabák[5], Mika Kivimäki[5], Dorte Vistisen[2]
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Objectives: Overweight and obesity are associated with autonomic dysfunction both in non-diabetic individuals and in people with prediabetes and diabetes. Furthermore, autonomic dysfunction has been associated with changes in glucose metabolism and development of cardiovascular disease and diabetic complications. However, it is not known how temporal changes in measures of body composition assessed by e.g. fat mass (FM) and fat free mass (FFM) may affect autonomic function(AF). Exploring patterns of changes in body composition parameters may present new risk factors and pathophysiological pathways that may be modified to prevent autonomic dysfunction. We aim to investigate the effect of changes in body composition on autonomic function in patients with and without dysglycemia.
Methods: Data on body composition and AF was collected twice in civil servants in 2002 and 2009. AF was assessed by measures of cardiovascular autonomic function: resting heart rate (HR) and several heart rate variability (HRV) indices. Body composition was assessed by body mass index (BMI), waist-to-hip ratio (WHR) FM and FFM.
In total 3,342 participants without CVD were included. Associations between 5-year changes in body composition indices and changes in AF measures were estimated with linear regression models adjusting for baseline level of the outcome and exposure, age, sex, ethnicity, dysglycemia, metabolic covariates and medication. Analyses including HRV were adjusted for resting heart rate. The HRV indices were log transformed before analysis. A modifying effect of dysglycemia was tested. Adjustment for multiple testing was applied using the Benjamini-Hochberg method.
Results: Increase in BMI (kg/m2), WHR, FM (kg) and FFM (kg) were associated with concurrent increases in resting HR (bpm) (BMI: 0.87 (95% CI: 0.68,1.05), WHR: 21.50 (14.9,28.2), FM: 0.44 (0.31,0.57), FFM: 0.37 (0.28,0.46)). Changes in body composition were not associated with changes in HRV indices after adjustment for multiple testing. There was no modifying effect of dysglycaemia on any association (Table 1).

Conclusions: Adverse changes in body composition assessed by BMI, WHR, FM, FFM are associated with an increase in heart rate but not autonomic dysfunction. In addition, changes in both FM and FFM seems to associate with heart rate similarly. The reason for this remains to be investigated.

Table 1

		BMI (kg/m2)		WHR		FFM (kg)		FM (kg)	
	Model	**Estimate**	**P**	**Estimate**	**P**	**Estimate**	**P**	**Estimate**	**P**
Resting Heart rate (bpm)	**1**	**0.9 (0.7;1)**	**<0.001**	**21.9 (15.3;28.5)**	**<0.001**	**0.4 (0.3;0.6)**	**<0.001**	**0.4 (0.3;0.5)**	**<0.001**
	2	**0.9 (0.7;1.1)**	**<0.001**	**21.5 (14.9;28.2)**	**<0.001**	**0.4 (0.3;0.6)**	**<0.001**	**0.4 (0.3;0.5)**	**<0.001**
SDNN (%-diff)	**1**	-0.5 (-1.6;0.6)	0.330	-24.8 (-48.3;9.4)	0.135	0.2 (-0.6;1)	0.611	-0.3 (-0.9;0.2)	0.219
	2	-0.6 (-1.7;0.5)	0.290	-20.5 (-45.6;16.3)	0.234	0.2 (-0.6;1)	0.656	-0.4 (-0.9;0.2)	0.189
RMSSD (%-diff)	**1**	-0.5 (-2.1;1)	0.508	-19.2 (-52.4;37)	0.427	0.5 (-0.6;1.6)	0.388	-0.4 (-1.1;0.4)	0.315
	2	-0.7 (-2.2;0.9)	0.394	-21.6 (-54.2;34.1)	0.371	0.4 (-0.7;1.5)	0.496	-0.4 (-1.2;0.3)	0.238
Low frequency power(%-diff)	**1**	-1.4 (-3.8;1.1)	0.262	-49.6 (-78.2;16.3)	0.107	0.1 (-1.6;1.9)	0.897	-0.7 (-1.9;0.5)	0.246
	2	-1.4 (-3.8;1.1)	0.257	-38.6 (-73.7;43.4)	0.258	0.1 (-1.6;1.8)	0.915	-0.7 (-1.9;0.5)	0.248
High frequency power (%-diff)	**1**	-2 (-4.7;0.7)	0.144	-29.9 (-72.7;80.4)	0.460	0.5 (-1.4;2.5)	0.584	-1.3 (-2.6;0.1)	0.061
	2	-2.4 (-5.1;0.4)	0.092	-32.5 (-74.2;76.2)	0.419	0.4 (-1.6;2.4)	0.706	**-1.4 (-2.7;-0.1)**	**0.037**

Table 1 Effect (with 95% CI) of one population standard deviation 5-yearincrease in body composition measures on SDNN, standard deviation of normal-to-normal R–R intervals; RMSSD, the root mean square of the sum of the squares of differences between consecutive normal-to-normal R–R intervals. The associations are adjusted for age, sex, ethnicity and baseline value of the outcome studied, and BMI (model 1) and further adjusted for physical activity, smoking, systolic blood pressure, total cholesterol, triglycerides, tricyclic antidepressants, diuretics and β blockers (Model 2). Models with HRV indices as out comes were adjusted for resting heart rate. Models where BMI was the determinant was not adjusted for BMI.

OR.17 HEART RATE RESPONSE DURING A STRESS TEST AND EFFECTS OF A CARDIAC REHABILITATION PROGRAMME IN PATIENTS WITH KNOWN DIABETES AND WITH NEWLY-DETECTED GLYCEMIC DISORDERS

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Objectives: Some papers suggest the high prevalence of unknown glycemic disorders among coronary patients. Heart rate (HR) response to a stress test is modulated by autonomic nervous system activity and has been shown to be impaired in diabetes. An abnormal HR response has a predictive value for sudden death. We aimed to analyse HR response to a stress test before and after one month of an ambulatory programme of cardiac rehabilitation in patients with known diabetes (KD), with newly-detected glycemic disorders (NDGD) and in normoglycemic patients.
Methods: We included 838 patients, 79% men, 75% with coronary disease (mostly after an acute coronary syndrome), 375 with KD. An OGTT was performed (plasma glucose measured at fasting and 2 hours after the glucose challenge) in the patients without KD, and a stress test at admission and at the end of the programme.
Results: Among the 463 patients free of KD, 189 (41%) had NDGD: diabetes (n=42), isolated fasting hyperglycemia (FH, n=45), glucose intolerance (IGT, n=70), both FH and IGT (n=32), and 274 were normoglycemic. HR at rest (HRrest), and maximal HR (HRmax), VO2 max and the percentage of HR reserve (%HRreserve) during the stress test differed significantly between the 6 groups (KD and the 5 NDGD groups) (p2 max and %HRreserve the lowest in KD patients, without significant differences between NDGD groups nor between NDGD and normoglycemic patients. The same profile was found when comparing these parameters in KD, NDGD taken altogether and normoglycemic patients (p2 max and %HRreserve (p=0.03 to
Conclusion: The data confirm the high prevalence of unknown glycemic disorders and the diagnostic value of the OGTT in coronary patients. The higher HRrest and the defect in HR reserve in the patients with known diabetes are likely to result from autonomic dysregulation and may be improved by a cardiac rehabilitation programme.

DAY 2 SATURDAY 28 AUGUST 2021, ORAL ABSTRACT

OR.18 ASSOCIATION BETWEEN URINARY ENDOTHELIAL GROWTH FACTOR LEVELS AND INDICES OF CARDIOVASCULAR AUTONOMIC NEUROPATHY IN PATIENTS WITH TYPE 1 DIABETES

Yu Kuei Lin[1], Emily Tanner[2], Yuee Wang[3], Wen Ye[4], Lynn Ang[1], Wenjun Ju[3], Rodica Pop-Busui[1]

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Objective: Current outcome measures for diabetic cardiovascular autonomic neuropathy (CAN) involve labor-intensive and time-consuming evaluations, thus identifying reliable and simple CAN biomarkers is needed. As prior research reported the relationship between CAN and diabetic nephropathy, we assessed whether the urinary endothelial growth factor (uEGF), an established urinary biomarker for chronic kidney disease progression, may be used as an effective CAN screening/diagnostic tool.

Methods: A cohort of 44 patients with type 1 diabetes (T1D) was phenotyped for CAN with the standardized battery of cardiovascular reflex tests (deep breathing, Valsalva, and response to standing) at baseline and annually during 3-year follow-ups. The uEGF was measured in spot urine samples obtained at baseline using Human EGF Immunoassay Quantikine ELISA (R&D Systems) and normalized to urine creatinine (uEGF/Cr). Spearman correlation was used to assess the association between uEGF/Cr levels and measures of CAN at baseline. Mixed effects models were conducted to assess the relationship between baseline uEGF/Cr levels and changes in CAN measures over time.

Results: The mean age of this cohort was 43±17 years, 49% were female, and diabetes duration was 22 ±15 years. Baseline uEGF/Cr levels positively correlated with expiration/inspiration (E/I) ratio ($r=0.37$, $PP<0.05$).

Conclusions: These data suggest that uEGF may serve as a non-invasive biomarker that could be used as a predictor for CAN progressions in patients with T1D. Further evaluations confirming these findings with covariate adjustments in other larger cohorts could enable large-scale populational CAN assessments and would also support the use of this biomarker for CAN assessment in clinical care.

OR.19 CARDIOVASCULAR AUTONOMIC NEUROPATHY AND RISK OF HEART FAILURE IN PARTICIPANTS WITH TYPE 2 DIABETES ENROLLED IN DEVOTE TRIAL

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Objective: Heart failure (HF) is emerging as one of most prevalent cardiovascular complication in patients with diabetes. Although mechanisms are complex, recent evidence suggest that cardiovascular autonomic neuropathy (CAN) may be an important player. We evaluated whether CAN is associated with an increased risk of HF in patients with type 2 diabetes (T2D) enrolled in the DEVOTE trial.

Methods: DEVOTE was a randomized, double-blind trial comparing the impact of insulin degludec to glargine 100 units/mL on cardiovascular outcomes. HF was an adjudicated secondary outcome. CAN was assessed by indices of heart rate variability (HRV) derived from 10-sec standard electrocardiograms at enrollment in 6347 T2D participants with HRV data available. Values below the 5th percentile of the cohort were defined as abnormal. Time to first hospitalization due to HF was analyzed using Kaplan–Meier survival curves and the log-rank test.

Results: A total of 369 (5.8%) DEVOTE participants had CAN at baseline. Participants with and without CAN had significant different [mean (standard deviation)] age [63.4 (7.3) and 64.9 (7.3) years], hemoglobin A1c [8.9 (1.9) and 8.4 (1.6) %], body mass index [33.0 (7.4) and 33.6 (6.8) kg/m2] and number of subjects from minority ethnicity [19.5 and 15.2%], respectively (P[hazard ratio=1.47 (95% confidence interval:1.04-2.06); P=0.028] over follow-up period (Figure).

Conclusion: These data indicate that CAN may be used for risk stratifying in patients with T2D at risk for developing symptomatic HF.

DAY 2 SATURDAY 28 AUGUST 2021, ORAL ABSTRACT

OR.20 LESIONS OF THE SMALL FIBERS OF THE AUTONOMIC NERVOUS SYSTEM AND GRADATION OF THE DIABETIC FOOT RISK IN PATIENTS WITH DIABETES

Olivier Bourron[1], Agnès Hartemann[1], Abdul Moutairou[2], Jean-Henri Calvet[3]
[1]Diabetology, Pitié-Salpêtrière, Paris, France
[2]Statistics, Impeto Medical
[3]Medical, Impeto Medical

Objectives: Foot lesions are a common, serious and costly complication of diabetes. The examination of the foot allows the evaluation of the diabetic foot risk according to the international classification ranging from grade 0 to grade 3. The sweat glands are innervated by the small fibers C of the autonomic nervous system and the evaluation of the plantar sudoromotor function allows detection and follow-up of peripheral vegetative neuropathy. Our objective was to evaluate the association between the grade of diabetic foot risk and a marker of the severity of small fiber neuropathy estimated by a non-invasive, objective, rapid and quantitative method.
Methods: 404 patients from one diabetology department and including, 251 patients with type 2 diabetes and 142 with type 1, had gradation of the risk for diabetic foot in the course of the treatment and a Sudoscan test allowing assessment of sudomotor function of the feet through measurement of the electrochemical skin conductance (ESC, µS). Thresholds for ESCs were:
Results: The characteristics of the patients were: 47% of women, age: 55 ± 13 years, HbA1C: 9.9 ± 1.9%. Feet ESC decreased significantly with grade; grade 0: 70 µS [55-78]; grade 1: 65 µS [41-75]; grade 2: 55 µS [33-74]; grade 3: 31 µS [25-46] (results expressed in median [Q1-Q3], $p < 0.05$).
Conclusion: This study revealed a link between the neuropathy of the small fibers of the autonomic nervous system and the gradation of the diabetic foot risk carried out during the treatment, confirming the clinical interest of Sudoscan. This work needs to be completed on a larger population to study the possible predictive character of the neuropathy of small fibers on the development of future lesions of the foot.

15:50 – 17:05 | ORAL SESSION 5: From Men to Mice
Chairs: **C. S. Hansen** - Denmark, **N. Papanas** - Greece

OR.21 RISK FACTORS ASSOCIATED WITH PROGRESSION OF DIABETIC NEUROPATHY

Georgios Ponirakis[1], **Rayaz Malik**[2]
[1]Medicine, PhD
[2]Medicine, Weill Cornell Qatar

Objective: There are limited longitudinal studies assessing the risk factors associated with the evolution of diabetic peripheral neuropathy (DPN).
Methods: Patients with type 2 diabetes (T2D) (n=78) and control participants (n=26) underwent clinical, metabolic and neuropathy phenotyping using corneal confocal microscopy (CCM), vibration perception threshold (VPT) and DN4 questionnaire at baseline and 2-year follow-up.
Results: The prevalence of DPN and painful DPN (pDPN) was 18% and 26%, respectively. Patients with T2D had a higher VPT (P≤0.01) and lower corneal nerve fiber density (CNFD), branch density (CNBD) and fiber length (CNFL) (P≤0.0001) compared to controls. Over a 2-year follow-up period, there was a significant decrease in HbA1c (P≤0.001), body weight (P≤0.05) and LDL (P≤0.05). There was no change in the prevalence of DPN (P=0.28), but there was a significant improvement in DN4 in patients who had painful neuropathy at baseline (P≤0.0001). VPT (P=0.57) and CNFD (P=0.28) did not change and there was a decrease in CNBD and CNFL (P≤0.05). However, there was a significant increase in CNFD (P≤0.01) and CNFL (P
Conclusions: Despite a modest improvement in HbA1c, body weight and LDL in patients with T2D there is evidence of progressive small nerve fiber degeneration. However, physical activity was associated with small nerve fiber regeneration, whilst inactivity was associated with progressive nerve fiber degeneration.

DAY 2 | SATURDAY 28 AUGUST 2021, ORAL ABSTRACT

OR.22 NADPH OXIDASE 5 PROMOTES NERVE DAMAGE IN METABOLIC DISEASE

Stephanie Eid[1], Faye Mendelson[1], John Hayes[1], Crystal Pacut[1], Kai Guo[2], Junguk Hur, Eva Feldman[1]

[1]Neurology, University of Michigan

[2]Biomedical sciences, University of North Dakota

Objectives: Peripheral neuropathy (PN) is a disabling complication that affects over 30% of normoglycemic patients with metabolic disease and 60% of type 2 diabetic (T2D) patients. Beside hyperglycemia, dyslipidemia has emerged as an important mediator of metabolic disease-dependent nerve injury. However, the mechanisms by which dyslipidemia leads to injury in murine and human PN remain unclear. While dyslipidemia favors a highly oxidizing environment in complication-prone tissues, how dyslipidemia intersects with specific sources of reactive oxygen species (ROS) to contribute to nerve damage is unknown. NADPH oxidase (NOX) enzymes are specialized for ROS production, and of the 7 members (NOX1-5, Duox1 and 2), the NOX5 isoform is only present in higher mammals, and not in rodents. In this study, we examined the role of NOX5 in human peripheral nerves and in in vitro models of PN.

Methods: NOX5 methylation status, gene and protein expression were assessed in sural nerve biopsies from patients with PN. At the cellular level, human Schwann cell (SC) and neuronal cultures were exposed to high concentrations of the saturated fatty acid palmitate to evaluate NOX5 gene and protein expression, NOX-derived ROS generation, redox sensitive transcription factor NF-E2-related factor-2 (Nrf2) nuclear translocation, and caspase-3 dependent apoptosis. We also assessed the NOX4-NOX5 interaction by co-immunoprecipitation.

Results: Evaluation of sural nerve biopsies of T2D patients with PN revealed NOX5 promoter hypomethylation in patients with worse PN that was associated with increased NOX5 gene and protein expression. In vitro, our results show that palmitate treatment increases NOX5 gene expression in cultured neurons with increased ROS generation at early and late time points. Nrf2 nuclear translocation was initially increased by palmitate exposure, but overtime was suppressed by treatment. Translocation had no effect on dyslipidemia-induced injury determined by upregulated caspase 3 protein expression at early and late time points. Similar results were observed in SCs, with preliminary data pointing toward a potential NOX5-NOX4 interaction following palmitate treatment.

Conclusions: Our findings provide evidence of a previously unrecognized role of NOX5 as a critical target for dyslipidemic oxidative stress that may injure PN-relevant cell types and contribute to the development of PN during metabolic stress.

OR.23 IMPACT OF CHOLESTEROL DYSREGULATION ON THE DEVELOPMENT OF PERIPHERAL NEUROPATHY

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University of Reunion Island, Diabète - Athérothrombose - Thérapies Réunion Océan Indien (DéTROI), Réunion, France

Diabetes mellitus (DM) represents one of the most common chronic disorders worldwide, with epidemic levels affecting about 8.5 % of the human population. DM can damage the peripheral nervous system in various ways presenting diverse disorders with differing anatomic features, clinical courses, and phenotypes. The most common presentation is the symmetric distribution of sensory abnormalities in the lower limbs, known as distal symmetric diabetic polyneuropathy (DPN). Despite the global prevalence, the pathophysiological mechanisms of DPN have not yet been fully elucidated. Although glucose metabolism has been the focus of research to understand the pathophysiology of this complication for decades, glycemic control shows a limited correlation with DPN. Accumulating data from several large-scale trials of patients with Type 2 DM also link dyslipidemia as a major independent risk factor for the development of diabetic neuropathy. Clinical evidence has shown that increased low-density lipoprotein (LDL) cholesterol and triglyceride (TG) levels associate with a faster progression to peripheral neuropathy in patients with DM. The nervous system is highly enriched in lipids and cholesterol plays an important role as a structural and functional molecule important for the nerve health. In this work, we hypothesized that a dysregulation of cholesterol metabolism could impact the development of peripheral neuropathy. In order to address this question, we characterized the behavioral phenotype of different mouse models of dysregulated cholesterol metabolism, using a number of sensory tests (Von Frey, Hargreaves, pinprick, brush test) and motor behavior (Rotarod) that may indicate peripheral deficits. In parallel, we used western blot and immunohistochemical analysis to analyze the expression of major lipoprotein receptors: LDLR (low-density lipoprotein receptor), VLDLR (very low-density lipoprotein receptor) and LRP1 (lipoprotein receptor-related-protein-1) in the sciatic nerve. Our preliminary behavioral analysis did not show a significant difference between hypercholesterolemic mice tested (LDLR -/-) and (ApoE -/-: Apolipoprotein E-/-) compared to control mice. We show the expression of different receptors: LDLR, VLDLR and LRP1 in the adult sciatic nerve. In conclusion, this work shows that systemic increase of cholesterol levels in knock-out mice does not seem to result in behavioral neuropathic symptoms. It will be interesting for future studies to test HFD (High-Fat Diet) fed mice as a model of lipid dysregulation and evaluate the onset of neuropathic symptoms.

DAY 2 | SATURDAY 28 AUGUST 2021, ORAL ABSTRACT

OR.24 FOLLOW UP OF PERIPHERAL POLYNEUROPATHY SIGNS AND SYMPTOMS IN SEVERELY OBESE PATIENTS FOLLOWING BARIATRIC SURGERY

Helena Schmid[1], Otto Nienov[2], Fernanda Dapper Machado[2], Rodrigo Menguer[2], Luiz Alberto De Carli[3]

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[3]CTO, Santa Casa de Proto Alegre

Objectives: Peripheral polyneuropathy (PPN) is a complication of Diabetes Mellitus (DM) and obesity. After bariatric surgery (BS), persistence and clinical manifestations (signs and symptoms) of PPN are not well defined. Our purpose is to report the follow up of patients with grade II and III obesity from time of the surgery until 6 months after BS.

Methods: A prospective, longitudinal study, with 96 patients with PPN and grade II and III obesity before BS (18 with DM, 39 with PreDM and 39 without diabetes (NoDM)) was performed. PPN was defined as positive when Michigan Neuropathy Screening Instrument (MNSI) had a score ≥2.5 on physical exam and at least one symptom. Patients were also followed up with Neuropathy Symptom Score (NSS) and Neuropathy Disability Score (NDS) measures. NDS was considered positive if ≥3 points were given. Figure 1 shows a flowchart explaining the inclusion and exclusion criteria used.

Results: After BS, PPN signs and symptoms ameliorate, without difference between the groups in MNSI examination (p=0.156), MNSI questionnaire (p=0.958), NSS (p=0.519) and NDS (p=0.480). PPN persistence decreased in all (DM, preDM and NoDM; p

Conclusion: In patients with PPN and obesity grade II and III, PPN presence as well as its signs and symptoms decrease 6 months after BS.

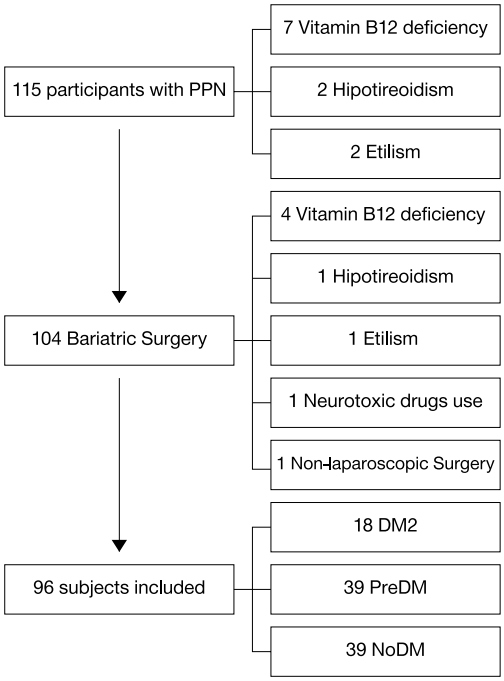

Figure 1: Flowchart of the inclusions and exclusions of participant's who gave consent to the study.

OR.25 OMEGA-3 POLYUNSATURATED FATTY ACIDS IN THE TREATMENT OF DIABETIC PERIPHERAL NEUROPATHY: IS THE SOURCE IMPORTANT?

Mark Yorek
University of Iowa and Iowa City VA Healthcare System

In 2015, 9.4% of the United States population had diabetes and about 50% of these patients will have developed diabetic peripheral neuropathy (DPN). The only treatment for DPN is glycemic control, which is less effective in subjects with type 2 diabetes. Thus, there is a critical need of a treatment. Our pre-clinical studies have demonstrated that treating diabetic rodents with omega-3 polyunsaturated fatty acids (PUFA) derived from menhaden (fish) oil initiates nerve damage repair and reverses DPN. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are the predominate omega-3 PUFA found in fish oil and are the precursors of E and D series resolvins, respectively, which have anti-inflammatory and neuroprotective properties. We have shown that these metabolites alone elicit repair of nerve damage caused by diabetes when administered endogenously. As we initiate plans to advance omega-3 PUFA to a clinical trial for DPN there remains several questions to be addressed. One poorly explored question has been what is the best source or composition of omega-3 PUFAs that will provide the most favorable and safe outcome? We have shown that treating type 2 diabetic rats with fish oil that achieved an omega-3 PUFA concentration in serum that was obtained in human subjects treated with 4 g of fish oil/day is an efficacious treatment for DPN. However, is fish oil the best source of omega-3 PUFA for the treatment of DPN or are the ethyl ester derivatives of EPA and/or DHA more efficacious? Ethyl esters of EPA (Vascepa®) or the combination of EPA and DHA (Lovaza®) are pharmaceutical compounds and represent a highly purified and concentrated source of EPA and DHA. Besides these pharmaceutical compounds are there other “healthy” alternatives to fish oil? Commercially available algae’s that primarily produce EPA or DHA or a combination of EPA and DHA may be a more environmental friendly and safe source of omega-3 PUFA. Studies have shown that EPA and DHA and their metabolites have different molecular targets. Since the etiology of DPN is complex having both vascular and neural pathological pathways it is likely that a combination of EPA and DHA as found in Lovaza® or in algae’s that produce an equivalent amount of EPA and DHA will be needed for an effective treatment of DPN. Our past studies with fish oil and their metabolites for the treatment of DPN and the potential use of these alternative sources of omega-3 PUFA will be discussed.

CONGRESS NEURODIAB 2021

ORAL ABSTRACT DAY 3

Aristotelous Square in Thessaloniki, Greece

DAY 3 | SUNDAY 29 AUGUST 2021, ORAL ABSTRACT

08:30 – 09:45 | ORAL SESSION 6: Central Mechanisms
Chairs: **S. Tesfaye** - UK, **F. Piccon**i - Italy

OR.26 ALTERATIONS IN THE FUNCTIONAL BRAIN NETWOK IN TYPE 1 DIABETES

Suganthiya S. Croosu[1,2,3], Johan Røikjer[2,4], Carsten D. Mørch[5], Niels Ejskjaer[2,3], Jens B. Frøkjær[1,3], Tine M. Hansen[1,3]
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[2]Dept. of Endocrinology, Steno Diabetes Center North Denmark,
[3]Dept. of Clinical Medicine, Aalborg University Hospital & Aalborg University, Aalborg, Denmark
[4]Dept. of Health Science and Technology, Aalborg University Hospital & Aalborg University, Aalborg, Denmark
[5]Dept. of Health Science and Technology, Aalborg University, Aalborg, Denmark

Objectives: Diabetes has been suggested to alter the brain default mode network (DMN), which is activated at rest. The network is linked to cognitive function and has also been suggested to be influenced by pain. However, it is uncertain whether the potential reorganization of DMN is attributed to diabetes per se or the complications coexisting with diabetes including peripheral neuropathy and neuropathic pain. This study aimed to investigate the DMN in adults with type 1 diabetes mellitus (T1DM) with and without peripheral neuropathy and neuropathic pain.
Methods: The study is a part of a larger project MEDON (Methods of Early Detection of diabetic peripheral Neuropathy). These preliminary results are based on resting-state functional MRI performed on 19 T1DM and neuropathic pain (mean age 51.5 ± 9.8 years, 10 females), 15 with T1DM and neuropathy (mean age 54.1 ± 8.7 years, 5 females), 19 subjects with T1DM (mean age 51.6 ± 9.8 years, 9 females), and 20 healthy controls (mean age 51.5 ± 9.2 years, 10 females). Seed-to-voxel analyses were performed for four DMN seeds: Medial prefrontal cortex, posterior cingulate cortex and right/left lateral parietal cortex. The strength of DMN connectivity (mean z-score) was calculated using the mean of seed-to-seed correlation between all four seeds.
Results: Increased connectivity between left lateral parietal (DMN seed) and right operculum ($p=0.001$) and decreased connectivity between left lateral parietal (DMN seed) and interior frontal cortex/precentral cortex/middle frontal cortex ($p = 0.003$) were observed in T1DM with neuropathy compared to controls. The overall connectivity of DMN was stronger in T1DM group (mean±SD, 0.65 ± 0.19) compared to controls (0.49 ± 0.17), (Bonferroni, $p = 0.04$). However, the values for the strength of DMN connectivity in the group with T1DM and pain neuropathy (0.54 ± 0.18) and in the group with T1DM and neuropathy (0.59 ± 0.18) were intermediate between the other two groups.
Conclusions: These preliminary data confirmed the altered DMN connectivity in individuals with T1DM. Altered connectivity was especially found in the left and right lateral parietal in T1DM with neuropathy compared to controls with increased connectivity to operculum, which is involved in higher-order processing for somatosensory perception and decreased connectivity to frontal regions involved in cognition. The strength of DMN connectivity was stronger in those T1DM without neuropathy and pain, which could suggest DMN functioning as a cognitive compensatory system, also confirmed by other studies. However, this is still urged to be investigated.

DAY 3 SUNDAY 29 AUGUST 2021, ORAL ABSTRACT

OR.27 DEEP LEARNING TREATMENT RESPONSE CLASSIFICATION OF DIABETIC PAINFUL NEUROPATHY

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[2]Department of Human Metabolism, University of Sheffield, Sheffield, UK

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Objectives: Disabling pain in the lower and upper limbs affe cts a quarter of all patients with diabetic peripheral neuropathy (DPN). This results in considerable disability and suffering and pharmacotherapy is often used for symptomatic relief. However, only a third of patients achieve a 50% reduction in pain intensity. We recently demonstrated how functional magnetic resonance (MR) imaging can be used to assess and stratify patients with painful DPN. This supports the idea of using neuroimaging as a mechanism-based technique to individualise therapy for patients with painful DPN. The aim of this study was to develop and validate different machine learning algorithms to predict treatment response in patients with painful DPN.

Methods: Twenty-three consecutive patients who received intravenous lidocaine treatment for painful DPN were assessed. All subjects (responders n=13 and non-responders n=10) underwent detailed clinical and neurophysiological assessments including quantitative sensory testing using the German Network on Neuropathic Pain (DFNS) protocol to phenotype their pain sensory profile. Subjects also underwent resting state brain magnetic resonance (MR) imaging. After pre-processing we performed a group concatenated ICA set to 30 components and obtained subject specific spatial maps. From these we automatically choose 7 highly correlated ($p<0.05$) ICA components from well know resting state functional connectivity networks. A 3D CNN (convolutional neural network) classification framework was trained using a VGG-Net based architecture with 100 epoch and a learning rate of 0.001. This deep learning architecture was used to compare models using (1) 7 highly correlated ICA networks 2) All 30 ICA networks generated.

Results: The mean age and duration of pain were 57.2 and 8.2 years respectively. Also mean NTSS-6 scores for all patients were 13.86. The deep learning treatment response classification model using 7 ICA spatial maps has a mean AUROC of 0.91 and an accuracy score of 0.85. However, with the extra information of all 30 ICA maps the mean AUROC increased to 0.94 with an accuracy score of 0.89.

Conclusion: Our results show that we can predict treatment response to a high AUROC and accuracy rate. We have also shown that additional information can be extracted with extra ICA spatial components as an input to our deep learning model. To our knowledge this is the first study utilising deep learning methods to classify treatment response in painful DPN. Our dataset cohort is small by machine learning standards and future works would benefit if expanded to a larger cohort.

OR.28 CLASSIFYING SENSORY PHENOTYPES IN PAINFUL DPN: MULTIMODAL MAGNETIC RESONANCE IMAGING AND A MACHINE LEARNING APPROACH

D. Selvarajah[1], K. Teh[2], I.D. Wilkinson[2], F. Heiberg-Gibbons[1], M. Awadh[1], A. Kelsall[3], S. Pallai[3], G. Sloan[3], S. Tesfaye[3]

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[3]Diabetes Research Department, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK

Objectives: A common distressing complication of diabetes that is discordant with the degree of peripheral nerve pathology is painful diabetic neuropathy (DN). Very little is known about the cerebral processes involved in pain processing in painful DN. Here we investigated resting-state brain connectivity associated with prolonged pain in DN.

Methods: 142 subjects and 36 matched controls were compared with regard to both behavioural measures of pain perception and resting-resting state functional Magnetic Resonance Imaging. The resting-state fMRI brain connectivity was investigated using 20 seed regions located in cardinal pain processing brain regions. Resting-state fMRI analysis was performed using the NITRC Functional Connectivity (CONN) Toolbox and SPM8 (welcome Trust Centre for Neuroimaging London, UK) in Matlab 2014a (the MathWorks, Natick, MA, USA). Functional connectivity matrices between the pre-specified seeds were calculated and the HV versus painful DN phenotype interaction examined.

Results: Relative to controls, painful DPN patients displayed increased brain connectivity predominately for the supplementary motor areas and the primary sensorimotor cortex (b=0.23, T(93)=3.7, p-FDR=0.004). Similar results were found when painful DPN subjects were compared with those with no DPN (b=0.23, T(96)=4.01, p-FDR=0.001). Conversely, we observed an increase in brain connectivity between the primary somatosensory cortex and cingulate cortex (b=0.13, T(101)=3.18, p-FDR=0.039), prefrontal cortex and amygdala (b= -0.14, T(101)=-3.59, p-FDR=0.01) between painful and painless DPN patients.

Conclusion: Our study provides experimental evidence of increased connectivity between frontal midline regions that are implicated in affective pain processing and bilateral sensorimotor regions in painful DPN patients.

DAY 3 | SUNDAY 29 AUGUST 2021, ORAL ABSTRACT

OR.29 INCREASED FUNCTIONAL CONNECTIVITY OF THE THALAMUS TO THE PRIMARY SOMATOSENSORY CORTEX AND INSULAR CORTEX FOLLOWING TREATMENT WITHDRAWAL: A POTENTIAL BIOMARKER OF PAINFUL-DPN

Sloan G.[1], Selvarajah D.[1,2], Teh K.[3], Wilkinson, I.D.[2], Tesfaye S.[1]

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[2]Department of Oncology and Human Metabolism, University of Sheffield, Sheffield UK

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Objectives: Altered functional connectivity has been identified in key brain regions involved in somatosensory perception in patients with painful diabetic peripheral neuropathy (painful-DPN), using resting state functional-magnetic resonance imaging (fMRI). However, these studies have not looked at the impact of neuropathic pain treatments. A greater understanding of treatment upon these pain processing areas might lead to greater understanding of the mechanisms of these pharmacotherapeutic agents and also development of new treatments that target these brain regions.

Methods: A total 15 participants (Age, 62.1 ± 9.0; HbA1c 65.4 ± 16.2 mmol/mol; 13 type 2 diabetes, 1 type 1 diabetes and 1 MODY; 13% female) enrolled in the OPTION-DM clinical trial (ISRCTN17545443) underwent neuroimaging. All participants had clinical and neurological assessments, including the modified Toronto Clinical Neuropathy Score, Doleur Neuropathique 4 and Neuropathic Pain Symptom Inventory. Participants underwent fMRI imaging using 3T (Achieva, Phillips Healthcare) when the participants were on maximum tolerated medication (Treatment Scan) and one week after washout of these medications (Washout Scan). The data was analysed using Conn Functional Connectivity Toolbox in SPM.

Results: There was a significant increase in Pain Numeric Rating Scale (NRS) from Treatment Scan (4.0 ± 2.1) to the Washout Scan (6.1 ± 2.4, p=0.044). There was a significantly greater functional connectivity between the Primary Somatosensory Cortex (S1) and the Thalamus, and the Insular Cortex and Thalamus (p false discovery rate [FDR] = 0.041) during the Treatment Scan compared with the Washout Scan. Moreover, there was a significant difference in the change between scans in S1 - Thalamic functional connectivity in participants with Severe-Pain (NRS ≥8 at baseline: Age, 64.5 ± 10.1; 10% Female; -0.372 ± 0.275) compared to participants with Moderate-Pain (NRS ≤7: Age, 57.4 ± 3.0; 20% Female; -0.051 ± 0.180, p=0.035). The change in S1-Thalamic connectivity also correlated with a number of variables including baseline pain (r -0.585, p=0.022), NPSI (r -0.597, p=0.019) and the difference in NRS at the Treatment Scan and Baseline pain (r -0.513, p=0.050).

Conclusions: This is the first study to look at the impact of neuropathic pain medication withdrawal on functional connectivity of pain matrix brain regions. On neuropathic pain medication withdrawal there is an increase S1 – Thalamus and Insular Cortex – Thalamus functional connectivity. Moreover, the change in S1 – Thalamus functional connectivity from the Treatment Scan to Withdrawal Scan differentiated participants with high and low baseline neuropathic pain and correlated with baseline pain. This study further demonstrates that the thalamus is a key area for the central mechanisms of painful-DPN and its functional connectivity to the S1 and Insular Cortex has the potential to act as a biomarker of painful-DPN.

OR.30 THALAMIC H1-MRS METABOLITE PARAMETERS ARE RELATED TO MOOD DISORDERS

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Background: Our group has previously demonstrated increased relative blood volume and preserved HMRS neuronal metabolite ratios in the thalamus of subjects with painful diabetic peripheral neuropathy (P-DPN). We hypothesised that perfusion measures and neuronal function measured by metabolite ratios may be related. Additionally, as brain metabolite ratios may also be affected by mood disorders, common in P-DPN, there is a need to investigate if there are significant correlations.

Methods: 52 type 1 diabetes (T1D) subjects (18 P-DPN, 23 DPN, 13 T1D without neuropathy-DM-NN) and 1 non-diabetic healthy volunteers (HV) took part in the study. 1HMRS examination was performed at 3T (Ingenia, Philips, Netherlands). Single voxel spectra were obtained from a 2.25cm3 (15x10x15mm) cubic volume of interest within the left thalamus, TE=135ms, TR=1600ms, NSA=256 using point resolved (PRESS) technique. Fitted metabolite area ratios were calculated for choline (Cho) at 3.2ppm, Creatine (Cr) at 3.0ppm, and N-Acetyl Aspartate (NAA) at 2.02ppm. MR-DSC images were obtained at 3T using a T2*-weighted technique (TR/TE=1250/35ms; 72 dynamics) to assess the passage of a bolus of intravenous gadolinium-chelate through the left thalamic vascular bed. ANOVA was performed to compare the group means for 1HMRS metabolite ratios. Pearson's r correlations were performed between perfusion parameters: regional blood volume (RBV), regional blood flow (RBF), mean transit time (MTT), time to peak (TTP) concentration; and 1HMRS metabolite ratios. 1HMRS metabolite ratios were correlated using Pearson's R(R) with baseline characteristics and scores on validated questionnaires measuring symptoms of mood disorders.

Results: There was significant negative correlation between NAA/Cr (measure of neuronal function) and measures of depression: Hospital anxiety and depression scale (HADS): R= -0.33 (p=.01), Becks depression inventory (BDI) R= -0.25 (p=.048); and anxiety: State-Trait Anxiety inventory- State (STAI-S) R= -.37 (p=.002), STAI- Trait (T) R= -.32 (p=.01) and Behavioural Inhibition (BIS) R= -0.25 (p=.04). There were no significant correlations between perfusion measures and metabolite ratios. There was no difference in metabolite ratios between the groups.

Conclusion: This is the first study to find thalamic 1HMRS metabolite ratios are correlated with symptoms of mood disorders and measures of neuropathy in subjects with T1D. It is likely that the high prevalence of mood disorders in P-DPN and DPN have significantly confounded previous 1HMRS studies and may explain conflicting reports in the literature. The link between neuropathy and mood disorders needs further exploration to understand whether depression and neuropathy may arise from a common neurobiological pathway.

DAY 3 | SUNDAY 29 AUGUST 2021, ORAL ABSTRACT

10:45 – 11:45 | ORAL SESSION 7: Case Reports and Observation Studies
Chairs: **S. Sharma** - UK, **G. J. Bönhof** - Germany

OR.31 SEVERE ATYPICAL AMYOTROPHY (RADICULOPLEXUS NEUROPATHY) IN A PATIENT WITH NEWLY DIAGNOSED TYPE 2 DIABETES AND COVID-19 INFECTION – A CASE REPORT

Anna Korei, Magdolna Békeffy, Edit Román, Ildikó Istenes, Zsuzsanna Putz, Noémi Hajdú, Dóra Tordai, Orsolya Vági, Péter Kempler
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Diabetic amyotrophy is a rare neurological complication of diabetes. Viral infections may cause radiculopathies and COVID-19 has already been postulated being associated with a variety of neurological disorders.
The 62-year-old male (BMI: 27.1 kg/m2) was admitted to hospital due to blood glucose values above 30 mmol/l and newly-onset diabetes. As his COVID-19 antigen test was positive, he was referred to the COVID-19 care unit. By admission, he had experienced a severe, increasing pain in the hip, thighs and buttocks for 3 weeks. Interestingly, he had a more pronounced pain in the shoulders and upper arms and it was accompanied by severe muscle weakness of the upper extremities. He also experienced a 15 kg weight loss during the last month.
During his stay in hospital, he developed COVID-pneumonia. Hence he was treated with vitamin D3, LMWH, dexamethasone and remdesivir. His HbA1c was 13.8% and we initiated. multiple daily insulin injections.
On neuropathy examination, by using the Neurometer (Neurotron Inc.), hypaesthesia of all sensory nerve fibre types was established. The tuning fork showed slightly impaired vibration perception on the two upper and the right lower limb. The protective sensation assessed by monofilament was preserved. Only a mildly elevated warm thermal perception threshold of the left upper limb was detected when small-fibre neuropathy was evaluated by Q-Sense (Medoc Ltd.). No cardiovascular autonomic neuropathy could be established.
In respect of the treatment of his neuropathy, both pathogenetically (alpha-lipoic acid and benfotiamine) and symptomatic treatment options (pregabaline+duloxetine) were implemented.
Conclusions: Based on the clinical scenario and results of the neuropathy tests, the patient suffered from severe symmetrical radiculoplexus neuropathy with upper extremity predominance being uncommon for patients with diabetes. COVID-19 infection in diabetes mellitus may cause a more severe and atypical presentation of amyotrophy with a combined involvement of the cervical and lumbosacral plexus.

OR.32 PERIPHERAL NEUROPATHY AND COVID-19

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Objectives: Diabetic peripheral neuropathy (DPN) is one of the major chronic complications of diabetes and leading high-risk factor of foot ulcers/amputations. About 60-70% of diabetic patients will eventually develop DPN. Causes of diabetic neuropathy are multifactorial, including poor diabetes control, diabetes duration, metabolic/vascular factors, ect.

COVID-19 ia A highly contagious respiratory disease caused by the SARS-CoV-2 virus. SARS-CoV-2 is thought to spread from person to person through droplets released when an infected person coughs, sneezes, or talks. The most common signs and symptoms of COVID-19 are fever, cough, and trouble breathing. Fatigue, muscle pain, chills, headache, sore throat, runny nose, nausea or vomiting, diarrhea, and a loss of taste or smell may also occur.

Nerve pain and skeletal muscle injury, Guillain-Barré syndrome, cranial polyneuritis, neuromuscular junction disorders, neuro-ophthalmological disorders, neurosensory hearing loss, and dysautonomia have been reported as PNS manifestations in patients with COVID-19.

Our aim was to see how covid 19 correlate with peripheral neuropathy in Georgian patients with type 2 diabetes mellitus (T2DM).

Methods: Patients supervised and treated at our Center were selected: 20 T2DM patients (11males and 9 females) with previously diagnosed T2DM and Medium severity COVID19, their mean age was 40±5 years; their diabetes duration varied from 5 to 7 years. HbA1c in was 8.3±1.5%. All neurological tests and examination with Sudoscan (a non–invasive method for the assessment of the small fiber function, Impeto Medical, France) were performed in all patients. results of all neurological tests (monofilament test, tip-term/temperature test, vibration test) were positive 17 out of 20 patients. Sudoscan examination revealed presence of small fiber neuropathy in these patients. Patients had the following symptoms after transmission of the COVID infection: pain, numbness, and weakness in the lower extremities.

Results: Patients who had diabetes mellitus (did not have diabetic neuropathy) developed symptoms of peripheral neuropathy after Covid 19 transfer.

Conclusions: This study shows that COVID 19 may develop peripheral neuropathy in diabetic patients who did not have diabetic peripheral neuropathy prior to Covid infection. Observations will continue.

DAY 3 | SUNDAY 29 AUGUST 2021, ORAL ABSTRACT

OR.33 INFLUENCE OF DIABETIC POLYNEUROPATHY ON THE SEVERITY OF SARS-COV-2 INFECTION

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Objectives: The 2019 Coronavirus pandemic, caused by a new type of coronavirus (SARS-CoV-2), has claimed more than 3.85 million lives worldwide so far. Data from several countries have shown that mortality and morbidity are higher among people with chronic disease, including diabetes. The aim of this study is to observe whether the presence of polyneuropathy had an impact on the form of COVID-19 disease, or on the outcome of the patients.
Methods: We evaluated 57 patients with type 1 and type 2 diabetes mellitus, hospitalized at the Nicolae Malaxa Clinical Hospital in Bucharest, with SARS-CoV-2 infection. Statistical data were analysed using IBM SPSS.
Results: Out of N=57 patients with diabetes, 22 (38.6%) were women and 35 (61.4%) men, with a mean age of 64.51 ± 10.64 years; 3 (4.3%) patients had type 1 diabetes (T1DM) and 54 (77.1%) type 2 diabetes (T2DM). Of the total, 14 (24.6%) had a diagnosis of peripheral diabetic polyneuropathy. The mean duration of DM in patients with polyneuropathy was 10.06 (CI 95% 7.34-12.72) years. The mean glycated haemoglobin values in patients with polyneuropathy were 8.78 ± 2.23 %. There were no statistically significant differences in the gender distribution of polyneuropathy. Among patients with polyneuropathy, 1 (7.14%) had a mild form of SARS-CoV-2 infection, 9 (64.26%) had a moderate form and 4 (28.56%) had a severe form ($p < 0.691$). The average length of hospitalization of patients with polyneuropathy was 17.21 ± 12.19 days, compared with those without polyneuropathy of 16.95 ± 9.82 days ($p < 0.837$). Among the patients with polyneuropathy, 14.3% (N=2) presented anosmia, respectively 0% dysgeusia, compared to patients without polyneuropathy: 8.9%, respectively 5.4%. There were no statistically significant differences between patients with polyneuropathy and those without, in terms of the early manifestations of SARS-CoV-2 infection-anosmia, dysgeusia ($p=0.292$, $p=0.357$).
Conclusions: No correlation was found between the presence of peripheral diabetic polyneuropathy and the severity of the form of SARS-CoV-2 infection or the length of hospitalization of patients in our clinic. Also, there are no statistically significant correlations between the occurrence of anosmia, dysgeusia, caused by SARS-CoV-2 infection and the diagnosis of polyneuropathy.

OR.34 CEREBRAL AND PERIPHERAL MICROCIRCULATION IN TYPE 2 DIABETES MELLITUS AND OBESITY, INFLUENCE OF NEUROPATHY AND C-PEPTIDE LEVELS

Miklós Káplár[1], Regina Esze[1], Márton Mikó[2], Zita Képes[2], Sándor Somodi[1], György Paragh[1], Péter Kempler[3], Miklós Emri[4], Ildikó Garai[5]

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Objectives: Microcirculation is damaged in diabetic patients and it has also been observed in obesity. Damage to microcirculation affects both cerebral and peripheral microvessels and is one of the main pathogenetic factors in the development of neuropathy. C-peptide ameliorate microcirculation and vascular endothelial growth factor (VEGF) is an angiogenic factor.
Our aim was to investigate the cerebral and peripheral microcirculation, peripheral neuropathy and to find any association between them in obesity and type 2 diabetes.
Methods: Participants (diabetic group: 16 female and 24 male, mean age: 50.9±6.9 year, BMI: 32.9±5.1 kg/m2; obesity group: 18 female and 14 male, mean age: 51.4±1.0 year, BMI: 38.8±6.0 kg/m2) were involved after a written consent was obtained.
Tc99m HMPAO dynamic SPECT/CT (technetium-99m hexamethyl propylenamine oxime single photon emission computed tomography) studies were performed to assess cerebral and peripheral microcirculation.
Neurometer was used to determine neuropathy and three groups of patients - severe, mild and no neuropathy – were created.
Results: Leg perfusion was significantly lower in the diabetic group (p
There were no significant differences in hemispheral and regional brain perfusion neither between T2DM and obese patients nor among neuropathy groups.
C-peptide levels were non significantly lower in mild and higher in severe neuropathy patients compared to those without neuropathy, but significant difference between mild and severe groups was found (p=0.0066).
VEGF levels were significantly elevated in severe neuropathy patients compared to no neuropathy group (p=0.049).
Lower limb microcirculation correlated significantly with C-peptide (p<0.05, rho: 0.29) but not with VEGF levels. There was also positive correlation between C-peptide levels and cerebral microcirculation (p<0.05, rho: 0.27).
Conclusions: C-peptide levels highly and positively contribute to the changes in lower limb microcirculation in patients with neuropathy.
Cerebral microcirculation was not altered in our study, but positive correlation with C-peptide levels was found.

DAY 3 | SUNDAY 29 AUGUST 2021, ORAL ABSTRACT

13:45 – 14:45 | ORAL SESSION 8: Pathogenesis 3
Chairs: **M. Yorek** – USA, **R. Malik** – Qatar

OR.35 PROGRESSION AND REGRESSION OF SMALL AND LARGE NERVE FIBER PATHOLOGY AND DYSFUNCTION IN RECENT-ONSET TYPE 1 AND TYPE 2 DIABETES: A 5-YEAR PROSPECTIVE STUDY

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[3]GDS Group

Objectives: It has been traditionally suggested that the early development of diabetic sensorimotor polyneuropathy (DSPN) is characterized by a predominant and progressive injury to small nerve fibres followed by large fibre impairment. We tested an alternative hypothesis that small and large fibre damage due to DSPN in type 1 and type 2 diabetes could develop in parallel and may not only be progressive but also reversible.
Methods: Participants from the German Diabetes Study baseline cohort with recent-onset type 1/type 2 diabetes (n=350/570) and age-matched glucose-tolerant control individuals (con1/con2: n=114/190) were assessed by nerve conduction studies (NCS), thermal detection thresholds (TDT), vibration perception threshold (VPT), Neuropathy Symptom Score (NSS), Neuropathy Disability Score (NDS), and intraepidermal nerve fibre density (IENFD) in skin biopsies (type 1/type 2 diabetes: n=102/225; con1/con2: n=109/208). Subsets of participants with type 1/type 2 diabetes were followed for 5 years (n=184/307; IENFD subset: n=18/69). DSPN was defined by the Toronto Consensus criteria.
Results: At baseline, DSPN was present in 8.1% and 13.3% of the type 1 and type 2 diabetes groups, respectively. The most frequently abnormal tests in the lower limbs below or above the 2.5th and 97.5th centile of the controls were IENFD (13.7%) and individual NCS (up to 9.4%) in type 1 diabetes participants and IENFD (21.8%), malleolar VPT (17.5%), and individual NCS (up to 11.8%) in those with type 2 diabetes, whereas TDT abnormalities did not differ between the control and diabetes groups. The risk factors most consistently associated with impaired peripheral nerve tests across the groups studied were higher age, height, and weight. IENFD correlated variably with both small and large fibre function tests in the control and diabetes groups. After 5 years in the type 2 diabetes group, the highest progression rates from the normal to the abnormal range were found for IENFD (18.6%), malleolar VPT (18.4%), and NDS (15.0%), while vice versa the highest regression rates were observed for NDS (11.2%), sural nerve amplitude (9.1%), IENFD (8.7%), and NSS (8.2%). In type 1 diabetes participants, no major progression was seen after 5 years, but subclinical DSPN regressed in 10.3%.
Conclusions: These findings point to an early parallel damage to both small and large nerve fibres in well-controlled recent-onset type 2 and, to a lesser extent, type 1 diabetes. After 5 years peripheral nerve pathology and dysfunction progresses in type 2 diabetes, but initial nerve alterations are also reversible to a meaningful degree.

OR.36 EFFECTS OF PROGRESSIVE RESISTANCE TRAINING IN PATIENTS WITH TYPE 2 DIABETIC POLYNEUROPATHY; A RANDOMIZED SINGLE-BLINDED CONTROLLED TRIAL

Khan K.S., Overgaard K., Devantier L., Tankisi H., Gregersen S., Pop-Busui R., Dalgas U., Andersen H.

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Objective: To evaluate the effects of progressive resistance training (PRT) on muscle strength, and motor function in patients with type 2 diabetes with and without polyneuropathy (DPN) and to compare these adaptations to healthy controls.

Methods: A total of 109 participants in three groups (type 2 diabetes with DPN (N=42), type 2 diabetes without DPN (N=32) and healthy controls (N=35)) underwent within-group randomization to either supervised PRT or to non-PRT for 12-weeks. The primary outcome was muscle strength measured as the peak torque of the extensors and flexors of the knee and ankle, while secondary outcome measures included the six-minute walk test (6MWT), five-time-sit-to-stand-test (FTSST) and postural stability index obtained by static posturography.

Results: PRT resulted in muscle strength gains of the knee extensors and flexors in all three groups using comparative analysis with similar improvements when comparing PRT versus Non-PRT groups, p

Conclusion: In patients with type 2 diabetes and DPN, PRT improved strength of the knee extensors and flexors and motor function at a level comparable to both diabetes patients without DPN and healthy controls.

DAY 3 SUNDAY 29 AUGUST 2021, ORAL ABSTRACT

OR.37 THE EFFECTS OF 12-WEEKS PROGRESSIVE RESISTANCE TRAINING ON CUTANEOUS INNERVATION IN PATIENTS WITH DIABETIC POLYNEUROPATHY; A RANDOMIZED SINGLE-BLINDED CONTROLLED TRIAL

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Objective: The present study aimed to examine the effects of 12-weeks of progressive resistance training (PRT) on cutaneous re-innervation in patients with type 2 diabetes with and without DPN and in healthy controls. This study was part of a randomized controlled trial investigating the effects of PRT in individuals with diabetes.
Methods: A total of 109 individuals were included; type 2 diabetes with DPN (N=42), type 2 diabetes without DPN (N=32), and healthy controls (N=35). Individuals were randomized to 12-weeks of supervised PRT or no training. Skin biopsies were obtained, and intra-epidermal nerve fiber density (IENFD), nerve fiber branching, and growth-associated protein (GAP-43) fiber density were assessed. DPN was determined based on clinical evaluations and nerve conduction studies.
Results: Individuals with type 2 diabetes with DPN (N=24), without DPN (N=20), and healthy controls (N=27) were included. PRT did not result in change in skin biopsy parameters in any of the three groups IENFD: (DPN: non-PRT: 0.25±1.57; vs. PRT: -0.04±0.96, p=0.53), (non-DPN: PRT: -0.67±2.33; vs. non-PRT: 0.74±1.33, p=0.10), (Healthy controls: PRT: 0.93±1.29; vs. non-PRT: -0.14±1.63, p=0.08) and GAP-43: (DPN: PRT: 0.33±1.14; vs. non-PRT: -0.21±1.42, p=0.28), (non-DPN: PRT: -0.11±1.59; vs. non-PRT: 0.75±1.36, p=0.38), (Healthy controls: PRT: 0.50±1.39; vs. non-PRT: -0.51±2.24, p=0.19).
Conclusion: Twelve weeks of progressive resistance training did not result in any changes in IENFD, nerve fiber branching, or GAP-43 of ankle skin biopsies in individuals with and without DPN and healthy controls.

OR.38 CHANGES OF THE PLASMA MRNA LEVELS OF SOME GENES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Background and aims: Better understanding of the pathogenesis of diabetes mellitus and its complications requires the investigation of the genetic factors involved in the utilization of oxygen and glucose. Recently, the role of the mammalian target of rapamycin (mTOR) and hypoxia-inducible factor 1 (HIF-1) was suggested as the possible factors involved in the pathogenesis of type diabetes mellitus and some of its complications. However, the data regarding the expression of the genes of these factors in patients with diabetes mellitus are scarce. The aim of our study was to examine the levels of the mRNA encoding mTOR and HIF-1 in patients with long-term type 2 diabetes.

Materials and methods: We enrolled 24 patients with type 2 diabetes mellitus (6 males and 18 females, mean age 61.6±9.26, HbA1c – 9.4±2.53%, diabetes duration - 13.35±5.73 years, data are presented as mean+SD) and 11 patients without diabetes (6 males and 5 females, mean age 50.0±2.71 years) as the control group. Real-time PCR analysis was performed for quantitative evaluation of mTOR and HIF-1 mRNA in the blood. The statistical analysis was performed using Student test.

Results: We found statistically significant elevation of the plasma levels of the HIF-1 mRNA in patients with type 2 diabetes mellitus compared to control group – 29.5±2.45 vs 1.4±0.47, $p<0.05$. It was the trend toward decrease of the levels mTOR mRNA in the blood in patients with type 2 diabetes mellitus compared to control group - 29.49±2.45 vs. 35.19±10.36, $p<0.1$.

Conclusions: The revealed changes of the plasma levels of mRNA of HIF-1 and mTOR in patients with long-term poorly controlled type 2 diabetes mellitus could indicate the changes of the expression of those genes and possible role for the impairments of the production of those factors in the pathogenesis of diabetes and its complications. The clinical significance of the revealed changes of the genes expression requires the further investigation.

CONGRESS NEURODIAB 2021

ORAL ABSTRACT DAY 4

White Tower Museum in Thessaloniki, Greece

09:40 – 10:40 | ORAL SESSION 9: Autonomic Neuropathy 3
Chairs: **V. Spallone** – Italy, **C. Brock** - Denmark

OR.39 DOES THE DIAGNOSTIC VALUE OF THE QUESTIONNAIRE FOR AUTONOMIC SYMPTOMS COMPASS 31 DIFFER BETWEEN TYPE 1 AND TYPE DIABETES?

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Objectives: Composite Autonomic Symptom Score (COMPASS) 31 has been validated for diabetic cardiovascular autonomic neuropathy (CAN) and the value of 16.44 proposed as the best cut-off for abnormality with sensitivity up to 80% and specificity up to 65%. However, autonomic symptoms might be more weakly associated with autonomic deficits in type 2 than in type 1 diabetes. Thus, this study aimed to evaluate if the diagnostic performance of COMPASS 31 for CAN and diabetic polyneuropathy (DPN) differs between type 1 and type 2 diabetes.
Methods: Seventy-nine patients with type 1 (age 42±13 years, duration 25±13 years) and 143 with type 2 diabetes (age 63±8 years, duration 12±9 years) completed the COMPASS 31 questionnaire before undergoing four cardiovascular reflex tests (CARTs) and assessment of neuropathic symptoms, signs (using MDNS), vibration and thermal thresholds. Early and confirmed CAN were defined by 1 and 2 abnormal CARTs, and DPN by 2 abnormalities among symptoms, signs and sensory thresholds.
Results: The COMPASS 31 total weighted score (TWS) was higher in presence of CAN (early and confirmed) and DPN for both patients with type 1 (with Vs. without CAN: 30.8±22.5 Vs. 20.3±19.8, P=0.0132; with Vs. without DPN: 34.8±22.1 Vs. 14.3±15.1, P
Conclusions: While confirming the diagnostic validity of COMPASS 31 for both CAN and DPN, this study documents that its diagnostic performance for confirmed CAN is better in type 1 than in type 2 diabetes. As opposed to type 1 diabetes, no single domains of COMPASS 31 reached acceptable diagnostic accuracy for CAN in type 2 diabetes.

Table. Diagnostic characteristics of COMPASS 31 TWS for CAN and DPN: area under the curve (AUC) and sensitivity and specificity (at the cut-off of 16.44) (95% confidence intervals).

	CAN (early and confirmed)		**Confirmed CAN**		**DPN**	
	AUC		AUC		AUC	
Type 1 diabetes	0.651 ± 0.066 (0.522-0.780)		0.725 ± 0.073 (0.583-0.867)		0.753 ± 0.059 (0.637-0.868)	
Type 2 diabetes	0.650 ± 0.056 (0.541-0.759)		0.606 ± 0.077 (0.456-0.756)		0.682 ± 0.045 (0.594-0.769)	
Cut-off 16.44	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**
Type 1 diabetes	65.5% (48.2-82.8)	62.0% (48.5-75.4)	81.2% (62.1-100)	60.3% (48.2-72.4)	76.3% (62.8-89.8)	78.0% (65.4-90.7)
Type 2 diabetes	68.7% (52.7-84.8)	52.2% (43.0-61.5)	66.7% (42.8-90.5)	49.2% (40.6-57.9)	61.9% (51.5-72.3)	61.0% (48.6-73.5)

DAY 4 MONDAY 30 AUGUST 2021, ORAL ABSTRACT

OR.40 EVALUATION OF THE AUTONOMIC AND PERIPHERAL SENSORY NERVOUS SYSTEM FUNCTION IN YOUNG PATIENTS WITH TYPE 1 DIABETES AT THE TIME OF THE TRANSITION FROM PEDIATRIC TO ADULT-ORIENTED HEALTH CARE SYSTEM

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Objectives: The prevalence of neuropathic lesions in young patients with type 1 diabetes (T1DM) at the time of transition from pediatric care to adult-oriented health care system is poorly studied. A comparative study with healthy volunteers to assess the possible neuropathic condition of this special population and to define the potential earlier screening demands, has not been performed yet.

29 young patients with T1DM [age: 22.4 ± 2.9 years; body mass index (BMI): 22.8 ± 3.0 kg/m2; HbA1c: 8.5 ± 2.1 %, mean T1DM duration: 12.2 ± 5.8 years; 13 men/16 women; (mean ± SD)] and 30 healthy volunteers (age: 21.5 ± 1.6 years; BMI: 22.3 ± 3.7 kg/m2; HbA1c:5.3±0.3 %; 12 men/18 women) were enrolled in the study.

Methods: Autonomic function was assessed by the four standard cardiovascular reflex tests. The peripheral neuronal function was determined by Neurometer®, Neuropad®-test, Tiptherm®, Monofilament® and Rydel-Seiffer tuning fork tests.

Results: The vibratory sensation on the radial nerve on both sides was significantly impaired in the T1DM group compared to the controls with Rydel-Seiffer tuning fork test (perception threshold at right: 7.5 ± 1.0 vs. 7.9 ± 0.3; at left: 7.5 ± 0.9 vs. 7.9 ± 0.3, $p < 0.05$, separately). The Tiptherm®-test also proved a significant impairment in T1DM patients (11 sensing failures vs. 1 failure, $p < 0.001$). No significant differences with Neurometer®, Neuropad®, Monofilament® or by the cardiovascular reflex tests were detected between the two groups.T1DM patients had significantly higher diastolic blood pressure than controls (80±9 vs. 74±8 mm Hg, $p < 0.01$), but there was no significant difference in the systolic parameter (127±26 vs. 121±13 mm Hg).

Conclusion: Cardiovascular autonomic neuropathy was not found in this young type 1 diabetic population. However, peripheral sensory neuronal impairments were detected with Rydel-Seiffer tuning fork and Tiptherm®-tests at the time of transition of their diabetes care.

OR.41 CHARACTERIZATION OF THE AUTONOMIC AND SENSORY FUNCTIONS IN PATIENTS WITH DIFFERENT DURATIONS OF TYPE 1 DIABETES

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Introduction: Long-term diabetes exposure is a well-known risk factor of diabetic neuropathy, but the details of the neuronal dysfunctions in patients with different disease durations has not been described yet. The exploration of the characteristics of neuropathy with different durations of type 1 diabetes would enhance the prevention of this complication. The aim of our study was to determine the cardiovascular autonomic (CAN) and peripheral sensory neuropathy in patient groups with diabetes durations shorter than 10 years, among 10-20 years and longer than 20 years.

Patients, methods: 40 patients with type 1 diabetes were included in our study, divided into 3 groups according to disease duration (14-14-12 patients per group). To study CAN, 4 cardiovascular reflex tests (CRT) were performed, and peripheral sensory function was assessed by Neurometer.

Results: 2 out of 4 CRT results showed a significantly worsening trend between groups according to diabetes duration (Valsalva ratio: 2.1±0.5 vs 1.8±0.4 vs 1.5±0.6 $p<0.05$, orthostasis: 4.7±1.6 vs 7.5±2.8 vs 10.8±7.3 mmHg, $p<0.05$, mean±SD, less than 10 years vs 10 to 20 years vs more than 20 years diabetes duration). Heart rate response during deep breathing was not significantly reduced between groups (21±6.7 vs 16.5±7.8 vs 15.8±8 beats/min, $p>0.05$.) Peripheral sensory function was more abnormal in large myelinated fibres with longer disease duration in the lower limb (peroneal nerve 2000 Hz stimulation thresholds: 4.04±0.3 vs 4.32±0.4 vs 5.70±0.5 mA $p<0.05$).

Conclusions: Creating patient groups by disease duration, we found that tests based on the changes of heart rate or systolic blood pressure might become abnormal over 20 years. Impaired function of the large myelinated sensory fibres of the lower limb is also expected. The data suggest that cardiac parasympathetic and sympathetic regulation as well as lower limb sensory function both deteriorate progressively over more than 2 decades in type 1 diabetes. Efforts should be made to prevent or slow down this recognized process.

DAY 4 | MONDAY 30 AUGUST 2021, ORAL ABSTRACT

OR.42 CARDIOVASCULAR AUTONOMIC NEUROPATHY IN CONTEXT OF OTHER COMPLICATIONS OF TYPE 2 DIABETES MELLITUS

Andra-Elena Nica[1,2], Emilia Rusu[1,2], Carmen Dobjanschi[1,2], Sivu Claudia[1,2], Gabriela Radulian[1]

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Objectives: Among chronic diabetic complications, cardiac autonomic neuropathy (CAN) is one of the most common, but it is also one of the most frequently ignored. Currently, a general consensus exists that CAN is an independent risk factor for cardiovascular events. Its high mortality rate is related to cardiac arrythmias, silent myocardial ischemia, sudden death, perioperative cardiovascular and cardiorespiratory instability. The aim of this study was to investigate the relationship between CAN and other micro and macrovascular complications of type 2 diabetes (T2DM).

Methods: We included, in this study, 269 patients with T2DM. 51,3% (n=138) were female. Mean age was 61,15 ± 9,13 years and mean evolution of T2DM was 9,19 (CI 95% 8,23 – 10,15) years. We evaluated their cardiovascular risk factors, demographic data and any major micro and macrovascular of their diabetes. Assessments of CAN were based upon Ewing's battery. Neuropathic symptoms as assessed based sensory tests include pinprick sensation, light touch, vibration and temperature perception. We also evaluated Peripheral Neuropathy using sudomotor test.

Results: 53,2% of patients presented different degrees of CAN: 19,7% (n=53) mild CAN, 23,4% (n=63) moderate CAN and 10% (n=27) severe CAN. In the severe CAN group, the duration of diabetes, systolic blood pressure and HbA1c were all significantly higher than those with other forms of CAN (all p<0,05). 24,9% (n=47) of patients had at least one microvascular complication, 30,7% (n=58) had two microvascular complications and 21,2% (n=40) had three microvascular complications. CAN was correlated with the presence of other microvascular complications. During Ewing tests heart rate min was higher in severe CAN group (p=0,001). All patients with severe CAN had another microvascular complication (p=0,017). Albumin creatinine ratio in the group with severe CAN was higher, 233,7 (95% CI 21,6-489,13) than those with mild or moderate types of CAN, 139,33 (95% CI 46,35-232,31). Also, all patients with severe CAN had peripheral diabetic polyneuropathy. In the severe CAN group the BMI, lipid levels and creatinine were not significantly higher than those in other groups. In our study severe CAN did not correlate with macrovascular complications.

Conclusions: Our study results reinforced the concurrent development of CAN and other microangiopathic complications (retinopathy, chronic kidney disease (CKD) and peripheral neuropathy). We found a link between increasing severity of CAN and increasing prevalence and severity of peripheral neuropathy, CKD and retinopathy, which are markers of microangiopathic complications.

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