North Europe Young Diabetologists (NEYD) Annual Meeting 2017

Patricia Thomas reports on the NEYD Annual Meeting held at the Woodside Hotel, Warwickshire on 17th-19th May 2017

Held in scenic Warwickshire countryside in central UK, the 3-day North Europe Young Diabetologists (NEYD) annual meeting provided a unique opportunity for 30 young diabetes researchers to discuss and present their research to peers. Delegates came from the UK, Denmark, the Netherlands and Belgium, and comprised outstanding clinicians and basic scientists from a wide range of disciplines within diabetes research. The nature of the meeting was to allow for discussion of research in a more stimulating way than can occur at big international diabetes meetings. Additionally, experts in the field attending, including Professor Stephanie Amiel and Professor Sir George Alberti, gave invaluable constructive feedback which you would not receive at other meetings. Each presenter had 15 minutes to present their work and then discussions ensued, which continued over a plentiful supply of tea, coffee and cakes, and long into the evening over dinner. The comfortable venue of the Woodside Hotel made for an easy atmosphere and the afternoon game of softball in the grounds encouraged friendships and collaborations to be made which spanned the north of Europe. There were many highlights in the meeting and a few are outlined below.

The debate between the distinguished Professors Filip Knop and Max Nieuwdorp entitled "This house believes microbiota modulation will revolutionise the treatment of metabolic diseases" was a particular highlight. Professor Nieuwdorp was assigned the 'against' house position, which was a source of great amusement due to the numerous grants and honours that he has received for his work supporting a role for the gut microbiome in metabolism and inflammation in obesity and diabetes. His argument however prevailed, with more attendees voting for the 'against' house. A further highlight was the inspiring talk by Professor Amiel who used the analogue of the Three Princes of Serendip to discuss the key players in diabetes research and how they influenced her career. Her invaluable advice to be successful as a researcher was to not let failure knock you back and that those who were successful had 'fire in their belly'.

The main themes of the research presented by delegates were the role of diet in glycaemic control, clinical trials of new therapies being developed, genetics and the underlying physiological mechanisms of diabetes.

Low carbohydrate diets (<50 g/day) and caloric restriction (450–1000 kcal/day) were reported to lower plasma glucose and promote weight loss in type 2 diabetes (T2D) by Samkani *et al*, Ranjan *et al* (University of Copenhagen) and Van Eyka *et al* (Leiden University). As little as one week on a low carbohydrate diet reduced hypoglycaemia and glucose variability in type 1 diabetes (T1D), as well as increasing time spent in euglycaemia. Collectively, these outcomes validate current UK dietary interventions and can be extrapolated to other countries. However, in the UK, dietary compliance is problematic with poor attendance on structured education programmes such as DAPHNE (dose adjustment for normal eating) and DESMOND (diabetes education and self-management for ongoing and newly diagnosed). A recent survey of adults with T1D, conducted by Dr Harris at King's College London, identified four types of non-attenders: (1) those who acquired information elsewhere; (2) those who have the knowledge but don't use it; (3) those who have low self-esteem associated with educational experience; and (4) those who have diabetes denial. Adapting the course according to patient type would encourage a greater attendance at structured education programmes and patient self-management of diabetes.

Trunk-Black Juel *et al* and Foghsgaard *et al* (University of Copenhagen) reported their work on incretin mimetics, specifically GLP-1 (glucagon-like peptide-1) receptor agonists. Secreted by intestinal cells in response to food, GLP-1 stimulates insulin secretion and inhibits glucagon secretion. Therefore, agonists have long been investigated for their therapeutic potential. Researchers administered the GLP-1 receptor agonist liraglutide to women with prior gestational diabetes and who, therefore, have an increased risk of developing T2D. Liraglutide improved fasting blood glucose, HbA_{1c} and glucose tolerance compared with matched controls. In patients whose pancreas had been removed, the GLP-1 receptor agonist lixisenatide reduced postprandial glucose excursions by decelerating gastric emptying and reducing postprandial gut-derived glucagon release. Another interesting treatment was reported by van Baar *et al* (University of Amsterdam). They had observed that a catheter-based upper endoscopic procedure, which consists of hydrothermal ablation of the intestinal duodenum with subsequent mucosal healing, improves glycaemic and fatty liver disease markers in patients with T2D. This had added psychological benefits as patients reported they felt like they were actively doing something to treat their diabetes.

Engelbrechtsen *et al* (University of Copenhagen) reported the genotype-mediated effect of TCF7L2 rs7903146, a common gene variant with a strong association with T2D. In those patients with T2D and the gene variant, there were alterations in their postprandial response in triglycerides and triglyceride-rich lipoproteins. This implies that the TCF7L2 rs7903146 T-allele gene affects hepatic lipid regulation. A new T2D missense variant, CUBN, had also been identified by Ahluwalia *et al* (University of Copenhagen). CUBN was found to be associated with albuminuria, the main marker for decreased kidney function and end stage renal disease to which a third of patients with T2D progress. Thomas *et al* (University of Exeter, UK) described how they are using their database of gene variants in diabetes to develop a T1D genetic risk score, which they eventually want to make into a telephone app to help GPs to diagnose diabetes types correctly.

As a basic scientist investigating pancreatic β-cell biology, it was great to hear about the work of others studying fat, brain, liver and stomach cells and their

role(s) in diabetes progression. Additionally, learning about patient care strategies and difficulties that patients face on a day-to-day basis was highly beneficial. As researchers we strive to find ways to improve the quality of life of people with diabetes that are both patient-led and tailored to individual needs. This meeting delivered the current state-of-the-art in the field, and the mix of clinical and basic sciences provided for a compelling educational experience which is rarely found in larger conferences. It is easy to see why this meeting has continued for over 30 years; hopefully this is only the beginning.

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Top scoring abstracts from the NEYD annual meeting

Renal sinus fat and renal haemodynamics in overweight type 2 diabetes patients: a cross-sectional analysis

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Aim
Increased renal sinus fat (RSF) is associated with renal disease, but underlying mechanisms are incompletely understood. Mediation by glomerular hyperfiltration, hypertension or (local) inflammation is proposed. We evaluated whether RSF is associated with (intra-)renal haemodynamic alterations in type 2 diabetes (T2DM).

Methods
Fifty-one T2DM patients (age 63±7 years; BMI 31 (28–34) kg/m^2; GFR 83±16 mL/min/1.73m^2) underwent MRI scanning to quantify RSF volume and subcutaneous and visceral adipose tissue compartments (SAT and VAT, respectively). GFR and effective renal plasma flow (ERPF) were determined by inulin and PAH clearance, respectively. Effective renal vascular resistance (ERVR) was calculated. Intra-renal haemodynamics (glomerular hydraulic pressure (P_{GLO}) and afferent and efferent arteriolar resistances; RA and RE, respectively) were estimated by the Gomez formula.

Results
RSF correlated negatively with GFR (r=–0.38, p=0.006), P_{GLO} (r=–0.51, p<0.001) and ERPF (r=–0.38, p=0.006) and positively with R_A (r=0.51, p<0.001) and ERVR (r=0.45, p=0.001), which persisted after adjustment for VAT, MAP, sex and BMI. After correction for age, only ERVR and P_{GLO} remained statistically significant. RSF correlated with MAP (r=0.29, p=0.039).

Conclusions
In contrast to our hypothesis, higher RSF is associated with lower GFR, ERPF and P_{GLO} in overweight T2DM patients, driven by alterations in R_A. RSF-mediated increases in R_A may potentiate renal ischaemia, or conversely delineate a favourable renal haemodynamic state.

Unexpected effects of long-chain fatty acids on the viability of a human pancreatic beta cell line

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Aim
Long-chain fatty saturated acids (LC-SFA) can cause lipotoxicity in rodent β-cells whereas their mono-unsaturated counterparts are benign.[1] Patients with type 2 diabetes (T2D) often display elevated circulating fatty acids (FA), contributing towards lipotoxicity. Elevated odd-chain SFA (C15:0, C17:0) are associated with reduced T2D risk, but their impact on β-cell viability is unknown.[2] We have characterised the effects of LC-FA on human EndoC-βH1 cells.

Methods
EndoC-βH1 and rodent INS-1 cells were treated with LC-FA and viability determined with flow cytometry. FFA uptake was monitored with BODIPY FL C_{16} (palmitate derivative).

Results
C16:0 (≤1 mM) was well tolerated by EndoC-βH1 cells, even over 72 h of incubation. By contrast, the mono-unsaturate palmitoleate (C16:1) was moderately cytotoxic (dead cells: control 7.0±0.1%; C16:0 9.6±1.5%; C16:1 20.4±7.9; p<0.01). Surprisingly, C17:0 elicited a marked increase in EndoC-βH1 cell death (control 23.2±2.2%; 0.25 mM C17:0 25.8±0.2%; 0.5 mM 57.2±11.1%; 1 mM 97.5±0.9%). BODIPY FL C_{16} revealed that FFAs are taken up rapidly by β-cells and in INS-1 cells, unsaturated species were routed preferentially to lipid droplets. In EndoC-βH1 cells, both saturated and unsaturated species appeared to accumulate in lipid droplets.

Conclusions
The viability of human EndoC-βH1 cells is influenced by LC-FA in a manner that differs markedly from rodent β-cells, possibly because of differential routing of FFAs to lipid droplets.

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Top scoring abstracts from the NEYD annual meeting (continued)

Enhancing mental health inpatient diabetes care: a Quality Improvement (QI) project for admission assessment

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Background and aim

People with serious mental illness have reduced mortality of up to 20 years versus the general population.[1] They are at risk of developing type 2 diabetes from psychotropic medication, lifestyle and genetics.[2] Inpatient admission offers integrated holistic care opportunities,[3] but barriers exist: staff confidence, training and lack of medical care prioritisation.[4] We aimed to improve admission physical health assessment for all general adult and older patients at Leicester Partnership Mental Health Trust.

Methods

Using the Model for Improvement,[5] we developed and implemented electronic notes focused on diabetes risk assessment and key care processes via proforma development, educational implementation and an email reminder and feedback system.

Table 1: Admissions, HbA_{1c} actioning, diabetes risk assessment

Intervention stage	Timeline	Total admissions	HbA_{1c} actioned (%)	Diabetes UK risk score completion (%)	Overall risk assessment
Baseline	Week 1	24	12.50	0.00	0.00
Intervention period	*Week 8	29	0.00	3.70	3.70
	Week 18	**14**	**57.14**	**12.50**	**12.50**

*Intervention commenced week 8.

Results

Data were collected for all admissions over 11 weeks. Mean admissions per week: 25

Conclusions

Our data showed improvements in diabetes risk assessment, HbA_{1c} result actioning and diabetes patient admission care. At-risk patients received assessments and enhanced interpretation of HbA_{1c} results. Diabetes patients received improved assessment around medications, screening, acute and chronic complications. Introduction of a tested QI process with education and prompting can improve diabetes admission processes within inpatient psychiatry, supporting a new model of care. Future work surrounds sustaining improvement and improving care plan quality.

References

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Table 2: Four-weekly data for diabetes admissions care processes

Intervention stage	Timeline	Diabetes admissions total	Diagnosis correct (%)	Diabetes medication assessment (%)	Acute complications review (%)	Annual screens review (%)	Complications review (%)	Diabetes plan made (%)	Diabetes plan appropriate (%)
Baseline	Weeks 1–4	12	83.33	25.00	8.33	8.33	8.33	8.33	8.33
Intervention period	*Weeks 5–8	8	100.00	50.00	25.00	0.00	12.50	25.00	25.00
	Weeks 9–12	**4**	**100.00**	**100.00**	**75.00**	**50.00**	**50.00**	**75.00**	**50.00**

*Intervention commenced week 5.