## *Do differences in the brains of people with diabetes predict future neurological complications?*

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Our ability to assess brain function has been quite limited. Despite increasingly sophisticated imaging, the emphasis has been on defining structural differences, whereas assessment of functional ability has largely relied on questionnaires to test different aspects of cognition. The effects of large vessel disease on the brain are well known, and there is increasing evidence of long-term neurological damage from recurrent severe hypoglycaemia (Warren and Frier, 2005).

Newer techniques using magnetic resonance imaging (MRI) spectroscopy allow more dynamic testing of the brain, and investigations of the various degenerative disorders have revealed differences in chemistry and volume that correlate with neurocognitive and clinical assessments. Studies of central brain function in people with diabetic painful neuropathy have also shown changes not observed with conventional imaging (Selvarajah et al, 2008).

In this remarkable follow-up study from the Royal Children's Hospital, Melbourne, Australia (summarised alongside), young people with type 1 diabetes were studied, using MRI spectroscopy and neurocognitive questionnaires, 12 years after diagnosis and their results compared with those of individuals without diabetes. There were functional and biochemical differences in brain function as well as reductions in brain volume in the group with diabetes. These changes correlated with prior episodes of hypoglycaemia and poor metabolic control.

Whether these changes are reversible or predict future neurological impairment remains to be seen, but only with meticulous studies like these are we going to understand the natural history of diabetes complications and the role of metabolic disturbance.

Selvarajah D, Wilkinson ID, Emery CJ et al (2008) Thalamic neuronal dysfunction and chronic sensorimotor distal symmetrical polyneuropathy in patients with type 1 diabetes mellitus. *Diabetologia* **51**: 2088–92

Warren RE, Frier BM (2005) Hypoglycaemia and cognitive function. *Diabetes Obes Metab* **7**: 493–503

DIABETES, OBESITY AND METABOLISM

## Long-acting insulin analogues versus NPH human insulin

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| Readability | ✓✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓✓ |

1 A meta-analysis was undertaken to determine differences in $HbA_{1c}$, incidence of hypoglycaemia and weight gain between neutral protamine hagedorn (NPH) human insulin and long-acting insulin analogues.

2 A total of 285 RCTs comparing long-acting insulin analogues (detemir or glargine) and NPH insulin in people with type 1 diabetes were identified; of these, 20 met the eligibility criteria, giving 3693 and 2485 in the long-acting analogues and NPH groups respectively.

3 $HbA_{1c}$ and BMI as trial endpoints, and incidence of nocturnal and severe hypoglycaemia, were subjected to meta-analysis.

4 Overall, a small but significant reduction in $HbA_{1c}$ ($P$=0.026) was seen with long-acting analogues over NPH human insulin.

5 Weight gain with insulin detemir was significantly smaller than with human insulin ($P$=0.012).

6 Risk of nocturnal and severe hypoglycaemia was significantly lower with long-acting insulin analogues (all $P$<0.01).

7 Switching from NPH to long-acting analogues as basal insulin in people with type 1 diabetes has a small effect on $HbA_{1c}$, and also reduces the risk of nocturnal and severe hypoglycaemia.

Monami M, Marchionni N, Mannucci E (2009) Long-acting insulin analogues vs. NPH human insulin in type 1 diabetes. A meta-analysis. *Diabetes Obes Metab* **11**: 372–8

DIABETES CARE

## Long-term effects of type 1 diabetes on brain function

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓✓✓✓ |

1 Neurocognitive assessment and neuroimaging were used to examine central nervous system function 12 years after diagnosis in youths with type 1 diabetes ($n$=106) whose IQ at diagnosis matched that of healthy controls ($n$=75).

2 Verbal and full-scale IQs were lower in the diabetes group (both $P$<0.05).

3 The diabetes group also had lower *N*-acetylaspartate levels (indicative of neuronal death or decreased neuronal metabolism), and higher myoinositol and choline levels (linked with gliosis and demyelination) ($P$<0.05).

4 Grey matter in bilateral thalami and right hippocampal gyrus and insular cortex was decreased in the diabetes group, as was white matter in bilateral hippocampi, left temporal lobe and middle frontal area (all $P$<0.0005).

5 T2 relaxation times increased in the left superior temporal gyrus and decreased in bilateral lentiform nuclei, caudate nuclei and thalami, and the right insular area (all $P$<0.0005).

6 Hypoglycaemia was associated with lower verbal IQ and volume reduction in the thalamus; poor metabolic control predicted elevated myoinositol and decreased T2 in the thalamus; early-onset diabetes predicted lower performance IQ; and older age predicted volume loss and T2 change in the basal ganglia.

7 The findings in youths with type 1 diabetes are suggestive of several illness-related neuropathological processes including gliosis, demyelination and altered osmolarity.

Northam EA, Rankins D, Lin A et al (2009) Central nervous system function in youth with type 1 diabetes 12 years after disease onset. *Diabetes Care* **32**:445–50

DIABETES CARE

## Depression predicts sexual dysfunction in women with type 1 diabetes

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓✓✓✓ |

1 This study investigated prevalence, type, risk factors and predictors of female sexual dysfunction (FSD) in women with type 1 diabetes taking part in the long-term Epidemiology of Diabetes Interventions and Complications (EDIC) study.

2 Ten years into the study, 652 female participants were invited to complete a questionnaire on sexual function, and underwent standardised history and physical examinations, laboratory testing and mood assessment.

3 This report is based on results from the 424 sexually active women responding to the questionnaire and answering the question on FSD.

4 Overall prevalence of FSD in sexually active women in the study was 35%.

5 Types of FSD included: loss of libido (57%); problems with orgasm (51%), lubrication (47%) and sexual arousal (38%); and pain during intercourse (21%). Low overall sexual satisfaction was reported by 25%.

6 Univariate analyses found a positive association between FSD and age ($P$=0.0041), marital status ($P$=0.0016), menopausal status ($P$=0.0019), microvasculopathy ($P$=0.0092) and depression ($P$=0.0022), but in multivariate analysis, only depression ($P$=0.004) and marital status ($P$=0.003) were significant predictors of FSD.

7 FSD is common in women with type 1 diabetes, with depression being the major predictor.

Enzlin P, Rosen R, Wiegel M et al; DCCT/EDIC Research Group (2009) Sexual dysfunction in women with type 1 diabetes: long-term findings from the DCCT/ EDIC study cohort. *Diabetes Care* **32**: 780–5

DIABETES CARE

## Pedometers and text messaging fail to increase motivation

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| Readability | ✓✓✓✓ |
| Applicability to practice | ✓✓ |
| WOW! factor | ✓✓ |

1 The use of pedometers and text messaging to increase physical activity in adolescents with type 1 diabetes was assessed in a 12-week randomised controlled trial undertaken in New Zealand.

2 The 78 participants were aged 11–18 years; 36 were male.

3 The intervention group ($n$=38) wore an open pedometer and were sent weekly motivational text messages. The control group ($n$=40) received standard care.

4 Median daily step count was 11 063 (range 1541–20 158) at baseline; at 12 weeks it had reduced by 840 in the control group and 22 in the intervention group ($P$=0.4).

5 Mean self-reported moderate or vigorous physical activity increased by 38.5 and 48.4 minutes/week in the control and intervention groups respectively ($P$=0.4).

6 In this adolescent group, the use of pedometers and text messaging as motivational tools did not increase physical activity.

Newton KH, Wiltshire EJ, Elley CR (2009) Pedometers and text messaging to increase physical activity: randomized controlled trial of adolescents with type 1 diabetes. *Diabetes Care* **32**: 813–15

DIABETES, OBESITY & METABOLISM

## Lipohypertrophy – does it matter?

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| Readability | ✓✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓✓✓ |

1 Eight people with type 1 diabetes underwent 72 hours of continuous blood glucose monitoring (CBGM) while on a standardised diet and injecting all their insulin into either lipohypertrophic or non-lipohypertrophic areas.

2 Overall, the prevalence of hypoglycaemia (CBGM readings <4 mmol/L) was similar between the two sites ($P$=0.1).

3 The effects of injecting into lipohypertrophic tissue is small compared with the usual clinical variation observed with insulin injections.

4 Advising people to refrain from injecting into lipohypertrophic tissue to improve glycaemic control is not supported by these findings.

Overland J, Molyneaux L, Tewari S et al (2009) Lipohypertrophy: does it matter in daily life? A study using a continuous glucose monitoring system. *Diabetes Obes Metab* **11**: 460–3

DIABETES CARE

## BGM partly explains depression–$HbA_{1c}$ link

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓ |

1 This study of 276 adolescents with type 1 diabetes investigated whether the association between depressive symptoms and glycaemic control is mediated by blood glucose monitoring (BGM).

2 Depressive symptoms were linked with lower BGM frequency ($P$=0.04) and higher $HbA_{1c}$ levels ($P$=0.05), and lower BGM frequency was linked with higher $HbA_{1c}$ levels ($P$<0.001); however, when depressive symptoms and BGM frequency were combined, only BGM frequency was linked with $HbA_{1c}$, and depressive symptoms were not significant ($P$=0.19).

3 The results showed that 38% of the depression–$HbA_{1c}$ link in adolescents with type 1 diabetes can be explained by BGM. More specifically, those with depressive symptoms are likely to experience problems with BGM, with implications for glycaemic control.

McGrady ME, Laffel L, Drotar D et al (2009) Depressive symptoms and glycemic control in adolescents with type 1 diabetes: mediational role of blood glucose monitoring. *Diabetes Care* **32**: 804–6

> *"Advising people to refrain from injecting into lipohypertrophic tissue to improve glycaemic control is not supported by these findings."*