Management of type 1 diabetes

Does hypoglycaemia cause permanent memory problems in children?

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The available evidence strongly supports the view that for people with diabetes, striving to achieve near-normal levels of blood glucose reduces the risk of complications. It is clear that, using current treatments, the rate of hypoglycaemic episodes is inversely related to how successful we are at lowering blood glucose levels towards normal levels. Hypoglycaemia is at best disruptive to life and at worst occasionally fatal. Hypoglycaemia is therefore a major obstacle in our fight to reduce the burden of blindness, kidney disease, nerve damage and amputations associated with diabetes. Any clinician working with type 1 diabetes will be acutely aware of the impact of even a single episode of hypoglycaemia on an individual's life.

Having said that, we are still not certain whether hypoglycaemia results in permanent impairment of cognitive function. It can be seen from two papers in this quarter's section that the answer remains a definite maybe. The question is most important in young children, where the developing brain may be most susceptible to damage. Part of the problem is that it is extremely difficult to perform the right study to obtain a clear answer.

The paper by Strudwick et al (see below) compares a small group of children with type 1 diabetes previously documented to have had severe hypoglycaemia with an age-matched group without documentation of previous severe hypoglycaemia. They conclude that there is no difference in cognitive function between the groups. In contrast, Hershey et al (see right) conclude that high frequency of and early exposure to severe hypoglycaemia results in impairment of a specific cognitive task – spatial delayed response (measured by the ability to remember the position of a cross appearing on a computer screen). They do, however, acknowledge the weakness of using a retrospective design and the difficulty in matching groups.

The study design and subsequent conclusions in both papers are equally valid but unfortunately they are both small studies with less than ideal methodology. We are left with no clear answer to what is an important question for both children and adults.

JOURNAL OF PEDIATRICS

No evidence for cognitive defects resulting from coma or seizure

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

1 This population-based study of children aged 6–15 years with early-onset type 1 diabetes examined whether severe hypoglycaemia led to cognitive abnormalities.

2 Forty-one participants with a history of hypoglycaemic coma or seizure were compared with 43 individuals with no such history.

3 Memory and learning tests, and behavioural and intellectual measures were all employed.

4 No significant between-group differences were found for any of the test results or measures.

5 The authors note that laboratory-based assessment of cognitive function may miss subtle problems with cognition.

6 In addition, the need for further investigation involving pathophysiological measures and longitudinal follow-up is acknowledged.

Strudwick SK, Carne C, Gardiner J, Foster JK, Davis EA, Jones TW (2005) Cognitive functioning in children with early onset type 1 diabetes and severe hypoglycemia. *Journal of Pediatrics* **147**(5): 680–5

DIABETES CARE

Timing of severe hypoglycaemia affects long-term spatial memory

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

1 It is believed that repeated severe hypoglycaemia impairs long-term spatial memory in children with type 1 diabetes.

2 This investigation aimed to establish whether the age at which severe hypoglycaemia occurs affects the extent of the impairment.

3 Data were pooled from three studies to obtain a sample of 103 children aged between 6 and 18 years with type 1 diabetes, and 60 controls.

4 All three studies assessed previous severe hypoglycaemic episodes as well as using the spatial delay response task to test short-delay (5 s) and long-delay (60 s) spatial memory.

5 Individuals in the type 1 diabetes group were categorised into having had zero, one or two, or three or more severe hypoglycaemic episodes, and also as having had the first episode before or after turning 5 years old; chronic hyperglycaemia data were also collected.

6 It was found that repeated severe hypoglycaemia (three or more episodes), especially when the first episode was before the age of 5, resulted in impaired long-delay spatial memory.

7 Chronic hyperglycaemia was not found to influence spatial memory, and neither was age of onset of type 1 diabetes.

Hershey T, Perantie DC, Warren SL, Zimmerman EC, Sadler M, White NH (2005) Frequency and timing of severe hypoglycemia affects spatial memory in children with type 1 diabetes. *Diabetes Care* **28**(10): 2372–7

'CSII use was deemed to represent good value for money.'

DIABETES

Farming exposure not linked to reduced type 1 diabetes risk

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

1 It has been hypothesised that contact with microbial compounds in a farming environment at an early age could reduce the risk of autoimmune diseases; this case-control study tested the hypothesis for type 1 diabetes.

2 Type 1 diabetes risk was not found to be linked to drinking unpasteurised farm milk in the first year of life, living on a farm or regular contact with farm animals in stables.

Radon K, Windstetter D, Solfrank S et al (2005) Exposure to farming environments in early life and type 1 diabetes. *Diabetes* **54**(11): 3212–6

DIABETIC MEDICINE

CSII predicted to be more cost-effective than MDI in the UK

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

1 This investigation's objective was to predict long-term costs and outcomes of continuous subcutaneous insulin infusion (CSII) and multiple daily injections (MDI) in people with type 1 diabetes in the UK.

2 The CORE Diabetes Model was used to simulate the progression of diabetes (from baseline characteristics taken from UK studies) and model the effect of treatment with CSII and MDI.

3 CSII treatment resulted in a mean quality-adjusted life expectancy improvement that was 0.76 years greater than the improvement with MDI.

4 Mean direct costs to the National Health Service were £19 407 higher with CSII than with MDI.

5 Combining the two factors led to an incremental cost-effective ratio of £25 648 per quality-adjusted life year gained for CSII relative to MDI; CSII use was deemed to represent good value for money.

Roze S, Valentine WJ, Zakrzewska KE, Palmer AJ (2005) Health-economic comparison of continuous subcutaneous insulin infusion with multiple daily injection for the treatment of Type 1 diabetes in the UK. *Diabetic Medicine* **22**(9): 1239–45

DIABETOLOGIA

Targeted inhibition of beta-cell loss may reverse type 1 diabetes

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

1 In some people with long-standing type 1 diabetes, insulin secretion can be detected, which indicates that either a small proportion of their beta-cells have survived or their beta-cells are continually renewed but with ongoing autoimmune destruction.

2 This study's goal was to explore these possibilities; pancreatic sections were obtained from 42 people with type 1 diabetes and 14 without.

3 The number of beta-cells – present in 88% of people with type 1 diabetes – was not related to either diabetes duration (which ranged from 4 to 67 years) or age at death (range, 14–77 years).

4 Beta-cell apoptosis in type 1 diabetes was roughly double the level found in controls ($P<0.001$).

5 Given the ongoing apoptosis, beta-cell presence led the authors to conclude that there must be concomitant beta-cell formation and that targeted inhibition of this apoptosis may thus reverse type 1 diabetes or at least lead to some beta-cell mass regeneration and improvement in function.

6 In terms of a mechanism for the formation, it is conceivable that islets could originate from ductal precursor cells, as is seen with prenatal islet origin.

Meier JJ, Bhushan A, Butler AE, Rizza RA, Butler PC (2005) Sustained beta cell apoptosis in patients with long-standing type 1 diabetes: indirect evidence for islet regeneration? *Diabetologia* **48**(11): 2221–8

DIABETOLOGIA

First-born weight may predict second-born macrosomia

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

1 In a regression analysis, first-born birthweight but not maternal HbA_{1c} was significantly associated with the birthweight of second-born children ($P<0.001$) of mothers with type 1 diabetes.

2 The birthweight of an earlier-born child may thus be a useful predictor of the risk of macrosomia in a subsequent child.

Kerssen A, de Valk HW, Visser GH (2005) Sibling birthweight as a predictor of macrosomia in women with type 1 diabetes. *Diabetologia* **48**(9): 1743–8

'The birthweight of an earlier-born child may be a useful predictor of the risk of macrosomia in a subsequent child.'