

# **Høye blodsukker hos barn – hvor skadelig er det?**

Dag Veimo

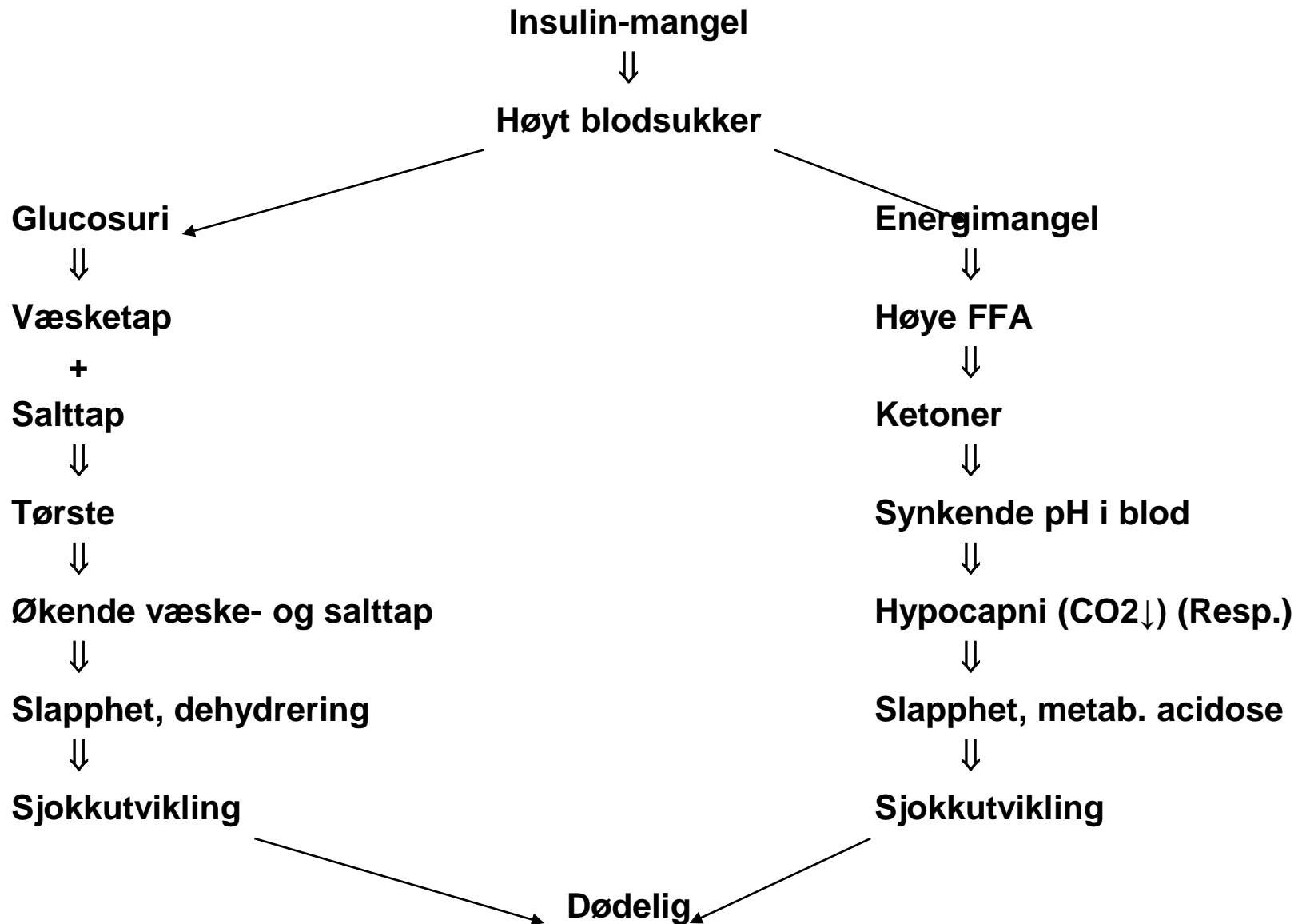
Overlege

Barneavd. NLSH, Bodø

# Høye blodsukker hos barn

- **Hva (hos friske barn)**
  - fastende >6 (DM >7)
  - postprandialt > 8 (DM >10-11)
- **Hvordan**
  - stressblods.
  - insulinmangel
- **Skadelige effekter**
  - somatisk
    - kort sikt
    - senkomplikasjoner
  - cerebralt
    - ødem, tromboser
    - psykologiske
    - cognitive defekter
- **Behandling**
  - insulin
- **Forebygging**
  - insulin o.a.

# Hva skjer i kroppen ved diabetes?



# Senkomplikasjoner (klassiske)

- **Nyrer**
- **Øyne**
- **Hjerte-/kar**
- **Nevropati**
- **Hudsår**
- **Andre (cerebrale o.a)**

# Effekter av hyper-G

- **Kjente akutt-effekter av hyper-G på kroppen, indirekte på CNS?**
- **Langtidsvirkning av hyper-G:**
  - lett/moderat hyper-G
  - alvorlig hyper-G
- **Cognitive akutt-effekter av hyper-G?**
- **Cognitive sen-effekter av hyper-G?**
- **Klassiske senkomplikasjoner inkl. arteriosklerotiske**

# Mål for diabetes-behandlingen

- **Her og nå:**
  - Minst mulig **hypoglykemi** / føling
  - Unngå ketoacidose ("insulin-mangel")
  - Minst mulig blodsukker-svingninger **/hyperglykemi**
  - Nok insulin til måltidene – til riktig tid**
  - God **livskvalitet** barn / foreldre
- **Senskader:**
  - God blodsukker-kontroll / HbA1c lav (<7-7,5)
  - Normal vekst og utvikling
- **Vi vet at:**
  - God / intensiv regulering gir mindre senskader (DCCT)
  - Det er lettere å oppnå god regulering med I-pumpe enn med mangeinjeksjons-behandling**

(Archives of Internal Medicine 2001;161:2293)

# Hvorfor viktig med god regulering?

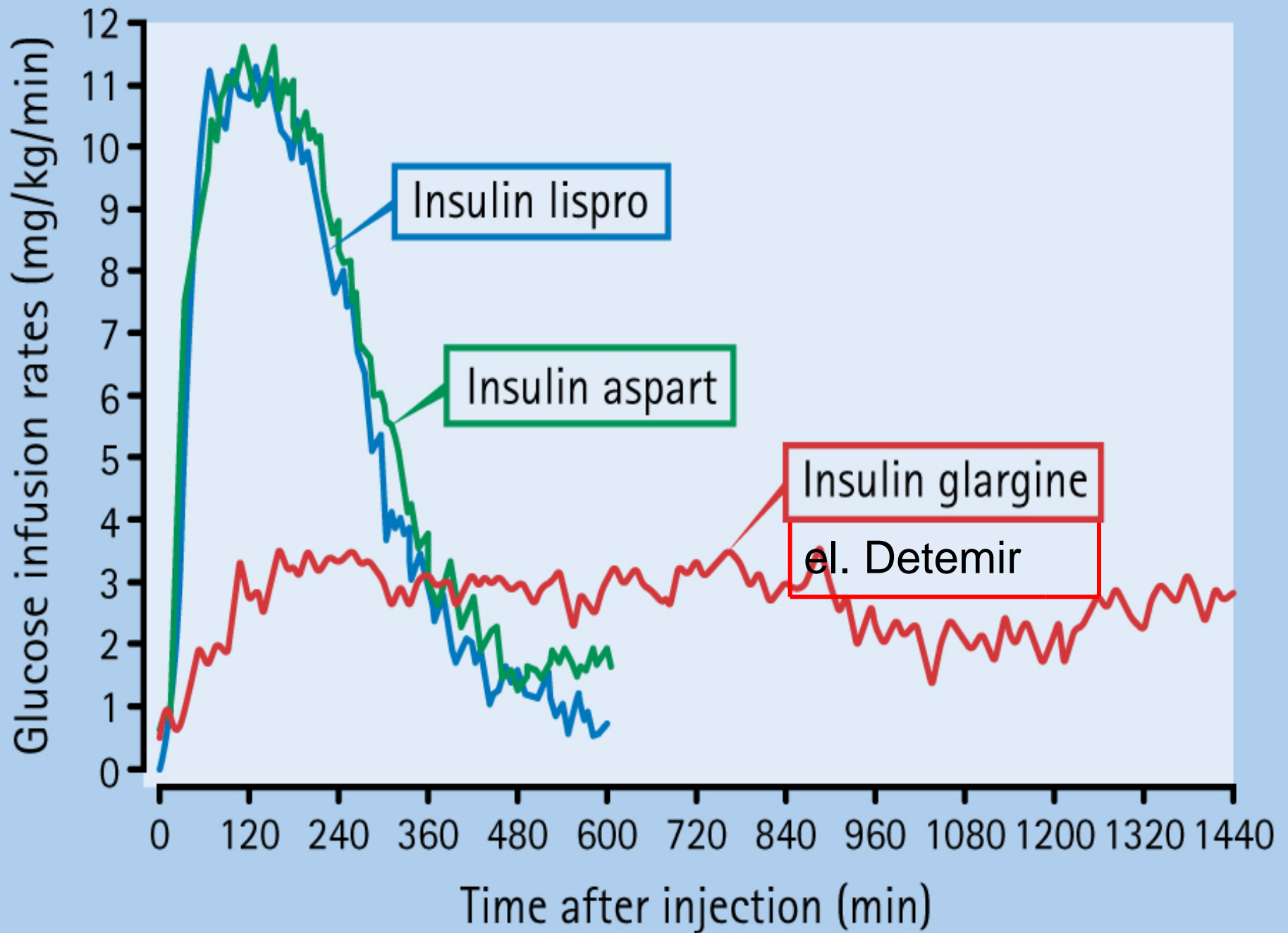
- **DCCT-studien**
- Data vedr. **hypo-glykemi**
- Nye data vedr. **hyper-glykemi**
- Nye data vedr. blodsukker-stabilitet, inkl. **CGM**
- Vektutvikling
- Livskvalitet

# Problemer m. I-behandling

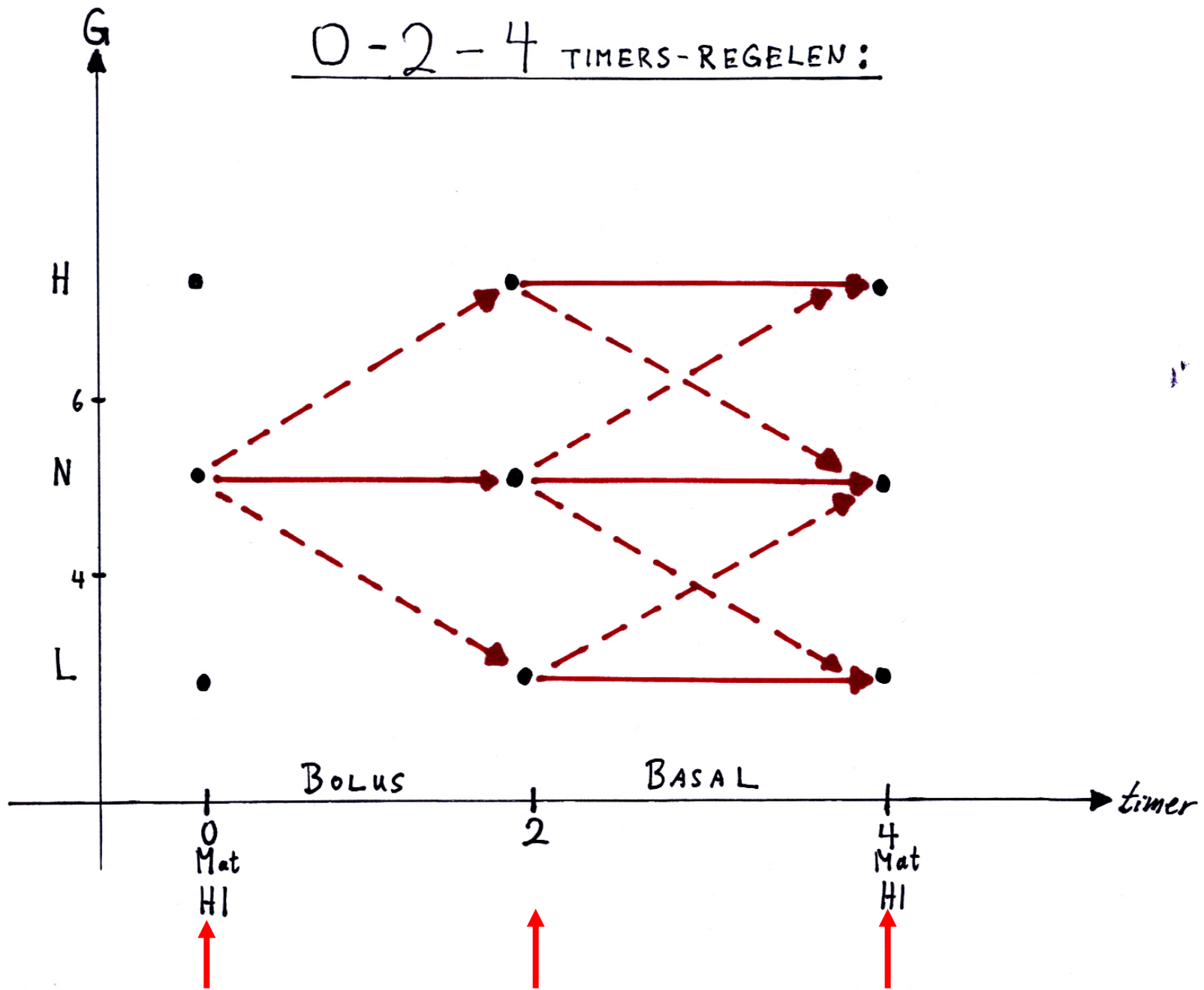
- **Må alltid gjennomføres - hver dag - resten av livet**
- **Kan være smertefull**
- **Kan være komplisert å få til godt**
- **Blodsukker må måles ofte**
- **Gir ikke alltid normalt eller stabilt blodsukker**
- **Gir ikke alltid god langtids-regulering**
- **Kan gi hypoglykemi og føling**
- **Kan gi komplikasjoner i seg selv (vektøkning, o.a.)**
- **Kan ikke alltid skjules**
- **Kan innvirke på dagliglivet (arbeid, skole, idrett, samliv)**
  
- **Innvirker på cognitive evner?**

# Kontrollopplegg

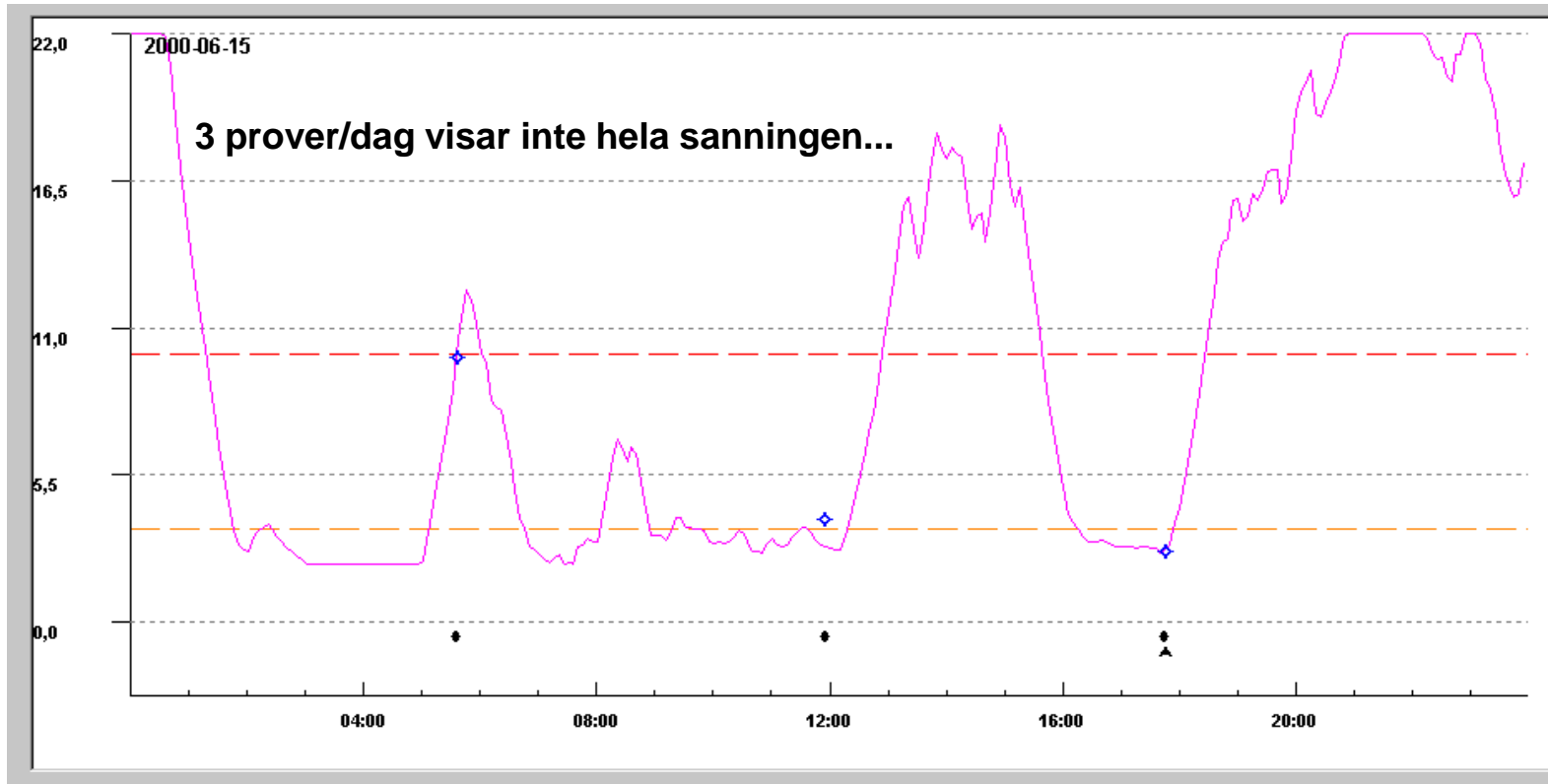
- **Vanlige kontroller**
  - Blodsukkeranamnese
  - HbA1c
  - Stikkesteder
  - Klin.us.
  - Annet
  - Endring av insulinregime?
  
- **Årskontroller**
  - Alt under vanlige kontroller +
  - Øyebunnsus. (e. 3-5 års sykdom / 15 år)
  - Urinus. (samme som øyebunnsus.)
  - H, V, BT, pubertet
  - Lipider, FT4/TSH, glutenantistoffer
  - Føtter, sensibilitet
  - Årskontrollskjema → Norsk Barnediabetes-register
  - Bechmarking-prøver



0-2-4 TIMERS-REGELN:



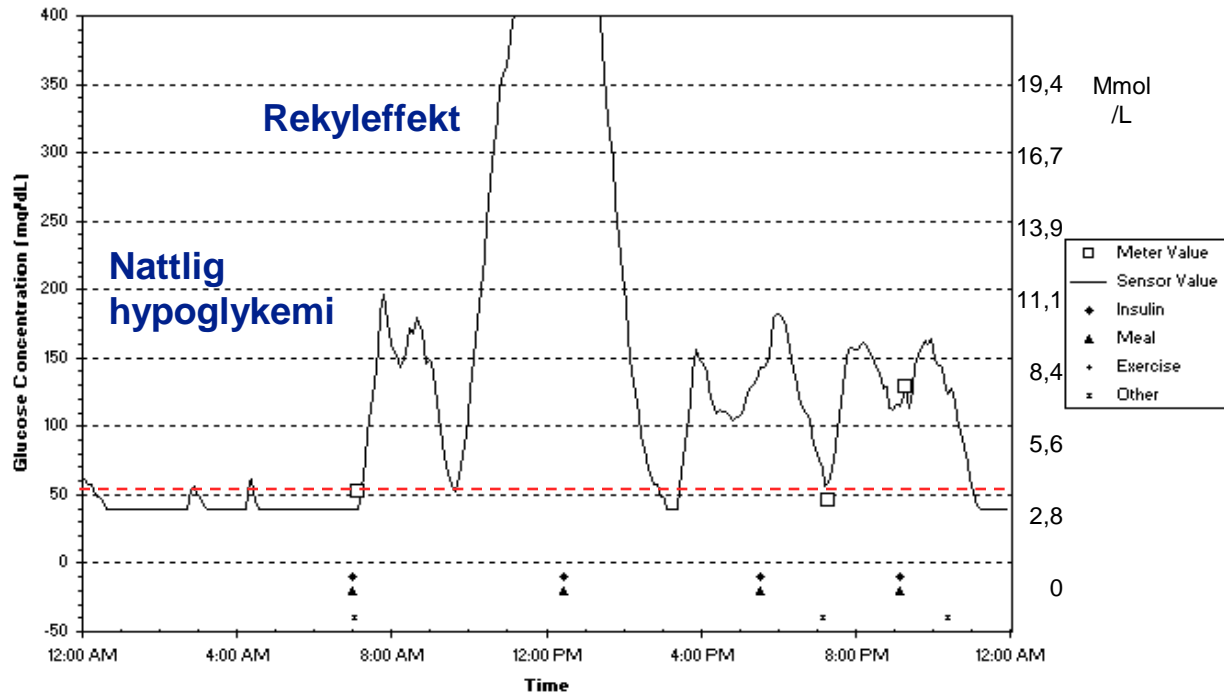
# Högt blodsocker



## Hyperglykemier (> 15,0 mmol/L)

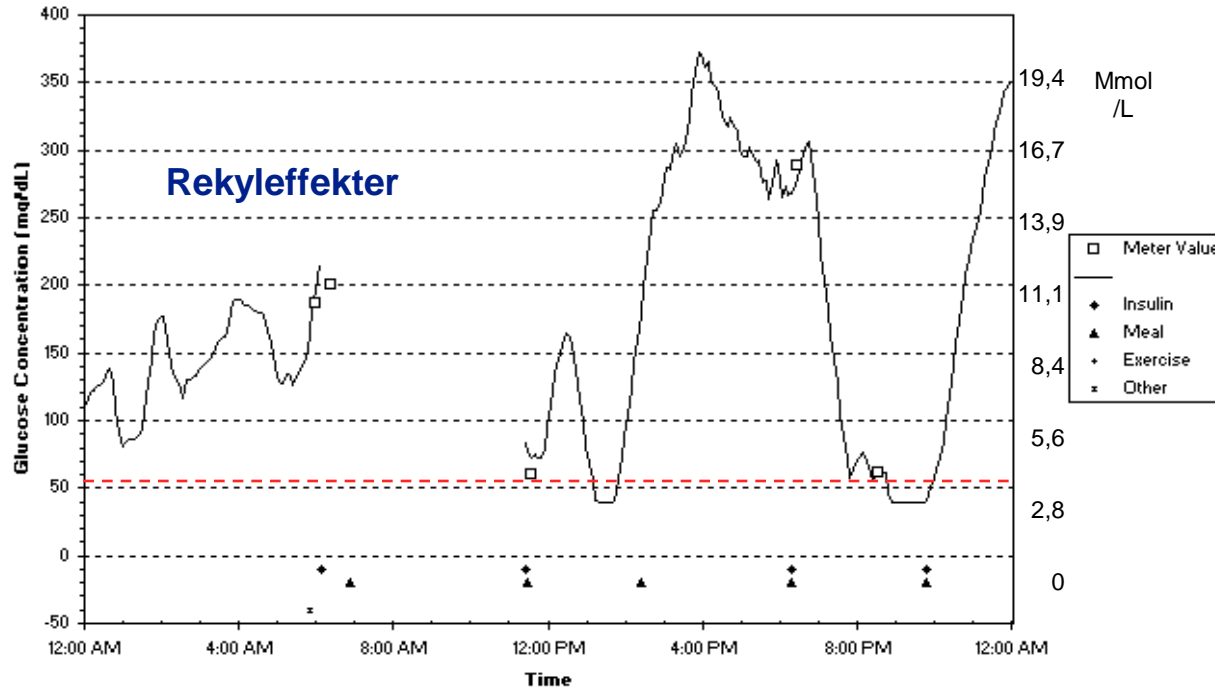
- ➡ 1,5 episoder/dag, duration 126 33 min. (kl 06 - 22)
- ➡ 0,6 episoder/natt, duration 177 83 min. (kl 22 - 06)

# Hypoglykemieer



- ➔ 26/27 patienter hadde hypoglykemieer dagtid ( $\leq 3,0$  mmol/L)  
0,8 episoder/dag, duration 58 29 min. (kl 06 - 22)
- ➔ 27/27 patienter hadde nattliga hypoglykemieer (kl 22 - 06)  
0,4 episoder/natt, duration 132 81 min.

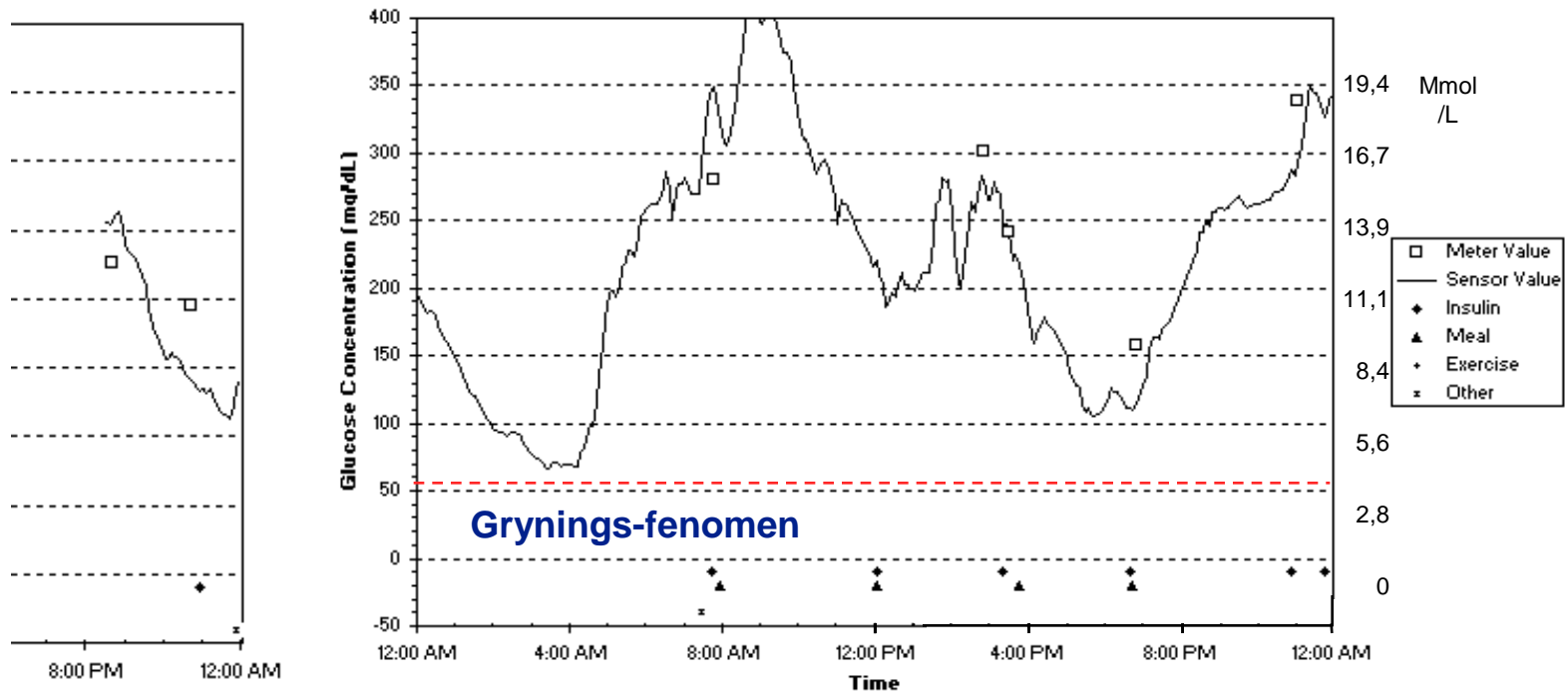
# Rekyleffekter



Rekyleffekter dagtid fanns hos 24/27 patienter  
( $\leq 3,0$  mmol/L och  $\geq 10$  mmol/L stegring på  $< 3$  tim)

⇒ syntes på 25,7 % av kurvorna

# Grynings-fenomen (Dawn)



Grynings-fenomen fanns hos 10/27 patienter  
( $> 3,0$  mmol/L och  $\geq 7$  mmol/L stegring till uppvaknandet)

➡ syntes på 5,3 % av kurvorna

# Mental utvikling (tidligere synspunkter)

- **Diabetes har ingen direkte effekt på mental og kognitiv utvikling**
- Barn med dårlig regulert diabetes eller mye hypoglykemier kan få en (midlertidig) påvirkning av sin cerebrale funksjon
- Mange, langvarige og kraftige **hypoglykemier**, spes. med **kramper**, før **4-5-årsalder**, kan gi **ned satt læreevne** senere
- Etter denne alder ikke påvist sikre slike effekter av hypoglykemier
- **Kronisk hypoglykemi** påvirker våkenhet, **konsentrasjon** og innlæringsevne, slik at skolerresultater blir dårligere
- Svært dårlig regulering med mye **høye blodsukker**, har en egen depressiv effekt på hjernen
- Det er imidlertid **ikke påvist sikre senskader** etter dette



### **Symptoms:**

- **Faint**
- **Sweaty**
- **Hungry**
- **Cold**
- **Nauseated**
- **Abdominal pain**
- **Headache**
- **Blurred vision**
- **Difficulty in speaking**



### **Signs:**

- **Pale**
- **Sweaty**
- **Tachycardia**
- **Appears distant**
- **Aggressive, noisy, naughty behaviour**
- **Tearful**
- **Tremulous**

Fig. 14.2. Common features of hypoglycaemia in children.

# Hva er hypo-glykemi?

- Vanlige betraktninger; glukose < 3,5-4,0
- **Jonny Ludvigsson (Sundvolden -09):**
- "Erfaringer fra CGM hos friske ikke-diabetiske barn, har lært oss at de kan ha fhv. lave blodsukker i løpet av natten eller om morgenen uten kliniske symptomer. Likedan i skoletiden."
- "Vi har sett blodsukker på 3,0-3,5 hos disse barna, uten tegn på "følinger" eller andre problemer."
- "Vi mener derfor at man må slutte å være så engstelige for moderat lave blodsukker hos barn, og ikke over-behandle dem"

? Severe hypoglycemia

? Recurrent asymptomatic hypoglycemia

Cognitive Impairment

? Psychosocial effects

? Chronic hyperglycemia



# Cerebrale effekter av hyper-G (1)

- **Kjente akutt-effekter av hyper-G på kroppen, indirekte på CNS**
- **Langtidsvirkning av hyper-G:**
  - lett/moderat hyper-G
  - alvorlig hyper-G
- **Klassiske senkomplikasjoner inkl. arteriosklerotiske cerebrale forandr.**
- **Innvirkning på synapse-dannelsen?**
- **Kognitive akutt-effekter av hyper-G?**
- **Kognitive sen-effekter av hyper-G?**

## **Cerebrale effekter av hyper-G (2)**

- **Diverse dyrestudier mht. virkning på hjernens utvikling inkl. grå og hvit substans, glia osv.**
- **Diverse studier mht. kognitive effekter av tidlig diabetes, diabetesvarighet, hypo-/hyper-G o.a. ved type 1 DM**
- **Diverse studier vedr. kognitive effekter av type 2 DM hos voksne og spes. eldre**
- **Diabetes vs. utvikling av Alzheimers sykdom**

# Cognitive Dysfunction and Diabetes Mellitus

Christopher T. Kodl and Elizabeth R. Seaquist

Endocrine Reviews 29 (4): 494-511

The deleterious effects of diabetes mellitus on the retinal, renal, cardiovascular, and peripheral nervous systems are widely acknowledged. **Less attention has been given to the effect of diabetes on cognitive function.** **Both type 1 and type 2 diabetes mellitus have been associated with reduced performance on numerous domains of cognitive function.**

The exact pathophysiology of cognitive dysfunction in diabetes is not completely understood, but it is likely that hyperglycemia, vascular disease, hypoglycemia, and insulin resistance play significant roles.

Modalities to study the effect of diabetes on the brain have evolved over the years, including **neurocognitive testing, evoked response potentials, and magnetic resonance imaging.**

Although much insightful research has examined cognitive dysfunction in patients with diabetes, **more needs to be understood about the mechanisms** and natural history of this complication in order to develop strategies for prevention and treatment.

# Why is cognitive dysfunction associated with the development of diabetes early in life?

Ryan et al., *Pediatric Diabetes* 2006;7:289-97

- The impact of hypo- and hyperglycemia vs. matched controls
- Neurocognitive dysfunction appears **soon after diagnosis** (2-3 y)
- Early onset of diabetes: a potent predictor of dysfunction
- The Diathesis hypothesis:
  - few of the childrens experience seizures in early life, during the "critical cerebral period"
  - young childrens at greater risk of poor metabolic control, both more hypo-G and hyper-G
  - hyper-G can be at least as harmful as hypo-G
- Because of this a good metabolic control is very important from the beginning of therapy for this illness

# The Effects of Type 1 Diabetes on Cognitive Performance

## A meta-analysis

[Augustina M.A. Brands](#), MSC123, [Geert Jan Biessels](#), PHD, MD1, [Edward H.F. de Haan](#), PHD13, [L. Jaap Kappelle](#), PHD, MD1 and [Roy P.C. Kessels](#), PHD13  
*Diabetes Care March 2005 vol. 28 no. 3 726-735*

**CONCLUSIONS**—In patients with type 1 diabetes, cognitive dysfunction is characterized by a slowing of mental speed and a diminished mental flexibility, whereas learning and memory are spared. **The magnitude of the cognitive deficits is mild to moderate, but even mild forms of cognitive dysfunction might hamper everyday activities** since they can be expected to present problems in more demanding situations.

# Neurocognitive Functioning in Children Diagnosed with Diabetes Before Age 10 Years

F. Kaufmann et al.,

[Journal of Diabetes and its Complications](#), Vol. 13(1), Jan 1999: 31-38

- Our objective was to determine scores on tests of neurocognitive functioning in children diagnosed with diabetes before age 10 years and to determine the association of age of diagnosis, duration of diabetes, subtle hypoglycemia, severe hypoglycemia, and history of hypoglycemic seizures with these neurocognitive test scores. Fifty-five of 62 eligible patients with a mean age of  $7.9 \pm 1.6$  years, tests to evaluate the following domains: memory/attention, visual-perceptual, broad cognitive function, academic achievement, and fine motor speed/coordination. Age-matched siblings served as controls. The mean HbA1c was  $7.8 \pm 1.1\%$  for the year prior to testing.
- Our results showed that the overall mean scores for the extensive neurocognitive battery were within the normal range and were comparable to the scores of the age-matched sibling controls.
- Age of diagnosis and duration of diabetes did not relate to neurocognitive test results.
- **Mean HbA1c had a negative association** with some tests of memory/attention ( $p < 0.03-0.04$ ) and academic achievement ( $p < 0.005-0.03$ )
- **There was no association of neurocognitive test scores with severe hypoglycemia**, but subjects with history of hypoglycemic seizures had a decrease in scores on tests assessing memory skills ( $p < 0.03$ ) including short term memory and memory for words.
- **These data suggest that overall neurocognitive test scores were within the normal range and comparable to controls.**
- However, specific aspects of neurocognitive functioning may be adversely affected by having had a hypoglycemic seizure, but not by episodes of severe hypoglycemia without seizure.
- Lower HbA1c and an increase in the number of blood glucose levels less than 70 mg/dL (subtle hypoglycemia) which were associated with higher scores in some domains of academic achievement and memory suggests that **stable glycemia may positively influence cognitive abilities and/or that successful diabetes management requires cognitive skills.**

# Influence of an Early-Onset Age of Type 1 Diabetes on Cerebral Structure and Cognitive Function

Ferguson et al.

*Diabetes Care June 2005 vol. 28 no. 6 1431-1437*

- **OBJECTIVE**—Children who develop type 1 diabetes before age 7 years (early-onset diabetes; EOD) have comparatively poorer cognitive abilities.

Whether this relates to psychosocial consequences of chronic illness or organic factors related to diabetes and its complications remains unresolved.

- **CONCLUSIONS**—An early childhood onset of type 1 diabetes was associated with mild central brain atrophy and significant differences in intellectual performance in adulthood, implying that neurodevelopment may be adversely affected by EOD.

The differences observed in brain structure support an organic contribution to their etiology but do not exclude a coexistent contribution of psychosocial factors.

- **Cognitive function in children with type 1 diabetes: a meta-analysis.**

- [Gaudieri PA](#), [Chen R](#), [Greer TF](#), [Holmes CS](#). *Diabetes Care*. 2008 Sep;31(9):1892-7

- **OBJECTIVE:** To quantify the magnitude and pattern of cognitive difficulties in pediatric type 1 diabetes as well as the effects associated with earlier disease onset and severe hypoglycemia.
- **RESEARCH DESIGN AND METHODS:** Pediatric studies of cognitive function since 1985 were identified for study inclusion using MEDLINE and PsycInfo. Effect size (ES, Cohen's d) between the diabetic and control groups, expressed in SD units, were calculated within cognitive domains to standardize meta-analysis test performance.
- **RESULTS:** The meta-analysis sample of 2,144 children consisted of **1,393** study subjects with type 1 diabetes and 751 control subjects from 19 studies.

Overall, **type 1 diabetes was associated with slightly lower overall cognition** (ES -0.13), with small differences compared with control subjects across a broad range of domains, excluding learning and memory, which were similar for both groups.

**Learning and memory skills, both verbal and visual (-0.28 and -0.25), were more affected for children with early-onset diabetes (EOD) than late-onset diabetes (LOD), along with attention/executive function skills (-0.27).** Compared with nondiabetic control subjects, EOD effects were larger, up to one-half SD lower, particularly for learning and memory (-0.49).

Generally, **seizures were associated with a negligible overall cognition ES** of -0.06, with slight and inconsistent cognitive effects found on some measures, possibly reflecting the opposing effects of poorer versus better metabolic control.

**CONCLUSIONS: Pediatric diabetes generally relates to mildly lower cognitive scores across most cognitive domains.** Cognitive effects are most pronounced and pervasive for EOD, with moderately lower performance compared with control subjects. Seizures are generally related to nominal, inconsistent performance differences.

- **Attentional functioning in children and adolescents with IDDM.**

- [Rovet J](#), [Alvarez M](#). University of Toronto, Canada. [jrovet@sick-kids.on.ca](mailto:jrovet@sick-kids.on.ca)

**OBJECTIVE:** To determine whether specific attentional cognitive processes are disrupted in children and adolescents with IDDM.

**RESEARCH DESIGN AND METHODS:** We tested 103 children and adolescents with IDDM and 100 healthy control subjects (age range 9.3-18.3 years) for intelligence and attention. Subjects were given multiple clinical tests of attention and a computerized vigilance test, all of which served to provide information about multiple components of attentional processing. Specific components studied were the abilities to focus, select, shift, suppress, inhibit, and sustain attention. A diabetic history was obtained for the IDDM group, and blood glucose levels were determined before and after computerized attention testing.

**RESULTS:** Across tests, **IDDM subjects differed from control subjects only in the select component of attention**, which was accounted for mainly by the poorer performance of children with early-onset diabetes (< 6 years). When subgrouped by history of **seizures from hypoglycemia**, those having had seizures demonstrated a lower verbal IQ and greater difficulty with select, focus, and inhibit attentional components, whereas sustain, suppress, and shift attentional components were unaffected.

**Correlation analyses showed that higher concurrent blood glucose levels were associated with less adequate ability to inhibit impulsive responses**, whereas multiple regression analyses indicated that inhibit and focus were best predicted by onset age and concurrent blood glucose.

- **CONCLUSIONS:** **In children and adolescents with IDDM, attention is poorer in several but not all aspects of attention; these aspects are affected by a history of seizures from hypoglycemia and higher ambient blood glucose levels at time of testing.** These results suggest both organizational and activational effects of diabetes on specific subcomponents of attention in diabetes.

- **School performance in children with type 1 diabetes-  
-a population-based register study.**

- [Dahlquist G, Källén B; Swedish Childhood Diabetes Study Group. Diabetologia. 2007 May;50\(5\):957-64. Epub 2007 Feb 27.](#)

- **AIMS/HYPOTHESIS:** We examined the school marks of diabetic children in Sweden at the time of leaving compulsory education. Marks were examined in comparison with non-diabetic children and with special regard to age at onset of diabetes.
- **SUBJECTS AND METHODS:** The study involved **5,159** children who developed diabetes between 1 July 1977 and 1 July 2000, and **1,330,968 non-diabetic children**. We linked the nationwide Swedish Childhood Diabetes Register to the Swedish School-Mark Register, which contains school marks for all children in Sweden at the time of leaving compulsory education (usually at 16 years old). Adjustment was made for potential confounders such as year of birth, maternal age, parity and educational level.
- **RESULTS:** The mean of all numerical school marks for diabetic children was slightly but statistically significantly lower than those of the referent children (3.15 +/- 0.01 [mean + SD] vs 3.23,  $p < 0.001$ ). The lowest mean score was among children with diabetes diagnosis before the age of 2 years (2.97 +/- 0.09 vs 3.08-3.17 in the older age groups,  $p = 0.10$ ). When individual subjects were studied (sports, mathematics, English and Swedish), a more complex picture emerged. In four subjects (mathematics, English, Swedish and sports) the risk of a diabetic child not getting a school mark or not passing was increased; in **sports and English** the diabetic children had significantly reduced odds of getting a high mark.
- **CONCLUSIONS/INTERPRETATION:** Despite a well-developed diabetes care system, we have not succeeded in preventing the disease from affecting school achievements. Among children with a young age at onset and therefore longer duration, the negative effects tend to be greater.

# Impact of Diabetes and Its Treatment on Cognitive Function Among Adolescents Who Participated in the DCCT

[Gail Musen](#) et al.

*Diabetes Care* October 2008 vol. 31 no. 10 1933-1938

- **OBJECTIVE**—The purpose of this study was to evaluate whether severe hypoglycemia or intensive therapy affects cognitive performance over time in a subgroup of patients who were aged 13–19 years at entry in the Diabetes Control and Complications Trial (DCCT).
- **RESEARCH DESIGN AND METHODS**—This was a longitudinal study involving 249 patients with type 1 diabetes who were between 13 and 19 years old when they were randomly assigned in the DCCT. Scores on a comprehensive battery of cognitive tests obtained during the Epidemiology of Diabetes Interventions and Complications follow-up study, ~18 years later, were compared with baseline performance. We assessed [the effects of the original DCCT treatment group assignment](#), mean A1C values, and frequency of severe hypoglycemic events on eight domains of cognition.
- **RESULTS**—There were a total of 294 reported episodes of coma or seizure. [Neither frequency of hypoglycemia nor previous treatment group was associated with decline on any cognitive domain.](#) As in a previous analysis of the entire study cohort, [higher A1C values were associated with declines in the psychomotor and mental efficiency domain \( \$P < 0.01\$ \);](#)
- **CONCLUSIONS**—[Despite relatively high rates of severe hypoglycemia, cognitive function did not decline over an extended period of time in the youngest cohort of patients with type 1 diabetes.](#)

# Central Nervous System Function in Youth With Type 1 Diabetes 12 Years After Disease Onset

[Elisabeth A. Northam](#) et al.

*Diabetes Care* March 2009 vol. 32 no. 3 445-450

- **OBJECTIVE**—In this study, we used neurocognitive assessment and neuroimaging to examine brain function in youth with type 1 diabetes studied **prospectively from diagnosis**.
- **RESEARCH DESIGN AND METHODS**—We studied type 1 diabetic ( $n = 106$ ) and control subjects ( $n = 75$ ) with no significant group difference on IQ at baseline 12 years previously by using the Wechsler Abbreviated Scale of General Intelligence, magnetic resonance spectroscopy and imaging, and metabolic control data from diagnosis.
- **RESULTS**—Type 1 diabetic subjects had lower verbal and full scale IQs than control subjects (both  $P < 0.05$ ). White matter was decreased in bilateral parahippocampi, left temporal lobe, and middle frontal area (all  $P < 0.0005$  uncorrected). Early-onset disease predicted lower performance IQ, and hypoglycemia was associated with lower verbal IQ and volume reduction in thalamus; poor metabolic control predicted elevated myoinositol and decreased T2 in thalamus;
- **CONCLUSIONS**—This study documents brain effects 12 years after diagnosis in a type 1 diabetic sample whose IQ at diagnosis matched that of control subjects. Findings suggest several neuropathological processes including **gliosis, demyelination, and altered osmolarity**.

# Cognitive Ability and Brain Structure in Type 1 Diabetes Relation to Microangiopathy and Preceding Severe Hypoglycemia

[Stewart C. Ferguson](#) et al.

*Diabetes January 2003 vol. 52 no. 1 149-156*

- Type 1 diabetes is associated with chronic hyperglycemia and exposure to intermittent severe hypoglycemia.  
The long-term cerebral effects of these consequences of diabetes are ill defined. In this study, the history of preceding severe hypoglycemia and the presence of background retinopathy were examined in relation to cognitive ability (neuropsychological test battery) and brain structure (magnetic resonance imaging) in a cross-sectional evaluation of 74 young people with type 1 diabetes.
- **DISCUSSION:** In the present study, no significant relationship was identified between previous exposure to severe hypoglycemia and cognitive ability. This is consistent with the observations of the DCCT ([10](#),[12](#)) and the Stockholm Diabetes Intervention Study (SDIS) ([11](#)), both of which evaluated cognitive function in young adults who had been exposed to recurrent severe hypoglycemia.
- In the present study, **structural abnormalities of the brain were not observed in association with a history of preceding severe hypoglycemia.** No relationship was identified between the frequency of previous severe hypoglycemia and cerebral atrophy

# Absence of Adverse Effects of Severe Hypoglycemia on Cognitive Function in School-Aged Children With Diabetes Over 18 Months

[Tim Wysocki](#) et al.

*Diabetes Care* April 2003 vol. 26 no. 4 1100-1105

- **OBJECTIVE**—Some children with type 1 diabetes may be at risk of cognitive impairments, but mechanisms of this effect have not been confirmed. The objective of this study was to determine whether severe **hypoglycemia** (SH) in children with type 1 diabetes is associated with cognitive decline over 18 months.
- **RESULTS**—Over 18 months, 58 of 142 patients (41%) experienced 111 SH episodes, with a RR of SH of 1.12 for IT over UC. Neither occurrence nor frequency of SH was associated with decline in full-scale intelligence quotient (IQ), standard scores for planning, attention, simultaneous processing, or successive processing, or scaled scores on any of eight subtests. The same findings emerged when only patients who had experienced hypoglycemic seizures or coma were included in the SH group for analyses.
- **CONCLUSIONS**—SH did not induce adverse changes in the measures of cognitive function administered to 6- to 15-year-old children with type 1 diabetes in this study. Although SH should be avoided in all children with diabetes, these episodes did not have adverse effects on cognition in this age-group over 18 months.

# Pathophysiology of central nervous system complications in diabetes mellitus.

[Mooradian AD.](#) Clin Neurosci. 1997;4(6):322-6.

It is now generally accepted that diabetes can alter central nervous system (CNS) function. Even in the absence of overt cerebrovascular accidents or repeated hypoglycemic reactions, **uncontrolled hyperglycemia is associated with cognitive changes**. These changes are documented both in patients with diabetes as well as in animal models of experimental diabetes.

The cognitive impairment can be **ameliorated with optimization of blood glucose control**.

The potential causes of CNS dysfunction in diabetes can be broadly categorized as either **vascular** causes including changes in the blood-brain barrier and **metabolic** changes. The latter causes include repeated hypoglycemic episodes, hyperglycemia, hyperosmolality, acidosis, ketosis, neuroendocrine or neurochemical changes.

The **other contributory causes** of CNS dysfunction in diabetes include the presence of hypertension, uremia, peripheral and autonomic neuropathy and multiple drug use.

# Postprandial plasma glucose excursions and cognitive functioning in aged type 2 diabetics

A. M. Abbatecola et al.

NEUROLOGY 2006;67:235-240

- **Conclusions:** Exaggerated postprandial glucose (PPG) excursions are associated with a derangement of both global, executive, and attention functioning. A tighter control of PPG may prevent cognitive decline in older diabetic individuals.

# Increased Glucose Levels Are Associated With Episodic Memory in Non-diabetic Women

[Olov Rolandsson](#), [Anna Backeström](#), [Sture Eriksson](#), [Göran Hallmans](#) and [Lars-Göran Nilsson](#)

*Diabetes February 2008 vol. 57 no. 2 440-443*

- **OBJECTIVE**—Patients with type 2 diabetes have an increased risk of a reduction in cognitive function. We investigated the hypothesis that plasma glucose is associated with a reduction in episodic and/or semantic memory already in **nondiabetic** subjects.
- **RESULTS**—In an adjusted multivariate model, fasting plasma glucose (fPG) and 2-h plasma glucose (2hPG) were significantly negatively associated with episodic memory (fPG: B  $-0.198$ , SE  $0.068$ ,  $\beta$   $-0.209$ ,  $P = 0.004$ ; and 2hPG: B  $-0.061$ , SE  $0.031$ ,  $\beta$   $-0.148$ ,  $P = 0.048$ , respectively) in women but not in men. The association was not found in relation to semantic memory.
- **CONCLUSIONS**—We conclude that an increase in plasma glucose is associated with impairment in episodic memory in women. This could be explained by a negative effect on the hippocampus caused by raised plasma glucose levels.

# Relationships Between Hyperglycemia and Cognitive Performance Among Adults With Type 1 and Type 2 Diabetes

[Daniel J. Cox](#) et al.

*Diabetes Care January 2005 vol. 28 no. 1 71-77*

- **OBJECTIVE**—Hyperglycemia is a common event among patients with type 1 and type 2 diabetes. While the cognitive-motor slowing associated with hypoglycemia is well documented, the acute effects of hyperglycemia have not been studied extensively, despite patients' reports of negative effects. This study prospectively and objectively assessed the effects of hyperglycemia on cognitive-motor functioning in subjects' natural environment.
- **RESULTS**—Hyperglycemia (blood glucose >15 mmol/l) was associated with slowing of all cognitive performance tests ( $P < 0.02$ ) and an increased number of mental subtraction errors for both type 1 and type 2 diabetic subjects. The effects of hyperglycemia were highly individualized, impacting ~50% of the subjects.
- **CONCLUSIONS**—Acute hyperglycemia is not a benign event for many individuals with diabetes, but it is associated with mild cognitive dysfunction.

# Cognitive Function Is Disrupted by Both Hypo- and Hyperglycemia in School-Aged Children With Type 1 Diabetes: A Field Study

[Linda A. Gonder-Frederick](#) et al.

*Diabetes Care* June 2009 vol. 32 no. 6 1001-1006

- **CONCLUSIONS**

- Based on these findings, naturally occurring episodes of acute hypo- and hyperglycemia during daily routine can be associated with cognitive-motor disruptions in school-aged children with diabetes.

To our knowledge, this is the first study comparing the negative impact of hypo- and hyperglycemia on cognitive function in this pediatric population.

Somewhat surprisingly, **the decline in performance at both glucose extremes was equivalent.**

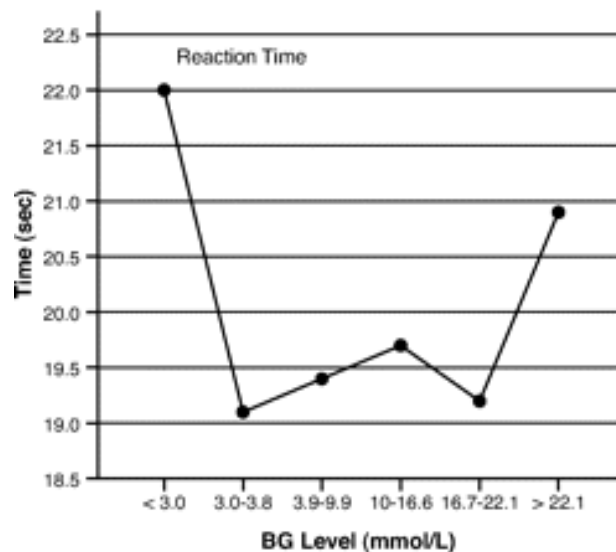
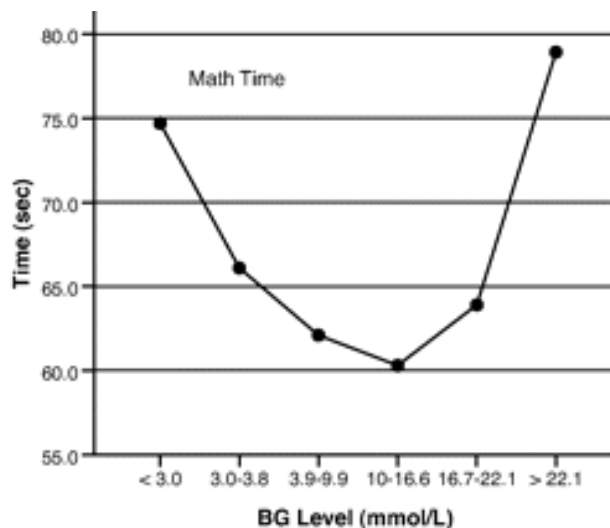
However, a significant decline in performance was not seen until hyperglycemia became quite profound. In addition, blood glucose extremes affected only the time to complete tasks and not the number of correct responses. This finding replicates results from adult studies ([2,3](#)) and adds to the data suggesting that **the initial effect of blood glucose extremes is a decrease in mental efficiency and speed and not a decrease in accuracy.**

Thus, people with diabetes of all ages may compensate behaviorally for blood glucose–related cognitive disruptions by first slowing down their performance and consequently sacrificing efficiency to preserve accuracy. A similar type of behavioral compensation plays a key role in models of aging and cognitive functioning ([16](#)).

- **The finding that children varied greatly in the extent to which they were affected by glucose extremes replicates findings from studies of adults with diabetes ([3,6](#)).** The mechanisms underlying these individual differences in vulnerability remain difficult to identify. In this study, demographic variables such as age and sex were not associated with individual differences. Exploratory correlations to examine the role of clinical variables indicated that
- **higher A1C levels and frequency of severe hypoglycemia may be related to more impairment when blood glucose levels are very high.**

# Mental math time and reaction time across blood glucose (BG) ranges.

Dvs. hjernen fungerer dårligere både ved høye og lave blodsukker



*Gonder-Frederick L.A et al. Diabetes Care 2009;32:1001-1006*

- **Hvor farlig er hypoglykemi? Hva sier vi til familiene? Vad säger vi till småbarnsföräldrar?**
  - **Barn har god motregulation; de dör inte av obehandlad hypoglykemi!**
  - **Ingen/Mycket liten risk för nedsatt intellektuell förmåga av sporadiska svåra hypoglykemier**
  - **Insulinchock/svår hypoglykemi gör sin största skada via föräldrars rädsla för hypoglykemi vilket kan leda till HYPERglykemi!**
  - **Små barn förblir ofta opåverkade trots mycket låga blodsockernivåer!**
  - **Kan behöva viss extra tillsyn då de inte alltid känner igen hypoglykemi**
- Johnny Ludvigsson

- **Situationer då hypoglykemi kan vara farligt**
  - I trafiken: Trafikolyckor
  - På hög höjd: Fall-olyckor
  - I båten/vid vatten: Drunkningsolyckor?
  - Vid svår kyla: Köldskada/Ihjälfrysning
  - Vid depression: Suicid
  - Vid alkoholkonsumtion: Hjärnskada/Dead-in-bed
  - Efter många års diabetes, ssk om för högt HbA1c: Autonom neuropati kan ge Dead-in-bed
  - Vid viss hormonell sjukdom: Addison kan öka risken för dead-in-bed
- Johnny Ludvigsson

- **Hvor farlig er hypoglykemi? Hva sier vi til familiene?**

- **1. Hypoglykemi är obehagligt och KAN vara farligt, men **HYPERGLYKEMI är farligare!****
- **2. Hypoglykemi leder till obehagliga symtom som i sig inte skadar kroppen.**
- **3. Berätta ärligt om akuta och sena komplikationer!  
Alla har rätt att veta vad som gäller!**
- Johnny Ludvigsson

# Egne erfaringer

- **Pasienter med dårlig regulering er mer depressive**
- **"Høna og egget"?**
- **Bedre regulering gir**
  - lavere totalt insulin-behov
  - mindre svingninger i blodsukker
  - bedre fysisk form (egne utsagn)
  - mindre depresjoner
  - fungerer bedre (egne utsagn)
  - bedre skoleprestasjoner?
- **Økt mestringsfølelse når reguleringen bedres, større insatsvilje/-evne**
- **Mindre foreldremas**

# Hva nå?

- Det er tydelig at høye blodsukker er skadelig for kognitive funksjoner både på kort og lang sikt, mer enn lave blodsukker sannsynligvis
- Det blir derfor viktigere enn før å konsentrere seg om å unngå store fluktuasjoner i blods. og spes. svært høye blodsukker
- Hva vil dette ha å si for beh.praksis og opplæring?
  1. Informere om dette
  2. Karbohydrat-telling o.a. teknikker
  3. Lære å sette riktige bolusdoser (0-2-4 timers-opplegget)
  4. Kombinere de "beste" insulinene (hurtig- og langsomt-analoger)
  5. Evt. insulin-pumpe
  6. Kontinuerlig glukose-måling (CGM(S))? (Refunderes i Sverige)
- Regelmessig psykolog-hjelp?
- Rgm. testing av kognitive profiler som en del av kontroll-opplegget?

# Kontrollopplegg

- **Vanlige kontroller**
  - Blodsukkeranamnese
  - HbA1c
  - Stikkesteder
  - Klin.us.
  - Annet
  - Endring av insulinregime?
  - **(Psykol./cognitiv fungering??)**
- **Årskontroller**
  - Alt under vanlige kontroller +
  - Øyebunnsus. (e. 3-5 års sykdom / 15 år)
  - Urinus. (samme som øyebunnsus.)
  - H, V, BT, pubertet
  - Lipider, FT4/TSH, glutenantistoffer
  - Føtter, sensibilitet
  - Årskontrollskjema → Norsk Barnediabetes-register
  - Bechmarking-prøver
  - **(Psykol./cognitiv fungering?)**

