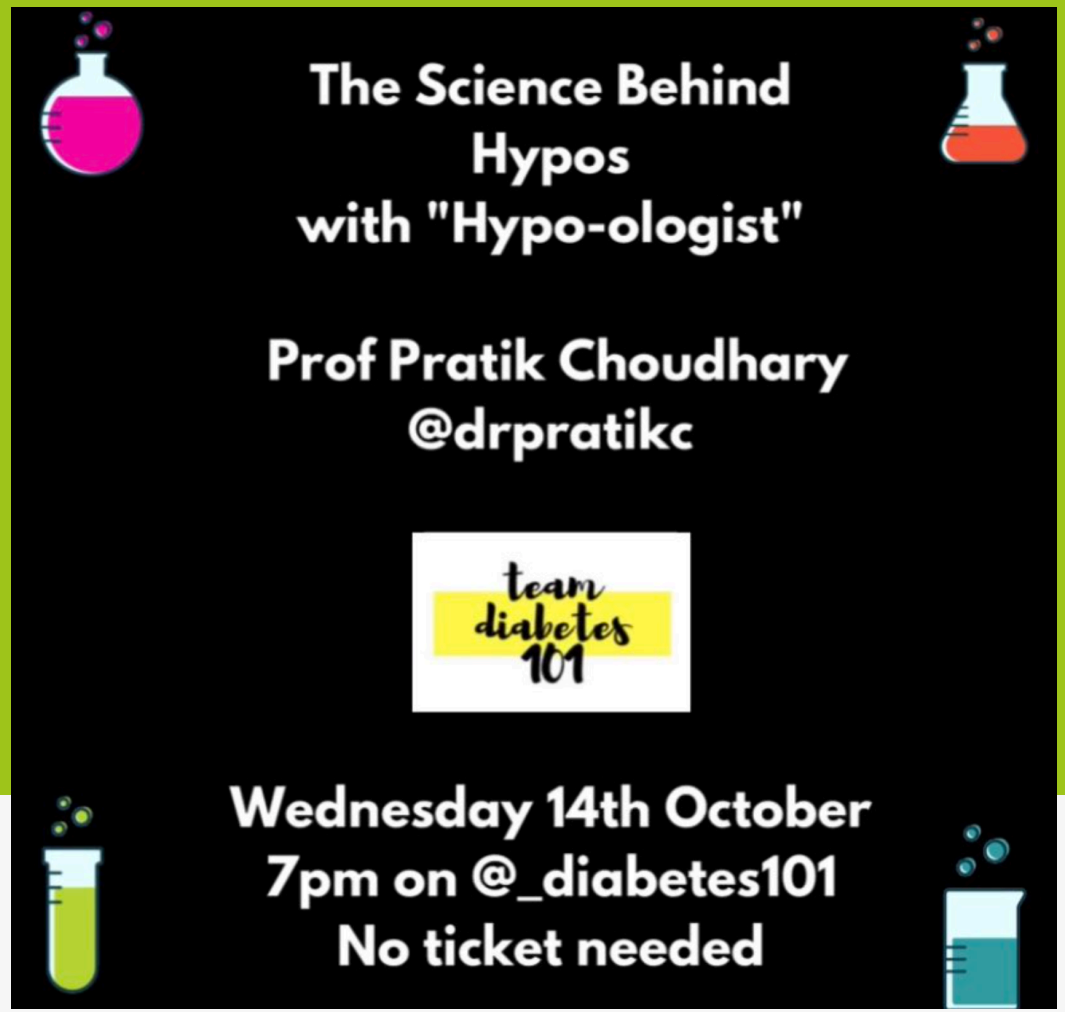


UNIVERSITY OF LEICESTER

NHS
University Hospitals of Leicester
NHS Trust

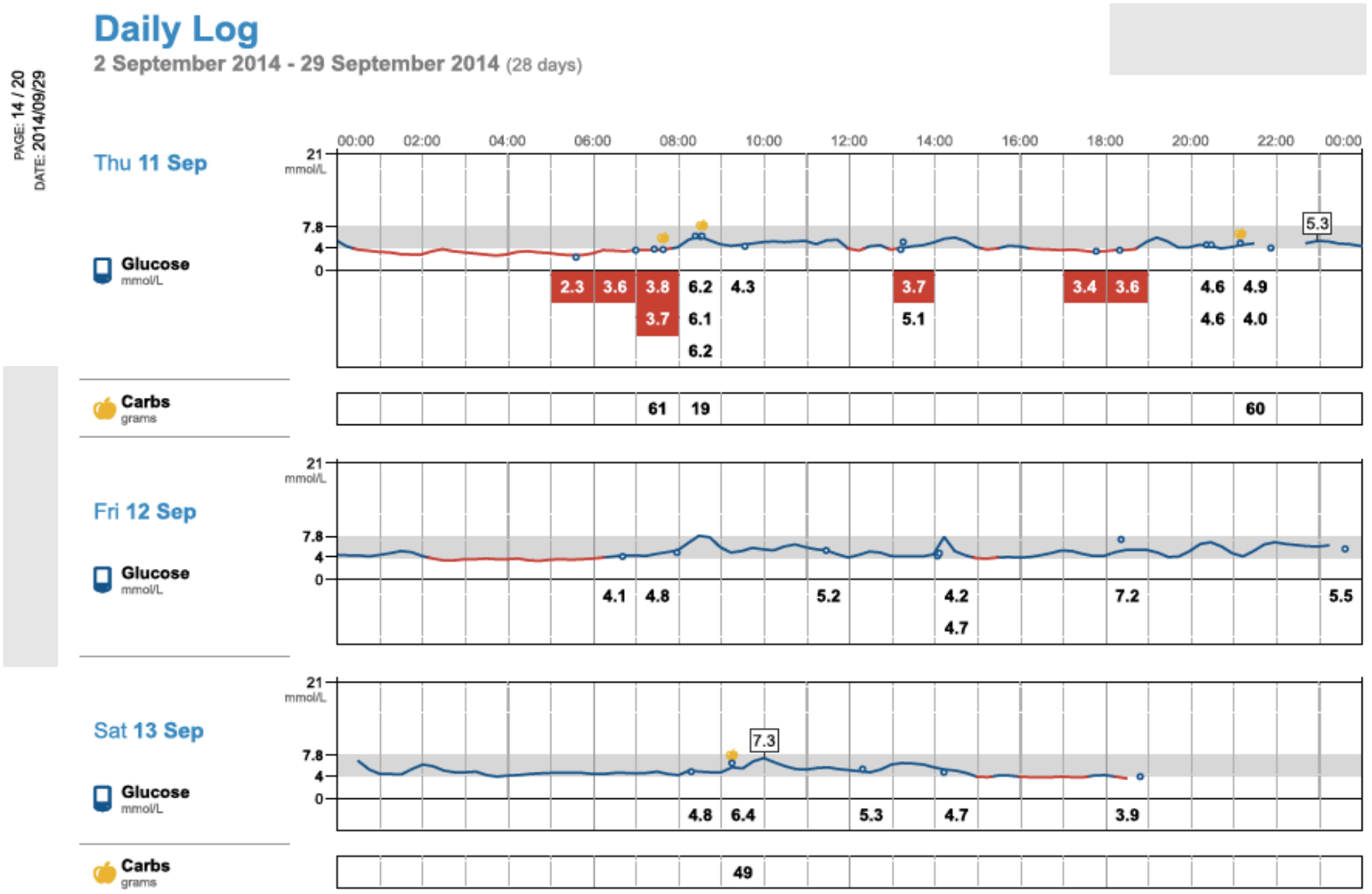
Leicester Diabetes Centre


Control
Hypoglycaemia

How common is Hypoglycaemia

- 25 – 30% of T1D develop impaired awareness of hypoglycemia
- 30% of T1D have a Severe hypo each year
- 5% of T1D have multiple severe hypoglycemia
- 2-3 episodes of self-treated hypos / week
- 1:10 nights will have a low glucose on sensors
- Much lower rates of hypoglycaemia in type 2 diabetes

What is normal …? What is hypo?

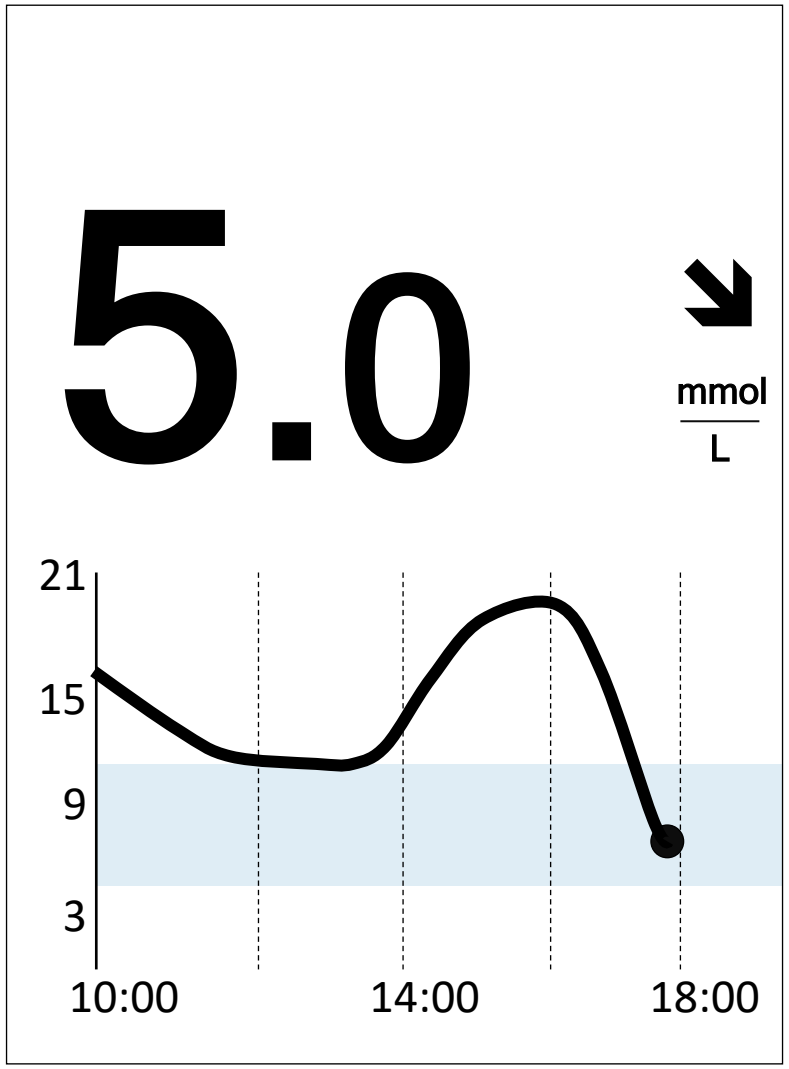


Incidence of CGM hypos

- Low sensor glucose occurs in between 10-20% of nights with CGM. You may only pick these up when you scan.
- 2-5% of nights will have prolonged hypoglycemia [> 2 hours] on CGM[2]
- This is within normal limits – even non-diabetic people have nights when glucose is between 2 – 3 mmol/l
- In a recent Danish study, patients classified as having good awareness of hypoglycemia were unaware of almost 60% of hypoglycaemic episodes captured on blinded CGM

[2]Chase et al, Diabetes care, 2010

Defining hypoglycaemia



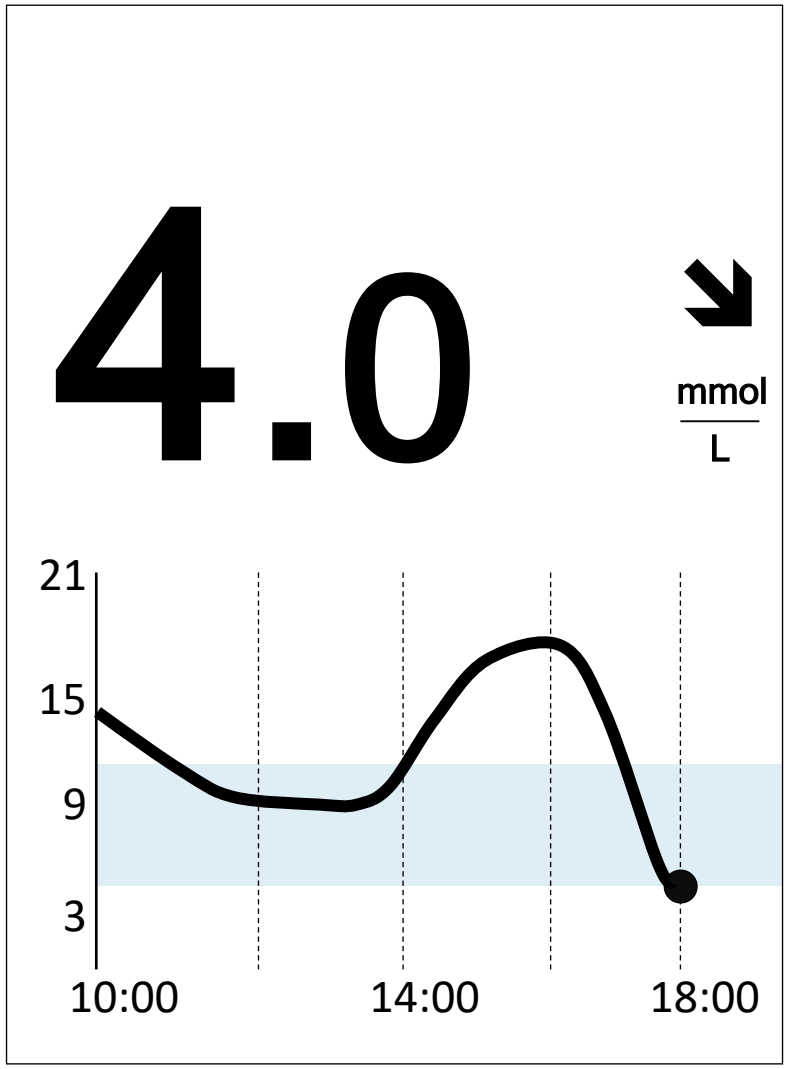
Although some people can feel their glucose falling or get hypo symptoms at high glucose levels, this isn't true hypoglycaemia

However, because sensors are reading glucose in the skin not the blood, sometimes your blood glucose may be low even though the sensor glucose is not showing a hypo [is above 4 mmol/l]

IF YOU FEEL LOW, AND THE SENSOR SHOWS A FALLING GLUCOSE, DOUBLE CHECK WITH A FINGERSTICK READING

If you are not yet low, but glucose is falling consider taking 5-10 grams of carbs
[1-2 jelly babies or dextrose tablets]

Defining hypoglycaemia



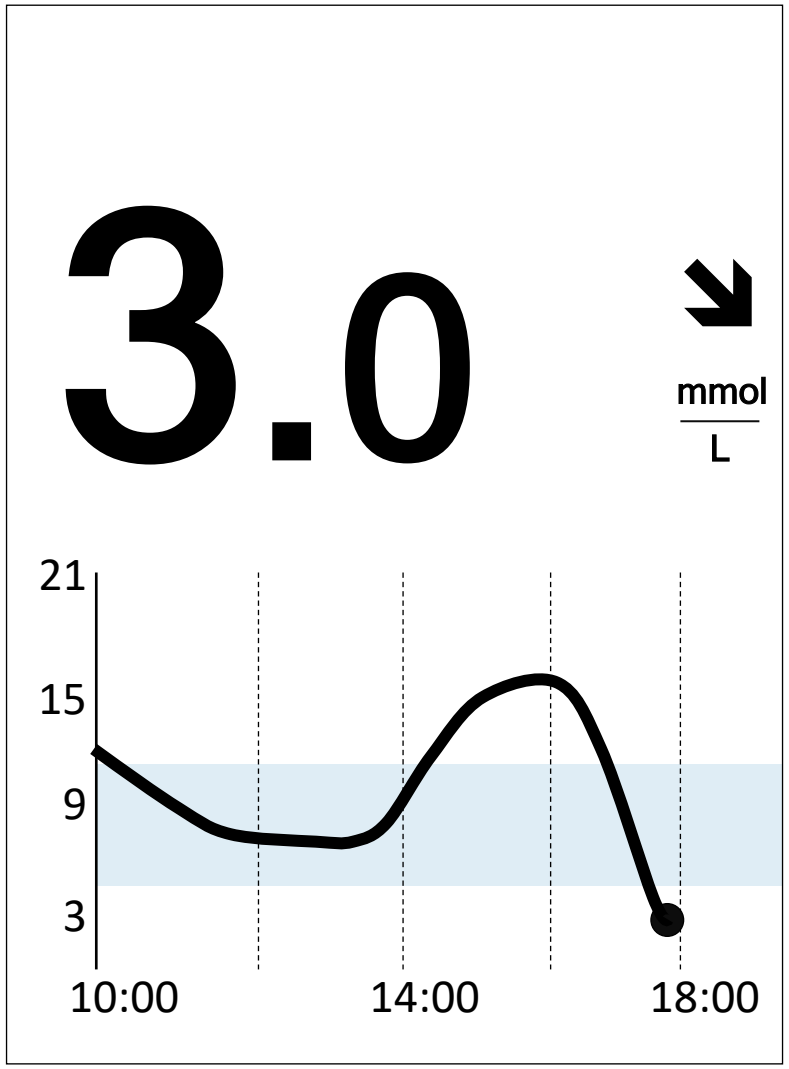
A blood glucose of less than 3.9mmol/l has been defined as a hypo ALERT value

You should take action here to avoid further drop and be aware that your blood glucose value may be lower. Check a fingerstick glucose.

DAFNE hypo treatment:
Below 3.5mmol/l: 15-20g rapid acting carbohydrate (lucozade or orange juice or 3-4 dextrose tablets)
Below target but above 3.5mmol/l: eat 10g of carbs

IF YOU FEEL LOW, AND THE SENSOR DOES NOT SHOW THIS, DOUBLE CHECK WITH A FINGERSTICK READING

Defining hypoglycaemia



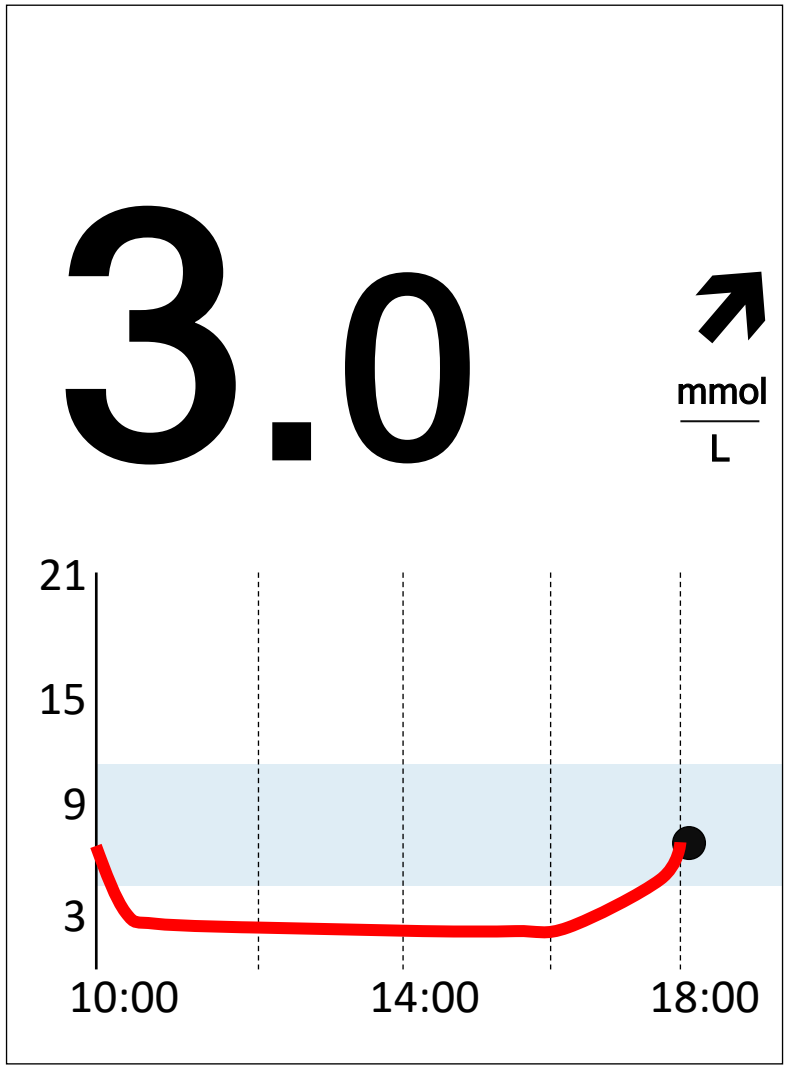
3 mmol/l and below is defined as SERIOUS hypoglycaemia.

Below this level, there is usually some slowing of brain function, and people can experience confusion and drowsiness.

Repeated episodes below this level increase the risk of severe hypoglycaemia

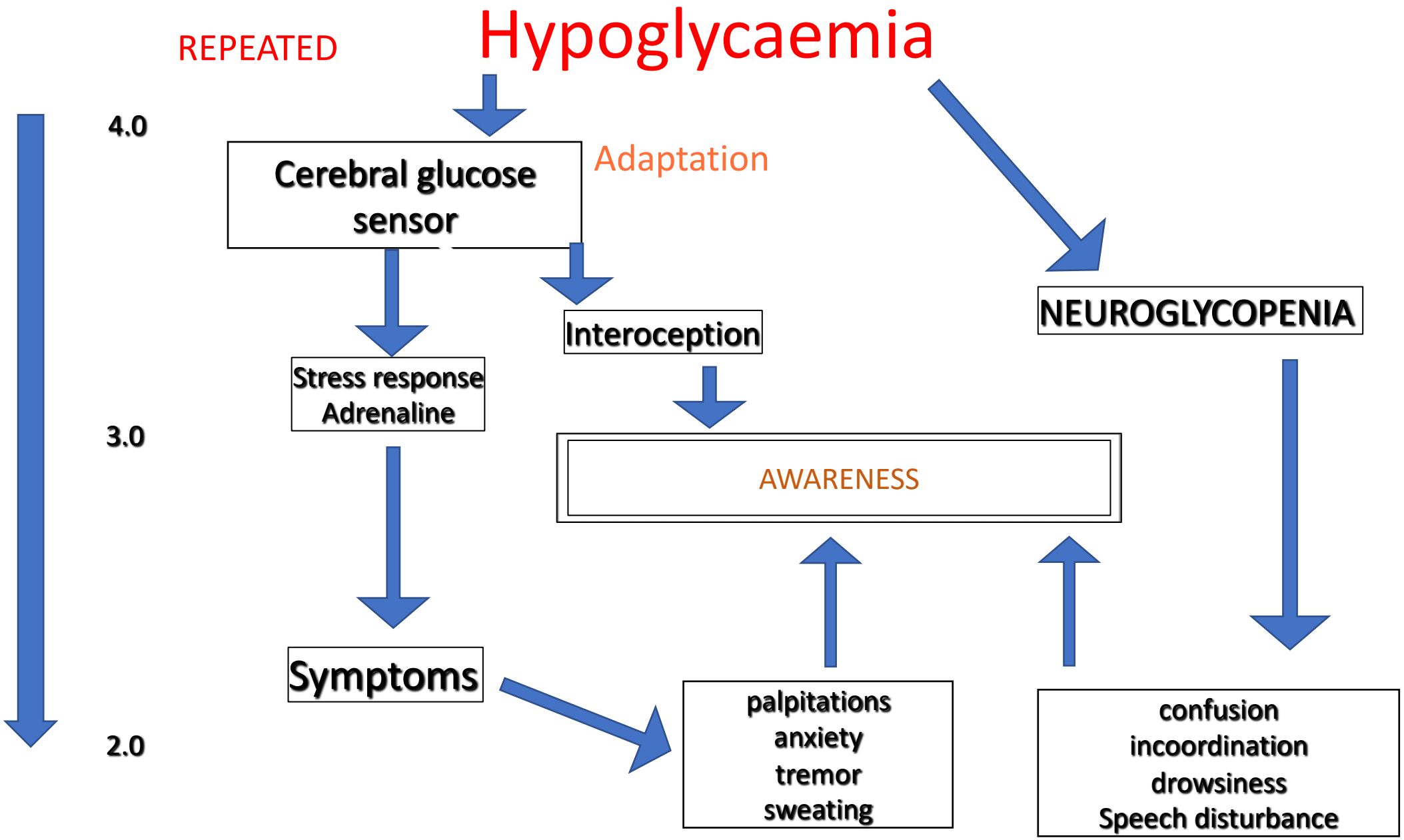
TREAT URGENTLY
15-20g of rapid acting carbohydrate [150 mls of lucozade or orange juice or 3-4 dextrose tablets] and recheck in 15 mins

Defining hypoglycaemia

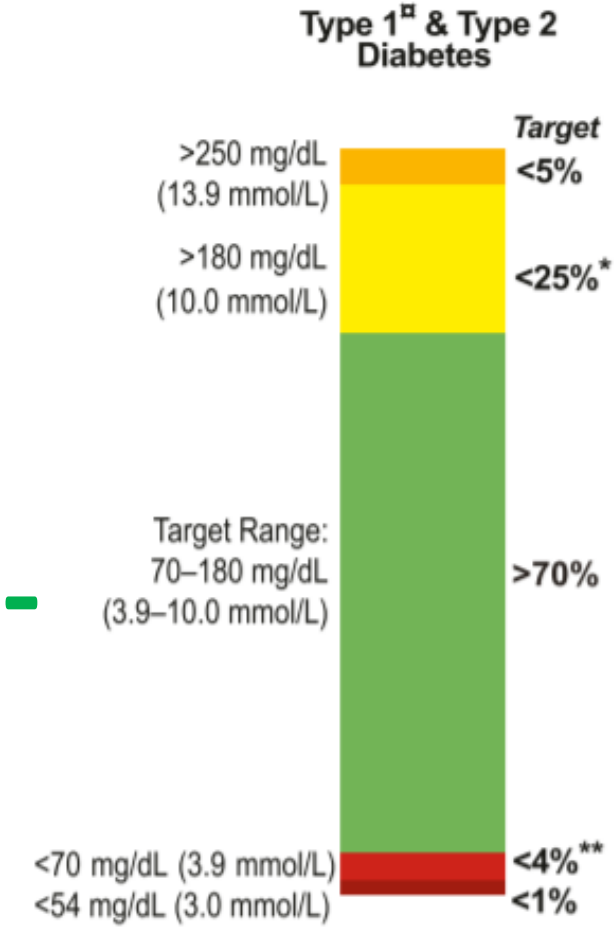


PROLONGED HYPOGLYCAEMIA

OVER 2 HOURS BELOW 3 mmol/l is defined as prolonged hypoglycaemia


REPEATED
Hypoglycaemia
4.0
3.0
2.0
Cerebral glucose sensor
Adaptation
Interoception
NEUROGLYCOPENIA
Stress response
Adrenaline
AWARENESS
Symptoms
palpitations
anxiety
tremor
sweating
confusion
incoordination
drowsiness
Speech disturbance

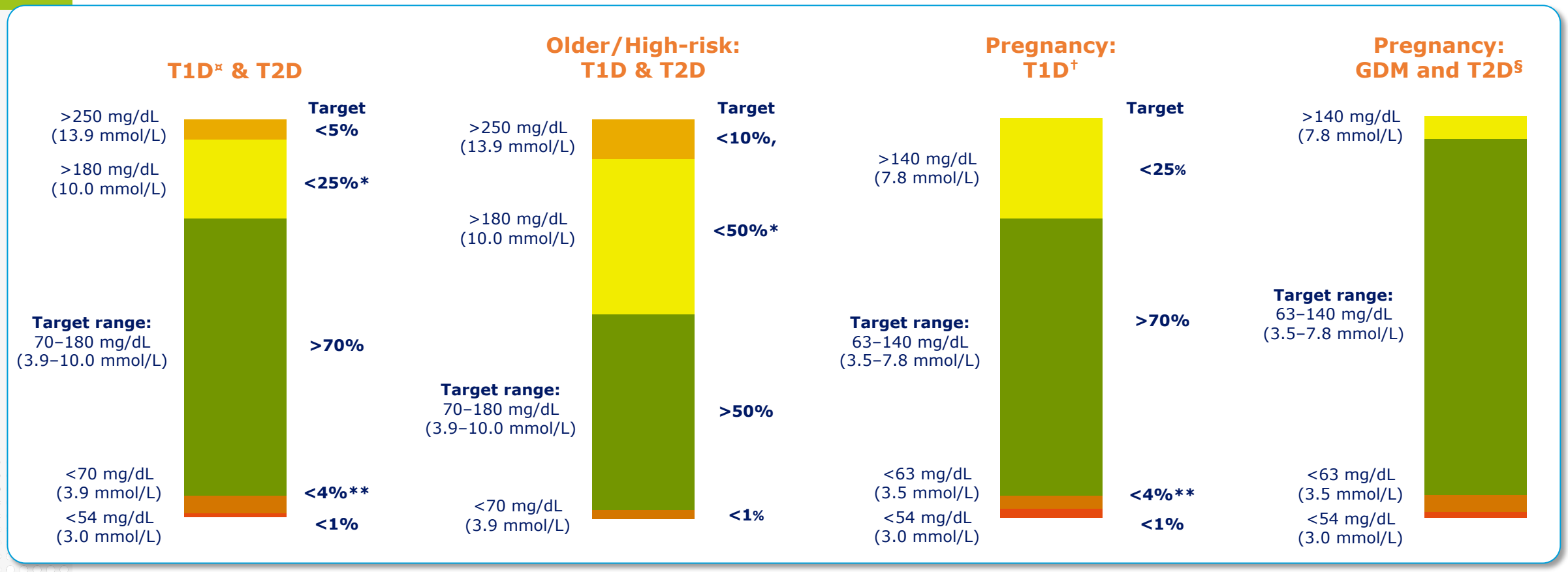
Time in range



3.9- **10mmol/l**

Battelino et al. Diabetes Care 2019 International Consensus on Time in Range

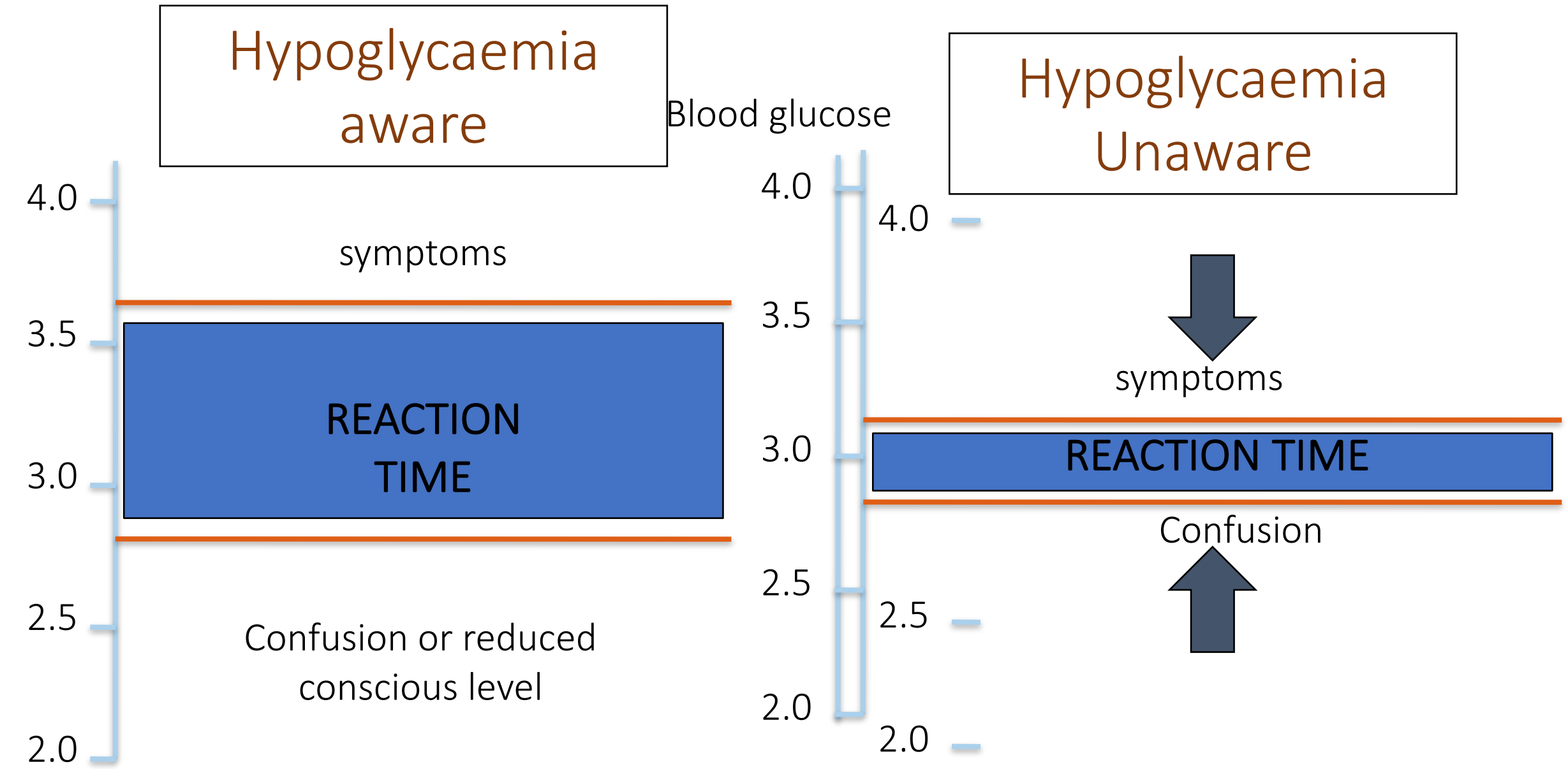
Different glycaemic targets for different populations



¶For age <25 years, if A1C goal is 7.5%, then set TIR target to approximately 60% (see *Clinical Applications of Time in Ranges* section in the text for additional information regarding target goal setting in pediatric management). †Percentages of time in ranges are based on limited evidence – more is required. ††Percentages of time in ranges have not been included because there is very limited evidence in this area – more is required. See *Pregnancy* section in text for more considerations on targets for these groups. *Includes percentage of values >250 mg/dL (13.9 mmol/L). **Includes percentage of values <54 mg/dL (3.0 mmol/L).

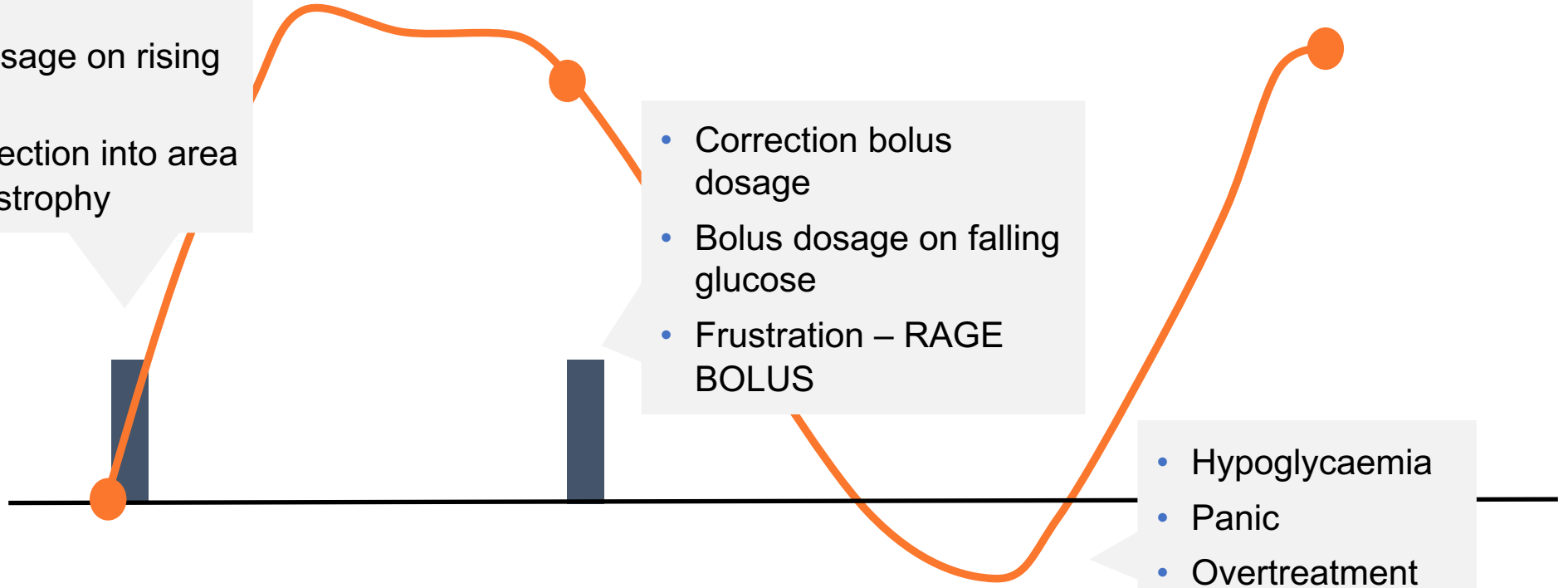
GDM, gestational diabetes mellitus; T1D, type 1 diabetes; T2D, type 2 diabetes

Battelino T. *Diabetes Care*. 2019 Aug;42(8):1593-1603. doi: 10.2337/dci19-0028. Epub 2019 Jun 8


Hypoglycaemia aware
Blood glucose
Hypoglycaemia Unaware
4.0
symptoms
3.5
REACTION TIME
3.0
2.5
Confusion or reduced conscious level
2.0
4.0
3.5
symptoms
REACTION TIME
3.0
Confusion
2.5
2.5
2.0
2.0

Common theme

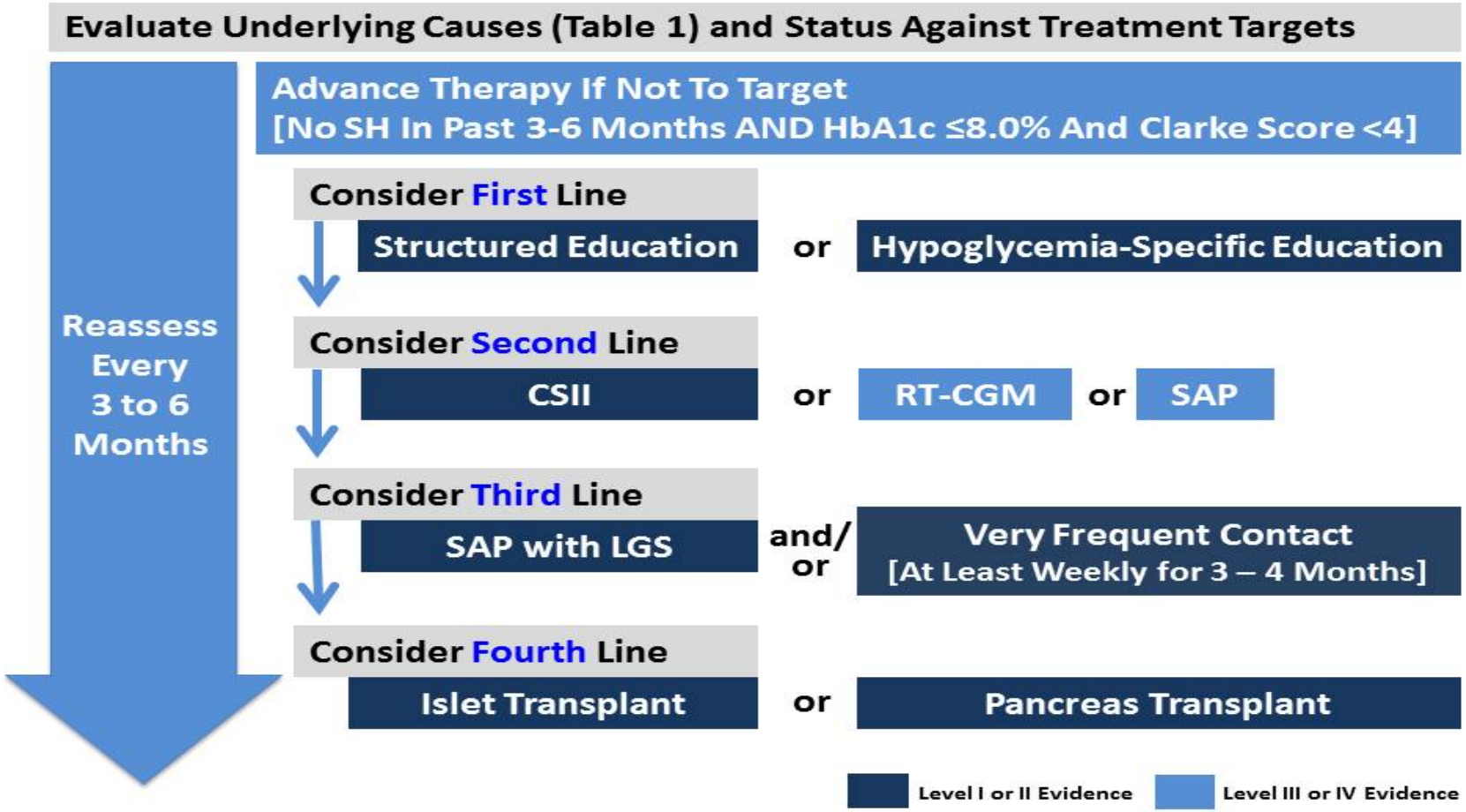
- Inadequate bolus dosage
- Bolus dosage on rising glucose
- Bolus injection into area of lipodystrophy



- Correction bolus dosage
- Bolus dosage on falling glucose
- Frustration – RAGE BOLUS

- Hypoglycaemia
- Panic
- Overtreatment

Algorithm for problematic hypoglycaemia



Choudhary; Diabetes Care 2015

Why do people have problematic hypoglycemia?

- Age
- Long duration of ds
- Impaired awareness
- Absent C-peptide
- Contributing co-morbidities
  - Renal failure
  - Gastroparesis
- Unpredictable insulin action
  - Lipohypertrophy
  - Insulin antibodies
- Mismatch of insulin requirements and delivery
- Imbalanced insulin regime
- education [CHO counting]
- exercise
- Striving for very tight control

Choudhary et al; PMJ 2011
Little et al; Diab Met Res Rev; 2014

Risk factors for hypoglycaemia in T2D

- Duration of diabetes
- Age
- Previous hypoglycaemia
- Low BMI
- Insulin therapy > 10 years
- NOT HBA_{1c}

- - Impaired cognitive function
- - Impaired renal function

BMI, body mass index

Cariou *et al. Diabetes Metab* 2014. doi: 10.1016/j.diabet.2014.10.007 [Epub ahead of print]

The Psychology of recurrent SH

- Different cognitions and behaviors around SH
  - Emphasis on avoiding hyperglycemia
  - Belief they can function normally during hypoglycemia
  - Take less / delayed action to prevent / avoid hypoglycemia
- Neuroimaging data identifies
  - Reduced stress / anxiety response
  - Reduced “ emotional salience” of hypoglycemia
- Motivation to avoid hyperglycemia >> Motivation to avoid hypoglycemia

Margiotta et al ; EASD 2016
Rogers et al; Diabetic Medicine 2011

Dunn et al, Diabetes 2007
Nwokolo et al; Oral 154

Disabling hypoglycaemia

Disabling hypoglycaemia is defined as the repeated and unpredictable occurrence of hypoglycaemia that results in persistent anxiety about recurrence and is associated with a significant adverse effect on quality of life.

Severe hypoglycemia – an episode REQUIRING the help of a third partyu

Indications for islet transplantation

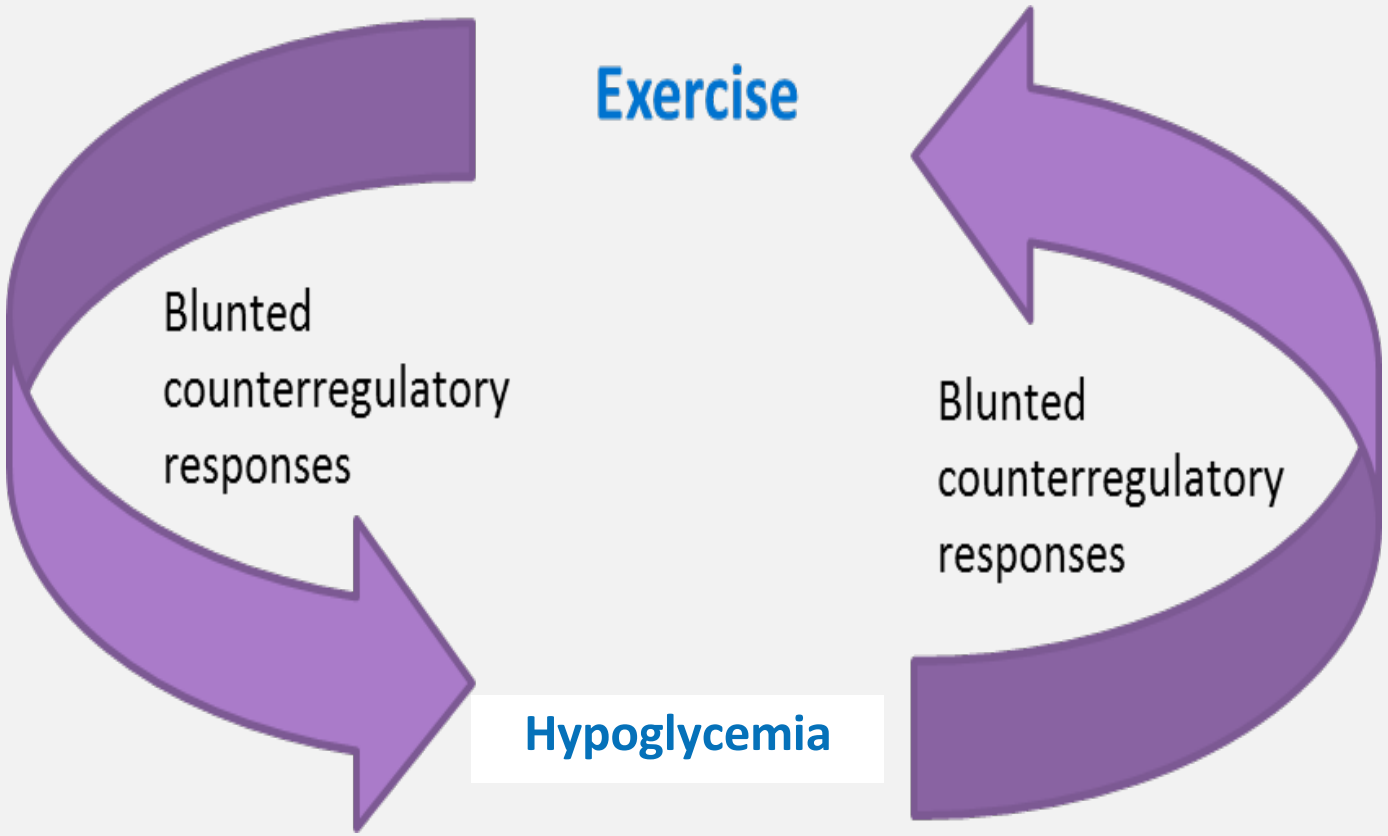
- Patients with type 1 diabetes [C-peptide –ve] who….

- Recurrent severe hypoglycaemia [at least 2 in the last 2 years] despite optimised medical therapy
  - [Education → pumps → sensors]

OR

Islet after Kidney in those with functioning renal graft who are unable to maintain appropriate glucose control OR have problematic hypoglycemia

Vicious Cycle of Hypoglycemia and Exercise



What Is the Role of Transplant?

- Islet / pancreas transplantation is life saving / changing

- BUT - While
- - transplantation is dependent on cadaveric donors
- - requires life long immuno- suppression

- Precious resource Reserved for those who cannot be managed conventionally

Causes of hypoglycaemia

- Imbalance between insulin
  insulin needs and insulin delivery

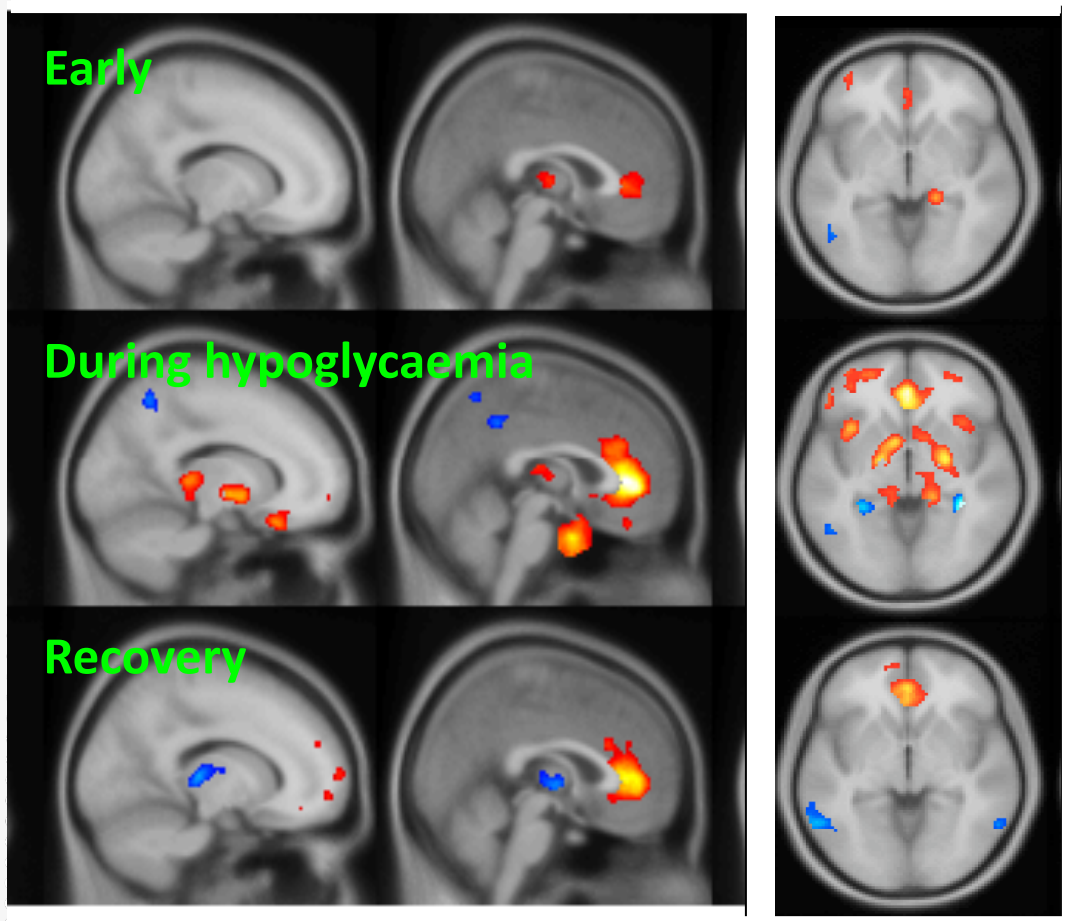
- Exercise
- Alcohol
- Error in carb counting
- Over-correction of high readings
- Late insulin injection

- Secondary

- Low cortisol
- Undetected coeliac ds
- Liver or kidney dysfunction

- Memory impairment

The symptomatic responses to hypoglycaemia ([^{15}O]-H_2O-PET)

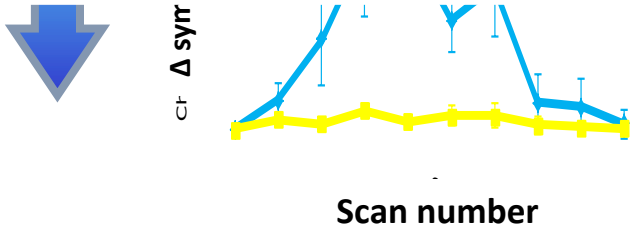


Vigilance
Arousal

Recognition of fearful stimuli
Feeding
Stress response

Aversion
Memory
Balance

Arousal



Teh et al, Neuroimage, 2010

Interpretation..

HA perceives hypoglycaemia as

- Stressful
- Unpleasant
- Unrewarding
- With Emotional memory of this response

Internal motivation to avoid future episodes

IAH perceives hypoglycaemia as

- NOT stressful
- Possibly pleasant / rewarding
- With NO Emotional memory of this response

NO internal motivation to avoid hypoglycaemia

Summary

- Hypos can be common - and we need to identify and count them before we can reduce them

- Education and then technology can effectively reduce hypos

- Hypos can be reduceed effectively with technology

Recurrent hypos can reduce awareness- but hypo avoidance can restore this too.

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