

HOW TO GET THE RIGHT MEAL TIME INSULIN DOSE WITH TYPE 1 DIABETES



PROTEIN AND FAT

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ABBREVIATIONS

AA = Amino Acid

ADP = Adenosine Di Phosphate

ATP = Adenosine Tri Phosphate

AUC = Area Under the Curve

BCAA = Branches Chain Amino Acids

Ca = Calcium

CGM = Continuous Glucose Monitoring

FFA = Free Fatty Acid

FPU - Fat and Protein Units

GDH = Glutamate Dehydrogenase

GI = Glycaemic Index

GL = Glycaemic Load

GLP-1 = Glucagon-like peptide-1

GIP = Gastric Inhibitory Polypeptide

GPCR = G-Protein Coupled Receptor

I:G = Insulin to Glucagon ratio

ICR = Insulin to carbohydrate ratio

MDI = Multiple Daily Injections

MUFA = Monounsaturated Fatty Acids

KATP = ATP-regulated potassium channel

mTOR = mammalian target of rapamycin

SFA = Saturated Fatty Acid

TCA = Tri-Carboxyl-Acid cycle

WHAT DOES THE PANCREAS DO WHEN PROTEIN AND FAT ARE CONSUMED?

INSULIN

Put simply, the B-Cells secrete extra insulin to move AA into the cells for anabolism, and promote FFA storage. The same regulators of B-Cell insulin secretion that have already been detailed are at play here. Most notably the increase in GLP-1, and the increased substrates for B-Cell glycolysis.

The big difference here is that the increase insulin requirement is not as immediate, it is more gradually over time. The stomach empties at a constant energy rate (8.4 kJ/min), therefore because fat is very energy dense, gastric emptying and consequent insulin signalling is delayed(33).

GLUCAGON

Put simply, the A-Cells secrete extra glucagon to prevent hypoglycaemia, and later to stimulate FFA oxidation and gluconeogenesis. The same regulators of A-Cell glucagon secretion that have already been detailed are at play here. Most notably the increased positive regulation from GIP, and negative regulation from insulin.

For the person with Type 1 diabetes, if no insulin is administered for a fat and protein meal, the I:G will drop leading to liver glycogenolysis and Gluconeogenesis. Also the AA's will not be used for anabolism.

RESEARCH

In 2010 Utoff and colleagues assessed the effect of three carb free meals with no bolus insulin on ten males with type 1 diabetes. The three carb free meals all consisted of <3g carbohydrate, 32-34g protein and 48-52g fat, 580-612kcal (68). They first did a fasting test to ensure the background insulin was set appropriately. The glucose level stayed stable over the four hour fasting test (7.2 - 6.8mmol/l), suggesting adequate background insulin.

For each of the three carb free meals, there was a consistent glucose rise of more than 3mmol/l over four hours. The researchers showed the glucose would have very likely kept rising if the study continued to measure past four hours, possibly up eight hours. This is supported by the consistent observation of the late post-prandial hyperglycaemia effect of both fat and protein in type 1 diabetes (28, 29).

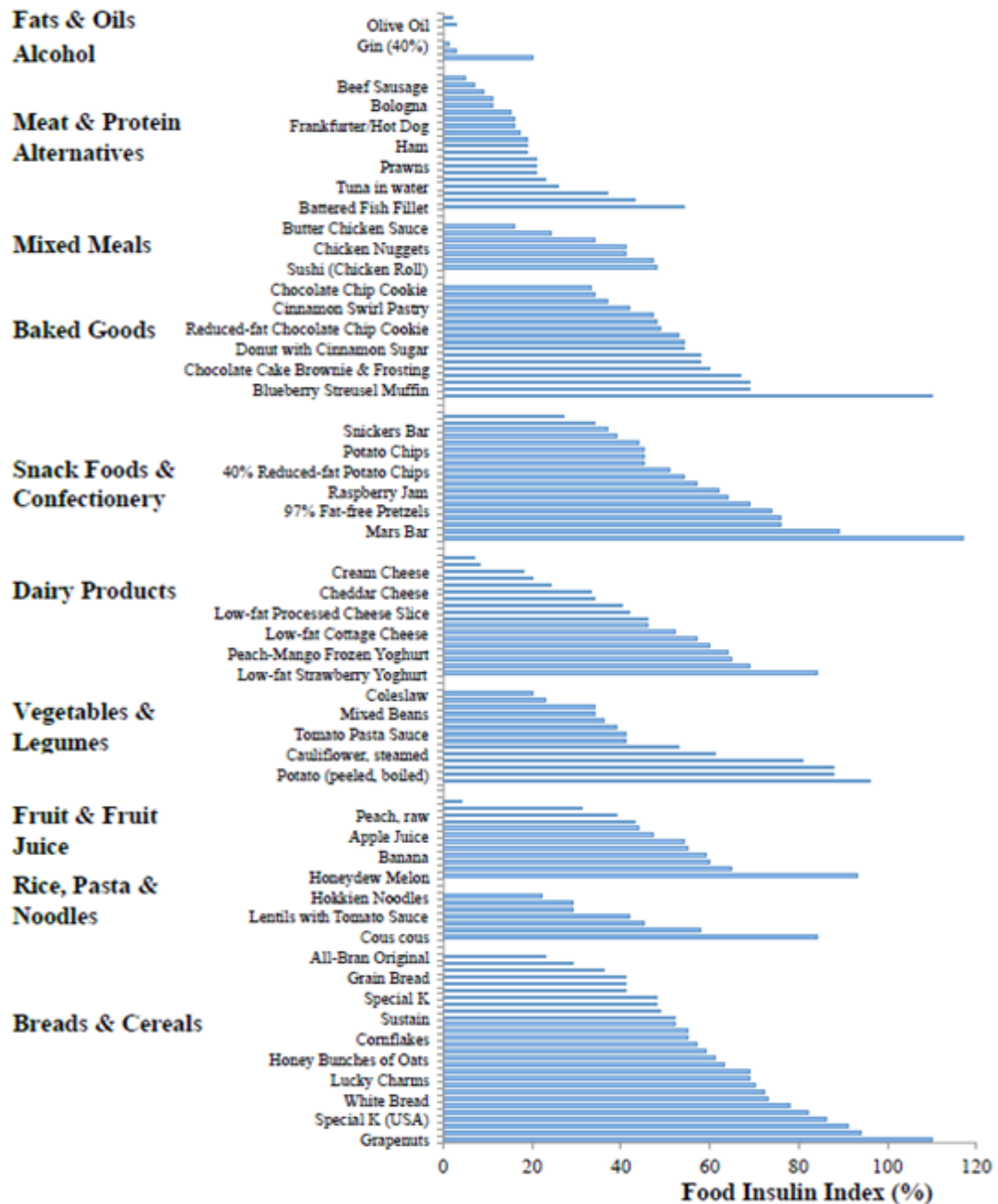
WHAT ABOUT TYPE 1 DIABETES STUDIES WHERE INSULIN WAS DELIVERED FOR FAT AND PROTEIN MEALS?

First we need to understand the Food Insulin Index (FII).

The FII is a measure based of the insulin response to a fixed 1000kj portion of food over two hours, performed on 10 healthy men aged 18-65yrs. The insulin response elicited by glucose is given a score of 100% as the reference.

So far 147 foods have been tested over 20 years. Each food has been given a FII score based on the percentage of incremental area under the curve of plasma insulin compared to that elicited from glucose. (See Bell Thesis, chapter 3, Appendix 3 (67)). The FII is unique in that it measures the insulin response to foods, therefore measures exactly what the person with Type 1 Diabetes needs to administer.

The FII produced some very interesting and unexpected results. For example 1000kj of Tuna (FII=23) produced a very similar insulin response to 1000kj of porridge (FII=29) over two hours. See the below graphic to see the different FII scores.



Copied from Bell (70)

It must be highlighted the FII only measures insulin response over two hours, therefore it will likely underestimate the insulin requirement for protein and fat over 5-6 hours. However, the FII does show the importance of considering the insulin requirement for foods as a whole over two hours after eating. Rather than just considering the carbohydrate content.

Interestingly when the FII researchers isolated low carbohydrate (<10g) foods, they found protein was the strongest predictor of insulin response, explaining 54% of the variance in those foods (70).

Bell (66) conducted a study on 11 people with Type 1 Diabetes to determine if a new insulin dosing algorithm based on the Food Insulin Index (FII) would achieve better blood glucose control than carbohydrate counting over three hours, for commonly eaten high protein foods.

Each study participant ate six different high protein foods (Beef steak FII 37, battered fish FII=54, poached eggs FII=23, low fat yoghurt=84, baked beans FII=88 and peanuts FII=15) on two occasions. On the first occasion they gave insulin for the food based on counting the carbohydrate and apply their ICR. On the second occasion they gave an insulin dose based on the FII score, but adjusted for the portion size to give an insulin dose based on a Food Insulin Demand (FID) score. Each participant had a unique FID ratio. The effect on blood glucose was measured over the next three hours.

The table below shows the insulin doses delivered for the same food, using the different methods. You can see the FID insulin doses were significantly higher than carbohydrate counting alone.

Table 4.1: Nutritional information and serving size for the six test foods

Food	Weight (g)	Energy (kJ)	Fibre (g)	Fat (g)	Protein (g)	CHO* (g)	Avg Insulin Dose using CHO (units)	FID†	Avg Insulin Dose using FID (units)
Beef Steak	225	1350	0	11.4	59.8	0	0.0	31	3.7
Battered Fish	105	945	1.0	14.3	12.4	14	1.6	31	3.7
Poached Egg	180	1080	0	20.3	23.6	2	0.1	15	1.8
Low-fat Strawberry Yoghurt	300	1200	1.2	5.8	13.8	45	5.4	57	6.9
Baked Beans	330	990	16.0	1.9	15.0	36	4.3	49	5.9
Salted Peanuts	150	3900	7.9	78.9	39.5	19	2.4	35	4.2

* CHO, available carbohydrate including sugars and starch and excluding fibre.

† FID, Food Insulin Demand. (FID = FII x kJ in food portion /1000) scaled using the FID and carbohydrate content of 1000 kJ of glucose powder (100/59)).

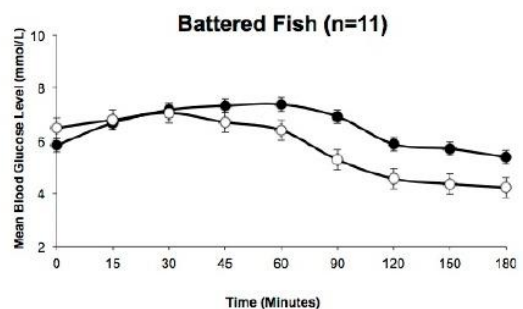
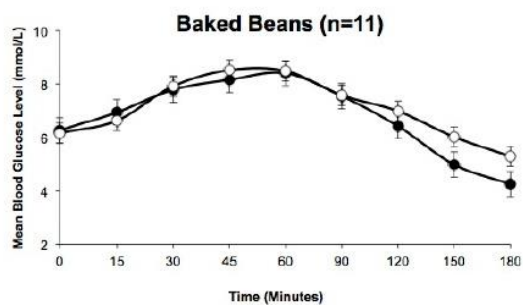
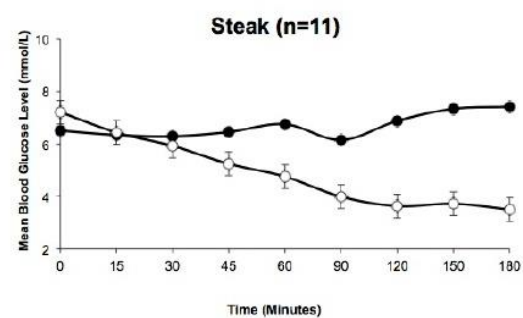
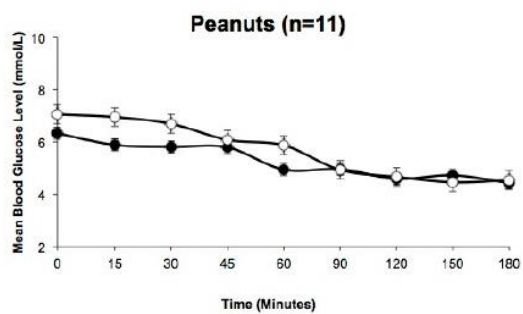
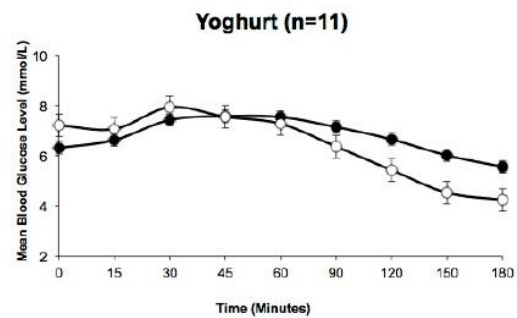
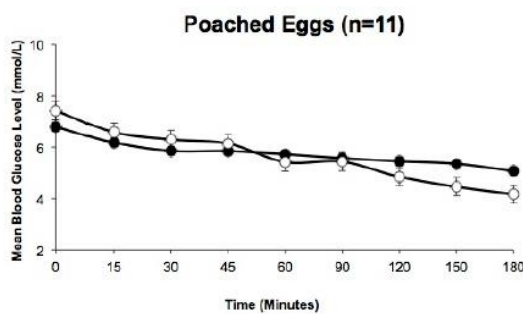
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The focus of this section is high protein fat foods with low carbohydrate. From the table above you can see the difference in insulin doses:

- Three poached eggs, 0.1units from carb counting vs. 1.8units for FID
- Huge 225g Beef steak, 0.0 units for carb counting vs. 3.7units for FID.
- Peanuts, 2.4 units for carb counting vs. 4.2 units for FID

SO WHAT HAPPENED TO THE BLOOD GLUCOSE LEVELS WHEN ALL THIS EXTRA INSULIN WAS GIVEN?

In the three hours after eating, the average blood glucose was significantly lower in the FID group (5.7mmol/l vs. 6.5mmol/l). The rate of hypoglycaemia between the two different methods was not significantly different. Take a look at the profiles over three hours for the individual foods in the below graphs. The blood glucose profiles of the carb counting group are the black dots, and FID group in white dots.



Copied from Bell (70)

The FID Beef Steak group had a lot more hypos, with 8 of the 11 people going low after bolusing on average 3.7units vs. 0.0units for carb counting, where only two participants went hypo.

However, If you exclude the beef steak example, you can see that extra insulin is required for people with Type 1 Diabetes when consuming high protein high fat foods. Certainly much more than just carb counting alone would suggest. The peanuts and eggs had a perfect profile with the FID insulin dose.

This adds credence to the fact that people with Type 1 Diabetes need insulin to transport AA for protein synthesis when high protein high fat meals are consumed. Also the risk of hypoglycaemia will not be increased with the extra insulin, unless the amount delivered is extremely high, as it was for the Beef Steak example!

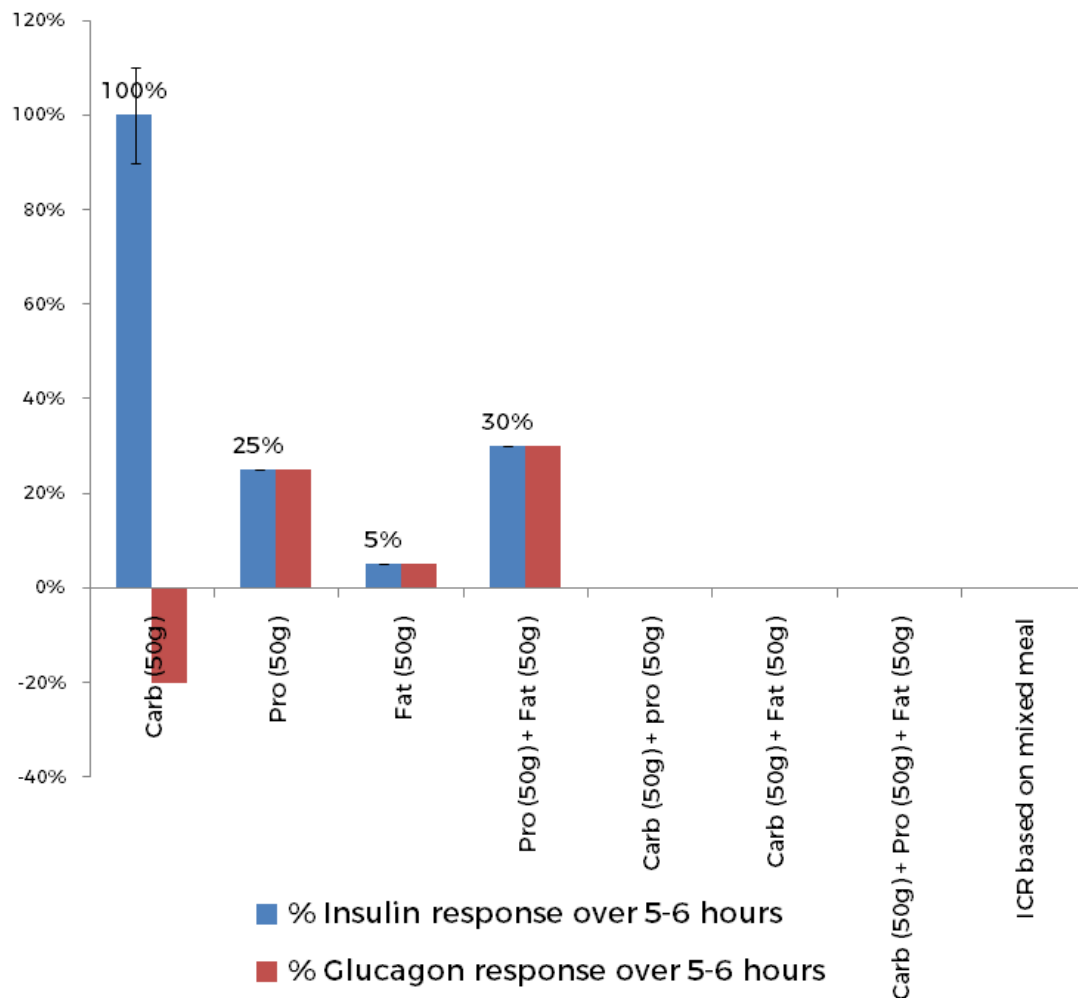
SUMMARY

Very simply, when protein and fat are together both at 50g, both Insulin and glucagon increase, therefore not altering the I:G. This allows AA to be used for anabolism, FFA to be stored as fat or used for oxidation, all whilst maintaining the glucose levels. This is regulated by an increase in GLP-1 stimulating insulin secretion, and an increase in GIP stimulating Glucagon secretion.

The job of the person with Type 1 Diabetes is to match the amount of insulin the pancreas would release for protein and fat combinations. Too little leading to catabolism and hyperglycaemia, too much leading to hypoglycaemia.

HOW MUCH INSULIN TO DELIVER FOR PROTEIN AND FAT ON A GRAM BASIS?

Taken together these two studies discussed strongly suggest protein and fat together require insulin. It would seem protein exerts the majority of the insulin response initially, with fat becoming more prevalent later. The graphic includes an expected response of 30% for both insulin and Glucagon.



In terms of delivering insulin for high protein and fat meals, it is likely more insulin is needed upfront to cover the protein. An extended bolus on a pump or second small injection may be justified to cover the late glucose rise from fat. This may not be practical for most people, and they may choose to have a slightly elevated background insulin to deal with the late rise.

Insulin delivery options:

Initial bolus.

Insulin load = protein (g) x 0.25

Later extended bolus over 2-5 hours or second injection in 60-90 minutes, if background insulin not increased.

Insulin load = Fat (g) x 0.05

The average person with type 1 Diabetes will rarely encounter this issue for a number of reasons:

- They rarely have large carb free meals
- Even if they do, they are generally eating in the next 3-4 hours so will not encounter the later raise in glucagon, and covered in next meal time insulin dose.

Times when the person with Type 1 Diabetes will have encountered this:

- Change of breakfast on a Sunday from usual cereal with milk, to a protein and fat breakfast (bacon, egg, sausage). Result, high glucose level.
- Carb free meal before bed not want another injection but hungry! Probable high glucose on waking. However, this strategy has been shown to be successful in preventing night time hypos, especially after a heavy day of exercise (76-78).

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