



PPS-jaarrapportage 2018

Algemene gegevens	
PPS-nummer	AF-16127
Titel	Assessment of the glycaemic effects of infant nutrition at weaning on long term metabolic and gastrointestinal health in the Göttingen Minipig model.
Thema	Voeding & Gezondheid (Nutrition and Health)
Uitvoerende kennisinstelling(en)	Wageningen Livestock Research (WLR) and Wageningen BioVeterinary Research (WBVR)
Projectleider onderzoek (naam + emailadres)	Sietse Jan Koopmans, sietsejan.koopmans@wur.nl
Penvoerder (namens private partijen)	Eurídice Castañeda Gutiérrez, Nestlé Research Center, Lausanne, Switzerland
Contactpersoon overheid	Cor Wever, c.j.g.wever@minez.nl
Totale projectomvang (k€)	1000.1
Adres projectwebsite	
Startdatum	01-01-2017
Einddatum	31-12-2019

Goedkeuring penvoerder/consortium

De jaarrapportage dient te worden besproken met de penvoerder/het consortium. De TKI's nemen graag kennis van eventuele opmerkingen over de jaarrapportage.

De penvoerder heeft namens het consortium de jaarrapportage

- goedgekeurd
- niet goedgekeurd

Eventuele opmerkingen over de jaarrapportage:

Planning en voortgang (indien er wijzigingen zijn t.o.v. het projectplan svp toelichten)

Loopt de PPS volgens planning?	The in vivo phase of the PPS project was executed according to the protocol, measurement and analyses of some blood parameters and some tissue parameters take more time than expected and will be completed in the first 6 months of 2019. Publication of the results are planned before the end of 2019.
Zijn er wijzigingen in het consortium/de projectpartners?	No
Is er sprake van vertraging en/of uitgestelde opleverdatum?	Yes, publication of the results are planned in 2019
Is er sprake van inhoudelijke knelpunten, geef een korte beschrijving	Delayed measurement and analyses of some blood and tissue parameters.
Is er sprake van afwijkingen van het ingezette budget/de begroting?	No, just a delay into 2019

Korte omschrijving inhoud/doel PPS

Wat is er aan de hand en wat doet het project daaraan?

Wat gaat het project opleveren en wat is het effect hiervan?

Introduction and aim:

Increasing evidence suggests that early life environment can influence health and disease later in life. Optimization of nutrition during infancy could decrease the risk of non-communicable diseases thus having an important potential impact on public health and economy.

In this study, we hypothesize that diets promoting a high postprandial glucose response during the weaning period have a detrimental effect on metabolic health later in life, by affecting organ function and development. The alterations will result in metabolic programming of metabolic disease.

We will approach this question by feeding experimental diets eliciting high and low postprandial glucose response to weaned Göttingen Minipigs, then we will monitor their metabolic health until adulthood.

Wat is er aan de hand? (What is the situation?)

In adults, frequent consumption of high-postprandial- glucose-response diets is associated to greater risk of type 2 diabetes and cardiovascular disease. Up to now, the effect of carbohydrate choices in infants is not known. Several organs and systems are still in development at this stage and thus may be sensitive to be programmed.

Wat doet het project daaraan? (How does the project address this situation/question?)

We will approach this question by feeding experimental diets eliciting high and low postprandial glucose response to weaned Göttingen Minipigs, then we will monitor their metabolic health until adulthood. Göttingen Minipigs are the model of choice because of their similarities to the human infant in terms of digestive tract, and because they develop features of metabolic syndrome. Newly born minipigs reach adulthood within 6 months of age.

Wat levert het project op? (What are the results of the project?)

Generation of pre-clinical knowledge on the mechanisms by which high and low glycemic infant nutrition may affect health in later life.

Resultaten 2018

Geef een korte beschrijving van de high-lights van 2018

Geef een korte beschrijving van de projectdeliverables 2018

The following activities have been initiated and/or completed in 2018:

This project includes three different studies:

1) Diet validation.

Objective: To determine the postprandial glucose and insulin responses after consumption of experimental diets in 2-month old female Göttingen Minipigs.

Method and results: six experimental diets were formulated based on ingredients known to affect postprandial blood glucose and insulin concentrations. Various slow and fast digestible carbohydrates were used as well as proteins and amino acids known to affect insulin secretion. These 6 experimental diets were screened for postprandial glucose and insulin responses in 6 week old minipigs. Out of these 6 experimental diets, two contrasting glycemic-insulinemic diets were chosen for the remaining of the study. The chosen low and high glycemic diets differed more than 5-fold in their postprandial blood glucose ($p < 0.001$) and insulin responses (incremental area under the curve) in the 3 hour post-prandial time period. Subsequently, the 2 chosen glycemic diets were re-tested in more detail in 9-10 week old female minipigs. The low and high glycemic diets differed 4.5-fold ($p < 0.001$) in their postprandial blood glucose response (incremental area under the curve was 171 vs 772 min.mmol/L, respectively) in the 5 hour post-prandial time period. The low and high glycemic diets differed 2.9-fold ($p < 0.001$) in their postprandial plasma insulin response (incremental area under the curve was 148484 vs 423576 min.pmol/L, respectively) in the 5 hour post-prandial time period.

2) Effect of age on post-prandial glucose and insulin response.

Objective: To determine the postprandial response after consumption of the 2 chosen low and high glycemic diets in 10 month old female minipigs and compare that to the response in the same minipigs at the age of 9-10 weeks (see study 1).

Method and results: the female minipigs from study one were kept in group-housing and fed a normal SDS-minipig diet and restudied in the second half of 2018. The 2 chosen glycemic diets were re-tested in more detail in 10 month old female minipigs. The low and high glycemic diets differed ∞ -fold ($p < 0.001$) in their postprandial blood glucose response (incremental area under the curve was -69 vs 1055 min.mmol/L, respectively) in the 5 hour post-prandial time period. The low and high glycemic diets differed 4.7-fold ($p < 0.001$) in their postprandial plasma insulin response (incremental area under the curve was 172632 vs 815051 min.pmol/L, respectively) in the 5 hour post-prandial time period. We conclude that low and high glycemic diets, when tested in the infant or adult phenotype, show a greater contrast in postprandial blood glucose and plasma insulin responses in the adult phenotype.

3) Long-term study. Duration: 12 months

Objective: To determine the short- (3 months), medium- (6 months) and long-term (12 months) effects of the experimental low and high glycemic weaning diets on cardio-metabolic health of female Göttingen Minipigs.

Method and results: Forty-eight 3-week-old weaned female minipigs were balanced on body weights and litter to receive either the low or high glycemic diet for a period of 9 weeks (Stage I). Male suckling and male post-weaning minipigs (fed the low or high glycemic diet for a period of 2 weeks) were euthanized and blood and digesta samples were collected for baseline purposes. At the end of the short-term period, the female minipigs were studied for insulin sensitivity (hyperinsulinemic clamp), insulin secretion (hyperglycemic/arginine clamp), blood pressure and heart rate. After metabolic and cardiovascular testing, piglets were euthanized for portal and peripheral blood collection, digesta collection and tissue/organ collection for further detailed information on the phenotype and possible programming of the minipigs. Samples are currently being analyzed.

From 3 months to 6 months of age (Stage II), the remaining minipigs ($n=32$) were offered a controlled amount of regular chow diet in proportion to their body weight. Minipigs were studied at 6 months of age using the same techniques as used for the Stage I piglets. Samples are currently being analyzed.

From 6 months to 12 months of age (stage III), the remaining minipigs ($n=16$) were offered a controlled amount of obesogenic Western diet until the end of the experiment at 12 months of age. Minipigs were studied at 12 months of age using the same techniques as used for the Stage I and II piglets. Samples are currently being analyzed.

Preliminary analyses of the available data indicate that:

- 1) Early life glycemic nutrition affects insulin secretion in later life when fed a normal chow diet. Early life glycemic nutrition does not affect insulin secretion in later life when fed an obesogenic diet.
- 2) Early life glycemic nutrition affects blood pressure in later life when fed a normal chow diet. Early life glycemic nutrition does not affect blood pressure in later life when fed an obesogenic diet.
- 3) Early life glycemic nutrition does not affect baseline blood glucose, insulin, cholesterol, LDL, HDL, and triglycerides in later life when fed a normal chow diet. The effect of early life glycemic nutrition on blood glucose, insulin, cholesterol, LDL, HDL, and triglycerides in later life when fed an obesogenic diet is still under investigation.

The effect of early life glycemic nutrition on insulin action and on body composition in later life when fed a normal chow diet or an obesogenic diet is still under investigation.

Wat is het effect hiervan? (What is the effect of the outcome of the project?)

If our hypothesis is confirmed, this study will provide unique information on the importance of choosing diets that promote a low glycemic response during infancy in order to improve later health. For the industry it will constitute initial evidence indicating the direction for formulation of foods intended for infants. Moreover, these results will be communicated to health-care professionals on infant nutrition contributing to create awareness about carbohydrate choices during the complementary feeding period with potential beneficial societal impact.

Aantal opgeleverde producten in 2018 (geef in een bijlage de titels en/of omschrijvingen van de producten of een link naar de producten op de projectwebsite of andere openbare websites)			
Wetenschappelijke artikelen	Rapporten	Artikelen in vakbladen	Inleidingen/workshops
Too early	Too early	Too early	To early
Titels/omschrijvingen van belangrijkste producten in 2018 (max. 5) en hun doelgroepen			

Bijlage: Titels/omschrijvingen van alle producten in 2018 of een link naar deze producten op de projectwebsite of andere publieke websites