3

Developing the course "Assessment of Insulin Sensitivity in Metabolic Active Tissue"

Sara Gry Vienberg

Section of Integrative Physiology, CBMR, Faculty of Health and Medical Sciences, University of Copenhagen

Background

A big wish from several of the PhD students in our department as well as our neighboring departments at the Faculty of Health and Medical Sciences, University of Copenhagen is more PhD courses with "hands on" experience in the laboratory and not just PhD courses with a more theoretical approach of a given topic.

We are a newly established department within one of the Novo Nordisk Foundation sponsored research center clusters' and therefore do not have any obligations to teach. However, one of the missions within the Center for Basic Metabolic Research and our department of Integrative Physiology is to attract and educate world leading scientists. In an attempt to bridge this paradox of no teaching obligations and our vision for the center to educate world leading scientist as well as attract new young students for research, we plan to conduct a PhD course within our field of research with the title: "Assessment of Insulin Sensitivity in Metabolic Active Tissues". To fulfill the wishes of our PhD students we want to make this course practical so the students get the proper training in the laboratory and subsequently directly benefit from the taught techniques and experimental designs in their own research projects.

The aim of this project is therefore to plan the above mentioned PhD course, with a clear course description, intended learning objectives, teaching/learning activities and how the students learning outcomes are evaluated. The report therefore reflects my current effort to design and establish

this new PhD course and at the same time serves to meet the requirements for passing the course in university pedagogy.

The need for the intended PhD course

All our graduate (PhD) students are enrolled in the Health and Medical Science Graduate Program called Basic Metabolic Research. The overall goals for PhD students graduating from the Health and Medical Faculty are that they are capable of designing and executing research projects, acquire a broad knowledge base, as well as critical, creative and precise experimental skills. The graduate program within Basic Metabolic Research is meant to provide the training environment for metabolic research within the Copenhagen area, with special emphasis on glucose and fat metabolism, obesity and diabetes. Looking at the PhD course catalogue offered by the Basic Metabolic Research program at the Health and Medical Science Faculty and from related graduate programs from other universities, it becomes clear, why our PhD students are asking for more PhD courses specifically with a practical approach within diabetes and metabolism research, since very few are offered, at least during 2014. The intended PhD course will in other words fill in a gap in the current offered PhD courses.

Constructive Alignment

The planned PhD course will be designed, applying Biggs & Tang (2011) theory about constructive alignment. Constructive alignment basically states that the relation between the intended goals for a given topic, the teaching activities and the evaluation depends on the students learning before the intended goals can be achieved. Therefore, according to Biggs & Tang (2011) the key to obtain a course with a constructive alignment are the intended learning outcomes (ILOs). When the ILOs have been generated, then decision as to how they are taught and assessed are to follow. The ILOs should be expressed as which constructive activities are most likely to achieve them. As summarized in figure 3.1, activities are in this case verbs, so the verbs should specify what the students should do in order to learn the activity being taught.

In principle, constructive alignment of a given course should be reached when teaching/learning activities (TLAs) implement the verbs stated in the

intended learning outcomes, which are then used or acted upon in the TLAs and the assessment tasks.

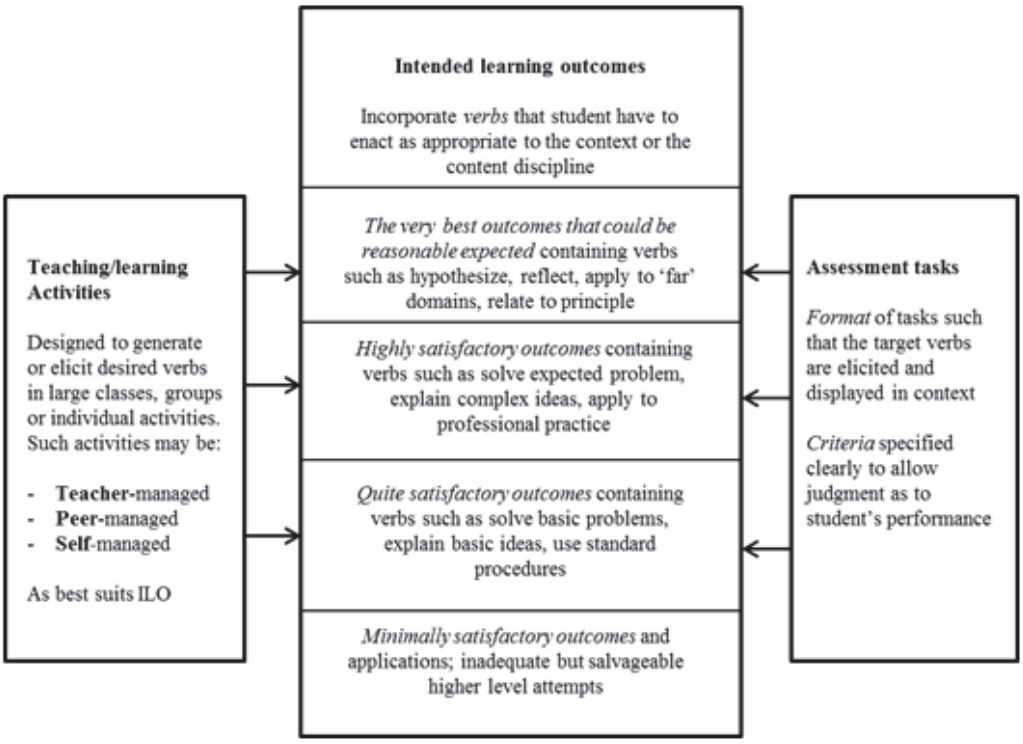

Fig. 3.1. Aligning intended learning outcomes, teaching and assessment tasks (Modified from Biggs & Tang (2011), p105)

Designing intended learning outcomes

The course I wish to design should particularly support the students' ability to design studies addressing insulin sensitivity in metabolic active tissue as well as conducting the studies/assays themselves and being able to critically analyze and evaluate their generated results during the course. From the principle of constructive alignment it is clear that designing the intended learning outcomes is the most essential element in the course design as it impacts both the teaching activities as well as the assessment tasks.

In order to design intended learning outcomes it is important to determine what kind of knowledge is to be learned, *declarative or functioning*. Biggs and Tang define declarative knowledge as knowledge about things or "know how" whereas functioning knowledge is knowledge that gives the

learner ability to do things (Biggs & Tang 2011, pp. 81). In other words, we want the students to develop competencies, where competencies are defined as a knowledge-based foundation to act appropriate in situations, which includes a specific kind of professional challenge Busch et al. (2004). It is also clear from our students' perspective that they wish a course which gives them functional knowledge and competencies, which make them able to add their already obtained declarative knowledge and research experience within metabolism.

Another consideration to do before writing the intended learning outcomes is what level of understanding is intended. Is it enough for the students to be able to do an experiment without knowing why they are doing it? Several learning taxonomies address this important point. The Structure of Observed Learning Outcomes (SOLO) taxonomy gives several examples on verbs to use in intended learning outcomes depending on what level of understanding is intended for the course (Rienecker et al. 2013, pp. 102). This learning taxonomy is divided into a multi-structural or quantitative and a relational or qualitative level of understanding. If the intended learning outcomes are at the quantitative level, then the learning outcomes should include verbs like mention, define, calculate, and describe. However, if a qualitative level of understanding is intended, then the intended learning outcomes should include verbs like; explain, analyze, use, discuss, evaluate and create. I clearly want the students not only to be able to describe a certain experimental method, but that they actually can perform the experiment as well as evaluate their results and put the results into a research context, so they themselves can use this technique to solve or address their own research questions. Hence, the goal for this PhD course is that the students obtain qualitative understanding and knowledge. Therefore, it is important that the verb in the intended learning outcomes reflects the appropriate level of understanding, the topic content the verb is supposed to address, and in which context of the content the verb is to be used. Of course there are also some technical and practical issues to consider, when planning a PhD course. Most PhD courses last only a week, which is also the intention for the planned PhD course. There are limits to what it possible to implement of knowledge and experience for the participants within a week, if, as stated above, the level of understanding should be relational and deep, rather than surface learning and multi-structural. The process of actually deciding the content of the course has been rather difficult, since I as well as my co-organizers/teachers for planning the course have not only different interests in science, but also very different approaches to what we

think are the most important topics to cover in the planned PhD course. This has given me some hard choices to make in order to decrease the suggested content of the course, so what is practical possible to do in the laboratory and what can actually be covered within only a week and still ensure the understanding becomes relational and not just multi-structural. Thus, in this short course, the intended learning outcomes are very closely related to the teaching activities in order for the participants to be able to succeed with the intended learning outcomes. The intended learning outcomes are given in the course description in appendix A.

Designing teaching/learning activities

Teaching/learning activities (TLAs) need to be aligned with the verbs stated in the intended learning outcomes, but besides that, there are also some general characteristics, which need to be fulfilled in the TLAs according to Biggs & Tang (2007) in order to achieve the ILOs. Those include:

a) An appropriate motivational context
b) A well-structured knowledge base
c) Relevant learner activity
d) Formative feedback
e) Reflective practice and self-monitoring

An appropriate motivational context includes that the students feel trusted and are able to make decisions, have time to make the right decisions and thereby take responsibility for own learning and that the teaching activities are not seen as trivial. In addition, it has to be done in an environment with clear policies and procedures as well as having reasonable probability for success. New knowledge, should build upon already learned skills and of course the activity has to be relevant. Giving formative feedback, while the students are learning in the middle of an activity is also important both for obtaining the success of the teaching activity as well as the intended learning outcomes. However, sometime we all make mistakes and those can be detrimental for a given experiment, not to mention very expensive, however, by self-monitoring and reflecting upon which mistakes were done or what went right this time, it is possible to correct the mistake, so it does not happen twice and thereby a valuable lesson has been taught/learned.

In order to succeed with the intended learning outcomes and give enough time for the teaching activities for the participants to feel free to

move and have time to make the right decisions and give formative feedback, I and the other co-organizers have had to cut a tremendously in what we to begin with, thought was a reasonable amount of content the participants should gain from our one week PhD course. The content of the PhD course is described shortly in at the course description in appendix A and appendix B shows the outline of the program for the week. Below are given a short description of the teaching activities planned and the reason for them.

Since this is a very labor and teaching demanding course with constant formative feedback, we expect no more than twelve participants and these will be divided into four groups of three. Each group will have an animal FELASA C license holder as instructor/teacher, not only to ensure formative feedback to the participants and that the experiments run smoothly, but also to ensure animal ethics and welfare.

All teaching activities are planned, so each new technique or exercise builds upon knowledge obtained from the previous exercise. The first teaching activity is to anaesthetize a mouse by intra-peritoneal injection. We expect that most participants have previous experience with animals, but in case there are a few, which does not, then this is a good opportunity to learn how to catch, handle and inject a mouse. If the injection is successful, the mouse will stop moving within a few minutes. When the mouse is anaesthetized then the participants will practice retro-orbital injections (this will be used in another experiment later in the week) followed by opening up the abdominal cavity in the mouse and try to do a vena cava injection before dissecting all the metabolic tissue. This might be a trivial exercise for participants with a lot of animal work experience, however, they should also know, that you cannot practice enough when it comes to animal experiments. There is always room for improvement and refinement.

This teaching activity will be followed up with doing vena cava injections on anesthetized mice, with either insulin or saline for five minutes before tissues (liver, fat and muscle) have to be removed and snap frozen in liquid nitrogen for further analysis of the insulin signaling pathway. The samples generated will be analyzed by Western blot during the week and will give a clear-cut answer about whether the vena cava injection with insulin was successful or not. To add an additional layer of context and give an idea about what this kind of experiment can be useful for in terms of insulin sensitivity assessment, the participants will be given mice which have exercised prior to the insulin stimulation or been sedentary. At the last day of the course, the participants will assess whether exercise leads to in-

creased insulin signaling as hypothesized or not in the tissues examined. The exercising of mice will not be performed by the participants, but they will be told the principle behind it and shown the custom-made treadmills we use for mice. The day will end with a 5 – 10 min presentation from half of the participants about their current research, so they partly get to know each other and partly can give feedback to each other about, where they can see the practiced methods being used in their own research. Since the day is already very packed, there will not be time for all participants to present their current work on Day 1, so the other half of the participants will present at the end of Day 2.

At the second day of the course, the participant will either perform isolation of primary adipocytes or do insulin stimulated glucose uptake in vivo using radioactive labelled glucose in mice. Both experiments require handling of the mice and i.p. injection of anesthetics, and dissection, repeating some of the techniques used at Day 1. Again, the participants will handle mice, which have been exercised or stayed sedentary prior to the experiments. The primary adipocytes will be examined for their insulin stimulated lipogenesis and inhibition of lipolysis also in the context of exercise, which is supposed to increase insulin sensitivity. The insulin stimulated glucose uptake, demands that the participants can perform retro-orbital injections as practiced on Day 1, do blood glucose measurements as well as dissect liver, muscle and fat to assess these tissues’ ability to take up and store glucose. Isolating primary adipocytes from fat instead of for example isolating hepatocytes from liver or muscle fiber from muscle, was chosen because it is rather easy and less time consuming than the other two techniques and therefore more likely to succeed. Furthermore, a lot of the PhD courses within metabolism and diabetes offered by the graduate school covers muscle biology. However, in order to assess whole body insulin stimulated glucose uptake covering all three tissues, we have chosen to include insulin stimulated glucose uptake using radioactive tracers. This method instead of the golden standard for measuring insulin sensitivity in vivo, e.g. hyperinsulinemic-euglycemic clamp, was chosen because this is durable to set up in all laboratories handling animals and does not require surgical expertise and therefore also more likely to succeed for the participants.

The Last teaching activity on Day 2 is 5-10 min presentation from the remaining half of the participants about their current research. Day 3 will be a copy of day 2, so all participants get through all methods. However,

instead of the participants' presentations at the end of Day 3, we will have an invited speaker covering adipocyte biology in the context of diabetes.

Day 4 will be a data collection day. Here all tissues and samples will be analyzed by Western blot analysis, scintillation counts, etc. and the participants will put together a presentation of their data for Day 5, where all groups will evaluate their results. The day will be ended by a keynote speaker, who will give a talk about how we assess insulin sensitivity in humans and connect the advantage and disadvantages with using mice as animal models for this type of research compared to humans.

Day 5 is the day of evaluation and assessment of the participants. There are several ways to evaluate the participants' performance, but we have chosen and oral group presentation and discussion with the rest of the participants, since we believe this will be most fruitful for all participants and perhaps give us as organizers a better idea of unintended but perhaps valuable learning outcomes, for our next course. The groups will present their results generated during the week. They should be able to explain why and how they assessed the insulin sensitivity and their results will indicate how well they applied the different techniques and give reasons to what went right or wrong and why. Since it is unknown, how acute exercise affect insulin sensitivity the results generated during this planned course might, in the best case scenario, end up in a publication. However, we at least expect that this intervention with or without exercise will be used as a base for how the techniques learned during this course can be used in a research context within the participants own research and how to design or not design new studies, whether this includes projects where mice with different genotypes, diabetic vs. normal, or mice treated with or without certain drug, etc. are analyzed and thereby fulfill the last of the intended learning outcomes in the course description.

A

Appendix A
GRADUATE SCHOOL OF HEALTH AND MEDICAL SCIENCES
University of Copenhagen

Assessment of Insulin Sensitivity in Metabolic Active Tissues

The course gives the participants capability to plan, apply and interpret their results within insulin stimulated end-point assays, carried out in typically active metabolic tissues such as liver, muscle and fat from mice.
In order to put the content of the course into relevant on-going research, the participants will either examine mice which have been acutely exercised prior to the course or mice which have been sedentary and assess their insulin sensitivity in different in vivo and ex vivo settings.

Learning Outcomes
The participants will be able to:

a. Explain why and how to assess insulin sensitivity in metabolic active tissues
b. Apply assessment of insulin sensitivity in metabolic active tissues
c. Evaluate the assessment of insulin sensitivity in metabolic active tissues and present the obtained data in a clear and concise way.
d. Design and create new studies, where the participants can apply, evaluate and benefit from the assessment of insulin sensitivity in their own research

Content
The content of the course includes handling of mice, i.p. injections as well as i.v. injections both retro-orbital and vena cava, besides dissecting the most relevant metabolic tissues. Furthermore, the course includes acute i.v. insulin stimulation through vena cava, and analysis of insulin signalling in muscle, fat and liver by Western blot. The participants will learn how to isolate primary adipocytes and assess lipogenesis and lipolysis as well as to do insulin stimulated *in vivo* glucose uptake using radioactive tracers.

Weight
5 ECTS

Participants
PhD students. Experience with animal work is an advantage, but not a requirement

Language
English

Form
The primary form will be exercises in the laboratory, but there will also be group work, discussions in plenum and lectures

Dates
Fall 2015

B

Appendix B

Assessment of Insulin Sensitivity in Metabolic Active Tissues, Fall 2015

Monday		Tuesday			Wednesday		
9-9.30 9:30-13	Introduction and practical information I.p. injectin of anaestaetics, Practise retro-orbital i.v. injection Practise i.v. vena cava injection and dissektion of tissue I.p injectin of anaestaetics, vena cava injections of saline or insulin, removal of muscle, fat and liver	9-16.00	Group A and B In vivo stimulated glucose uptake	Group C and D Adipocyte isolation Lipolysis Lipogenesis	9-17.00	Group A+B Adipocyte isolation Lipolysis Lipogenesis	Group C + D In vivo stimulated glucose uptake
13-14	Lunch		Lunch, when it fits			Lunch, when it fits	
14-17	Tissue homogenisation Protein concentration determination Make laemli samples as well as cast gels						
17-18	Presentations by participants	16-18.00	Presentations by participants		17-18.00	Lecture by invited speaker	
		18-19.00	Social hour with drinks and snack		18-19.00	Social hour with drinks and snack	

Thursday		Fridady	
9-13.00	All groups, run of western Collect counts from day 2 and 3	9.00-13	development of western and preparations of presentation
13-14.00	Lunch	13-14.00	Lunch
14-16.00	Data collection and assesment from previuos day	14-16.30	Group presentations of data Evaluation of data as well as where can the participants see the benefits of the learned assays in their own research
16-17.00	Lecture by invited speaker		
17-21.00	Social hours with dinner		

All contributions to this volume can be found at:

http://www.ind.ku.dk/publikationer/up_projekter/2014-7/

The bibliography can be found at:

http://www.ind.ku.dk/publikationer/up_projekter/

kapitler/2014_vol7_nr1-2_bibliography.pdf/