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HOW WE TEACH | *Classroom and Laboratory Research Projects*

Glucose metabolism from mouth to muscle: a student experiment to teach glucose metabolism during exercise and rest

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Engeroff T, Fleckenstein J, Banzer W. Glucose metabolism from mouth to muscle: a student experiment to teach glucose metabolism during exercise and rest. *Adv Physiol Educ* 41: 82–88, 2017; doi: 10.1152/advan.00124.2016.—We developed an experiment to help students understand basic regulation of postabsorptive and postprandial glucose metabolism and the availability of energy sources for physical activity in the fed and fasted state. Within a practical session, teams of two or three students (1 subject and 1 or 2 investigators) performed one of three different trials: *1*) inactive, in which subjects ingested a glucose solution (75 g in 300 ml of water) and rested in the seated position until the end of the trial; *2*) prior activity, in which the subject performed 15 min of walking before glucose ingestion and a subsequent resting phase; and *3*) postactivity, in which the subject ingested glucose solution, walked (15 min), and rested afterwards. Glucose levels were drawn before trials (fasting value), immediately after glucose ingestion (0 min), and 5, 10, 15, 20, 25, 30, 40, 50, and 60 min thereafter. Students analyzed glucose values and worked on 12 tasks. Students evaluated the usefulness of the experiment; 54.2% of students found the experiment useful to enable them to gain a further understanding of the learning objectives and to clarify items, and 44.1% indicated that the experiment was necessary to enable them to understand the learning objectives. For 6.8% the experiment was not necessary but helpful to check what they had learned, and 3.4% found that the experiment was not necessary. The present article shows the great value of experiments within practical courses to help students gain knowledge of energy metabolism. Using an active learning strategy, students outworked complex physiological tasks and improved beneficial communication and interaction between students with different skill sets and problem-solving strategies.

energy metabolism; glucose metabolism; postprandial; postabsorptive; physical activity

A PROFOUND KNOWLEDGE of the influence of physical activity (PA) on energy metabolism and the interaction with energy uptake is essential for health professionals. To understand metabolic regulation during and following physical activity, a basic understanding of external and internal energy resources and associated metabolic pathways is mandatory.

Specific challenges in the teaching of physiology are to illustrate the complex regulatory mechanisms of glucose metabolism at rest and during physical activity as well as to differentiate substrate utilization in the postabsorptive and postprandial states. Students should know at least three different carbohydrate sources (liver glycogen, muscle glycogen, external sources) and two regulating hormones (insulin, glucagon) to gain a basic understanding of glucose supply and demand. In the understanding of the contextual relationship, it is further necessary to learn the function of glucose transporters, pathways for intracellular glucose use, and storage as well as gastrointestinal absorption.

With regard to the amount and complexity of knowledge involved in the study of metabolic regulation, seminars and lectures should be supplemented with practical sessions.

Although the theoretical basis of metabolic regulation is described clearly in exercise physiology textbooks, innovative but feasible practical approaches for student-centered teaching are currently missing.

We developed an experiment to help students to understand basic regulation of glucose metabolism in the postabsorptive and postprandial states and the energy sources for physical activity in the fed and fasted states. Furthermore, we designed specific learning materials and used standardized diagnostic procedures to enhance the practical relevance. The aim of the present article is to describe the student experiment, present perceptions of students about its content-related value, and provide the materials for reproduction.

METHODS

Learning Objectives

The following learning objectives were defined for the practical course:

1. Glucose metabolism “From Mouth to Muscle,” including

- Gastrointestinal glucose absorption.
- Glucose transport and blood glucose.
- Cell-type specific glucose uptake (liver, muscle, and neural cells).
- Intracellular glucose turnover and storage (liver, muscle, and neural cells).

2. Properties of quickly available carbohydrates.
3. Estimation of calorific values.
4. Estimation of the basal metabolic rate.
5. Estimation of the energy expenditure during physical activity based on metabolic equivalent of task (2).

Setting

A course in physiology is obligatory for all undergraduate students in B.Sc. of Sports Sciences. The course program comprises a continuous lecture and a practical skills laboratory and is equivalent to lower-division courses. Prior to the practical classes in the skills laboratory, all students were advised to attend the respective lecture and to peruse the related chapters within an exercise physiology textbook (6). Students participated in the skills laboratory within

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seven classes with an average size of 18, each split into peer groups of approximately six to nine students. These classes took place from 8 AM to 12 PM. All groups performed a series of experiments on the basis of a laboratory manual. Prior to the experiments, the supervisors briefed the students shortly. He assisted the skills laboratory and helped students to adequately perform the required tasks. After completion of all tasks the supervisors discussed the results and conclusions with the entire class for 20–30 min.

Materials

The following materials were necessary and provided to the students:

1. Blood sampling protocol (see Fig. 2).
2. Plain version of flow chart of metabolic pathways (see Fig. 4).
3. Hand-held glucometer.
4. Lancing device and test strips.
5. Swabs, skin disinfection, and plasters.
6. Glucose solution (75 g in 300 ml of water).
7. Stopwatch.
8. Compendium of physical activities (2).

Experimental Setup

The experiment on glucose metabolism was newly implemented in the skills laboratory during the summer term of 2015. Students had been instructed previously that in every class some of them should arrive after overnight fasting or an at least 3-h fasting period.

With each peer group, the students had to appoint three people willing to voluntarily participate as test subjects. These test persons were randomly assigned to one of three different test conditions: *1*) inactive control, *2*) prior activity, or *3*) postactivity. Figure 1 gives an overview of the experimental timeline. All conditions lasted for 60 min and are detailed below. At some point the test person ingested a glucose solution (75 g in 300 ml of water). Blood glucose was sampled at baseline (fasting value) and following the glucose ingestion. Timing was accomplished with a conventional stopwatch. The time points for sampling are as follows: 0 min (i.e., immediately after glucose ingestion) and at 5, 10, 15, 20, 25, 30, 40, 50, and 60 min. The students recorded all measurements, and time courses of blood glucose were compared thereafter.

During the experiments and after they were finished, each peer group assembled and students had to analyze and discuss the experiment and their data based on the tasks and questions, which are detailed below. The supervisors encouraged the students for intragroup discussion and exchange of opinions. When necessary, the supervisors proposed answers or provided additional information. Students were allowed to work for 90–100 min.

Inactive group. First, the subjects ingested a glucose solution. The person then remained seated for the duration of the trial. Glucose levels were sampled for the next 60 min by the student group at the time points described above.

Prior activity group. Test persons had to perform brisk walking on a treadmill for 15 min. Immediately thereafter, the test persons ingested the glucose solution (see above) and were advised to remain seated with blood glucose being sampled as described above.

Postactivity group. Test persons ingested a glucose solution and then performed 15 min of brisk walking on a treadmill immediately thereafter. Blood glucose was sampled during walking and with subjects in a seated position once walking was finished according to the scheme described above.

Measurements

Blood glucose levels were assessed using hand-held glucometers in milligrams per deciliter. Supervisors did one exemplary measurement and supervised the students during all other assessments. Students were advised to wear gloves during all measurements. After disinfection of the puncture site, measurements were taken by pricking the tip of finger or earlobe (ideally only once) and collecting a blood drop periodically for 60 min, starting with a fasting value before the beginning of trials.

Tasks and Questions

In addition to the experiment, the peer groups had to complete and answer the following tasks and questions:

Energy expenditure.

1. Estimate the calorific value of the glucose solution (75 g of glucose).
2. Estimate the basal metabolic rate for the duration of the experiment (60 min) using the Harris-Benedict equation.
3. Estimate the energy expenditure during 15 min of brisk walking based on the metabolic equivalent of task (2).

Blood glucose.

4. Record all blood glucose values in your protocol (Fig. 2).
5. Plot the blood glucose values in the coordinate system beginning with *time point 0*.
6. Discuss the influence of the applied physical activity and glucose solution on subjects' blood glucose levels.

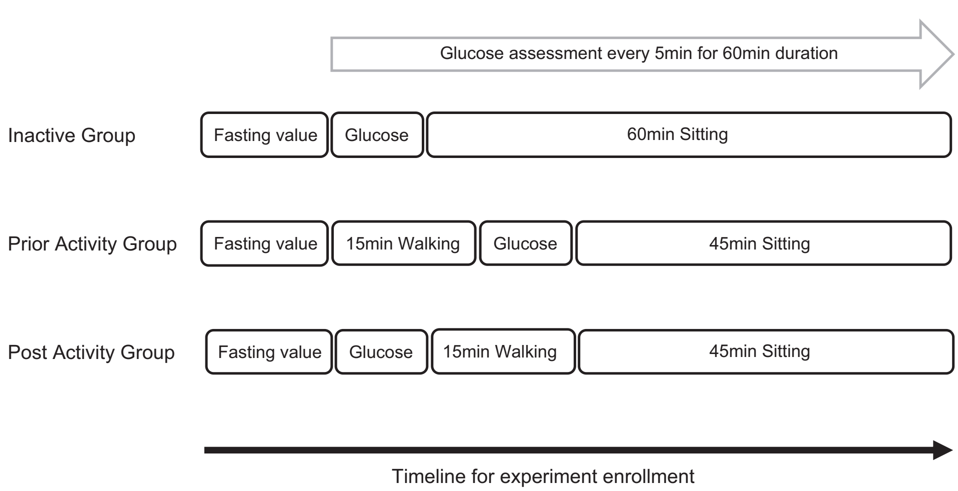

Fig. 1. Timeline of experimental conditions (inactive group, prior activity group, and postactivity group) indicating assessment of fasting value, walking, glucose ingestion, and subsequent sitting time.

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Time Point	Blood Glucose (mg/dl)	HR
Fasting value		
0min		
5min after glucose ingestion		
10min		
15min		
20min		
25min		
30min		
40min		
50min		
60min		
Maximum value ______min		
Minimum value _____ _min		
AUC value		

Fig. 2. Protocol for blood glucose assessment via hand-held device in mg/dl, including slots for fasting value, readings of *time points 0–60 min*, maximal and minimal values (including time points), and area under the curve (AUC). HR, heart rate.

7. Calculate the area under the curve (AUC) based on a linear connection between adjacent time points using the trapezoidal method (5).
8. Determine subjects' minimum (min) and maximum (max) glucose levels and the time to maximum (t_{max}) and minimum (t_{min}) (5).

Differences between trials.

9. Compare the results (AUC, max, min, t_{min}, and t_{max}) of all three trials (prior activity, postactivity, and inactive trial) within your group and describe differences.
10. Discuss possible explanations for the detected differences, i.e., which conclusions about the following subjects can be drawn: *1*) gastrointestinal glucose absorption, *2*) transport and concentration in the blood, *3*) glucose turnover and storage within liver and muscle cells, and *4*) underlying hormonal regulation (insulin and glucagon).
11. Use the flowchart to visualize main metabolic pathways and hormonal influence during trial conditions (Fig. 4).
12. Discuss limitations of the experimental design and methods for analysis (i.e., application of trapezoidal AUC based on linear relation of adjacent time points) (5) and confounders that may had lead to individual differences (consider anthropometric differences, sex, etc.)

After completion of all tasks and questions, the lecturers discussed the results and conclusions with the entire class for 20–30 min.

Evaluation

Students anonymously evaluated the usefulness of the practical session independently of the skills laboratory at the end of the term. The following questions have been used for assessment (4): During the course "Glucose metabolism during exercise and rest: From Mouth to Muscle," a practical experiment was completed. Students were asked to indicate whether the experiment was helpful in learning about glucose metabolism during rest and physical activity by checking one of the alternatives below:

A. The experiment was not necessary for me to understand the learning objectives and did not need to be carried out. By attending the theoretical class and studying the textbook and my notes I had understood all objectives.

B. The experiment was not necessary for me to understand the learning objectives. But it was useful to help me check whether I had understood the content.

C. The experiment was useful to enable me to gain a further understanding of the learning objectives. Although I had understood the content, the experiment enabled me to clarify details and/or allowed me to clear doubts and problems of comprehension.

D. The experiment was necessary to enable me to understand the learning objectives. By attending the theoretical class and studying the textbook and my notes alone I had not understood the learning objectives, and the experiment helped me understand the content addressed.

RESULTS

Answers to Tasks and Questions

Energy expenditure.

1. Calorific value calculation: 75 g/portion × 4 kcal/g = 300 kcal/portion.
2. Basal metabolic rate for men: BMR = 66.5 + (13.75 × weight in kg) + (5.003 × height in cm) – (6.755 × age in yr). Basal metabolic rate for women: BMR = 655.1 + (9.563 × weight in kg) + (1.850 × height in cm) – (4.676 × age in yr).
3. Exercise energy expenditure: 3.8 METS (walking, 3.5 mph, level, brisk, firm surface, walking for exercise; code: 17200) (2). Calculation: (3.8 $kcal \cdot kg^{-1} \cdot h^{-1}$) × (subjects weight in kg) × (0.25-h walking duration).

Blood glucose.

4. Protocol for blood glucose readings is shown in Fig. 2.
5. Example for plot of blood glucose values is displayed in Fig. 3.
6. Possible observations: beginning with 5 min after glucose ingestion, values probably rise until peak is reached during *minutes 20–40*. Thereafter, glucose concentration decreases but remains elevated compared with baseline until end of each trial. During the prior activity trial, exercise might lead to slightly elevated glucose values already at *time point zero*.

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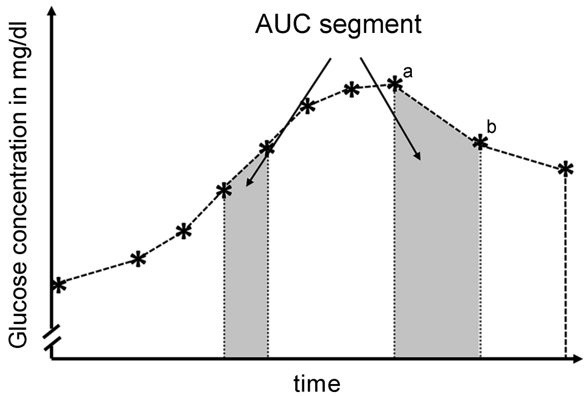

Fig. 3. Example for plot of blood glucose values with time on the *x*-axis and concentration of glucose in mg/dl on the *y*-axis. Exemplary trapezoids for area under the curve (AUC) analysis are displayed as gray areas within dotted lines. [a,b]Time points for an exemplary equation for 1 trapezoid (see *task no. 7* in *Tasks and Questions*); *assessment of blood glucose (each asterisk marks a time point of glucose assessment).

7. AUC calculation (linear trapezoidal method): based on a linear relationship between measurements, for each AUC segment (9 segments within each trial) a trapezoid has to be calculated using the equation stated above (5). Summation of all segments (as displayed in Fig. 2) leads to one overall AUC value for each trial (5). Exemplary equation for one time segment: ½ × (*glucose concentration a* + *glucose concentration b*) × (*time point b* – *time point a*).
8. Based on the linear relationship, subjects' minimum (min) and maximum (max) glucose levels and the time to maximum (t_{max}) and minimum (t_{min}) can be obtained from the protocol (5).

Differences between trials.

9. AUC and maximal values of subjects participating in the postactivity trial might be lower compared with values of inactive trial subjects. Furthermore, differences between the prior activity and postactivity trial might be found. The rise in glucose concentration during the prior activity trial could be increased, leading to shorter time to maximum and higher AUC values. Glucose concentration at the end of trials (*time point 60 min*) might be lower for subjects participating in postactivity trial.
10. *A*) Gastrointestinal glucose absorption could be influenced by physical activity; students should discuss whether absorption might be elevated due to increased overall blood flow or decreased due to lower peripheral vascular resistance and changes in blood flow distribution. *B*) Students should deduce the glucose absorption pathway from the gastrointestinal system into the blood and discuss possible differences of glucose uptake kinetics between trials. *C*) Glucose turnover and storage within liver and muscle cells should be estimated; furthermore, differences in the use of absorbed glucose, liver, and muscle glycogen during pre- and postprandial activity should be discussed, and students should assess how much glucose might be used during physical activity and why prior and postprandial activity might lead to different effects on muscular glucose uptake. *D*) Underlying hormonal regulation (insulin and glucagon) has to be described; students should discuss what impact prior activity might have on glucagon secretion and which interactions of insulin and physical activity might lead to differences observed between trial conditions.
11. The flow chart (Fig. 4) can be used to visualize main metabolic pathways and hormonal influence. Students may use copies of Fig. 4 to mark differences of metabolic pathways and hormonal regulation during the postprandial and postabsorptive state and the influence of gastrointestinal glucose uptake and physical activity. Students should differentiate four different metabolic

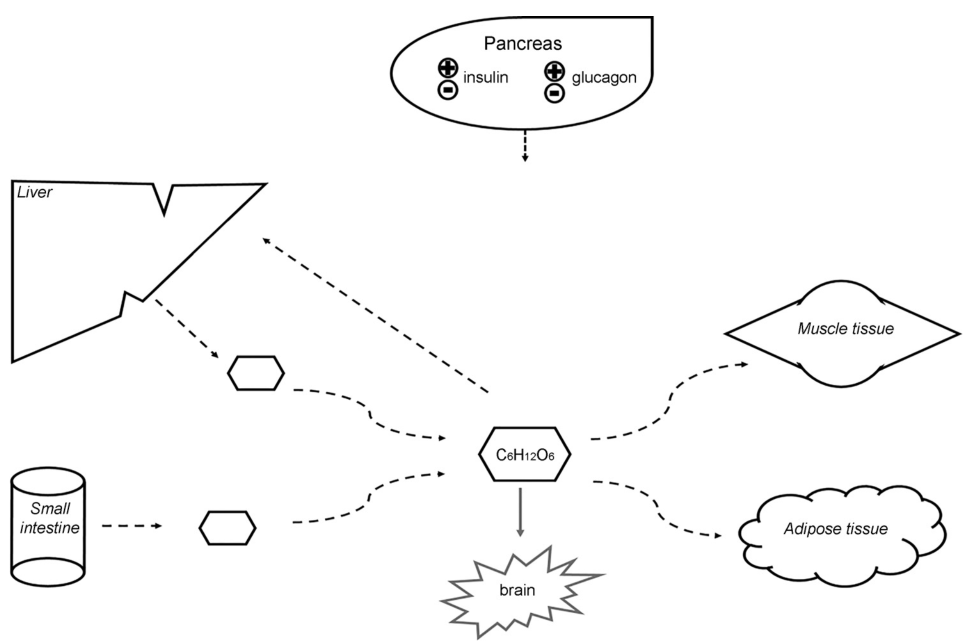

Fig. 4. Plain version of flow chart for metabolic pathways. Students should illustrate metabolic pathways used during different metabolic situations by drawing continuous lines based on the dashed arrows.

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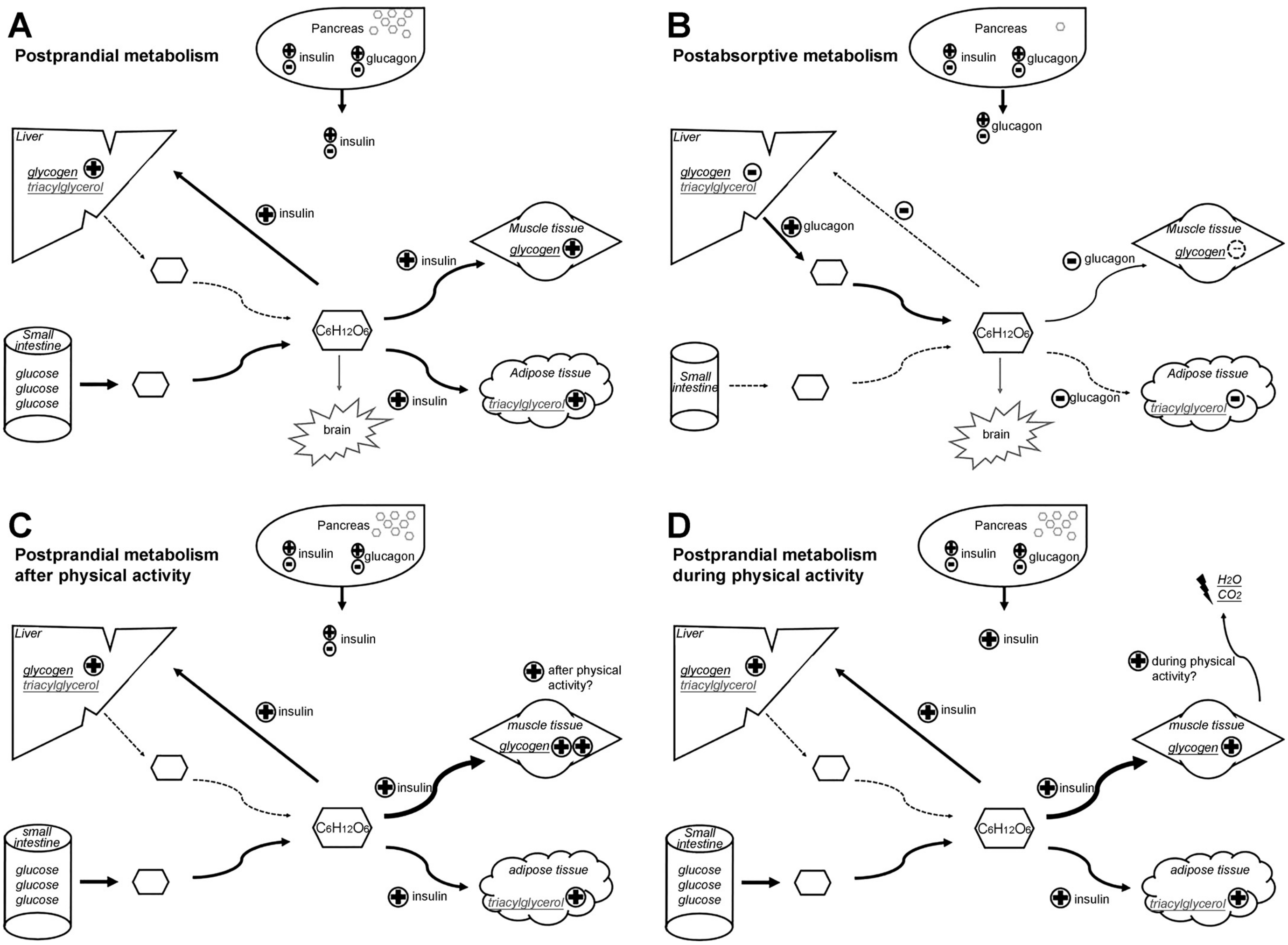

Fig. 5. Flow charts indicating main metabolic pathways for glucose storage or utilization, including effects of glucagon and insulin during postprandial metabolism after glucose ingestion (*A*), postabsorptive metabolism after overnight fasting (*B*), postprandial metabolism after physical activity induced depletion of muscular glycogen and subsequently elevated glycogen synthesis in muscle cells (*C*), and postprandial metabolism during physical activity, which leads to elevated glucose uptake of active muscle cells (*D*).

situations [postabsorptive (fasted) state, postprandial (fed) state, postprandial metabolism after physical activity, and postprandial metabolism during physical activity], which are displayed in Fig. 5. Students may use Fig. 4 for visualization by drawing continuous lines on the dotted arrows to highlight metabolic pathways used primarily during different metabolic situations. Furthermore, students should discuss the importance of glucose as the preferred fuel for neural cells and the impact of acute and chronic carbohydrate depletion on neural metabolism.

12. The noncrossover design without matched trial groups or the use of light physical activity is a major limitation to discuss. Confounders could be anthropometric differences, age, or sex as well as nutritional and physical activity behavior. Trapezodial AUC is used as an approachable and easy-to-understand calculation method, but more complex calculation methods might be more likely to illustrate realistic blood glucose kinetics. Students should be encouraged to discuss possible further analysis and appropriate statistical methods.

Evaluation Results

Students' evaluation of the practical sessions' usefulness for learning purposes showed that the majority of students found the experiment useful to enable them to gain a further understanding of the learning objectives and to clarify items (*answer C*; see *Evaluation*) (54.2%). For 44.1% the experiment was necessary to enable them to understand the learning objectives (*answer D*); 6.8% of the students answered that the experiment was not necessary but helpful to check what they had learned (*answer B*), and only 3.4% found that the experiment was not necessary and did not need to be carried out (*answer A*).

DISCUSSION

This evaluation shows the impact of a practical skills laboratory to supplement theoretical lectures on the perceived knowledge gain in students regarding the topic of energy metabolism within the field of exercise physiology. The majority of students found that the applied experiment was at least useful, if not necessary, to reach the intended learning objectives and clear doubts and problems of comprehension.

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Compared with other fields of human physiology like lung or cardiac function, practical experiments contributing to a better functional understanding of energy metabolism are less well established. The current experiment was developed as one of two lectures on the topic of exercise and energy metabolism within a skills laboratory, which was completed by three lectures covering the physiological background of the neuronal, cardiovascular, and respiratory systems.

Using a simple and cost-effective approach, we were able to illustrate the metabolic pathways from ingestion to intracellular utilization based on the example of glucose. All materials can be obtained easily, and running expenses for glucose strips, lancets, and other expendables are affordable. Because of the moderate intensity, short duration, and type of physical activity and the use of capillary blood, we minimized the risks for students in the role of subjects and investigators. However, students were trained to handle human fluid samples in hygienic laboratory conditions within this experiment.

The applied measurements were selected to provide a clinically oriented setting. Whenever possible, instructors provided background information about application and medical relevance of measurements and testing procedures. Hand-held devices are typically used for glucose or lactate measurements, and handling skills are important for prospective exercise physiologists. The basis for the inactive trial was the oral glucose tolerance test (OGTT) in the variation recommended by the World Health Organization (1) and, therefore, has great practical relevance. However, due to the time schedule, students were able to discuss 1- but not 2-h post-glucose ingestion OGTT values. A bout of 15 min of brisk walking was used as an example for guideline adhered (3) and applicable physical activity.

Due to the applied methods, students received an introduction in the sufficient analysis of serial measurements using a two-staged method for summary measures (AUC) and peak data analysis (max, min, t_{max}, t_{min}) (5). Within the setting of this course it was of great importance for the instructors to play an active part but not to give complete solutions during students' analysis and discussion within the work groups.

Interpretation of Metabolic Mechanisms

Based on the experimental conditions, students defined four basic metabolic states within two subsequent parts of a learning process. First, the students outlined metabolic pathways and the hormonal influence during fasting and fed situations, with the goal to define *1*) a postabsorptive (fasted) and *2*) a postprandial (fed) state. For some students, this part was mandatory to understand why glucose ingestion led to elevated glucose values and how steady glucose values were maintained during fasted state. The students had to discuss details of pancreatic insulin secretion and its effects on glucose uptake, glycogen synthesis in liver and muscle cells, and the conversion of glucose into fatty acids. Furthermore, they had to define possible glucose sources during the postabsorptive state and the influence of glucagon on glycogenolysis and gluconeogenesis. Using this approach, students were able to differentiate catabolic and anabolic pathways within muscle and liver cells as well as adipose tissue and the influence of insulin and glucagon.

For the second part of the learning process, the students used this basis to differentiate the use of internal and external glucose sources during *3*) postabsorptive physical activity and *4*) postprandial physical activity. The instructors placed particular value on the metabolic differences between fasted and fed exercise. Therefore, the students had to outline relevant metabolic pathways for both conditions on two different versions of Fig. 4. Using this concept, the students were able to deduce further metabolic consequences of physical activity. Most importantly, students had to differentiate the influence of postprandial and postabsorptive physical activity on insulin sensitivity. Students discussed by which pathways physical activity may have a greater influence on insulin sensitivity and non-insulin-dependent glucose uptake: *a*) postprandial activity, directly using ingested glucose within active muscle cells, or *b*) postabsorptive activity, leading to glycogen depletion and subsequent glycogen synthesis.

During the experiment, the instructors were able to detect and clarify some major misconceptions and problems of comprehension. Using the obtained data and learning materials like flow charts, the students were able to define and differentiate the role of liver and muscle glycogen and the utilization and storage of ingested glucose during rest and physical activity. Furthermore, students managed to identify the regulatory influence of insulin and glucagon on glucose transport, utilization, and storage. Instructors used this basis to discuss more complex topics like the function of passive glucose transporters within muscle cell and pancreatic β-cell membranes with the whole class.

Strengths and Weaknesses

A limitation of this experiment is that the applied physical activity is a rather small metabolic stimulus. In some of the student groups, anthropometrical differences between subjects led to insignificant differences between active and inactive trials. Higher intensity or longer duration could provoke greater differences between the trial conditions but may lead to a greater risk of injuries or adverse events. It was important to discuss the limitations and the exemplary character of the applied experiment to enable the students to deduce the effects of physical activity with higher intensity and longer duration on glucose metabolism.

We decided not to include specific information about fat metabolism to define clear learning objectives. Nevertheless, the influence of fat metabolism was discussed during most of the courses. To avoid excessive demands for the students, instructors advised the work groups to consciously exclude the issue during some parts of the discussion. Further studies could evaluate experimental designs on the topic of fat metabolism and should evaluate students' achievement of learning outcomes via objective data (i.e., exam scores).

Conclusion

The participation as investigators and subjects put students in the center of a teaching/learning process. Because of the combination of practical and theoretical elements, the instructors were able to promote the engagement of students with different skill sets. The course was designed to stimulate more kinesthetic students with a hands-on approach as well as auditory- and talking-oriented learners using the tasks and questions combined with a subsequent discussion. In conclusion, the present article shows the great value of student

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experiments and practical courses to help students gain knowledge and understand complex tasks using an active learning strategy and to improve beneficial communication and interaction between students with different skill sets and problem-solving strategies.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

T.E. and J.F. performed experiments; T.E. analyzed data; T.E., J.F., and W.B. interpreted results of experiments; T.E. prepared figures; T.E. and J.F. drafted manuscript; T.E., J.F., and W.B. edited and revised manuscript; T.E., J.F., and W.B. approved final version of manuscript.

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