"But We Don't Have Beta-Cells": Agent-Based Models to Support Health Education

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Abstract: This paper seeks to support science learning within the health-related education, the diabetes education domain. With this aim, we evaluated the impact of deep biochemical understanding on behavioral patterns of young patients with type 1 diabetes. The findings propose, a strong significant correlation between youths causal biochemical understanding to their behavioral patterns of glucose self-regulation. Consequently, in order to promote this biochemical understanding, we introduce an agent-based learning environment (SimDCell) which supports exploration of glucose equilibrium interactions that facilitate relation and connection of the biochemical processes to youth with type 1 diabetes own body functioning and to their daily based medical decisions.

Introduction

Health-related education has thus far occupied a modest space in the learning sciences (e.g. Reeve & Bell, 2009; Ching & Schaefer, 2015). To encourage additional learning sciences research in health education and to demonstrate the potential of applying existing approaches in this space, this paper presents an agent-based modeling approach to teaching the biochemical processes relating to the treatment of type 1 diabetes.

Type 1 diabetes mellitus (T1DM) is a life-threatening, chronic illness that affects youth and requires lifelong insulin therapy. The youth and their families must develop new routines for monitoring and tracking of blood glucose data (Lee, Thurston & Thurston, 2017). To maintain the delicate balance of blood glucose levels, adolescents must quickly learn to apply complex disease-related knowledge to daily self-treatment decisions. Much is still unknown about how learning interventions could better support type 1 diabetes management, a known problem for adolescent youth.

In response to this problem, we hypothesized that increased causal understanding of the biochemical processes underlying blood glucose might improve adolescents' glucose self-regulation. Based on the cross sectional study results, described below, this hypothesis appears to be supported. In light of this finding, we have developed an agent-based modeling environment, the Simulated Diabetes Cells (SimDCell), as a tool to support youth with type 1 diabetes examine and learn more about biochemical processes related to their disease. In this paper, we present vignettes from a single youth with type 1 diabetes interacting with this tool to illustrate the kinds of connections and discoveries characteristics that could be made with such an environment.

Simulated Diabetes Cells (SimDCell) learning environment

The SimDCell learning environment was designed in NetLogo (Wilensky, 1999), an agent-based modeling (ABM) environment, which is extensively used to model complex systems in science and to support learning about systems in classes (e.g., Dubovi, Dagan, Sader-Mazbar, Nasar & Levy, 2018; Jacobson & Wilensky, 2006; Levy & Wilensky, 2009). Complex systems are comprised of numerous micro-level entities, whose interactions emerge into a higher-order behavior, a macro-level phenomena. The diabetic process and its medical treatment is a prime example of a complex system. Many different molecules interact with one another, with drug molecules, and with normal body processes leading to the emergence of therapeutic or toxic effects. Medications are aimed at restoring physiological factors that maintain equilibrium in the body. However, equilibrium, as a complex phenomenon, is difficult to teach and to understand (Zion & Klein, 2015), since it encompasses dynamic processes that take place while the system is at a constant state.

The SimDCell learning environment is comprised of multiscale biochemical models embedded in a pedagogically-supportive e-learning management system (Figure 1). These agent-based models simulate the relevant anatomy of glucose equilibrium. Two central representations were used: 1) cell models (pancreas cells, muscle cells and liver cells), and 2) plots showing the numbers of various molecules. Each cell model includes the main organelles and molecules that participate in the metabolic processes and insulin mechanisms that maintain blood glucose equilibrium. The models are used to demonstrate the effects of various activities and diets on both healthy and T1DM body functioning. Participants can add different doses of insulin-based medications,

manipulate multiple characteristics and habits (such as fasting or sport activities), and observe the subsequent body reaction. The plots show the number of insulin and glucose molecules in the various relevant body parts. The use of multiscale models enables participants to zoom in on each type of cell separately or to zoom out to view how the different types of cells work synchronously for a more comprehensive exploration of glucose equilibrium.

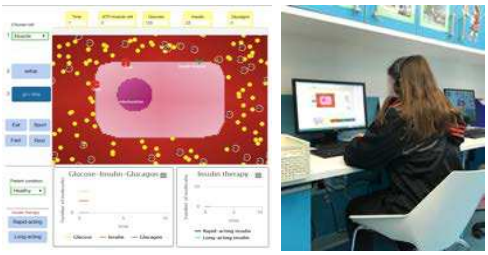

Figure 1. A screenshot of SimDCell environment and a picture of adolescent learning with the environment.

Methods

Research design and participants

A mixed methods approach was used to understand the relationship between adolescents' biochemical knowledge and glucose control effectiveness. We conducted a cross sectional employed research with type 1 diabetes adolescents between 12 and 18 years old (n=55) who are treated at the diabetes clinic in a large hospital in northern Israel. The sample comprised of patients who are treated with either insulin pump (n=34; 61%) or with multiple injections (n=21; 39%), and lived with T1DM for an average of 5±3.4 years. To examine how adolescents might use the SimDCell environment to learn about their disease, we employed case study methods with a 13-year-old female participant, "Michelle".

Data collection instruments and data analysis

The cross sectional study

Diabetic biochemical knowledge. We designed three open-ended questions to evaluate adolescents' knowledge about biochemical processes of glucose equilibrium. The *first question* asked participants to describe the role of insulin within human body by using terms such as cell, receptor, transporter, energy, ATP, etc. The *second question* presented the case of "John", who has T1DM and is currently experiencing high blood glucose levels. The participants were asked to explain whether high blood glucose levels enable John's cells to produce more energy compared to a heathy body. The *third question* asked the participants to describe the differences between insulin secreted from a human pancreas and insulin administered as a treatment. The content of the items was reviewed by diabetes experts to ensure accuracy. The language of the items was compared to school science curricula to ensure they were written at an appropriate level for the young participants. The responses were coded as correct or incorrect, and the total score was calculated as the percentage of correct answers.

Glucose control. Glycosylated Hemoglobin (HbA1C) is a blood test which estimates the glucose level average over a period of 2-3 months. HbA1C was obtained from the patients' medical records. In order to prevent diabetic complications, the clinic guidelines' recommendation for all adolescents is to keep HbA1C below 7.5% which is equivalent to a blood glucose level of 169 mg/dl.

Case study

For the case study, we used screen recording software to capture Michelle's interactions with the SimDCell learning environment. While leaning with SimDCell, Michelle was asked to use a think aloud protocol, with additional information elicited by a supporting researcher. A video-based discourse analysis was conducted to explain the interaction between the young participant, the learning environment, and the researcher (Jordan & Henderson, 1995). The researchers carefully transcribed then coded each video entry. The resulting codes were compiled into a codebook for illuminating how the participant used the provided data representations, how she interpreted the processes depicted, and how she resolved conflicts raised when comparing the SimDCell representations with her own bodily experiences.

Results

The association between biochemical knowledge and glucose control

A significant negative correlation was found between the level of biochemical knowledge and the glucose balance as measured by HbA1C (Pearson r =-0.57, p<0.001) among adolescents who used the insulin pump for treatment. Hence, the higher the biochemical understanding the lower HbA1C, which means better metabolic control. No significant difference was found among adolescents using treatment based on multiple daily injections (Pearson r =-0.23, p=0.29).

Learning with multiscale biochemical models

When introduced to the SimDCell learning environment, Michelle quickly began to manipulate the model cells. The learning environment was designed to expose the sophistication of the cell models gradually. On the first screen, only a single muscle cell is displayed; on subsequent screens, users can manipulate new characteristics and new organelles and cells are revealed. Michelle was eager to explore the new features of the model to advance through the screens. After exploring the muscle cell, Michelle moved to another screen to explore a beta (pancreas) cell. After a quick inspection of the cell model, Michelle's attention fell quickly to the presence of insulin in the cell representation.

Michelle:	[pointing to the beta cell model] So, if this cell is not insulin dependent, why does it still have an insulin inside it?
Researcher:	Please try to switch to the muscle cell, and then compare between the cells, between the beta and the muscle cells. [Michelle switches to the muscle cell, clicks several different buttons, then observes the effects for several seconds]
Michelle:	I see… The beta cell produces insulin and then secretes it. While the muscle cell uses this insulin as a mediator for glucose entrance within the cell.
Researcher:	[pointing to the beta cell] Now try to add glucose by clicking inside the model and see what happens.
Michelle:	[clicks rapidly on the screen, which creates multiple glucose molecules] It's fun! See… I filled it with glucose. [pauses for observation] More insulin is secreted now. Ah, I see, that's actually what is happening within a healthy body. *But we (people with type 1 diabetes) don't have beta cells*, *so we don't secrete insulin*. Here they called it bolus, we also call our injections "bolus". Only here it's a bolus of insulin in a healthy body.

By giving Michelle the opportunity to explore the function of muscle and beta cells and compare them, SimDCell prompted Michelle to compare the representations and the interactions to the function of her own body. Moreover, she was able to comprehend that the insulin bolus that she receives multiple times a day is actually a mimic of the insulin bolus secretion from a healthy pancreas. The understanding of normal beta cell function helps to clarify reasons for the T1DM insulin regimen, which includes different injections during the day. In the next excerpt, Michelle explores the function of another molecule she had used in her treatment—glucagon.

Michelle:	[exploring the liver cell at the model] I understand now. When insulin is attached to its receptor on the liver cell membrane, then the glycogen is constructed from glucose. And when glucagon is attached, it causes the breakdown of glycogen.
Researcher:	So then, why do you think you have to carry glucagon injections with you?
Michelle:	*So, when I am passing out*, the glucagon takes the glycogen out of the liver cell and breaks it down to glucose molecules, and then the blood glucose level will rise.
Researcher:	I hope you won't pass out.
Michelle:	*But if we, people with diabetes*, have normal glucagon in our body, why do we need these injections of glucagon if we already have it?
Researcher:	Try it with the model. See what happens when the model cells are in hypoglycemia.

Exploration of cells models in the SimDCell environment gave Michelle the opportunity to relate complex understanding of glucose equilibrium toward her own body and make sense of treatments that she is receiving (e.g., glucagon kit that she carries with her).

Discussion and conclusion

This study among adolescents with type 1 diabetes provides preliminary results showing the importance of young patients having causal biochemical knowledge about their disease (Lee et al., 2017). Our findings show that adolescents' glucose levels, measured by HbA1C, were significantly and strongly associated to the adolescents' causal understanding of biochemical processes. That is, when the level of biochemical understanding was higher, the glucose balance was better, i.e., the HbA1C was lower. A closer look at our data suggests this effect is true only for patients whose treatment is based on the insulin pump. This can be explained by the greater number of decision-making processes that insulin pump users have to make compared to treatment with multiple daily injections. Administration of insulin through multiple daily injections is based on blood glucose levels only, while insulin pump treatment also requires increased glucose monitoring, counting dietary carbohydrates and judging the impact of exercise on insulin infusion rates. This additional consideration illuminates the importance of causal biochemical understanding for such complex daily decisions.

The current study also builds upon previous research regarding the value of exploring computer models for science learning (e.g., in physics: Sengupta & Wilensky, 2009), by extending it to understand how models based on a complex-systems perspective may support adolescents learning to self-regulate their diabetes. The SimDCell environment is a novel approach in diabetes education and helps adolescents draw connections between pathophysiological-biochemical processes and their application to diabetes treatments. As they explore dynamic cell models, young people are able to relate the processes represented in the models to the functions of their own body and improve their mechanistic understanding about diabetes. More research is needed to explore the relation of casual biochemical explanations of a disease management and consequent health outcomes.

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