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Nursing students learning the pharmacology of diabetes mellitus with complexity-based computerized models: A quasi-experimental study

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ABSTRACT

Background: Pharmacology is a crucial component of medications administration in nursing, yet nursing students generally find it difficult and self-rate their pharmacology skills as low.
Objectives: To evaluate nursing students learning pharmacology with the Pharmacology Inter-Leaved Learning-Cells environment, a novel approach to modeling biochemical interactions using a multiscale, computer-based model with a complexity perspective based on a small set of entities and simple rules. This environment represents molecules, organelles and cells to enhance the understanding of cellular processes, and combines these cells at a higher scale to obtain whole-body interactions.
Participants: Sophomore nursing students who learned the pharmacology of diabetes mellitus with the Pharmacology Inter-Leaved Learning-Cells environment (experimental group; $n = 94$) or via a lecture-based curriculum (comparison group; $n = 54$).
Methods: A quasi-experimental pre- and post-test design was conducted. The Pharmacology-Diabetes-Mellitus questionnaire and the course's final exam were used to evaluate students' knowledge of the pharmacology of diabetes mellitus.
Results: Conceptual learning was significantly higher for the experimental than for the comparison group for the course final exam scores (unpaired $t = -3.8$, $p < 0.001$) and for the Pharmacology-Diabetes-Mellitus questionnaire ($U = 942$, $p < 0.001$). The largest effect size for the Pharmacology-Diabetes-Mellitus questionnaire was for the medication action subscale. Analysis of complex-systems component reasoning revealed a significant difference for micro-macro transitions between the levels ($F(1, 82) = 6.9$, $p < 0.05$).
Conclusions: Learning with complexity-based computerized models is highly effective and enhances the understanding of moving between micro and macro levels of the biochemical phenomena, this is then related to better understanding of medication actions. Moreover, the Pharmacology Inter-Leaved Learning-Cells approach provides a more general reasoning scheme for biochemical processes, which enhances pharmacology learning beyond the specific topic learned. The present study implies that deeper understanding of pharmacology will support nursing students' clinical decisions and empower their proficiency in medications administration.

1. Introduction

Registered nurses are the primary practitioners accountable for the daily preparation and administration of approximately 7000 medication doses and devote 20 to 40% of their time to this task (Westbrook et al., 2011). Near-error situations and adverse events are disproportionately associated with treatment by novice registered nurses (Hickerson et al., 2016). Therefore, a solid and fundamental knowledge of generic drug names and classes, indications of use, dosages and side effects, pharmacokinetics[1] and pharmacodynamics,[2] food and drug interactions, and the medication-administration process should be grounded in nursing education and training (Choo et al., 2010). Teaching safe and effective pharmacotherapy is challenging, however; it is strongly based on the interactions between basic science concepts

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[1] Pharmacokinetics is the study of drug concentrations during the processes of absorption, distribution, biotransformation, and excretion (McKenry et al., 2006). It is common to define these interactions as actions of the body on the drug.

[2] Pharmacodynamics is the study of interactions with specific macromolecular components in tissues, typically receptors (McKenry et al., 2006). It is common to define these processes as actions of the drug on the body.

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of the relevant physiology, anatomy, pathology, and microbiology (Banning and Cortazzi, 2004). Several studies have shown nursing curricula missing the required foundation of knowledge to undertake drug administration effectively and nurses lacking adequate knowledge of pharmacology (Meechan et al., 2011; Ndosi and Newell, 2009). Nurses and nursing students generally find pharmacology to be interesting but difficult, and they self-rate their pharmacology skills as low, especially for pharmacokinetics and pharmacodynamics. Studies have described the traditional education approach as causing "confusion, disinterest, inattentiveness … culminating in underachievement and poor learning outcomes" (Charles and Duffull, 2001; Dilles et al., 2011, p. 396). These findings call for implementing innovative teaching concepts to replace the traditional pharmacology courses methodology (Lim et al., 2014; Thomas and Schuessler, 2016).

1.1. Conceptual Understanding Through the Lens of Complex Systems

The domain of complex systems has evolved rapidly in the past 25 years with the development of novel ideas and tools and new ways of comprehending phenomena via basic and life sciences, computer science, and many other fields. Complex systems comprise micro-level entities (often referred to as *agents*), which interact with each other and with their environment. The interactions of numerous submicroscopic elements result in a higher-order or global behavior, a macro-level phenomenon. Such systems are emergent; although they are not regulated through a central control, they self-organize in coherent global patterns (Holland, 1995; Kauffman, 1995).

A pharmacological process is a prime example of a complex system. Many different molecules interact with one another, with drug molecules (pharmacodynamic processes), and with normal body processes (pharmacokinetic processes) that lead to the emergence of therapeutic or toxic effects (Katzung et al., 2011). Moreover, medications actions are aimed at restoring physiological factors that maintain homeostasis in the body. Homeostasis, as a complex phenomenon, is difficult to teach and to understand (Jacobson and Wilensky, 2006; Zion and Klein, 2015). Since homeostasis means dynamic stability of conditions, it is difficult to understand that equilibrium is a dynamic state (Katzung et al., 2011). Moreover, biological-physiological mechanisms occur simultaneously within interrelated and interdepended systems (such as blood glucose level and condition of stress) (Zion and Klein, 2015). Physiological homeostasis becomes even more complex when abnormal states of multiple morbidities and pharmacological processes change its level. These pharmacodynamic and pharmacokinetic nonlinear interactions within the body's homeostasis are unique for each medication and vary for different patient clinical conditions.

This paper presents the Pharmacology Inter-Leaved Learning-Cells (PILL-Cells) model-based learning environment, which enables students to learn the multi-level biochemical concepts related to diabetic mellitus drug actions, using agent-based computer models (Fig. 1) (Dubovi et al., 2014). The PILL-Cells environment was designed as part of a larger educational architecture aimed at bridging the gap between theory and practice in academic teaching for the nursing profession. The current study builds upon previous research on the value of computer models for learning science, by extending it to understand how models based on a complex-systems perspective may support pharmacology learning. Unique to the design of the computer models included in the environment are two factors. First is the complex-systems-based approach that parses the system to individual micro-level entities (e.g., molecules) and global macro-level phenomena (e.g., hypoglycemia). Second is the multi-level approach: interactions between molecules and organelles emerge into the cell's functioning; interactions between cells in distinct organs emerge into the function of organism as a whole. We hypothesized that double-staged presentation of mechanisms of human organisms increases the learnability of diabetic drug actions.

We selected the diabetic mellitus matter due to the multilevel and complex nature of the glucose–blood equilibrium, its dysregulation with respect to the molecular level and metabolic mechanisms, the organs it involves, and the requirement of polypharmacy management and intensive follow-ups (Bauer and Nauck, 2014).

1.2. Research Aim

The purpose of this study is to evaluate the effectiveness of multi-scale agent-based computer models for complex-systems levels of thinking to support nursing students' learning pharmacology, specifically diabetes molecular and somatic mechanisms and treatment-related medications. Moreover, in the current study we evaluate the use of the computer model environment in transferring conceptual pharmacology knowledge and complex-systems thinking to related topics of pharmacology other than diabetes mellitus.

2. Methods

2.1. Research Design

We conducted a quasi-experimental pre- and post-test design using a quantitative approach.

2.2. Participants and Procedure

Participants included volunteer sophomore nursing students who were attending the traditional lecture-based pharmacological course of 56 h in 14 weeks during the fall semester. The study comprised two groups of students: (1) an experimental group, who learned via the PILL-Cells diabetes pharmacology computer models for approximately 3 to 4 h (Fig. 1); and (2) a comparison group, who learned via the diabetes pharmacology lecture-based curriculum for a total of 4 h. The experimental group included 100 students. Of these, 94 (94%) students completed both the pre- and post-test questionnaires. The comparison group included 80 students, of whom 54 (68%) had taken both the pre- and post-test evaluations. Together, 148 students completed the pre- and the post-test evaluations.

The comparison group was recruited 1 year before the experimental group. Pre- and post-test evaluations were undertaken at the beginning and at the end of the semester (2 months before and 1 month after the activities on the last day of the semester). There were no statistically significant differences in demographic characteristics and baseline academic achievements between the experimental and the comparison groups (Table 1).

2.3. Data Collection Instruments

2.3.1. Pharmacology PILL-Cells Environment

We used an agent-based modeling (ABM)[3] computational paradigm, which is extensively used in the domain of complex systems. ABM has been applied to a wide range of biological and biomedical experiments, particularly for modeling pathophysiological processes with a significant spatial component (An and Wilensky, 2009; Bauer and Nauck, 2014; Bhattacharya et al., 2012). NetLogo[4] is one such modeling environment and was used to construct our PILL-Cells environment (Dubovi et al., 2014; Wilensky, 1999).

Learning with the PILL-Cells environment models was guided by worksheets that provided nursing scenarios, explained the

[3] ABM is a computational modeling paradigm that simulates complex dynamic systems by simulating each of their many autonomous and interacting elements (called entities or agents). By observing and experimenting with agent behaviors and interactions (micro-level), we demonstrate and understand the collective behavior (macro-level) that results from the aggregation of the individual behaviors and interactions.

[4] NetLogo is a widely used, general-purpose, open-source ABM language that enables users to explore and construct models of complex systems (http://ccl.northwestern.edu/netlogo).

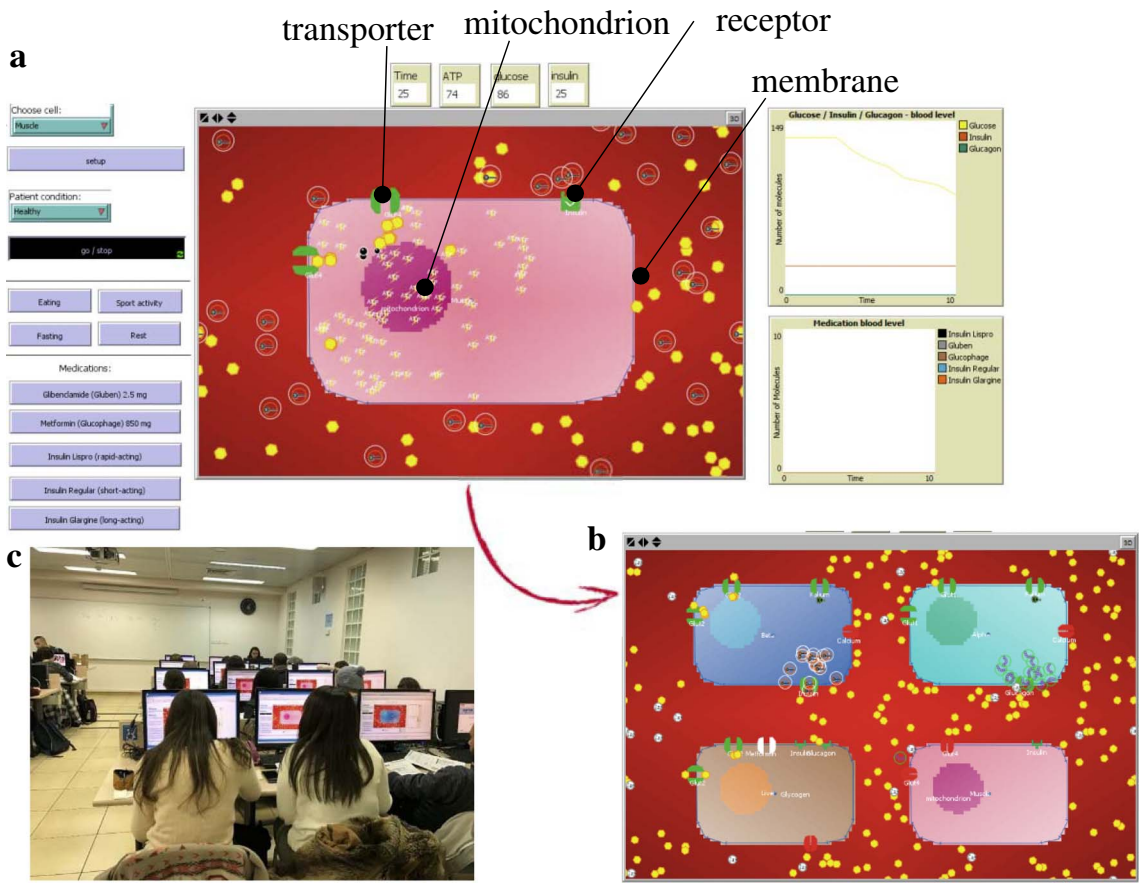

Fig. 1. The PILL-Cells environment and picture of students learning with the environment.
a and b. The PILL-Cells environment is a suite of multiscale molecular, cellular and organ interaction models within the sick or healthy cell organ. Using agent-based computer models, students can investigate the biochemical multi-level processes of medications. Students can zoom in on one cell type or zoom out on the four cell types responsible for glucose equilibrium (link for model sample of PILL-Cells environment: http://simnurse1.haifa.ac.il/Cells.html).
c. Nursing students learning pharmacology with the PILL-Cells environment. The learning included exploration of computerized models with guided activities.

Table 1
Demographic characteristics and university entrance and course achievements: comparisons between the experimental and comparison nursing student groups.

Demographics	Total sample (n = 148)	Experimental group (n = 94, 64%)	Comparison group (n = 54, 46%)	Statistics[a]
Age (years) (Mean ± SD)	23 ± 3	22.9 ± 2.8	22.7 ± 2.3	0.50 (p = 0.62)
Gender (n, %)				
Female	110 (74)	69 (73)	41 (76)	0.20 (p = 0.43)
Male	38 (26)	25 (27)	13 (24)	
Origin (n, %)				
Arabs				
Muslim	60 (40)	36(39)	24 (44)	1.2 (p = 0.73)
Druze	10 (7)	5 (5)	5 (9)	
Christian	29 (20)	20 (21)	9 (17)	
Jewish	47 (32)	32 (34)	15 (28)	
Other	2 (1)	1 (1)	1 (2)	
Entrance tests results to nursing school (Mean ± SD)				
Psychometric entrance-test score[b]	626 ± 43	604 ± 49	594 ± 41	0.28 (p = 0.77)
Hebrew test score (YAEL test)[c]	115 ± 12	113 ± 12	116 ± 10	− 1.36 (p = 0.17)
Course tests results during the first year (Mean ± SD)				
Chemistry course score	70% ± 24	67% ± 16	75% ± 34	− 1.9 (p = 0.07)
Microbiology course score	87% ± 9	88% ± 8	86% ± 8	0.74 (p = 0.45)
Cell-biology course score	91% ± 8	91% ± 8	91% ± 8	0.35 (p = 0.75)
Biology course score	90% ± 9	91% ± 8	89% ± 10	0.58 (p = 0.6)

Numbers represented: N (%) or Mean ± SD.
[a] Based on Chi-square test or independent sample t-test as appropriate.
[b] Psychometric Entrance Test is a standardized test in Israel, generally taken as a higher education admission exam. It covers three areas: mathematics, verbal reasoning, and English language.
[c] The YAEL test is a Hebrew-proficiency test. Students who take the Psychometric Entrance Test in any language other than Hebrew are also required to take the YAEL test. Here we report the mean scores of 27 students in the comparison group and 50 in the experimental group who took the YAEL test.

representations, called attention to particular events in the models, encouraged closed and open experimentation and, finally, required students to answer questions and to draw conclusions. Students explored the PILL-Cells environment, which consists of two central representations (Fig. 1): cell models and plots.

The cell models include four types of cells: *pancreas* (2 types), *muscle*, and *liver*. Each cell in the model represents the specific organelles and molecules that participate in the metabolic processes of the medication mechanisms involved in the blood-glucose-level equilibrium: (a) the *pancreas cells*, which include two cell types: alpha cells, responsible for glucagon secretion, and beta cells, responsible for insulin secretion; (b) the *muscle cells*, which normally use glucose for glycolysis (the pathway for producing ATP, or energy), via a complex mechanism which is mediated by insulin; and (c) the *liver cells*, which store glucose in glycogen molecules and generate glycogen breakdown in the glycolysis mechanism when blood glucose is low. The models can be used to explain healthy and diabetes mellitus type 1 or type 2 body functioning; they enable students to administer medications in different doses and to manipulate a patient's characteristics and habits, for example fasting or sport activity. Students can then observe the subsequent bodily reaction. Moreover, using these multiscale models allows students to zoom in on each cell type separately or to zoom out for a more comprehensive exploration of the glucose equilibrium by viewing how the four different types of cells interact. This ability to manipulate and to easily and repeatedly explore the diverse activity of the cell types in the model enables students to integrate biochemical reactions and glucose equilibrium, the relevant anatomy and physiology, and the different medications and patient behaviors.

The plots show the macro-level amounts of insulin, glucose, and medication molecules in the various relevant cell types. As the plots reflect an actual global count of the molecules in the models at each moment, they can easily be related to what is viewed as happening in the cells (Fig. 1).

We expected that exploration of multiscale cell models with guided activities would support causal understanding of the system based on the student's earlier biology and biochemistry knowledge. We also expected that the plots would connect to and bridge between the cell models and real healthcare situations. We hypothesized that the connection to real-world situations would support students' understanding of patients' glucose and medication levels during a medication-administration process. Thus, they would be able to make sense of and relate the interactions between medication molecules and the body's cells to the body's global behavior in terms of pharmacokinetics and pharmacodynamics.

2.3.2. Pharmacology-Diabetes Mellitus Questionnaire

The Pharmacology-Diabetes Mellitus questionnaire (PDM) questionnaire consists of 11 questions (8 multiple-choice, 3 open-ended) developed specifically for this study. The items were validated by experienced lecturers in our nursing department to ensure appropriate alignment of context and content and a suitable level of expertise. The questionnaire evaluates two dimensions: conceptual pharmacology knowledge, and components of complex-systems thinking.

The conceptual pharmacology content is divided into three subscales of pharmacology-diabetes medications: (1) glucose equilibrium, (2) glucose disequilibrium (diabetes mellitus disease), and (3) medications actions — influence on glucose equilibrium and side effects (Supplementary material). These three components build upon each other through a nesting relationship whereby glucose equilibrium is nested within glucose disequilibrium and both are part of the medications actions' component. This enables us to test students' proficiency with increasingly sophisticated problems.

The components of complex-systems thinking comprise three open-ended questions analyzed according to the construct of levels in a complex system (Jacobson, 2001; Wilensky and Resnick, 1999): (1) micro level, (2) macro level, and (3) transition between micro and macro levels.

Analysis of the PDM questionnaire using Cronbach's alpha yielded an internal consistency score of 0.71.

2.3.3. Course Final Exam

To evaluate transfer of conceptual pharmacology knowledge and complex-systems thinking to other related topics of pharmacology, we used the course's final exam, consisting of 40 questions related to the basic principles of pharmacology, organized according to body systems: (1) endocrine drugs (e.g., antidiabetic drugs), (2) cardio-vascular renal drugs (e.g., antihypertensives), (3) drugs that act on the central nervous system (e.g., analgesics), (4) chemotherapeutic drugs, and (5) other drugs (e.g., drugs for HIV and gastrointestinal diseases). The exam was written and validated by the course lecturers.

2.3.4. Demographic Questionnaire

A demographic questionnaire collected information about the participants' gender, age, religion, and previous work experience in health organizations. We also collected participants' entrance-test results and course tests results during the first year of nursing school.

2.4. Statistical Analysis

Responses to the PDM questionnaire were analyzed for the two dimensions of pharmacology concepts and complex-systems components. For the pharmacology concepts, responses were coded as correct or incorrect, and the total score was calculated as the percentage of correct answers. The pre- and post-test results were analyzed with descriptive statistics (Mean, SD). Learning gains were calculated for each student as post-test score minus pre-test score. Then, descriptive statistics for learning gains (Mean, SD) were calculated for the experimental and the comparison groups. Learning gain scores were compared using a Mann–Whitney U test for non-parametric data with an effect size as r (Fritz et al., 2012). For the complex-system components dimension, the pre- and post-test answers for the three open-ended questions were coded based on three central complex-system components: whether the system was described at the micro level (molecules, recaptures, transporters, and cells; for example, “There is no insulin; hence the glucose can't enter the cell and the ATP is not produced”), the macro level (system-wide properties and organs; for example, “High glucose level can harm different organs like neuropathy and retinopathy and nephropathy”); or transition between micro and macro systems (e.g., “During physical activity, the body needs more energy. The energy carried by the ATP molecules is produced during cell respiration”). For each participant, the number of system-reasoning components was calculated and analyzed with descriptive statistics (Mean, SD). Interaction effects between groups were evaluated using repeated measures ANOVAs. Final exam scores and their subscales for the experimental and comparison groups were compared using unpaired t-tests.

3. Results

To confirm the validity of our sample, we compared students who completed both the pre- and the post-test questionnaire to students who did not complete the post-test questionnaire. For the experimental study group, no significant difference was found in the pre-test scores between students who did not complete the post-test questionnaire and those who completed both the pre- and the post-test evaluations ($t = 1.18$, $p = 0.26$). Similarly, at the comparison group no significant difference was found for the pre-test scores between students who did not complete the post-test questionnaire and those who completed both evaluations ($t = -0.85$, $p = 0.40$).

3.1. Diabetes-Related Conceptual Knowledge

Results of the PDM pre- and post-test questionnaires are presented

Table 2
Comparisons of pre-test and post-test Pharmacology-Diabetes Questionnaire results: scores and learning gains for the two student nursing groups (N = 148).[a]

	Pre-test scores		Post-test scores		Learning gain[b]		Statistical tests	
	Exp. (n = 94)	Comp. (n = 54)	Exp. (n = 94)	Comp. (n = 54)	Exp. (n = 94)	Comp. (n = 54)	Mann–Whitney U	Effect size, r
Overall	34 ± 17	32 ± 17	75 ± 12	36 ± 24	39 ± 17	4 ± 23	662***	0.62
Subscales								
Glucose equilibrium	17 ± 25	16 ± 22	64 ± 31	20 ± 28	46 ± 38	4 ± 35	1072***	0.44
Disturbance of glucose equilibrium (diabetic mellitus diseases)	53 ± 33	44 ± 34	90 ± 16	48 ± 34	38 ± 34	5 ± 41	1321***	0.37
Medications actions	35 ± 22	36 ± 24	70 ± 17	39 ± 29	35 ± 29	3 ± 32	1197***	0.49

Exp., experimental group; Comp., comparison group.
[a] Data are presented in percentage Mean ± SD, range 0–100.
[b] Learning gain was computed to compensate for differences in prior knowledge of PDM questionnaire (postscore–prescore).
*** $p < 0.001$.

in Table 2. Overall, the learning gains in conceptual content knowledge for the experimental group were significantly higher than for the comparison group, with a large effect size (39 ± 17 vs. 4 ± 23, respectively; U = 662, $p < 0.001$). For the questionnaire subscales, the highest effect size was found in the medications actions subscale (35 ± 29 vs. 3 ± 32, respectively; U = 1197, $p < 0.001$).

3.2. Transfer of Conceptual Knowledge

Analysis of the course final exam revealed significantly higher scores with a moderate-to-strong effect size of Cohen's d = 0.68 in the experimental group compared with the comparison group (M = 74%, SD = 14 vs. M = 64%, SD = 16, respectively; unpaired $t = -3.8$, $p < 0.001$). For the exam's subscales, significant differences between the two groups were related to drugs that act in the endocrine, central nervous, and chemotherapeutic systems (Table 3).

3.3. Complex-Systems Reasoning

The three components of complex-systems reasoning are presented in Fig. 2. The only significant interaction effect between the groups occurred in the transition between micro and macro thinking levels (F(1, 82) = 6.9, $p < 0.05$), with a moderate-to-strong effect size of $\eta_p^2 = 0.8$. No significant interaction effect was found between the groups for micro-level thinking ($F(1, 82) = 0.71, p = 0.2$) or for macro-level thinking ($F(1, 82) = 0.04$, $p = 0.8$).

4. Discussion

Knowledge of medication processes is highly important for nurses, as they are the primary medication managers. To promote nursing students' robust understanding of pharmacology, we examined the effectiveness of learning with the PILL-Cells environment, which enables students to learn about a multi-level biochemical process through a complex-systems approach. We applied the complex-systems perspective to represent the relationship between changes and stabilities at different equilibrium points of pharmacological processes (Klein and Zion, 2015).

The main difference in students' learning outcomes between the PILL-Cells environment and the lecture-based curriculum involved understanding the concepts related to the pharmacology of diabetes mellitus. The results show significantly greater conceptual learning in the experimental group than in the comparison group, whose members learned via the lecture-based curriculum. While all components of conceptual knowledge showed a significant gain for the experimental group, the largest effect size was for the subscale related to administering medication and performing a follow-up with a diabetic patient, which is the most complex subscale (Supplementary material, example 3). The medications actions component is the most sophisticated subscale, requiring coordination between an understanding of other subscales, the normal and abnormal diabetic equilibrium, and the impact of a variety of medications.

To illuminate how multi-level biochemical models based on a complex-systems perspective may support pharmacology learning, we evaluated students' complex-system thinking. Our findings show that

Table 3
Comparisons of course final exam scores and the two student groups (N = 148).[a]

	Exp. (n = 94)	Comparison (n = 54)	Unpaired t-test	Effect size, Cohen's d
Total score	74 ± 14	64 ± 16	−3.816***	0.68
Subscales				
Endocrine drugs[b]	78 ± 17	69 ± 28	−2.08*	0.43
Cardiovascular-renal drugs[c]	70 ± 19	65 ± 17	−1.72	0.27
Drugs that act in the central nervous system[d]	75 ± 21	67 ± 17	−2.55*	0.41
Chemotherapeutic drugs[e]	76 ± 19	59 ± 26	−4.35***	0.79
Other drugs[f]	64 ± 34	55 ± 26	−1.67	0.29

Exp., experimental group; Comparison, comparison group.
* $p < 0.05$.
*** $p < 0.001$.
[a] Data are presented in percentage Mean ± SD, range 0–100.
[b] Includes questions (n = 7) related to drugs affecting the diabetic mellitus diseases, thyroid gland, and adrenal cortex.
[c] Includes questions (n = 15) related to antiarrhythmic drugs, antihypertensive drugs, diuretic drugs, vasodilators and blood-viscosity drugs, treatment of heart failure, and dyslipidemia.
[d] Includes questions (n = 6) related to antidepressant drugs, antianxiety drugs, analgesics, and central nervous system stimulants.
[e] Includes questions (n = 10) related to antibacterial drugs, antifungal drugs, and chemotherapy agents.
[f] Includes questions (n = 2) related to HIV treatment and gastrointestinal diseases.

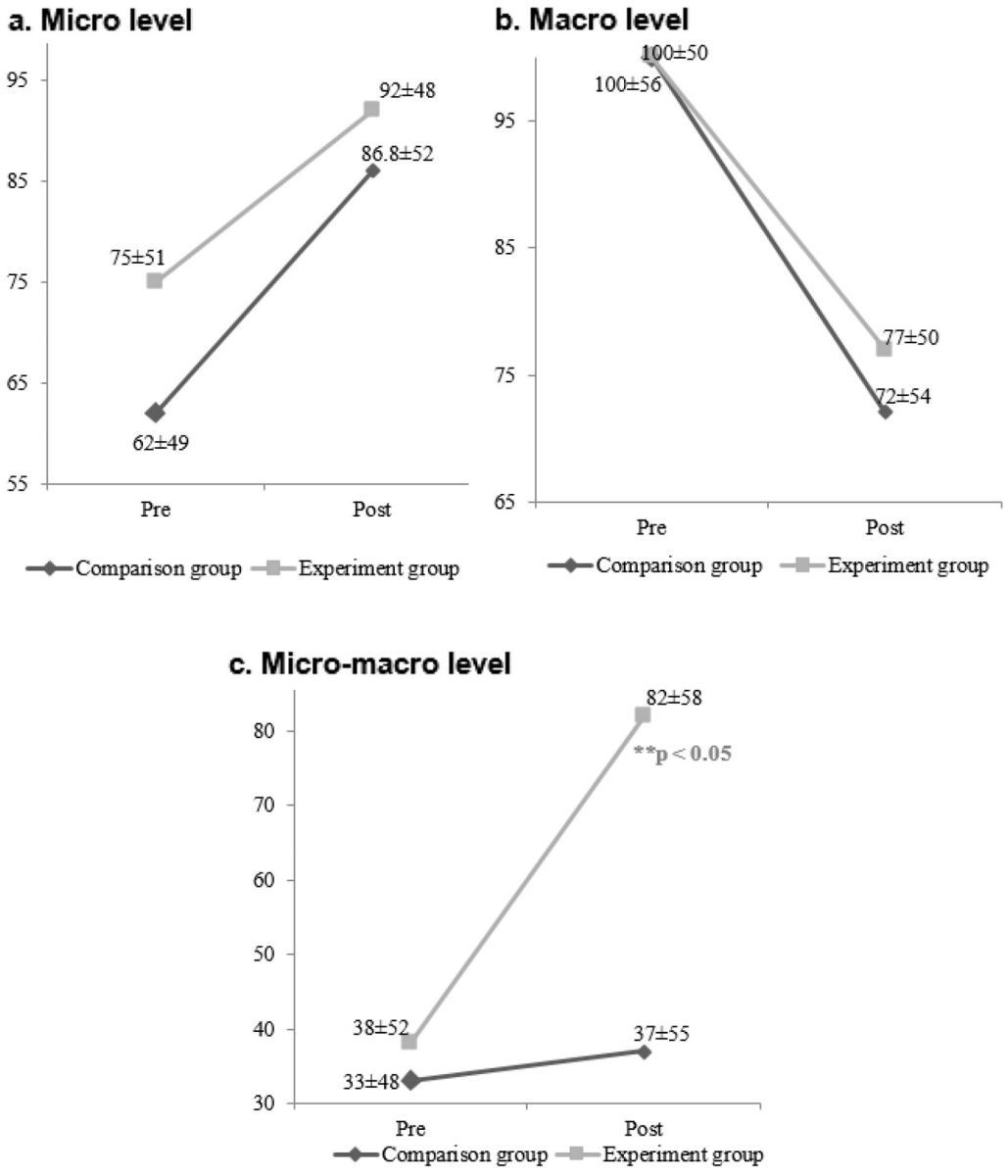

Fig. 2. Complex-system thinking components. Comparison of pre- and post-tests results (Mean and SD) based on three central complex-system components thinking: (a) micro level, (b) macro level, and (c) transition between micro and macro levels.

the main advantage for the experimental group, who learned with the PILL-Cells environment, was in transitioning between the micro and macro levels of the system. Therefore, the specific contribution of the PILL-Cells environment is how it helps nursing students to bridge simultaneous interactions between the system micro-level entities and their stochastic behaviors. For example, students understand better how, beginning with a hyperglycemic state (macro), a particular medication molecule (e.g., Glibenclamide) interacts with the beta-cell's receptors (micro), leading to the emergent macro-level phenomenon of an appropriate and stable glucose level in-vivo. The visual, dynamic, and linked representation of ABM distorts the physical phenomena by bringing the micro and macro levels closer. However, this distortion helps bridge the static behavior of homeostasis, at the macro level, and dynamic movement, at the micro level (Epstein, 2006; Goldstone and Janssen, 2005; Wilensky, 1999; Wilensky, 2001). Similar advantages in recognizing the interrelationships between system-level components have been shown in previous studies of complex-systems approaches (Gilbert and Treagust, 2009; Hirsh and Levy, 2013; Levy and Wilensky, 2009).

Interestingly, the grades for the final course exam show significantly greater conceptual learning for the experimental group than for the comparison group. Moreover, there is evidence for an extension of learning with the PILL-Cells environment above and beyond the learning gains about diabetes. We found that scores were higher not just for the endocrine drugs subscale (e.g., antidiabetic drugs) but also for drugs that act on the central nervous system and for chemotherapeutic drugs. Herein, we suggest that the PILL-Cells model-based learning environment provides not only understanding of the specific topic modeled but also a more general reasoning scheme for multi-level biochemical processes, and thus enhances understanding of other topics in the pharmacology curriculum.

Our research suggests that manipulating and exploring models based on an ABM paradigm of complex systems creates an explicit causal link between the micro-level elements of a system and its macro-level global behavior. Those small sets of entities and simple rules help to bridge and comprehend the associated complex processes of pharmacology. Thus, nursing students who learned with the PILL-Cells environment could better link the micro and macro levels, which contributed to higher conceptual knowledge compared with nursing students who learned with lectures only.

4.1. Limitations

The present study has several limitations. To prevent intervention diffusion between the experimental and comparison groups, we did not use random assignment in this study. To evaluate the advantages of learning with the PILL-Cells environment, further work should be performed on a larger scale with different categories of healthcare providers (e.g., registered nurses) and healthcare medical education.

4.2. Conclusion

There has been a growing emphasis on medication risk management and safety procedures, accompanied by allocated resources, in recent years. Despite advances in technological approaches, such as electronic medication management systems and barcode medication administration system, recurrent and significant errors still occur. Unfortunately, to date, quality reports conclude that healthcare has not necessarily grown any safer (Makary and Daniel, 2016). Here we are focusing on the human factor within an educational strategy specifically designed for nursing students. This factor aids in fostering a deeper understanding of medication administration and helps facilitate students' development of safer and more skilled medications administration behaviors.

Specifically, the present study illustrates how it is possible to enhance learning diabetes mellitus medications and to generalize pharmacology concepts and practice beyond the specific topics learned. Moreover, through a complex-systems perspective, this study introduces a powerful tool that can be implemented within nursing education curricula. Consequently, our cell models help nursing students combine human body biochemical processes with medication actions (Craft et al., 2017).

In closing, we suggest that integration of such educational strategies into the nursing curriculum promotes a deeper understanding of pharmacology and supports nurses' clinical decisions, empowering their competences and strengthening nurse-patient relationships.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nedt.2017.11.022.

References

An, G., Wilensky, U., 2009. From artificial life to in silico medicine. In: Adamatzky, A., Komosinski, M. (Eds.), Artificial Life Models in Software. Springer, London, pp. 183–214.

Banning, M., Cortazzi, M., 2004. Questioning student learning: an exploration of students' views on learning to become independent nurse prescribers. J. Furth. High. Educ. 28, 435–444.

Bauer, S., Nauck, M.A., 2014. Polypharmacy in people with Type 1 and Type 2 diabetes is justified by current guidelines—a comprehensive assessment of drug prescriptions in patients needing inpatient treatment for diabetes-associated problems. Diabet. Med. 31, 1078–1085.

Bhattacharya, S., Shoda, L.K.M., Zhang, Q., Woods, C.G., Howell, B.A., Siler, S.Q., Woodhead, J.L., Yang, Y., McMullen, P., Watkins, P.B., Andersen, M.E., 2012. Modeling drug- and chemical-induced hepatotoxicity with systems biology approaches. Front. Physiol. 3, 462.

Charles, B.G., Duffull, S.B., 2001. Pharmacokinetic software for the health sciences: choosing the right package for teaching purposes. Clin. Pharmacokinet. 40, 395–403.

Choo, J., Hutchinson, A., Bucknall, T., 2010. Nurses' role in medication safety. J. Nurs. Manag. 18, 853–861.

Craft, J., Christensen, M., Bakon, S., Wirihana, L., 2017. Advancing student nurse knowledge of the biomedical sciences: a mixed methods study. Nurse Educ. Today 48, 114–119.

Dilles, T., Vander Stichele, R.R., Van Bortel, L., Elseviers, M.M., 2011. Nursing students' pharmacological knowledge and calculation skills: ready for practice? Nurse Educ. Today 31, 499–505.

Dubovi, I., Levy, S., Dagan, E., 2014. PILL-CELL: Pharmacology InterLeaved Learning Cells, multiscale agent-based models. Created with Netlogo (http://ccl.northwestern.edu/netlogo). The Cheryl Spencer Department of Nursing and Systems Learning & Development Lab, University of Haifa, Israel.

Epstein, J.M., 2006. Generative Social Science: Studies in Agent-based Computational Modeling. Princeton University Press, Princeton, NJ.

Fritz, C.O., Morris, P.E., Richler, J.J., 2012. Effect size estimates: current use, calculations, and interpretation. J. Exp. Psychol. Gen. 141, 2–18.

Gilbert, J.K., Treagust, D.F., 2009. Towards a coherent model for macro, submicro and symbolic representations in chemical education. In: Gilbert, J.K., Treagust, D.F. (Eds.), Multiple Representations in Chemical Education. Springer, Netherlands, pp. 333–350.

Goldstone, R.L., Janssen, M.A., 2005. Computational models of collective behavior. Trends Cogn. Sci. 9, 424–430.

Hickerson, K.A., Taylor, L.A., Terhaar, M.F., 2016. The preparation–practice gap: an integrative literature review. J. Contin. Educ. Nurs. 47 (1), 17–23.

Hirsh, A., Levy, S.T., 2013. Biking with particles: junior triathletes' learning about drafting through exploring agent-based models and inventing new tactics. Technol. Knowl. Learn. 18, 9–37.

Holland, J.H., 1995. Hidden Order: How Adaptation Builds Complexity. Helix Books/Addison-Wesley, Cambridge.

Jacobson, M.J., 2001. Problem solving, cognition, and complex systems: differences between experts and novices. Complexity 6, 41–49.

Jacobson, M.J., Wilensky, U., 2006. Complex systems in education: scientific and educational importance and implications for the learning sciences. J. Learn. Sci. 15, 11–34.

Katzung, B.G., Masters, S.B., Trevor, A.J., 2011. Basic & Clinical Pharmacology. McGraw-Hill Medical: McGraw-Hill [distributor], New York; London.

Kauffman, S., 1995. At Home in the Universe: The Search for the Laws of Self-organization and Complexity. Oxford University Press, New York.

Klein, S., Zion, M., 2015. The characteristics of homeostasis: a new perspective on teaching a fundamental principle in biology. Sch. Sci. Rev. 97, 85–93.

Levy, S.T., Wilensky, U., 2009. Students' learning with the Connected Chemistry (CC1) Curriculum: navigating the complexities of the particulate world. J. Sci. Educ. Technol. 18, 243–254.

Lim, A.G., North, N., Shaw, J., 2014. Experiences of nurses as postgraduate students of pharmacology and therapeutics: a multiple case narrative study. Nurse Educ. Today 34, 985–990.

Makary, M.A., Daniel, M., 2016. Medical error—the third leading cause of death in the US. BMJ 353, i2139.

McKenry, L.M., Salerno, E., Hamelink, M.C., 2006. Mosby's Pharmacology in Nursing. Elsevier Mosby, St. Louis, MO.

Meechan, R., Mason, V., Catling, J., 2011. The impact of an integrated pharmacology and medicines management curriculum for undergraduate adult nursing students on the acquisition of applied drug/pharmacology knowledge. Nurse Educ. Today 31, 383–389.

Ndosi, M.E., Newell, R., 2009. Nurses' knowledge of pharmacology behind drugs they commonly administer. J. Clin. Nurs. 18, 570–580 (discussion 620).

Thomas, V., Schuessler, J.B., 2016. Using innovative teaching strategies to improve outcomes in a pharmacology course. Nurs. Educ. Perspect. 37, 174–176.

Westbrook, J.I., Duffield, C., Li, L., Creswick, N.J., 2011. How much time do nurses have for patients? A longitudinal study quantifying hospital nurses' patterns of task time distribution and interactions with health professionals. BMC Health Serv. Res. 11, 319.

Wilensky, U., 1999. NetLogo. Center for Connected Learning and Computer-Based Modeling. Northwestern University, Evanston, IL.

Wilensky, U., 2001. Modeling nature's emergent patterns with multi-agent languages. In: G.F. (Ed.), EuroLogo 2001: A Turtle Odyssey: Proceedings of the 8th European Logo Conference, 21–25 Avgust, Linz, Austria. Österreichische Computer Gesellschaft Wien, pp. 1–6.

Wilensky, U., Resnick, M., 1999. Thinking in levels: a dynamic systems approach to making sense of the world. J. Sci. Educ. Technol. 8, 3–19.

Zion, M., Klein, S., 2015. Conceptual understanding of homeostasis. Int. J. Biol. Educ. 4, 1–27.