Dynamic Mathematical Model of Infant Energy Imbalance, Body Composition Change, and Growth from Birth to 18 Years Old[1][2][3]

Aaron Gowins, Danielle Toupo, Carson Chow, and Kevin Hall

ABSTRACT

Background: Addressing the increasing prominence of childhood obesity will require an understanding of the underlying physiology and physical constraints. Clinicians and policy makers can benefit from the ability to compare the changes in body composition and energy use associated with healthy childhood growth to those associated with obesity.
Objective: We sought to develop a single model of the relationships between the intake and expenditure of energy and the deposition of tissue throughout childhood growth for both healthy weight and overweight subjects.
Design: By relating the changes in energy content in various tissues of children experiencing healthy growth to their nutrient intakes, we developed a computational simulation of the energy requirements and tissue deposition of healthy growth. We then extended this strategy to encompass the development of obesity.
Results: Our model accurately reproduces data from a variety of studies of healthy and overfed subjects other than those studies used to calibrate the model. After calibration, our model makes no reference to the calibration data, and relies only on the model parameters, the inputs of energy intake and expenditure, and age to produce simulations. We found that not only are overweight children taller on average than their peers, but that they are also shorter than their peers for their fat free mass value. We found that a single parameterized growth function of time is not sufficient to capture the body composition dynamics of the development of obesity for a model that begins at birth.
Conclusions: The model we present describes the typical deposition of fat and fat free tissue, as well as the growth of major organs, as a function of energy intake and expenditure dynamically throughout growth. Our model also predicts the distribution of tissue during periods of time where energy absorption differs from reference, as well as predicting the energy that must have been absorbed in order to reach a growth trajectory that differs from reference.

KEY WORDS

Infant growth, childhood growth, mathematical model, body composition, energy requirements, childhood obesity

INTRODUCTION

Despite widespread efforts to increase awareness and implement policy, the obesity epidemic continues to be a crisis in developed countries around the world. As obesity rates climb, an alarming number of children are being affected, and at ever younger ages.[Druet et. al., 2011]. However, studying the complex physiology that underlies childhood growth poses exceptional challenges. Measuring energy intake requires continuous monitoring of the energy content of the child's diet. The most precise methods of measuring energy expenditure, respiration calorimetry and the doubly-labeled water (DLW) method, are costly and require specialized laboratories. Accurate measurements of body composition of infants is especially rare, due primarily to the resistance of clinicians and patients' guardians to expose infants and small children to radiation during Dual-energy-X-ray-absorptiometry (DXA) measurements. Each of these methods introduce error, have prohibitive costs, and many requirements simply cannot be applied to infants in an appropriate and accurate manner. Our aim was to provide a method to produce estimates of the most difficult to measure and most important factors leading to childhood obesity using easier to obtain and less expensive measurements. Here we extend the well-validated model of [Hall et.al., 2013], by including ages from birth, introducing a number of revisions, and representing substantial additional physiology. Evidence indicates that body composition even prior to birth is associated with later body composition and obesity [McMillen et. al., 2009], highlighting the importance of understanding body composition changes and energy use in early growth. We present a mechanistic model based on established physiology and the physical properties of tissue and energy, and provide quantitative insights into the body composition changes related to varying energy intake and expenditure.

[1]From the Laboratory of Biological Modeling, National Institute of Diabetes, Digestive, and Kidney Diseases, National Institute of Health, Bethesda, MD
[2]Supported by the Intramural Program of the NIH, NIDDK
[3]Reprints not available, Address correspondence to

METHODS

Our mathematical model of energy partitioning between fat free mass (FFM) and fat mass (FM) from birth to adulthood is an extension of the previously published child and adult models [Hall et.al., 2013], and is presented in detail in the appendix. We begin with the fundamental observation that energy is in balance, and that changes in mass are governed by the ratio between energy absorbed through consumption and energy expended through maintenance and activity. The model is designed to predict the distribution of accumulated tissue between FFM and FM as a function of age, energy imbalance, and current body composition. Gender-specific trajectories for FFM and FM were fitted using age or mass dependent functions drawn from previously collected data on relevant physiological processes. Through combining these various independent functions, we constructed a model that substantially reproduces all calibration data and makes reasonable predictions of validation data, while providing insights into the physiological processes that underlie the dynamics of childhood growth.

Healthy Weight Model Calibration

In keeping with successful prior approaches, we developed an ordinary differential equation that we calibrated with data as shown in each figure. We began by reproducing the changing proportion of FFM and FM from [Fomon et.al., 1982, Haschke, 1989], as well as the energy required for both maintenance and deposition of mass. In order to establish the physiological mechanisms associated with this energy use and mass partitioning, we included a number of processes that occur as infants mature. These include the increasing energy density of FFM, the increase in cellularity, the growth of major organs and consequent changes in metabolic requirements, the thermic effect of feeding, adaptive thermogenesis, changes in physical activity, and changes in the glycolytic rate of the brain as it grows and matures.

A B

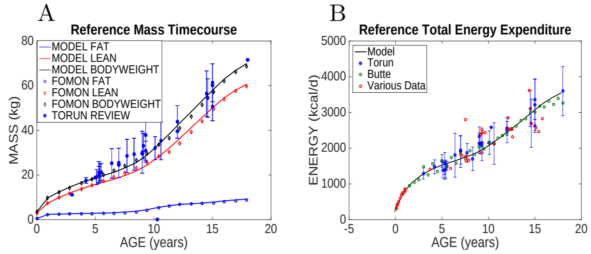


Figure 1. Model simulation of body composition for healthy weight male subjects (A) shown with body composition data from [Fomon et.al., 1982, Haschke, 1989, Torun, 2005] and Total Energy Expenditure (B) from [Torun, 2005, Butte, 2005]

A B

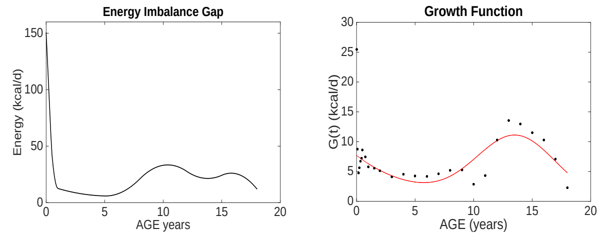


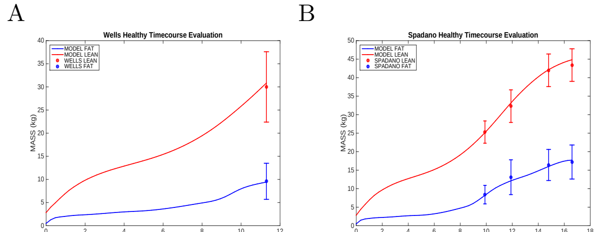
Figure 2. Energy Imbalance Gap as a function of age (A) and childhood growth represented as increased lean tissue deposition above adult Forbes partitioning ratio [Forbes, 1987] (B) for males.

The model is developed in Matlab® Version 8.4.0.150421(R2014b), using the Curve Fitting Toolbox Version 3.5(R2014b), and employs the ODE45 Runge-Kutta algorithm to numerically integrate. Some data uploading, subsetting, and exploration were done in R. The integrator function and all other codes are available in the appendix, in addition to a full description of model development.

Healthy Weight Model Validations

We validated the healthy weight model using a number of datasets not used for calibration. We included a number of studies of infants in addition to older subjects, including studies that were previously used in [Hall et.al., 2013], as well as others. Only energy intake values and initial conditions were altered to simulate validation data; birth weights were adjusted where they were included in the study and presumed to be identical to the calibration set where missing. No other model parameters were adjusted during the validations.

A B



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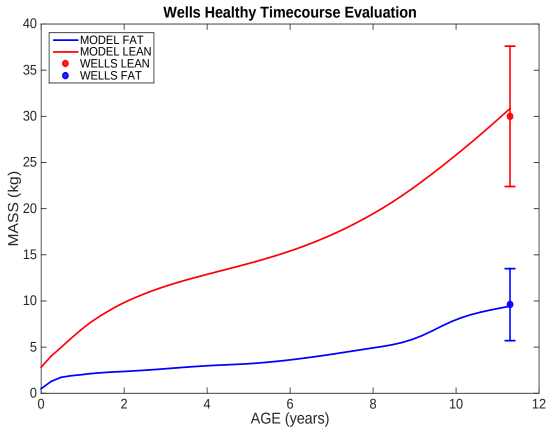

Figure 4. Healthy male subjects model validation from [Wells et.al., 2006]

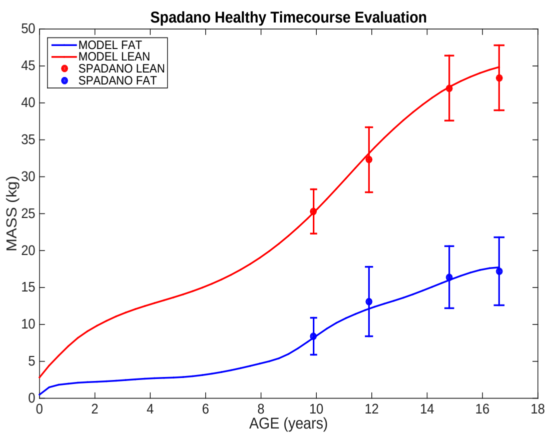

Figure 5. Healthy female subjects model validation from [Spadano et. al., 2005].

Overweight Model Calibration

We supplied the capability to model overfeeding by simulating an increase in energy intake and calibrating to [Wells et.al., 2006] for overfed subjects.

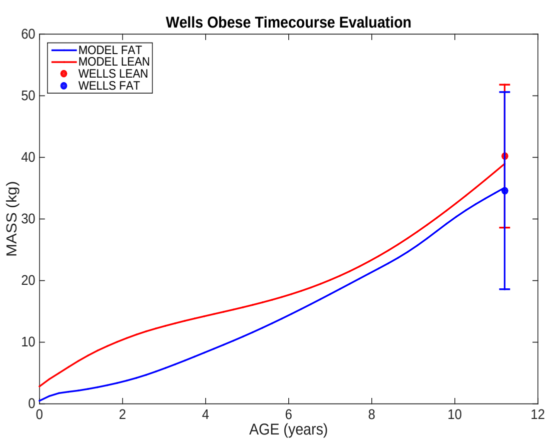

Figure 6. Overweight male subjects model calibration from [Wells et.al., 2006].

Overweight Model Validation

We then performed validation simulations similar to above, by simulating data not used in model calibration, and adjusting only initial conditions and energy intake values for validation.

Figure 7. Overweight male subjects model validation from [Spadano et. al., 2005].

Energy Intake and Expenditure

RESULTS

Defining Healthy Growth Trajectories

Simulating Body Compositions in Obesity

Simulating Energy Absorption, Intake, and Expenditure

DISCUSSION

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APPENDIX