Validation of energy intake during calorie restriction with the doubly labeled water method and changes in body composition

Dear Sir:

de Jonge et al (1) investigated the validity of estimates of energy intake (EI) during calorie restriction (CR) determined by the combination of doubly labeled water (DLW) and changes in body composition determined by dual-energy X-ray absorptiometry (DXA). They concluded that DLW + DXA overestimated EI by 8.7 ± 36.7% and, therefore, that “EI cannot be assessed accurately during CR by a combination of DLW and DXA.” over brief (ie, practical) periods of time, because of large interindividual variability caused by random errors in the measurement of changes in fat mass and fat-free mass by DXA. This disappointing conclusion may have been premature.

For 7 d, de Jonge et al measured the energy expenditure of 10 subjects by DLW in a room calorimeter while the subjects were fed a 30% CR diet prepared in the authors’ metabolic kitchen. The Bland-Altman plot in the authors’ Figure 2B provided the proper (2) comparison of their measurements of energy expenditure by DLW and calorimetry. This plot illustrated the authors’ encouraging finding that the 2 measurements differed by an average of only 1.3 ± 8.9%. However, the plot may also be interpreted as showing that the random variation of these differences increases with a CV of 30% of energy expenditure in excess of 1600 kcal/d. This is not encouraging.

The authors did not provide the corresponding Bland-Altman plot comparing their calculation of EI by DLW + DXA with the calculation of EI by those in the authors’ metabolic kitchen who prepared the food that was fed to the subjects. Because the comparison of these calculations was the stated purpose of the authors’ study, this was an unfortunate oversight. The missing Bland-Altman plot (Figure 1) was constructed from the data in the authors’ Figure 3A. Taken at face value, this plot appears to indicate that most of the differences between the 2 calculations of EI are not random, as the authors had concluded. Regression analysis suggests that the differences are strongly proportional ($R^2 = 0.82, P < 0.005$) and parallel (slope = 1 = 0.07 ± 0.18, $P = 0.7$) to EI above and below 1400 kcal/d. This proportionality appears to imply that an unidentified error in one calculation or the other could be corrected to reduce differences between the methods by 82%, which leaves a residual random error with an SEE of only 225 kcal/d (15%).

However, a probability plot of the data in the above regression analysis (Figure 2) shows that the regression analysis may not have faithfully represented the true relation between the 2 calculations. The highest and the 2 lowest data points do not fall on the same straight line as do the other normally distributed data points. What is worse, these extreme outliers with standardized residuals of −8.6, −7.5, and 16.6 from a regression line obtained without them have the strongest leverage on the regression analysis.

A second Bland-Altman plot constructed without these data points (Figure 3) shows that they accounted entirely for the apparent linear relation between the 2 calculations of EI. Neither the slope ($P = 0.65$) nor the intercept ($P = 0.85$) found by the second regression analysis is significant, and the residuals are normally distributed (plot not shown).

The mean ($± SD$) of the 7 remaining data points appears to indicate that DLW + DXA calculations yield estimates of EI that are $310 ± 116$ kcal/d higher than the calculations made by food preparers. Per this analysis, DLW + DXA estimates of EI during CR appear to be less accurate and more precise than the estimates made by de Jonge et al (1). Compared with the average EI calculated by both methods, DLW + DXA appears to overestimate EI by 100 × [(310 kcal/1511 kcal) ± (116 kcal/1511 kcal)] = 21 ± 8%. Whether the 21% bias resides in the DLW + DXA technique or in the authors’ metabolic kitchen cannot be determined from the authors’ data.

FIGURE 1. Bland-Altman plot of energy intake (EI) calculated by use of the doubly labeled water + dual-energy X-ray absorptiometry methods and by food preparers.

FIGURE 2. Probability plot of regression residuals. EI, energy intake.

FIGURE 3. Bland-Altman plot of energy intake (EI) calculated by use of the doubly labeled water + dual-energy X-ray absorptiometry methods and by food preparers, minus the outliers.
Thus, the Bland-Altman and regression analyses indicate that the authors' conclusion about DLW+DXA not being suitable for estimating EI during short-term CR studies may have been premature. Their experiment appears to have generated 3 widely spaced data points precisely suggesting one relation between the 2 calculations of EI (a large difference proportional to EI) and 7 closely spaced data points precisely suggesting a completely different relation (a large constant difference).

This data set is too small and heterogenous to warrant any further conclusion about how accurate and precise DLW+DXA may be, but accurate estimation of EI is of fundamental importance for everyone interested in CR. Therefore, investigators should be encouraged to collect and analyze more experimental data of this kind to search for potentially correctable sources of error in both calculations of EI and in the experimental methods that generate the data. If such sources are found and corrected, differences between the 2 calculations may be reduced to a random error of 8%.

One of the authors of the de Jonge et al article (LM Redman) was a postdoctoral scholar in the laboratory of ABL. LB and ABL have no financial or personal relationships with any research sponsor that would constitute a conflict of interest.

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REFERENCES

Reply to L Bowman and AB Loucks

Dear Sir:

We thank Bowman and Loucks for their interest in our study on the validation of energy intake during caloric restriction with the use of doubly labeled water (DLW) and changes in body composition (1), and we are glad to have the opportunity to address the issues raised. It is important to note that our study was designed to validate the methods for measuring both energy expenditure (EE) and energy intake (EI) during caloric restriction. More specifically, we tested whether DLW can be used in periods of caloric restriction to measure EE values for groups (average) and individuals and EI values when combined with dual-energy X-ray absorptiometry (DXA).

In regard to measures of EE under energy restriction, our findings clearly showed that the method can be used with good accuracy and reasonable precision. We found an average difference between DLW and respiratory chamber methods of 1.3 ± 8.9%. On the basis of the Bland-Altman plot provided, Bowman and Loucks state that the random variation seems to increase "with a CV of 30% of energy expenditure in excess of 1600 kcal/d." This conclusion is not warranted by the data, because the discrepancies between the 2 methods occurred in individuals with both low and high EE, and the maximum discrepancy was ≈13%.

In regard to the measurements of EI, our study examined the accuracy and precision of calculating EI in groups and individuals by using DLW and the changes in body energy stores measured by DXA over 7 d. Investigators knowledgeable in the field of energy balance rightfully do not expect that a combination of these 2 methodologies (DLW and DXA) over periods of 1–2 wk could provide reliable data to assess EI for a given individual because the changes in body energy stores (fat mass and fat-free mass) are too small to be detected precisely by DXA. The reason we undertook such a validation study was also to temper the common belief from many scientists that individual adherence to a caloric intake prescription can be derived by combining measures of DLW and body composition. In our study, this method yielded an estimate of average group EI that was reasonably consistent with actual EI, ie, 8.7% higher. However, for individuals with an overall precision of 36.7%, our data are consistent with the conclusion that the large differences between the DLW and DXA methods and actual EI reflect current technological limits of the DXA method, which is inadequate to detect small changes in body energy stores and therefore EI. As discussed in our article, limitations in the precision of the methods in the changes in body energy stores by DXA can produce intraindividual SDs of ≥400 kcal/d, which is a substantial proportion of daily EI for most individuals. Given these SDs, our observation that DLW- and DXA-based estimates of EI for some individuals had discrepancies from measured EI that substantially exceeded this magnitude is not surprising. Therefore, we do not feel that our conclusion that “the interindividual variability was too large to provide an assessment of CR adherence on an individual basis” was “premature.” In view of the above argument and of the small sample size, we do not believe that there is much value in speculating about the precision or accuracy of the method, on the basis of a Bland-Altman plot that compares the provided and the calculated EI values, whether or not the most discrepant values are excluded from the analysis. In preparation for our article, we made such a plot, but we elected not to present it because the number of subjects was too small to establish a firm conclusion that the differences between the 2 methods were truly proportional to estimated EI, even though the 2 lowest and the highest data points were mostly responsible for the potential proportionality. Eliminating 30% of the data points, as Bowman and Loucks suggest, does not seem appropriate.

We, however, do agree with Bowman and Loucks that our data set is too small to establish a concrete value for the accuracy and precision of the method, but this was not the aim of our study. As discussed in our article, under different conditions (eg, large rates of weight change and longer measurement intervals), the accuracy and precision of DLW-based measures of individual EI during weight loss may differ from our observed values, especially with improved methods to determine body composition. This could be explored in future studies. In conclusion, our study documented that, until better methods to measure intraindividual changes in energy stores are available, individual EE but not EI can be measured in periods of caloric restriction.

LMR spent 1 yr as a postdoctoral fellow with AB Loucks. None of the other authors had a financial conflict of interest.

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