11 and 15-month-old infants do not compensate immediately for energy variation, and no further adjustment occurs 12 or 24 hours later

Pauline Brugaillères, Sylvie Issanchou, Claire Chabanet, Sylvie Marty, Camille Schwartz

Title: 11 and 15-month-old infants do not compensate immediately for energy variation, and no further adjustment occurs 12 or 24 hours later

Authors' names: Pauline Brugaillères, Sylvie Issanchou, Claire Chabanet, Sylvie Marty, Camille Schwartz

Authors' affiliation: Centre des Sciences du Goût et de l'Alimentation, AgroSup Dijon, CNRS, INRAE, Université de Bourgogne Franche-Comté, Dijon, France

Sources of support: This work was supported by grants from ANR PUNCH (ANR-15-CE21-0014), the Conseil Régional Bourgogne Franche-Comté (PARI grant), the FEDER (European Funding for Regional Economic Development), the French Society of Nutrition (SFN 2015) and by a PhD fellowship from the French Ministry for Education and Research.

Conflict of interest and funding disclosure: The funders had no role in the planning, conduct, or interpretation of the study. The authors PB, SI, CC, SM, and CS declare no conflicts of interest.

Corresponding author: Camille Schwartz, UMR Centre des Sciences du Goût et de l'Alimentation, 17 rue Sully, 21000, Dijon, France. Tel.: +33 380 69 37 43; Email: camille.schwartz@inrae.fr

Abbreviations: EI: energy intake; ED: energy density; L/HED: low/high energy density; CV: coefficient of variation.

1. Introduction

Caloric compensation refers to the ability to adjust energy intake (EI) in response to the energy density (ED) of food. This ability to self-regulate contributes to maintaining the energy balance and remaining at a healthy weight status. An individual's caloric compensation ability can be tested in the laboratory using a preload paradigm (Birch & Deysher, 1985). This approach consists of offering a small amount of food (= preload) that is either low or high in ED (on two different days: a Low Energy Day [LED day] or a High Energy Day [HED day]), followed by an ad libitum meal after a fixed short period of time. To express the level of caloric compensation from the preload to the subsequent meal, a COMPX score is generally calculated. This score is obtained by dividing the difference in EI during the two ad libitum meals by the difference in EI from the two preloads, with the result multiplied by 100(Johnson & Birch, 1994): COMPX = [(EI of the meal after the LED preload – EI of the meal after the HED preload) / (EI of the HED preload – EI of the LED preload)] × 100. A COMPX of 100% reflects accurate compensation. In this case, the individual eats less food at the meal following the HED preload so that the total EI (preload + meal) in both conditions (LED, HED) are equal. A COMPX > 100% indicates overcompensation (i.e., the greater the COMPX increases over 100%, the greater the individual *undereats* after the HED preload, which leads to a lower total EI in the HED condition than in the LED condition), whereas a COMPX < 100% indicates undercompensation (i.e., the greater the COMPX decreases under 100%, the greater the individual *overeats* after the HED preload, which leads to a higher total EI in the HED condition than in the LED condition; COMPX values can extend into the negative range indicating in this case an even greater degree of undercompensation) (for details see Supplementary Figure 1).

The preload paradigm has been used in children (Birch & Deysher, 1985). To bridge a gap in knowledge with regard to energy adjustment abilities in infants, we recently adapted the preload paradigm for use in 11- and 15-month-old infants by offering a more or less caloric carrot puree 25 minutes before a meal (Brugaillères, Issanchou, Nicklaus, Chabanet, & Schwartz, 2019). In our longitudinal study, we observed that infants undercompensated the calories from the preloads (~ 43 kcal) at 11 and 15 months of age and that this undercompensation was more important at 15 months of age than at 11 months of age. This last result was in accordance with the hypothesis proposed by Fox et al., who suggested, on the basis of cross-sectional data, that appetite control abilities might deteriorate at approximately 1 year of age (Fox, Devaney, Reidy, Razafindrakoto, & Ziegler, 2006). Our work supports the hypothesis that infants at this age are not able to fully adjust for energy variation at the immediate meal following the preload. The question now turns to determining whether infants could improve their energy adjustment over longer periods of time.

Other studies with different methodologies can be scrutinized to gather some pieces of information concerning caloric adjustment over longer periods than a single meal. On the basis of several 24 h dietary recalls per participant, some studies have calculated a coefficient of variation (CV) as a measure of the intraindividual variability of EI for intakes at the meal occasion level and at the day level in young children (Birch, Johnson, Andresen, Peters, & Schulte, 1991; Shea, Stein, Basch, Contento, &Zybert, 1992) and in 8- to 16-month-old infants (Pearcey & De Castro, 1997).These studies all showed that the mean CV of EI is highly variable from meal to meal, whereas the mean CV of EI is less variable from day to day, providing evidence of a caloric adjustment over a 24-h period. Similarly, with another approach, a study based on 24-h dietary recalls reported a significant negative association between food ED and the average z-scores of the consumed portion size in infants from 4 to 11 months of age (Fox, Devaney, Reidy, Razafindrakoto, & Ziegler, 2006). The authors also concluded that infants of this age were able to adjust their EI by adapting the eaten quantities to the ED of food over the whole day. This group of studies suggests that a caloric adjustment may occur over periods longer than a single meal, that is, over several meals. However, this assumption has been challenged with a recent study based on weighed assessments of EI over 5 days by showing that increasing or decreasing the ED of some foods modified the daily EI in children 3-5 years old due to a weight adjustment instead of a caloric adjustment (i.e., the children ate a consistent weight of food regardless of the ED of the food) (Smethers et al., 2019).

In the present study, to advance the knowledge about infants' ability to adjust their energy intake beyond a single meal, we examined the extent to which energy adjustment occurs up to 24 h after a single meal preceded by preloads of varying ED when infants were 11 and then 15 months old. In other words, the aim was to compare the short-term caloric adjustment calculated at the meal level with the caloric adjustment assessed over 12 h and over 24 h. The predominant assumption from the previous literature would be in favour of an improvement of caloric adjustment over the day, although not all published findings are consistent. To achieve this aim, infants went through a preload paradigm meal in the laboratory (the results from this part were already published (Brugaillères et al., 2019)), and their consumption was then recorded at home until the next day (for up to approximately 24 h after the preload consumption and the ad libitum meal); this was done at 11 and 15 months old. Thus, we were able to calculate a COMPX score for different periods after the preload at each age.

2. Materials and methods

2.1. Participants

The study took place in Dijon (France). Parent-infant dyads were recruited from May 2015 to December 2016 using leaflets distributed to health professionals' consulting rooms using our internal database (Chemosens Platform's PanelSens, Commission Nationale de l'Informatique et des Libertés (CNIL), n° 1148039) and with the help of a recruitment agency. Sixty-nine parent-infant dyads were enrolled in this study, but as detailed in our previous paper, we obtained data on the infants' short-term caloric adjustment at 11 and/or 15 months of age for 50 infants (Brugaillères et al., 2019). The data were collected from December 2015 to July 2017.

Infants were included if they had no chronic health problems or food allergies, gestational age ≥ 37 weeks, birth weight ≥ 2.5 kg, no history of being tube fed and no history of being fed a hydrolysate formula. Infants of mothers with diabetes or celiac disease and infants of minor parents (< 18 years old) were excluded. This study was conducted according to the guidelines established in the Declaration of Helsinki and was approved by the local ethics committee (Comité de Protection des Personnes Est I Bourgogne, 2015-A000014-45). Written informed consent was obtained from both parents. The participants received a 60 € voucher for completing the measures.

2.2. Measurement of short-term caloric adjustment in the laboratory

We performed a laboratory-based assessment of the infants' short-term caloric adjustment ability by using the preload paradigm. This measure was performed twice for each infant, once when they were 11 months and once when they were 15 months old. The study design was detailed in our previous work (Brugaillères et al., 2019) and will thus be briefly described here. At each studied age, the measure required 2 visits to the laboratory on 2 non consecutive days at the same time of day. The preload consisted of 67 g of carrot puree that was either low or high in ED, depending on the day (LED day = 22 kcal, HED day = 65 kcal; the order was counterbalanced across infants). The HED preload was made by adding vegetable oil. Each infant was randomly assigned to a specific order group (LED/HED or HED/LED), and this order was the same at the two different ages. After a 25-min play period, the infants consumed an ad libitum meal composed of 300 g of vegetable and meat/fish puree followed by 195 g of a fruit puree. The maximal energy content of the meal was 296 kcal. The quantities served were chosen to be greater than the mean quantities consumed between 10 and 17 months old (Chouraqui, Tavoularis, Simeoni, Ferry, & Turck, 2020). These quantities were also approved by a paediatrician so that the infants could not feel uncomfortable even if they consumed the entire meal. Additionally, to respect the infants' food preferences, the recipes were beforehand chosen by the mother among our preselection of recipes with similar EDs. Each infant was offered the same ad libitum meal (the same recipes) at each studied age.

For both the preload and the meal, the infants were fed by the mother. While the preload had to be consumed entirely, the mother stopped offering each food item of the ad libitum meal after two consecutive refusals. The mother was blinded to the situation: she did not know the condition (HED vs. LED) or in which served food during the meal to which the vegetable oil had been added. The weight intake (g) of each meal component was assessed by weighing the bowl, as well as the infant's bib, before and after consumption (Soehnle, 1 g). The EI was then calculated according to the ED information from the manufacturers. At 11 and 15 months of age, as a result of the preload paradigm, a COMPX score was available for each infant; for additional details, refer to Brugaillères et al. (2019).

2.3. Food consumption diaries

To assess the caloric adjustment over longer periods after coming to the laboratory (approximately 12 h and 24 h), we used 24 h dietary records. For infants at 11 and 15 months of age, the mother (or the main caregiver) completed a food record booklet at home over a period of approximately 24 h following the 2 laboratory visits (the LED and HED days). For example, if the first day in the laboratory took place on Monday at lunch time, the mother completed the food record booklet until Tuesday, lunch included (Figure 1). The composition of the meals offered at home was left to the discretion of the caregivers.

The caregiver was asked to provide qualitative and quantitative information on all foods and drinks (including milk) consumed by the infant and to be as precise as possible (e.g., reduced-fat dairy, addition of butter). To ensure the quality of the recordings, the food record booklet contained detailed instructions. The qualitative description included the time of each food episode and the details of the offered foods: brand name for manufactured foods, the name and individual components for homemade preparations, and the estimated quantities of added caloric ingredients if applicable (e.g., 1 knob of butter, a pinch of grated cheese). Evaluations of eaten quantities were made by weighing each plate/bottle/cup before and after consumption with a scale that we provided to the parents (Soehnle, 1 g). The milk intake of breastfed infants (N = 6 at 11 months and N = 3 at 15 months) was assessed by weighing the infant before and after breastfeeding with a baby scale also provided to the parents (Soehnle professional 8310.01, precision: 10 g). The caregiver was also given a booklet of photographs of reference portion sizes adapted for infants up to 36 months of age as a complementary tool for estimating food quantities when weighing was not possible. This booklet was developed by the CREDOC (Centre de Recherche pour l'Etude et l'Observation des Conditions de Vie — Research Centre for the Study and Observation of Living Conditions, Chouraqui, et al., 2020). We completed this booklet by adding photographs of reference portion sizes for vegetables in pieces, non-caloric sweeteners and caloric ingredients (Chantilly cream and salad dressing) not included in the CREDOC version.

Please insert Figure 1

At each studied age, the 2 × 24 h dietary data collected were collated and reviewed by a registered dietician (SM). Based on the quantities consumed and the ED of each food, the dietician calculated the EI (kcal) of each consumed food. French national dietary databases were used: the 2016 CIQUAL (Centre d'Information sur la Qualité des Aliments — Centre for

Information on Food Quality) composition table or the 2013 CIQUAL composition table when the 2016 version did not contain the target food (CIQUAL, 2016). For manufactured foods and drinks (including infant formula), we used the ED provided by the manufacturers on the product label, or if that information was not available, we reported the ED of the closest average product listed in the CIQUAL table. When needed, these databases were supplemented with new foods based on manufacturer information and standard recipes. The breast milk ED was considered equal to 62.4 kcal/100 mL according to the value reported by Grote and colleagues (Grote et al., 2016) for 6-month-old breastfed infants.

Although many details were requested regarding the exact composition of each offered food, we sometimes had missing information regarding mixed dishes. In such cases, we used an estimation of the proportion of each ingredient (meat/fish, vegetable, starchy foods, and added caloric ingredients) based on the French nutritional guidelines (PNNS, Programme National Nutrition Santé — National Nutrition Health Programme) (PNNS, 2004 édition corrigée 2015) or based on the French guidelines for food service including nurseries (GEMRCN, Groupement d'Etude des Marchés en Restauration Collective et de Nutrition — public catering and nutrition market study group) when applicable (GEMRCN, 2015).For each infant and each day (the LED day and the HED day), EI was calculated for the 12-h period after preload consumption (i.e., if the laboratory test meal occurred at lunch time, this period encompassed all food consumption until midnight; Figure 1) and for the 24-h period after preload consumption (i.e., if the laboratory test meal occurred at lunch time, this period encompassed all food consumption until the next lunch; Figure 1). The same approach was applied if the laboratory meal occurred at dinner time (6% of the visits).

2.4. Statistical analysis

Analyses were performed using R software for Windows (version 3.6.1), and a linear mixed model was estimated using the nlme package (Pinheiro et al., 2020). The results are reported as the mean ± SD. Statistical significance was set at $P < 0.05$.

Based on the EI recorded during the laboratory test meals, we first calculated the short-term caloric compensation scores at 11 and 15 months of age (later referred to as 0h-$COMPX_{11mo}$ and 0h-$COMPX_{15mo}$). Based on the EI consumed during the 12- and 24-h periods after preload consumption, two variables related to caloric adjustment were calculated at each age: 12h-COMPX and 24h-COMPX. These variables were calculated according to the original COMPX equation (Johnson & Birch, 1994). In this equation, the numerator [(EI of the meal after the LED preload – EI of the meal after the HED preload)] was replaced by [(EI of meals during the 12/24 h period after the LED preload – EI of meals during the 12/24 h period after the HED preload)]. In these variables, we considered the EI from the ad libitum meal taken at the laboratory plus the EI from the meals taken at home during the period of interest (i.e., 12 h or 24 h). For example, the 12h-COMPX= [(EI of meals during the 12-h period after the LED preload – EI of meals during the 12-h period after the HED preload)/(EI of the HED preload – EI of the LED preload)] × 100. For each infant, we obtained at most 3 COMPX scores at each age (i.e., 0h-$COMPX_{11mo}$,12h-$COMPX_{11mo}$, and 24h-$COMPX_{11mo}$, and 0h-$COMPX_{15mo}$, 12h-$COMPX_{15mo}$, and 24h-$COMPX_{15mo}$).

A linear mixed model was used to evaluate the effect of age and of the period considered (3-level factor: 0 h, 12 h, 24 h) on the COMPX score. The fixed part of the model was age + period + age × period (two factors with interaction), and these effects were also considered random, using a general positive-definite matrix for the random-effects covariance matrix, that is, an unstructured variance-covariance matrix (6 rows, 6 columns). In other words, the variance was supposed to be heterogeneous across periods and across ages (6 different variances), allowing for the fact that variance could depend both on age and on the period considered, and the correlation matrix between COMPX scores was supposed to be unstructured, allowing for a higher correlation between a 12- and a 24 h-period COMPX score than between a 0 h- and a 12 h-period COMPX score. Such correlations account for the structural dependence between the 0 h- and 12 h-period COMPX, between the 0 h- and 24 h-period COMPX score, and above all between the 12 h- and 24 h-period COMPX score, induced by the calculation (partial coverage of the periods considered). Moreover, these correlations could account for a possible correlation between scores calculated at 11 months and at 15 months. Predictions and 95% confidence intervals were obtained with this model. Finally, non significant fixed terms were removed in a second model.

3. Results

The 50 infants (23 females) for whom we calculated a short-term COMPX at 11 and/or 15 months (i.e., 0h-COMPX$_{11mo}$ and/or 0h-COMPX$_{15mo}$) were characterized by a mean gestational age of 39.7 ± 1.4 weeks and a mean birth weight of 3.4 ± 0.4 kg (z-score BMI at birth = 0.4 ± 0.9).The durations of exclusive and total breastfeeding were 8.3 ± 8.7 weeks and 15.2 ± 19.1 weeks, respectively. The observed age at the start of complementary feeding of 4.9 ± 0.9 months was consistent with the age reported in a French representative cohort study (Bournez et al., 2018). The infants' z-scores BMI were -0.4 ± 1.0 at 11 months (N = 45) and at 15 months (N = 33). The mothers' characteristics were described in our previous paper (Brugaillères et al., 2019). Among the 46 infants for whom we obtained a 0h-COMPX$_{11mo}$, we had intake data to calculate the 12h-COMPX$_{11mo}$ for 31 infants (15 females) (Figure 2). Then, among these 31 infants, we had intake data to calculate the 24h-COMPX$_{11mo}$ for 22 of them (11 females). Among the 35 infants for whom we obtained a 0h-COMPX$_{15mo}$, we were able to calculate the 12h-COMPX$_{15mo}$ for 31 of them (14 females). From these 31 infants, we calculated the 24h-COMPX$_{15mo}$ for 24 (12 females). At both studied ages, the loss of participants for the calculation of the 12h- and 24h-COMPX was due to absent or incomplete information in the food diaries. On average, during the

12-h period after the laboratory visit (considered for the 12h-COMPX calculation), the infants consumed at home 5 and 6 food items at 11 and 15 months of age, respectively. The mean time period between the laboratory visit and the last food consumption recorded on the diaries until midnight (considered for the 12h-COMPX calculation) was 9 ± 2 h. During the 24-h period (considered for the 24h-COMPX calculation), the infants consumed at home an average of 9 and 10 food items at 11 and 15 months of age, respectively. The mean time period between the laboratory visit and the next lunch recorded on the diaries (or the next dinner when the laboratory visit occurred at dinner time) was 25 ± 1 h.

Please insert Figure 2

3.1. Description of the infant's energy intake (except EI from the preload)

At 11 months, the EI from the ad libitum meal taken at the laboratory was 138 ± 64 kcal on the LED day and 120 ± 57 kcal on the HED day (N = 46). The EI during the 12-h period post preload (N = 31) was 486 ± 103 kcal for the LED day and 480 ± 102 kcal for the HED day. The EI during the 24-h period post preload (N = 22) was 842 ± 145 kcal and 824 ± 165 kcal for the LED and HED days, respectively. At 15 months of age, the EI from the ad libitum meal taken at the laboratory was 119 ± 56 kcal on the LED day and 119 ± 53 kcal on the HED day (N = 35). The EI during the 12-h period post preload (N = 31) was 484 ± 95 kcal for the LED day and 508 ± 142 kcal for the HED day. The EI during the 24-h period (N = 24) was 886 ± 142 kcal and 920 ± 169 kcal for the LED and HED days, respectively. The same EI data are presented in Figure 3 for the infants for whom we had complete EI data at 11 months (N = 22, Figure 3A) and at 15 months (N = 24, Figure 3B).

Please insert Figure 3

3.2. COMPX: linear mixed model

The mixed model showed a significant age effect (*P* = 0.03), but no significant effect of the period considered (*P*=0.55), and no interaction between age and period (*P*=0.47). On average, the compensation was lower at 15 months than at 11 months (Table 1), and the data showed no adjustment over longer periods than the short term (COMPX scores at 0 h, 12 h and 24 h were not significantly different). Confidence intervals for the predictions (Figure 4) showed that the average scores were significantly lower than 100%, indicating undercompensation, except at 11 months for 24h-COMPX.

Please insert here Table 1

Table 1: COMPX scores: row means and standard deviations, estimated means, estimated standard errors and 95% confidence intervals corresponding to the fixed part of the linear mixed model.

	Row mean ± SD (N)	Estimated mean	Estimated Std error	95% Confidence interval
11 months				
$0h\text{-}COMPX_{11mo}$	44 ± 119 (N = 46)	44	17	[9,78]
$12h\text{-}COMPX_{11mo}$	14 ± 193 (N = 31)	17	34	[-50,84]
$24h\text{-}COMPX_{11mo}$	39 ± 371 (N = 22)	54	67	[-78,186]
15 months				
$0h\text{-}COMPX_{15mo}$	-16 ± 151 (N = 35)	-17	25	[-66,33]
$12h\text{-}COMPX_{15mo}$	-59 ± 269 (N = 31)	-62	48	[-157,33]
$24h\text{-}COMPX_{15mo}$	-87 ± 448 (N = 24)	-114	86	[-285,56]

In the second model, non significant fixed effects (i.e., the time effect and the interaction between time and age) were removed. The 95% confidence intervals for the COMPX scores were [5, 69] and [-69,24] for 11 and 15 months, respectively. They were significantly lower than 100%, showing undercompensation at both ages.

Please insert Figure 4

Figure 4: Estimated means and 95% confidence intervals for COMPX scores at 11 and 15 months over the 0-h period, over the 12-h period, and over the 24-h period following the preload (linear mixed model).

The random parameters of the 1st model (Table 2) showed that the variance of individual COMPX scores increased over the periods and was higher at 15 months than at 11 months. The general positive-definite structure of the random part (unstructured variance-covariance) accounted for the structural dependence between the COMPX calculated over shorter or longer periods. Indeed, at both 11 and 15 months, 12h-COMPX and 24h-COMPX were highly correlated (0.74 and 0.76), and 0h-COMPX showed a correlation with 12h-COMPX (0.48 and 0.25) and 24h-COMPX (0.51 and 0.08).

Table 2: Random part of the linear mixed model: standard deviations of estimated individual COMPX scores and correlations between estimated individual COMPX scores (general positive-definite structure).

	StdDev	Corr				
		0h-COMPX$_{11mo}$	12h-COMPX$_{11mo}$	24h-COMPX$_{11mo}$	0h-COMPX$_{15mo}$	12h-COMPX$_{15mo}$
0h-COMPX$_{11mo}$	105					
12h-COMPX$_{11mo}$	186	0.48				
24h-COMPX$_{11mo}$	359	0.51	0.74			
0h-COMPX$_{15mo}$	140	0.10	-0.06	-0.30		
12h-COMPX$_{15mo}$	263	0.15	0.06	0.09	0.25	
24h-COMPX$_{15mo}$	457	-0.07	0.10	0.25	0.08	0.76
Residual	55					

4. Discussion

In this study, we investigated the extent to which 11- and 15-month-old infants were able to adjust intake immediately following preloading of varying EDs (in the short term), as well as up to 12 and 24 h later. We showed that at both studied ages, the infants undercompensated their energy intake in the short term and that, on average, compensation did not improve over a longer period. In other words, energy compensation did not improve over time regardless of age. This result is aligned with the recent conclusions from Smethers et al. (Smethers et al., 2019).Clearly, this finding counters the predominant assumption in the literature that infants are able to adjust their energy intake on a daily basis and calls for more exploration.

Moreover, at both ages, the variance in COMPX scores increased over longer periods of time. This increase in the variance may be linked to the fact that the offered foods were different for all infants at home, and all the more so as the time elapsed was longer. In addition, the variance seemed to be more important at 15 months than at 11 months. We hypothesize that there are more differences in dietary intake (in terms of food and quantity) between infants at 15 months old than at 11 months old and that the 24 h dietary records may be less accurate at 15 months than at 11 months of age. A French survey revealed that the proportion of offered adult foods compared with specific infant foods increases around the age of 12 months (Ghisolfi et al., 2013). This complexification (more composite recipes) of the diet could make it more difficult for the parents to report their infants' dietary food intake at 15 months of age and for us to evaluate the ED of the foods, thus leading to a less accurate assessment of the caloric adjustment at 15 months old over the longer periods (12 h and 24 h).However, we tried to limit inaccuracies in reported food quantities by instructing the parents to weigh each plate and by giving the parents very precise instructions. In this regard, it seems that this limitation was unlikely, as demonstrated by the proximity between our mean EI values (over the 24 h periods) and the mean daily EI reported for infants of similar age ranges in France by others (850 and 913 kcal/d in 10- to 11- and 12- to 17-month-old bottle-fed infants, respectively) (Chouraqui et al., 2020).

The main limitation of this study was the loss of EI data collected at home. Consequently, we were not able to calculate the caloric adjustment over the 12-h period and particularly over the 24-h period for all participants. This effect reduced the power for the statistical analysis when comparing the COMPX scores. Nevertheless, our sample remains in the same range as other studies based on 24 h dietary records conducted of 8- to 16-month-old infants (N = 29) (Pearcey & De Castro, 1997) and of 2- to 5-year-old children (N = 15) (Birch et al., 1991).

Of course, the fall back solutions to the limitations linked to the fact that part of our study was conducted at home would have been to assess EI over longer periods under the controlled conditions of the laboratory. Owing to practical reasons, assessing food intake for 12 h (and even more for 24 h) in controlled conditions at the laboratory with infants of this age (and their parents) is extremely difficult to set up. Regarding our methodology, one can wonder whether the calories contributed by the preloads were too low to affect subsequent intake over a period as long as 24 h (LED provided 22 kcal and HED provided 65 kcal; a required minimal consumption of 85% of the preload was set so that the difference between the LED and HED preloads was at least 33 kcal).

Although different methodologies prevent easy comparisons between studies, the fact that the mean observed 0h-COMPX scores at 11 mo were within the range of reported values of some previous studies in children (21-70%) (Carnell, Benson, Gibson, Mais, &Warkentin, 2017; Johnson, 2000; Johnson & Birch, 1994; Remy, Issanchou, Chabanet, Boggio, & Nicklaus, 2015; Zandstra, Mathey, Graaf, & van Staveren, 2000), although different from other studies [77-105%] (Faith et al., 2004; Hetherington, Wood, & Lyburn, 2000; Kasese-Hara, Wright, &Drewett, 2002; Tripicchio et al., 2014), this is an argument in favour of our preloading paradigm, especially the chosen energy density for the preloads (LED preload= 22 kcal, HED day = 65 kcal, that is, 3-fold higher than the LED preload). For illustration, the difference of 43 kcal between LED and HED is not insignificant: it represents, for example, 130 g of plain carrot puree (ready-to-eat baby food) or 69 g of infant formula. The use of weighed dietary records is sufficiently precise considering what the difference in kcal between the LED and HED preloads represents in terms of the quantity of food.

Studies concerning appetite control abilities in infants are rare due to methodological and experimental constraints. Our main result requires the application of a public health perspective. Among infants between 11 and 15 months old, when the ED of a familiar food is modified, energy compensation occurs immediately but is partial (and more or less so depending on the individuals) and does not improve over the subsequent 24 h. To our knowledge, the present paper is the first to report this in this age range. This means that variations of the ED of a familiar food in the sense of an increase in ED (even quite slight) in the diet of infants as young as 11-15 months old might increase their daily energy intake. However, even a slight imbalance of the energy balance can promote rapid weight gain in the first few months if it is repeated, which is a risk factor for the development of an overweight condition. More research is warranted to unravel appetite control abilities in infancy, focusing on facilitators and barriers to efficient appetite control abilities.

This trial was registered at www.clinicaltrials.gov as NCT03409042 (https://clinicaltrials.gov/ct2/show/NCT03409042).

Acknowledgements

We thank M. Bournez (MD) for helping us prepare the protocol for the ethics committee, S. Nicklaus for her guidance and support, F. Bouillot (ChemoSens platform) for her help with recruiting participants, and V. Feyen for helping conduct the experimental tasks. The authors are very grateful to the reviewers for their valuable comments on the manuscript.

The authors' contributions were as follows—PB, SI, and CS: designed the project; PB and CS: conducted the research; SM: collated and reviewed the data; CC and PB: performed the statistical analysis; PB, SI, CC and CS: wrote the paper; PB: had primary responsibility for final content; and all authors read and approved the final manuscript.

References

Birch, L. L., & Deysher, M. (1985). Conditioned and unconditioned caloric compensation: evidence for self regulation of food intake in young children. *Learning and Motivation, 16*, 341-355. doi: https://doi.org/10.1016/0023-9690(85)90020-7

Birch, L. L., Johnson, S. L., Andresen, G., Peters, J. C., & Schulte, M. C. (1991). The variability of young children's energy intake. *The New England Journal of Medicine, 324*(4), 232-235. doi: https://doi.org/10.1056/NEJM199101243240405

Bournez, M., Ksiazek, E., Wagner, S., Kersuzan, C., Tichit, C., Gojard, S., Thierry, X., Charles, M.-A., Lioret, S., de Lauzon-Guillain, B., & Nicklaus, S. (2018). Factors associated with the introduction of complementary feeding in the French ELFE cohort study. *Maternal & Child Nutrition, 14*(2), e12536. doi: 10.1111/mcn.12536

Brugaillères, P., Issanchou, S., Nicklaus, S., Chabanet, C., & Schwartz, C. (2019). Caloric compensation in infants: developmental changes around the age of 1 year and associations with anthropometrics up to 2 years. *The American Journal of Clinical Nutrition, 109*(5), 1344–1352. doi: doi: 10.1093/ajcn/nqy357

Carnell, S., Benson, L., Gibson, E. L., Mais, L. A., & Warkentin, S. (2017). Caloric compensation in preschool children: Relationships with body mass and differences by food category. *Appetite, 116*, 82-89. doi: https://doi.org/10.1016/j.appet.2017.04.018

Chouraqui, J.-P., Tavoularis, G., Simeoni, U., Ferry, C., & Turck, D. (2020). Food, water, energy, and macronutrient intake of non-breastfed infants and young children (0–3 years). *European Journal of Nutrition*, 59, 67-80. doi: https://doi.org/10.1007/s00394-018-1883-y

CIQUAL. (2016). Table CIQUAL. https://ciqual.anses.fr/ Accessed 8 August 2018. Retrieved Accessed 8 August 2018, from https://ciqual.anses.fr/

Faith, M. S., Keller, K. L., Johnson, S. L., Pietrobelli, A., Matz, P. E., Must, S., Jorge, M. A., Cooperberg, J., Heymsfield, S. B., & Allison, D. B. (2004). Familial aggregation of energy intake in children. *The American Journal of Clinical Nutrition, 79*(5), 844-850.

Fox, M. K., Devaney, B., Reidy, K., Razafindrakoto, C., & Ziegler, P. (2006). Relationship between portion size and energy intake among infants and toddlers: evidence of self-regulation. *Journal of the American Dietetic Association, 106*(1, Supplement 1), 77-83. doi: https://doi.org/10.1016/j.jada.2005.09.039

GEM-RCN. (2015). Recommandation nutrition. Ministère de l'économie de l'industrie et du numérique.France, 123 pp., https://www.economie.gouv.fr/files/files/directions_services/daj/marches_publics/oeap/gem/nutrition/nutrition.pdf

Ghisolfi, J., Bocquet, A., Bresson, J. L., Briend, A., Chouraqui, J. P., Darmaun, D., Dupont, C., Frelut, M. L., Girardet, J. P., Goulet, O., Hankard, R., Rieu, D., Siméoni, U., Turck, D., &Vidailhet, M. (2013). Les aliments industriels (hors laits et céréales) destinés aux nourrissons et enfants en bas âge : un progrès diététique ? (Processed baby foods for infants and young children: a dietary advance? A position paper by the Committee on Nutrition of the French Society of Paediatrics). *Archives de Pédiatrie, 20*(5), 523-532. doi: https://doi.org/10.1016/j.arcped.2013.02.072

Grote, V., Verduci, E., Scaglioni, S., Vecchi, F., Contarini, G., Giovannini, M., Koletzko, B., & Agostoni, C. (2016). Breast milk composition and infant nutrient intakes during the first 12 months of life. *European Journal of Clinical Nutrition, 70*(2), 250. doi: https://doi.org/10.1038/ejcn.2015.162

Hetherington, M. M., Wood, C., & Lyburn, S. C. (2000). Response to energy dilution in the short term: evidence of nutritional wisdom in young children? *Nutritional Neuroscience, 3*(5), 321-329.

Johnson, S. L. (2000). Improving preschoolers' self-regulation of energy intake. *Pediatrics, 106*(6), 1429-1435.

Johnson, S. L., & Birch, L. L. (1994). Parents' and children's adiposity and eating style. *Pediatrics, 94*(5), 653-661.

Kasese-Hara, M., Wright, C., & Drewett, R. (2002). Energy compensation in young children who fail to thrive. *Journal of Child Psychology and Psychiatry, 43*(4), 449-456.

Pearcey, S. M., & De Castro, J. M. (1997). Food intake and meal patterns of one year old infants. *Appetite, 29*(2), 201-212. doi: https://doi.org/10.1006/appe.1997.0099

Pinheiro, J., Bates, D., DebRoy, S., Sarkar, D., R Core Team (2020). _nlme: Linear and Nonlinear Mixed Effects Models_. R package version 3.1-145, <URL: https://CRAN.R-project.org/package=nlme>.

PNNS. (2004 édition corrigée 2015). "Children and teens nutritional guide for all parents". In Retrieved 16th January 2018 from http://www.inpes.sante.fr/CFESBases/catalogue/pdf/688.pdf.

Remy, E., Issanchou, S., Chabanet, C., Boggio, V., & Nicklaus, S. (2015). Impact of adiposity, age, sex and maternal feeding practices on eating in the absence of hunger and caloric compensation in preschool children. *International Journal of Obesity, 39*(6), 925-930. doi: 10.1038/ijo.2015.30.

Shea, S., Stein, A. D., Basch, C. E., Contento, I. R., & Zybert, P. (1992). Variability and self-regulation of energy-intake in young-children in their everyday environment. *Pediatrics, 90*(4), 542-546.

Smethers, A. D., Roe, L. S., Sanchez, C. E., Zuraikat, F. M., Keller, K. L., & Rolls, B. J. (2019). Both increases and decreases in energy density lead to sustained changes in preschool children's energy intake over 5 days. *Physiology &Behavior, 204*, 210-218.

Tripicchio, G. L., Keller, K. L., Johnson, C., Pietrobelli, A., Heo, M., & Faith, M. S. (2014). Differential maternal feeding practices, eating self-regulation, and adiposity in young twins. *Pediatrics, 134*(5), e1399-1404. doi: 10.1542/peds.2013-3828

Zandstra, E. H., Mathey, M. F., Graaf, C., & van Staveren, W. A. (2000). Short-term regulation of food intake in children, young adults and the elderly. *European Journal of Clinical Nutrition, 54*(3), 239-246.

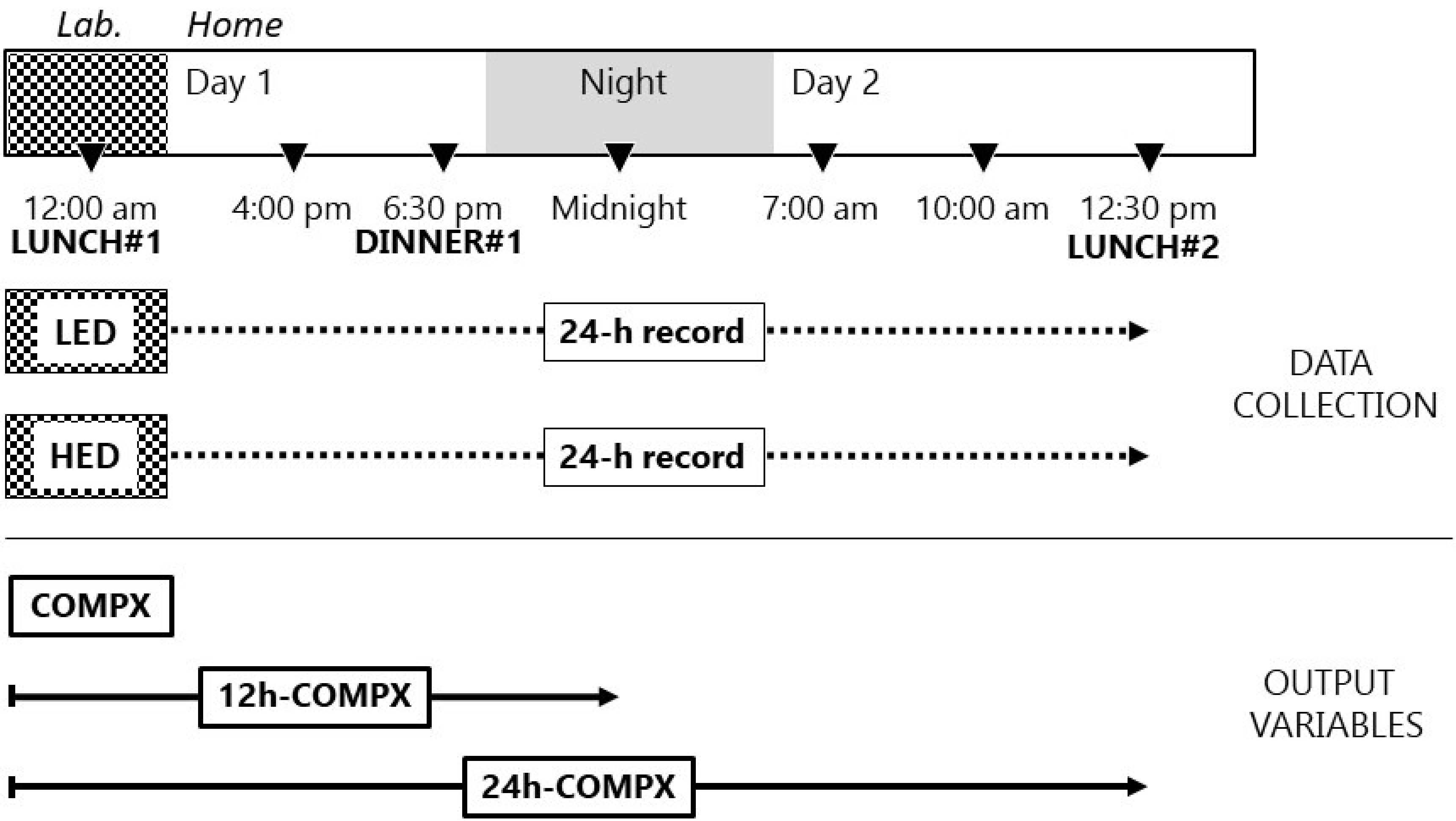
Figure captions

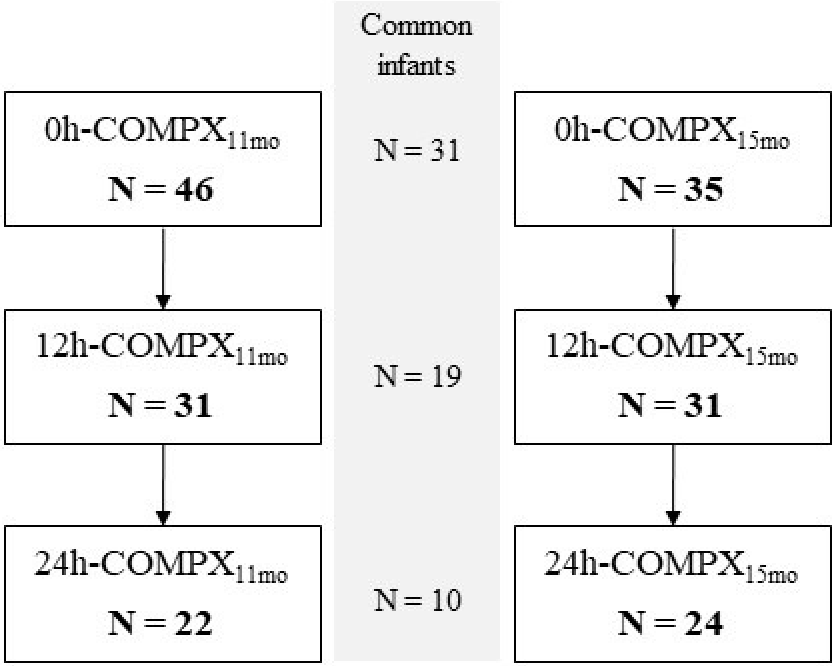
Figure 1: Schematic representation of the data collection and the output variables derived from it.

Figure 2: Flow-chart: number of individuals with 0h-COMPX, 12h-COMPX and 24h-COMPX values available at 11 and 15 months (N=50). The number of common infants between ages is 31, 19 and 10, respectively for the 0h-, the 12h- and the 24h- COMPX.

Figure 3: Mean energy intake (kcal) with 95% confidence intervals for each time period (0h = laboratory meal, 12h = 12h home record, 24 h = 24 h home record) following the preload consumption calculated at 11 months (N = 22, A) and at 15 months (N = 24, B). LED: Low Energy Density; HED: High Energy Density.

Figure 4: Estimated means and 95% confidence intervals for COMPX scores at 11 and 15 months, over the 0-h period, over the 12-h period and over the 24-h period following the preload (linear mixed model, N=50).


Lab.
Home
Day 1
Night
Day 2
12:00 am
LUNCH#1
4:00 pm
6:30 pm
DINNER#1
Midnight
7:00 am
10:00 am
12:30 pm
LUNCH#2
LED
24-h record
HED
24-h record
DATA COLLECTION
COMPX
12h-COMPX
24h-COMPX
OUTPUT VARIABLES



Common infants
0h-COMPX11mo
N = 46
N = 31
0h-COMPX15mo
N = 35
12h-COMPX11mo
N = 31
N = 19
12h-COMPX15mo
N = 31
24h-COMPX11mo
N = 22
N = 10
24h-COMPX15mo
N = 24