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Portion size and later food intake: evidence on the “normalizing” effect of reducing food portion sizes

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ABSTRACT

Background: Historical increases in the size of commercially available food products have been linked to the emergence of a worldwide obesity crisis. Although the acute effect that portion size has on food intake is well established, the effect that exposure to smaller portion sizes has on future portion size selection has not been examined.

Objective: We tested whether reducing a food portion size “renormalizes” perceptions of what constitutes a normal amount of that food to eat and results in people selecting and consuming smaller portions of that food in the future.

Design: Across 3 experiments, participants were served a larger or smaller portion of food. In experiments 1 and 2, participants selected and consumed a portion of that food 24 h later. In experiment 3, participants reported on their preferred ideal portion size of that food after 1 wk.

Results: The consumption of a smaller, as opposed to a larger, portion size of a food resulted in participants believing a “normal”-sized portion was smaller (experiments 1–3, \( P \leq 0.001 \)), consuming less of that food 1 d later (experiments 1–2, \( P \leq 0.003 \)), and displaying a tendency toward choosing a smaller ideal portion of that food 1 wk later (experiment 3, \( P = 0.07 \)), although the latter finding was not significant.

Conclusion: Because consumer preferences appear to be driven by environmental influences, reducing food portion sizes may recalibrate perceptions of what constitutes a “normal” amount of food to eat and, in doing so, decrease how much consumers choose to eat. This trial was registered at www.clinicaltrials.gov as NCT03241576.

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Keywords: portion size, food environment, eating behavior, nudging, energy intake, consumer preference

INTRODUCTION

The prevalence of overweight and obesity has increased dramatically in recent history in many parts of the developed world (1). The emergence of the obesity crisis coincided with changes in the food environment (2). During a relatively short time period, a combination of factors has resulted in an “obesogenic” food environment that promotes overconsumption (3–5). One aspect of the food environment that has changed is food portion size (6). The portion size of some commercially available foods has increased over time (7–9). This, coupled with evidence that portion size has an acute (10, 11) and prolonged effect on energy intake (12, 13), has led to suggestions that portion size has been a driver of population-level weight gain (9, 14). There have been calls for the need to “downsize” the default portion size of commercially available food products in order to tackle overweight and obesity (15, 16).

Reducing portion size has been shown to decrease acute energy intake, and this reduction may not be compensated for at subsequent meals (17, 18). However, it is less clear whether there would be other downstream consequences of reducing food portion sizes. We hypothesize that reducing the portion size of a food may “normalize” more appropriately sized portions and shift people toward selecting and consuming smaller portions of that food in the future. A key reason why the provision of smaller portion sizes could “renormalize” more appropriate portion sizes is because visual perception of what constitutes a normal size or amount is driven by what humans are used to seeing in their environment—otherwise known as their “visual diet” (19, 20). Human eating behavior and appetite control is also recognized as being flexible, in the sense that there is no tight physiologic control of energy intake and therefore no precise “correct” amount to eat (21–23). Portion size is thought to communicate information about what constitutes a normal amount of food to eat (24, 25). What has received less attention is how humans determine what

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a “normal”-sized portion is and how this affects decisions about meal size (25, 26). Although multiple factors affect the amount of food served at a meal, we hypothesized that perceptions of what constitutes a “normal” portion size play a central role. In the same way that it has been argued that the availability of supersized portions has normalized bigger portions (27), reducing food portion sizes could serve to “renormalize” more appropriately sized portions. In support of this, repeated visual exposure to images of larger compared with smaller portion sizes of a food has been shown to affect size judgments about an intermediate portion size of that food (19).

Across 3 experiments we tested the hypothesis that providing participants with smaller portion sizes of a food may recalibrate their perceptions of what constitutes a “normal” portion size and, in doing so, reduce the amount of that food that they choose to eat in the future. In experiments 1–3, participants were served and consumed either a larger or smaller portion of a lunch food, quiche. The next day, under the guise of a cover story, the same participants self-served and ate quiche (experiments 1 and 2). In experiment 3, 1 wk after being served a larger or smaller portion of quiche, participants selected the portion size of quiche they would most like to eat. We hypothesized that the provision of a smaller as opposed to larger portion size of quiche would result in participants choosing to eat less quiche in the future and that this would be explained by changes in the perception of the size of a “normal” serving of quiche.

METHODS

Experiment 1

Participants and sample size

Participants were recruited from staff and students at the University of Liverpool into a laboratory study described as examining “food, mood, and reasoning” (cover story). In experiment 1, we sampled women only and participants were required to indicate that they would be happy to eat quiche before participation. Potential participants with any history of food allergy or who were currently dieting for weight loss were ineligible. We based the smaller portion size on a serving that has been shown was palatable and acceptable to consume for lunch. In experiments 1 and 2, a broccoli-and-tomato quiche, varying in portion sizes from one-eighth of a quiche to a full family-sized quiche (200 g, 440 kcal), and the smaller portion size condition was one-quarter of half a family-sized quiche (100 g, 220 kcal, which equated to the manufacturer’s recommended amount for 1 serving).

Procedure

Participants attended a first session during a weekday lunchtime and were asked to abstain from eating for 2 h before the session. After checking for food allergies, the researcher bolstered the cover story by informing participants that they would complete mood questionnaires before eating lunch, and after eating lunch they would complete the same mood questionnaires and a cognitive task. Participants were then asked to complete a series of mood ratings (e.g., “how happy are you right now?”) on visual analog scales anchored with “not at all” and “extremely.” The mood ratings also included how hungry and full participants were. When participants had completed the ratings, the researcher returned with the lunch, which consisted of the randomly assigned (computerized random-number generator) larger or smaller portion of quiche with a 60-g side salad (lettuce leaves, red cabbage, and carrot) on a standard dinner plate, as well as a glass of water, and the researcher verbally asked the participant if they would “eat all of the meal.” The participant signaled when she had finished eating by pressing a buzzer. Participants then completed ratings about the palatability of the quiche by using the visual analog scales (anchors: “not at all” and “extremely”), including how much they liked the quiche, before completing the same mood rating as before lunch. To further corroborate the cover story, participants were then provided with a cognitive task, in which they had to identify missing letters in word stems to form words. Participants were informed that they had 5 min to complete as many word stems as possible and were provided with a stopwatch to keep track of how much remaining time they had. After 5 min, the researcher returned and explained that the first session was complete and reminded participants to return for their second session the following day.

Participants returned for the second session at lunchtime the next day and were informed that they would be completing a similar word completion task, but this time by lunch. After completing the word stem task, participants then completed the mood measures as in the first session. The researcher then returned with a tray consisting of a full family-sized quiche (400 g, 880 kcal) in a foil container, a full bag of salad (370 g), and a glass of water. The researcher explained that they had not had time to print the final questionnaires for the session, so told the participants they could serve themselves whatever they wanted to eat and that they would be back shortly. Once the participants had finished eating they alerted the researcher by pressing the buzzer and the researcher returned with the same mood measures and palatability questionnaire as in the first session. Next, participants were asked to write down what they thought the aims of the study were before completing a final questionnaire. In the final questionnaire, to measure perceptions of portion size normality, participants were asked “Which of the following portion sizes would you say is a normal portion size of quiche to eat for lunch?” and were shown 6 images of a broccoli-and-tomato quiche, varying in portion sizes from one-eighth of a quiche to a full family-sized quiche. Next, as a manipulation check, participants were shown the same images and asked which portion size they had been served in session 1. Finally, participants completed
a questionnaire that included demographic information, items on their eating habits, and a measure used to further probe demand characteristics. To further probe demand characteristics, participants were asked the extent to which they believed their food intake was measured by the researcher, and we planned to examine whether our main results were dependent on this (see Supplemental Methods for full details). Participants then had their height and weight measured before being debriefed, were provided with a small monetary payment, and were thanked for their time.

**Main analysis strategy**

We planned to examine the effect of portion size condition on the amount of quiche that participants consumed (calculated in grams from weighing the quiche and any leftovers pre-post lunch) during session 2 by using an independent-samples t test. We compared conditions on the portion size normality measure (ordinal data) by using a Mann-Whitney U test. To examine the effect of portion size condition on day 2 quiche consumption was explained by changes in portion size normality, we used the PROCESS macro for SPSS (29). All of the analyses were conducted in SPSS 24.0. (See Supplemental Methods for further information about the mediation analysis strategy and secondary analyses.) We planned to exclude any participants from analyses who had directly guessed the aims of the study (see Supplemental Methods for more information) or who did not follow key study instructions (e.g., consuming less than half of the quiche provided in session 1, eating nothing during session 2).

**Experiment 2**

In experiment 2, we aimed to replicate the findings of experiment 1 and we sampled men instead of women participants.

We used the same method as in experiment 1 except for an alteration to the food served during lunch. Pilot testing indicated that a lunch of quiche and salad may not be sufficient for some men, so in session 1 the lunchtime meal included a 25-g serving of potato chips and in session 2 a 25-g bag of unopened potato chips was included on the lunch tray.

**Experiment 3**

In experiment 3, we aimed to examine whether the effect of a smaller portion size on subsequent portion size selection would persist over a longer time period (1 wk later). We also designed experiment 3 to further rule out demand characteristics. When participants made their later portion size selection, they did so among a series of other measures they believed were part of an unrelated study being conducted by a different researcher.

**Participants and sample size**

Men and women were recruited from staff and students at the University of Liverpool into a study described as examining “hunger and executive functioning.” In experiments 1 and 2, we observed medium-large statistical effects of portion size condition on our dependent variables. Because we reasoned that the effect may be smaller 1 wk later, we aimed to recruit a sufficient number of participants to detect a medium-sized statistical effect ($\eta = 0.2$). We recruited slightly above this number as in experiments 1 and 2.

**Procedure**

We used a similar procedure as in experiment 2, although participants were served a cheese-and-onion quiche (279 kcal/100 g; Tesco Supermarket) in experiment 3. The portion sizes were the same as in experiments 1 and 2. Participants first completed a 3-min reaction time task in which they had to classify 40 letter strings as words or nonwords as quickly and accurately as possible to corroborate the cover story. Next, participants completed the mood measures before being provided with the randomly assigned smaller or larger portion size of quiche for lunch, along with the side salad, potato chips, and water. Participants completed the same mood measures again, before completing a similar reaction time task. Unlike experiments 1 and 2, participants did not complete any measures about the lunch food during session 1 to ensure that they were unaware of our interest in the quiche. At the end of the session, the researcher informed the participants that they would receive an e-mail in a week to complete a short online survey. One week later, participants were redirected to a survey site and first rated their hunger, as in experiments 1 and 2. Next, they completed a similar reaction-time task as in session 1. After this, they completed some filler personality items before being thanked for their time. On the next page, participants were asked to take part in a different survey being conducted by another researcher and that the study involved questions about food selection and eating habits. On consecutive individual pages, participants were shown 6 images of varying portion sizes of a common mealtime food. To disguise our interest in the target food (cheese-and-onion quiche), there were 4 foods in total, and for each of the foods, participants were asked “Which of the following portion sizes would you choose to eat for lunch?” and “Which of the following portion sizes would you say is normal to eat for lunch?” on separate pages. The cheese-and-onion quiche was always presented second, and the order of presentation of the selection and normality measure was counterbalanced. Next, participants completed the manipulation check, were asked questions about their eating habits (see Supplemental Methods), and guessed the aims of the study. Finally, participants were debriefed and thanked.

**RESULTS**

**Experiment 1**

**Participant characteristics**

Eighty-four participants were recruited. Four participants did not attend the second session, 4 correctly identified the aims of the experiment, and 1 did not follow study instructions (ate less than half of the quiche during session 1), which left a final sample size of 75 participants with a mean ± SD age of 31.9 ± 9.4 y and a mean ± SD BMI (kg/m$^2$) of 24.7 ± 4.8 (see Supplemental Figure 1).

**Session 1 food consumption**

During the first session, participants in the larger portion size condition consumed more quiche (mean ± SD: 176.5 ± 29.2 g)
portion size condition (99.2 ± 9.6 g) and, as expected, this difference was significant \[ t(73) = 15.50, P < 0.001, d = 3.56 \]. There was no significant difference \[ t(73) = 0.82, P = 0.41, d = 0.19 \] in salad consumption between the larger portion size condition (41.4 ± 19.1 g) and the smaller portion size condition (44.7 ± 16.1 g) during the first session.

**Session 2 portion size normality and subsequent consumption**

In line with our hypotheses, participants’ perception of a normal-sized portion was significantly smaller in session 2 if they had eaten the smaller \((n = 38)\) as opposed to the larger \((n = 37)\) portion size during session 1 \((U = 371.50, z = 3.76, P < 0.001, r = 0.43)\) (see **Table 1**). Moreover, participants served the smaller portion size (mean ± SD quiche consumed in session 2: 144.66 ± 72.36 g) as opposed to the larger portion size (mean ± SD quiche consumed in session 2: 189.81 ± 55.62 g) during session 1 on to freely serve themselves and consume significantly less quiche during session 2 \((t(73) = 3.02, P = 0.003, d = 0.70)\). There was no evidence that the effect that the session 1 portion size condition had on session 2 quiche consumption was influenced by whether or not participants believed their food intake would be measured by the researcher (see **Supplemental Results**). Mediation analysis confirmed that the effect of portion size condition on day 2 quiche consumption was explained by condition differences in portion size normality (see **Table 2**).

**Self-reported appetite and liking**

We examined whether self-reported fullness or hunger differed according to portion size condition pre- and postlunch during either session 1 or 2 by using a mixed ANOVA. As expected, participants felt less hungry and fuller after eating in both sessions. However, there was no effect of portion size condition or interaction between portion size condition and time point, indicating that the effect on food intake that the smaller portion size had did not result in participants reporting greater post-meal hunger or reduced post-meal fullness during either session (see **Supplemental Table 1**). Participants’ liking of the quiche in the smaller and larger portion size conditions did not differ (see **Supplemental Table 2**).

**Experiment 2**

**Participant characteristics**

Eighty-three participants were recruited. This sample size was consistent with our power analysis for experiment 1 and provided adequate statistical power to detect the effects observed in experiment 1. Two participants correctly identified the aims of the experiment, and 3 did not follow study instructions (ate less than half of the quiche during session 1), which left a final sample size of 78 participants with a mean ± SD age of 24.5 ± 7.0 y and a mean ± SD BMI of 25.2 ± 4.5 (see **Supplemental Figure 2**).

**Session 1 food consumption**

During the first session, participants in the larger portion size condition consumed more quiche (mean ± SD: 195.1 ± 15.1 g) than did participants in the smaller portion size condition (99.4 ± 11.2 g), and as expected, this difference was significant \([t(76) = 31.83, P < 0.001, d = 7.20]\). There was a significant difference \([t(76) = 2.20, P = 0.03, d = 0.50]\) in salad consumption between the larger portion size condition (51.5 ± 14.8 g) and the smaller portion size condition (57.2 ± 6.3 g) during the first session. There was no significant difference \([t(76) = 0.31, P = 0.76, d = 0.07]\) in potato chip consumption between the larger portion size condition (23.4 ± 4.5 g) and the smaller portion size condition (23.7 ± 4.5 g) during the first session.

**Table 1** Perception of portion size normality in experiments 1–3

|                | Larger portion size condition (%) | Smaller portion size condition (%) | Effect of condition (Mann-Whitney U test) |
|----------------|-----------------------------------|------------------------------------|------------------------------------------|
|                | One-eighth | One-fourth | Three-eighths | One-half | Three-fourths | One |                | One-eighth | One-fourth | Three-eighths | One-half | Three-fourths | One |                |
| Experiment 1 (n = 75) |          |            |              |         |              |     |                | 0          | 18.9       | 48.6        | 27.0     | 5.4          | 0    | (U = 371.50, z = 3.76, P < 0.001, d = 3.56) |
| Experiment 2 (n = 78) |          |            |              |         |              |     |                | 0          | 18.4       | 39.5        | 34.2     | 5.3          | 2.6  | (U = 422.00, z = 3.54, P < 0.001, d = 0.40) |
| Experiment 3 (n = 124) | 1.8       | 33.9       | 28.6         | 28.6    | 1.8          | 5.4  |                | (U = 1304.00, z = 3.24, P = 0.001, d = 0.29) |

1Values refer to the proportion of participants choosing each response option by each condition. Responses to “Which of the following portion sizes would you say is a normal portion size of quiche to eat for lunch?” with response options “one-eighth” to “one” indicate proportion of a family-sized quiche.

**Table 2** Mediation results in experiments 1–3

|                | Relation between condition (IV and PS normality (M)) | Relation between PS normality (M) and DV | Indirect effect | Proportion of total effect explained by indirect effect, % |
|----------------|-----------------------------------------------------|----------------------------------------|----------------|----------------------------------------------------------|
| Experiment 1 (n = 75) | 9.62 (4.84, 14.39) | 3.09 (1.82, 4.36) | 29.75 (14.05, 52.39) | 65.88 |
| Experiment 2 (n = 78) | 11.53 (5.48, 17.58) | 2.46 (1.22, 3.70) | 28.33 (11.49, 50.98) | 30.12 |
| Experiment 3 (n = 124) | 7.13 (0.67, 13.59) | 0.78 (0.64, 0.91) | 5.54 (0.71, 11.20) | 91.89 |

1Values are \( \beta \)s (95% CIs) unless otherwise indicated. Process mediation analysis was used. Because the direct effect of portion size condition on portion selection in experiment 3 was negative after including the mediator in the model \((\beta = -0.49, SE = 2.46, P = 0.84)\), we calculated the total effect from the absolute regression coefficients based on the recommendation by Alwin DF, Hauser RM. The decomposition of effects in path analysis. Am Sociol Rev 1975;40(1):37–47. Total effect = direct effect + indirect effect. DV, dependent variable; IV, independent variable; M, mediator; PS, portion size.
Experiment 3

Participant characteristics

A total of 140 participants were recruited. Three participants did not complete the second questionnaire, 1 participant correctly identified the aims of the experiment, and 12 participants did not follow study instructions (ate less than half of the quiche during session 1). The final sample of 124 participants (46 men, 78 women) had a mean ± SD age of 27.7 ± 9.2 y and a mean ± SD BMI of 23.6 ± 4.1 (see Supplemental Figure 3).

Session 1 food consumption

During the first session, participants in the larger portion size condition consumed more quiche (mean ± SD: 179.6 ± 31.9 g) than did participants in the smaller portion size condition (97.6 ± 12.9 g), and as expected, this difference was significant [t(122) = 19.38, P < 0.001, d = 3.37]. There was no significant difference [t(122) = 0.42, P = 0.68, d = 0.07] in salad consumption between the larger portion size condition (24.4 ± 9.2 g) and the smaller portion size condition (23.8 ± 6.9 g) during the first session. There was no significant difference [t(122) = 0.96, P = 0.34, d = 0.29] in potato chip consumption between the larger portion size condition (21.3 ± 12.2 g) and the smaller portion size condition (29.4 ± 38.1 g) during the first session.

Portion size normality and selection at follow-up

Participants’ perception of a normal-sized portion was significantly smaller 1 wk later if they had eaten the smaller (n = 68) as opposed to larger portion size (n = 56) during session 1 (U = 1304.00, z = 3.24, P = 0.001, r = 0.29) (see Table 1). Moreover, participants who ate the smaller as opposed to the larger portion size during session 1 tended to select a smaller size portion at follow-up (U = 1562.5, z = 1.80, P = 0.07, r = 0.16), although this difference was not significant. Mediation analysis confirmed that the effect of condition on later portion size selection was explained by condition differences in portion size normality (see Table 2).

Self-reported appetite

As in experiments 1 and 2, there were no effects of portion size condition on self-reported appetite (Supplemental Table 5).

DISCUSSION

In 3 experimental studies that served participants a smaller as opposed to a larger portion size of food resulted in them later perceiving a “normal”-sized portion of that food to be smaller. In experiments 1 and 2, this also resulted in participants selecting and eating less of that food the next day. In experiment 3, this resulted in participants tending to select a smaller ideal portion size of that food 1 wk later, although this finding was not significant (P = 0.07).

The present research was motivated by the observation that the portion size of many commercially available food products has increased over time and “supersized” products are now common (7, 14). It has also been suggested that larger portions of food have distorted consumer awareness of the recommended serving sizes of foods (30, 31) and that one of the reasons why food portion size affects acute energy intake is because portion size may signal a “normal” amount to eat (24). We reasoned that because humans will base perceptions of stimulus normality on what they encounter in their environment (19), downsizing the portion size of a food product should result in consumers adjusting their perceptions of what a normal-sized serving of that food is and this would affect future behavior. To our knowledge, the present experiments provide the first empirical evidence in support of this.

There have been suggestions that shrinking the portion size of commercially available food products could be one approach to reducing overconsumption and tackling population-level obesity (9, 15, 32). The present findings indicate that if portion sizes of commercially available foods were reduced, these smaller, more appropriate portion sizes may “normalize.” Across all 3 experiments, we also found no evidence that smaller portion sizes were associated with reduced fullness or increased hunger postmeal. These findings corroborate other laboratory studies, which show that decreasing portion size can reduce food intake without causing later compensatory eating (33, 34). More generally, the present findings are in keeping with current theoretical accounts of human eating behavior, which suggest that there is no “tight” control of energy intake on a meal-by-meal basis (21, 23). Thus, there is a flexible range of meal sizes that are likely to be acceptable to consumers. Dependent on what is “normal” in a consumer’s food environment, this flexibility in acceptable meal sizes can presumably result in chronic over- or undereating. What is unclear from the present studies is whether the consumption of a smaller portion size of food is required for smaller portions of that food to “normalize” or whether similar effects would be observed vicariously (e.g., seeing others consume smaller portions
may alter perceptions of portion size normality). Likewise, we focused on one food in the present studies, so it is unclear whether similar effects would be observed for foods that are more (or less) frequently consumed. It is plausible that perceptions of portion size normality for foods that are frequently eaten are less malleable than less familiar foods.

There are many historical examples of public health policies that may have seemed like a substantial change at the time or were met with some initial reactance but soon normalized. For example, since the turn of the century, the amount of salt in food products has decreased and as a result consumers are now eating less salt, which has been of benefit to public health (35, 36). Likewise, the implementation of smoke-free legislation in the United Kingdom, the United States, and many other countries has “de-normalized” smoking and in doing so likely saved thousands of lives (37). There is now consensus that, irrespective of their level of popular appeal, similar large-scale environmental changes are required in order to renormalize the food environment and effectively tackle the obesity crisis (2, 3, 5).

The present research has strengths and limitations. Findings were replicated across 3 experiments and the use of cover stories minimized demand characteristics. Yet, although we made efforts to minimize the potential influence of demand characteristics in our experiments, the replication of our findings under “free-living” conditions in which demand characteristics would be minimal may be valuable. A limitation is that we sampled a predominantly young, white, middle-class population. Although demographic characteristics such as social class are thought to influence nutrition (38), we do not know of a strong rationale as to why our main findings would be different across other populations and this remains an empirical question. A further limitation of the present experiments is that some of our self-report measures were not widely used validated instruments. For example, the measure of portion size normality did not include a full range of possible portion sizes of quiche, and this may have introduced measurement bias due to fewer response options at the upper end of the scale. Although this bias would be observed across both experimental conditions, it may have resulted in a less-precise measurement of portion size norm perceptions.

An unanswered question from the present research is how long the effects we observed would last. For example, the effects observed on food intake 1 d later in the laboratory (experiments 1 and 2) were larger than when portion size preference was observed 1 wk later outside of the laboratory (experiment 3), although other methodologic differences between the experiments may account for this observation. On the basis of the notion that perceptions of portion size normality are environmentally driven, we presume that these effects would persist, provided that consumers continue to encounter smaller-sized portions of the food item in question more frequently than supersized portions. The present studies are also unable to tell us about the extent to which changing the portion size of one type of food item would affect portion size preferences for other similar food items (a form of “transfer” effect), and this would be an interesting question to answer. In addition, the present studies do not allow us to draw conclusions about the independent effects that smaller and larger portion sizes have on changes in perceptions of portion size normality. The smaller and larger portion sizes used in the present studies differed somewhat in their shape as well as size, so standardizing shape across portion sizes would be preferable in future research. Finally, because of practical constraints, we measured portion size normality in experiments 1 and 2 after session 2 food intake and it is possible that the amount that participants ate during session 2 affected their perceptions of portion size normality.

Conclusions

In conclusion, serving participants a smaller portion size of a food affected their perceptions of what constitutes a normal-sized serving and resulted in them choosing to eat less of that food in future. Because consumer preferences are, in part, driven by environmental influence, reducing food portion sizes may recalibrate perceptions of a “normal” amount of food to eat and, in doing so, decrease how much consumers freely choose to eat. These results suggest that downsizing the default size of food products may result in the “renormalization” of smaller food portion sizes.

The authors’ responsibilities were as follows—ER: designed and oversaw the data collection of experiments 1 and 2; IK: oversaw the data collection of experiment 3; and both authors: designed experiment 3 and were responsible for data analysis, had full access to the data, and read and approved the final manuscript. The authors reported no competing interests.

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