

## Short Communication

# Increased meal frequency does not promote greater weight loss in subjects who were prescribed an 8-week equi-energetic energy-restricted diet

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There have been reports of an inverse relationship between meal frequency (MF) and adiposity. It has been postulated that this may be explained by favourable effects of increased MF on appetite control and possibly on gut peptides as well. The main goal of the present study was to investigate whether using a high MF could lead to a greater weight loss than that obtained with a low MF under conditions of similar energy restriction. Subjects were randomised into two treatment arms (high MF = 3 meals + 3 snacks/d or low MF = 3 meals/d) and subjected to the same dietary energy restriction of  $-2931$  kJ/d for 8 weeks. Sixteen obese adults ( $n$  8 women and 8 men; age 34.6 (SD 9.5); BMI  $37.1$  (SD  $4.5$ ) kg/m<sup>2</sup>) completed the study. Overall, there was a 4.7% decrease in body weight ( $P < 0.01$ ); similarly, significant decreases were noted in fat mass ( $-3.1$  (SD  $2.9$ ) kg;  $P < 0.01$ ), lean body mass ( $-2.0$  (SD  $3.1$ ) kg;  $P < 0.05$ ) and BMI ( $-1.7$  (SD  $0.8$ ) kg/m<sup>2</sup>;  $P < 0.01$ ). However, there were NS differences between the low- and high-MF groups for adiposity indices, appetite measurements or gut peptides (peptide YY and ghrelin) either before or after the intervention. We conclude that increasing MF does not promote greater body weight loss under the conditions described in the present study.

### Meal frequency: Weight loss: Gut peptides: Appetite

Investigating dietary patterns that may minimise sensations of hunger and maximise sensations of fullness is relevant in the context of improved control over body energy reserves. Increased feeding frequency has often been proposed to convey favourable effects on body weight<sup>(1–4)</sup>, adiposity<sup>(5,6)</sup> and energy intake<sup>(7,8)</sup>, but controversy persists<sup>(9–12)</sup>. It has been hypothesised that the favourable effect of increased meal frequency (MF) could emanate from a more sustained release of gastrointestinal hormones<sup>(13)</sup>; however, more studies are needed to confirm this postulation.

The main objective of the present study was thus to investigate whether using a high-MF pattern (3 meals + 3 snacks/d), with snacks being individually timed, could lead to greater weight loss than a low-MF pattern (3 meals/d) in response to an 8-week equi-energetic dietary energy restriction. The secondary objectives of the present study were to examine the effects of MF on: (1) appetite and on; (2) concentrations of total peptide YY and ghrelin.

### Methods

#### Subjects

Eighteen subjects (nine men and nine women) were recruited; of these subjects, sixteen completed the study (eight men

and eight women), whose results are presented herein. They were obese ( $30$  kg/m<sup>2</sup> < BMI <  $45$  kg/m<sup>2</sup>), non-diabetic, non-smokers, non-pregnant, sedentary (<30 min of continuous exercise performed  $\leq 2$  times/week), weight stable for  $\geq 6$  months ( $\pm 2$  kg) and aged between 18 and 55 years. Only pre-menopausal women with a regular menstrual cycle (28–35 d) were recruited, including those using oral contraceptives. Subject characteristics before and after the weight loss programme are presented in Table 1. Apart from being characterised by an increased adiposity, subjects were apparently healthy, i.e. free from any illnesses and medication that could have influenced the outcome of the programme. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the University of Ottawa Research Ethics Committee and the Montfort Hospital Research Ethics Board. Written informed consent was obtained from all subjects.

#### Procedures

The present study was conducted as a randomised approach with two parallel treatment groups. Participants were randomised to one of the two groups as follows: the high MF (3 meals + 3 snacks/d) and the low MF (3 meals/d). Women

Abbreviation: MF, meal frequency.

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**Table 1.** Characteristics of subjects in the high-meal frequency (HMF) and low-meal frequency (LMF) groups before and after weight loss (Mean values and standard deviations)

Variables	Before wt loss				After wt loss				MF†	Time‡	MF × time§
	HMF		LMF		HMF		LMF				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Age   (years)	34.6	9.5	36.3	7.4	–	–	–	–	NS	–	–
Body wt (kg)	114.1	24.6	101.0	16.6	109.5	23.6	95.7	17.4	NS	**	NS
Fat mass (kg)	48.9	11.4	38.3	5.6	45.7	10.0	35.2	7.4	NS	**	NS
Lean body mass (kg)	62.1	17.2	58.4	13.7	60.3	16.5	56.2	13.9	NS	*	NS
BMI (kg/m <sup>2</sup> )	37.1	4.5	34.8	4.0	35.6	4.7	32.9	4.5	NS	**	NS

Mean values were significantly different: \* $P < 0.05$ , \*\* $P < 0.01$ , respectively.

† Effect of MF = significant difference between the LMF and HMF groups.

‡ Effect of MF × time = a significantly different response of dependent variables to the intervention between the LMF and HMF groups.

§ Effect of time = significant effect of the weight loss programme on dependent variables.

|| Age at the onset of weight loss.

( $n = 8$ ) and men ( $n = 8$ ) were stratified equally in both groups. Both groups were prescribed a  $-2931$  kJ/d energy restriction for a period of 8 weeks and had to follow a meal plan according to the recommendations from the Canadian Diabetes Association's food exchange system<sup>(14)</sup>, as previously described<sup>(15)</sup>. A period of at least 4 h but not more than 6 h between main meals during the day, i.e. breakfast, lunch and supper, was imposed for both low- and high-MF groups. Supper had to be consumed at least 3 h before bedtime (2 h for snacks in the high-MF group). Ingestion of the pre-lunch and pre-supper snacks for the high-MF group was set at specific times for each subject. This time was determined at baseline based on the time to achieve peak fullness in response to a test meal of 1256 kJ (two slices of whole wheat toast, one tablespoon natural peanut butter and 125 ml of 2% milk). Meal timing for snacks was then set by subtracting the time to achieve peak fullness from the time at which the main meals were consumed. A 'meal' had to be composed from at least three food groups from the Canadian Food Guide, and a 'snack' was represented by one source of carbohydrate (grain products or fruits and vegetables) and one source of protein (meat and substitutes or milk products). Because all subjects were prescribed a 2931 kJ deficit during the weight loss programme, the resulting daily energy intake varied among subjects. In order for the snacks in the high MF to not represent a disproportionate amount of energy intake, the mean energy content for snacks was adjusted for each individual in the high-MF group and on average was 849 (SD 205) kJ (range 599–1059 kJ).

#### Pre- and post-weight loss measures

During the first day of measurement before and after weight loss, subjects were weighed. Following this, subjects rested in the supine position for 30 min before a resting energy expenditure measure was performed. Fullness levels were then assessed with a visual analogue scale following a standardised snack test meal in order to determine the fullness peak and the time fullness remained elevated. These results were used to determine meal timing for the 8-week diet of the high-MF group. At the end of both sessions, a dual X-ray absorptiometry scan was performed to assess body composition. All methods have been previously described

elsewhere<sup>(16)</sup>. During the second day of measurements before and after weight loss, appetite ratings and blood samples were taken fasting and hourly for 6 h for the two groups (high-MF and low-MF), while subjects were either served three meals (low-MF group) or three meals and three snacks (high-MF group) according to their respective dietary restriction. From the blood samples, total peptid YY (includes both peptid YY<sub>1-36</sub> and peptid YY<sub>3-36</sub>) and total ghrelin (includes both acyl and des-acyl ghrelin) were assayed in duplicates with commercially available ELISA (total peptid YY (catalogue no. EZHPYYT66K) and total ghrelin (catalogue no. EZGRT-89K) ELISA Kits, Millipore, Billerica, MA, USA). In our laboratory, the intra-kit CV for total peptid YY and total ghrelin used in the present study was 2.4 and 3.9%, respectively.

#### Statistical analysis

SPSS Software 17.0 (SPSS, Inc., Chicago, IL, USA) was used for all analyses. A series of repeated-measures ANOVA with MF as a between-subject factor were used for all dependent variables. All effects were considered significant at  $P < 0.05$ . Data are presented as means and standard deviations except if otherwise specified.

## Results

#### Anthropometric measures

A 4.7% decrease in body weight was observed after 8 weeks ( $P < 0.01$ ) (Table 1). Fat mass ( $-3.1$  (SD 2.9) kg;  $P < 0.01$ ), lean body mass ( $-2.0$  (SD 3.1) kg;  $P < 0.05$ ) and BMI ( $-1.7$  (SD 0.8) kg/m<sup>2</sup>;  $P < 0.01$ ) were also significantly reduced. There was NS difference in body weight loss between the low-MF ( $-5.3$  (SD 3.1) kg) and high-MF ( $-4.6$  (SD 2.4) kg) groups. The decrease in fat mass, lean body mass and BMI was not different between the low-MF and high-MF groups.

#### Appetite measures

As expected, the changes for desire to eat, hunger, fullness and prospective food consumption over the 6 h were significant ( $P < 0.01$ ). There were NS effects of MF or MF by weight loss interaction for appetite measurements. No effects of

weight loss or MF by weight loss interaction were noted for the integrated response (area under the curve) of appetite measurements.

### Total ghrelin and peptide YY

As expected, significant effects of time ( $P < 0.001$ ) delineating the variations of total ghrelin throughout the 6-h period and weight loss ( $P < 0.01$ ) were observed (Fig. 1(a)). NS effects of MF (low-MF *v.* high-MF) or MF by weight loss interactions were observed. Significant effects of time delineating the variations of total peptide YY throughout the 6-h period were also observed ( $P < 0.001$ ) (Fig. 1(b)). A significant effect of MF by time was observed, indicating that the different meal patterning significantly affected the 6-h total peptide YY profile ( $P < 0.05$ ). Finally, a significant weight loss by time interaction for peptide YY was also noted ( $P < 0.01$ ).

### Discussion

The premise underlying the present study was that increasing MF would lead to better short-term appetite regulation and increased dietary compliance; furthermore, it was hypothesised

that these predicted beneficial effects of increased MF could have resulted from more favourable gut peptide profiles, potentially leading to greater weight loss. Under the conditions described in the present study, all three hypotheses were rejected. First, although the energy restricted diet did cause a approximately 5% weight loss, NS group differences were noted for changes in body weight or any other marker of changes in body energy reserves. Second, as expected a significant time effect was noted for appetite sensations, but no MF or MF by weight loss effects were noted. Finally, no notable trends indicative of a significant effect of increased MF on total peptide YY or ghrelin were observed.

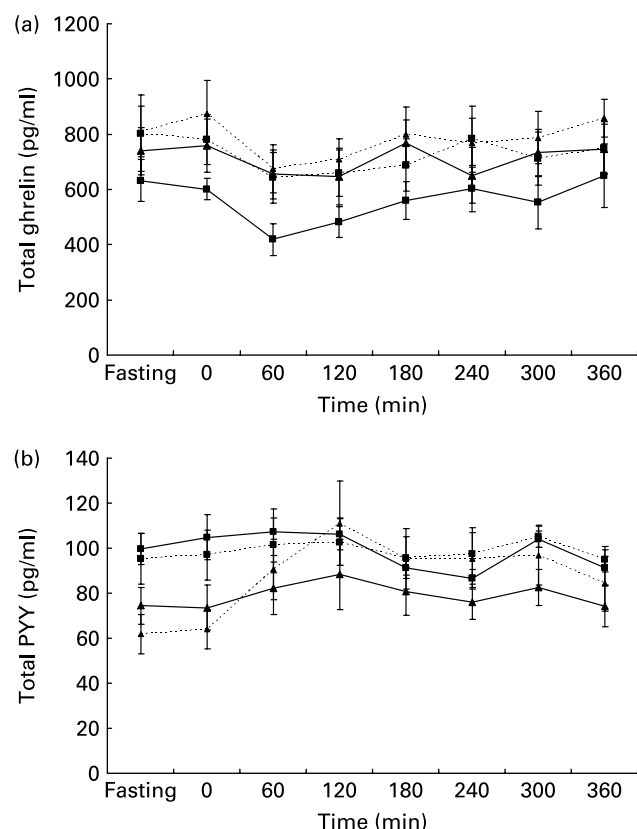
We had postulated that increasing MF would enhance the compliance to the energy restricted diet thus leading to greater weight loss, an effect possibly mediated by increased fullness. The present results do not support this hypothesis. In fact, both groups lost similar amounts of body weight and adiposity. Although many studies have reported positive effects of increased MF on overall energy intake and adiposity<sup>(1,2,4,6-8)</sup>, there are several reports showing no relationship between MF and BMI<sup>(9,12)</sup>, body weight<sup>(10,11)</sup> or body fat composition<sup>(10,11)</sup>. Further complicating an already divided topic, several authors have found that when dietary under-reporters<sup>(12)</sup> or behavioural factors such as eating restraint<sup>(9)</sup> or physical activity participation<sup>(17)</sup> are taken into account, previous findings of inverse relationships between MF and adiposity disappear. It is thus possible that the inverse relationship between MF and adiposity may in fact result from a combination of increased MF to increased physical activity and/or increased dietary restraint and possibly other factors as well.

It was also hypothesised that increasing MF could attenuate large meal-to-meal excursions of peptide YY and that total daily ghrelin, but more particularly pre-meal ghrelin levels, would also be reduced with increased MF. Since pre-meal appetite ratings have been shown to be predictors of energy intake<sup>(16)</sup>, the study design also included individual timing of the snacks in the high-MF conditions, so that peak fullness would actually coincide with lunch and dinner. Collectively, we had postulated that these effects could have in turn facilitated greater adherence to the energy-restricted diet in the high-MF group. According to the present results, increasing MF did not change the daily profiles of peptide YY or ghrelin, nor did it favourably impact appetite parameters.

In summary, we show that imposing a higher feeding frequency under equi-energetic dietary energy restriction does not promote greater weight loss in obese human subjects. Evidently within the context of an 8-week diet, there seems to be little difference in changes in appetite over differing degrees of periodicity of eating. It seems that the dietary manipulations that we used in the present study were not robust enough to elicit changes in the concentrations of peptide YY or ghrelin to a degree at which they would have had a significant impact on appetite and a downstream effect on energy intake and ultimately on body energy stores. We thus conclude under the conditions described in the present study that increasing MF does not promote increased body weight loss.

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**Fig. 1.** Total ghrelin (a) and total peptide YY (PYY; b) measured for 6 h before and after the 8-week weight loss programme in the high-meal frequency (HMF) and low-meal frequency (LMF) groups. For total ghrelin (a), significant effects of time and weight loss at  $P < 0.01$  were noted. NS effect of MF or MF by weight loss interaction was noted. For total PYY (b), significant effects of time ( $P < 0.01$ ), time by weight loss ( $P < 0.01$ ) and time by MF ( $P < 0.05$ ) interactions were observed. NS interaction of time by MF or MF by weight loss was noted. —▲—, HMF pre; —■—, LMF pre; ---▲---, HMF post; ---■---, LMF post.

J. D. C., M.-J. C. and E. D. were involved in the conception of the study. J. D. C. and M.-J. C. collected the data. J. D. C. and E. D. analysed and interpreted the data. J. D. C. and E. D. wrote the paper. All authors critically revised the paper. The authors of the present paper declared no conflict of interest.

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