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Ambulatory blood glucose measurement, dietary composition and physical activity levels in otherwise healthy women reporting symptoms that they attribute to hypoglycaemia

Elizabeth J. Simpson*, Michelle Holdsworth† and Ian A. Macdonald

University of Nottingham, School of Biomedical Sciences, Queen's Medical Centre, Nottingham, NG7 2UH, UK

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Reactive hypoglycaemia (RH) is a condition that has been popularised in the media and lay literature, particularly that targeting women, over the past 30 years. The objective of the present study was to investigate whether a non-patient group reporting symptoms that they attributed to a low blood glucose level would demonstrate biochemical hypoglycaemia when symptomatic and whether their habitual diet and activity level differed from those of controls. Thirty non-obese, healthy women (aged 19–45 years) reporting symptoms more than once a week that they attributed to hypoglycaemia (RH group), and eighteen controls, measured their finger-prick blood glucose level 3 h after breakfast and lunch, and recorded their diet and activity daily for 7 d. The RH group also measured their blood glucose when symptoms were being experienced. Symptoms less than 4 h after eating were classed as postprandial. The mean postprandial blood glucose level in the RH group when asymptomatic (4·66 (SEM 0·08) mmol/l) was significantly lower than that of controls (5·05 (SEM 0·11) mmol/l; $P < 0·01$). Symptoms occurred 2·6 (SEM 0·13) h after eating, at a lower blood glucose level (4·18 (SEM 0·10) mmol/l; $P < 0·001$) than when the women were asymptomatic. On symptomatic days, the RH group were more physically active than the controls (1·64 (SEM 0·04) *v.* 1·50 (SEM 0·03) multiples of resting energy expenditure; $P < 0·05$), with a lower energy intake (7901 (SEM 311) *v.* 9332 (SEM 227) kJ; $P < 0·001$). In conclusion, subjects reporting symptoms they associated with hypoglycaemia generally did not demonstrate biochemical hypoglycaemia but did have significantly lower blood glucose levels than controls. Higher physical activity and a failure to match energy intake to estimated energy requirement may be important in the aetiology of symptoms.

Reactive hypoglycaemia: Women: Diet: Physical activity

Postprandial or reactive hypoglycaemia (RH) is a condition that has been popularised in the media and lay literature, particularly that targeting women, over the past 30 years (Brun *et al.* 2000). These sources and anecdotal evidence claim that many people who are otherwise healthy experience periodic symptoms such as faintness, irritability, tremor, hunger and anxiety, which can be attributed to a low blood glucose level (hypoglycaemia). Indeed, in several countries, the number being referred to medical agencies for this condition has reached epidemic proportions (Yager & Young, 1974), although this is considered to have been less marked in the UK (Snorgaard & Binder, 1990). A recent survey of randomly selected women from Nottinghamshire, UK, supports this, only 0·5 % of those reporting symptoms that they attributed to hypoglycaemia having sought medical help (Simpson *et al.* 2006). It does not, however, appear that there is an absence of the phenomenon in the UK. This recent survey in Nottinghamshire revealed that more than a third reported symptoms that they attributed to a 'low blood sugar', with over 18 % reporting these symptomatic episodes more than once a week (Simpson *et al.* 2006). Whether these individuals are actually experiencing biochemical hypoglycaemia is unclear.

A Canadian study measuring ambulatory blood glucose level in a referral population of patients with suspected RH demonstrated that the mean blood glucose concentration when individuals were symptomatic was lower than that of non-symptomatic controls, 17 % of readings taken when patients were symptomatic being less than 3·3 mmol/l (Palardy *et al.* 1989). Whether these findings are reflected in a non-referring but symptomatic population has not previously been investigated.

The insulin regulation of blood glucose has been of particular interest in the physiology of RH, with insulin sensitivity being demonstrably higher in many patients (Tamburrano *et al.* 1989; Brun *et al.* 1995). With insulin sensitivity being shown to be higher in those who are more physically active (Mayer-Davis *et al.* 1998), and in those consuming a high-carbohydrate–low-fat diet (Himsworth, 1935), it is postulated that habitual activity level and diet may be important in the development of this condition (Brun *et al.* 2000).

Abbreviations: MET, multiple of resting energy expenditure; RH, reactive hypoglycaemia.

* **Corresponding author:** Miss E. J. Simpson, fax +44 (0) 115 9709259, email liz.simpson@nottingham.ac.uk

† Present address: UR106 Nutrition, Alimentation et Sociétés, Institut de Recherche pour le Développement, 34394 Montpellier, Cedex 5. France.

The purpose of this current study was to investigate whether women who report symptoms that suggest RH, but who have not been referred for a clinical problem, have a concomitant biochemical hypoglycaemia, and to assess whether their habitual diet and daily activity levels differ from those of controls.

Methods

Protocol

Forty non-obese, healthy women who reported symptoms that they attributed to hypoglycaemia, occurring more than once a week (RH group), and twenty weight- and age-matched, non-symptomatic controls were invited to participate in the current study. These individuals had taken part in a previous health survey of the general female population of Nottinghamshire, UK, and had expressed an interest in participating in further research studies (Simpson *et al.* 2006). All subjects were asked to complete a medical screening form, to ensure that they were healthy, and the SF-36 Health Survey Questionnaire to assess physical and mental components of their health status. BMI was calculated from reported height and weight.

Following training and familiarisation with the measurement techniques to be used, all subjects were asked to take free-living blood glucose measurements 3 h after breakfast and 3 h after lunch for 7 d, using finger-prick samples. Those in the RH group took additional measurements whenever symptoms were experienced during the initial 7 d period. During the next 7 d, the RH group took blood samples only when they experienced symptoms. A diet and activity diary was completed by all participants over the study period.

The study was approved by the Nottingham University Medical School Ethics Committee.

Health status

Health exclusions, including depression, were identified by 'yes' and 'no' answers to specific health screening questions. The SF-36 questionnaire was used to assess mental health status. Scores obtained were normalised with respect to the 1998 general US population data (Ware *et al.* 1998) and aggregated into 'mental health' component scores to allow comparisons between groups.

Symptoms of hypoglycaemia

To avoid biasing the responses, symptoms of hypoglycaemia were not defined for participants, and any experiences that an individual attributed to a low blood 'sugar' were taken as a symptomatic event. All such events were recorded in the diet diary with time of occurrence and symptoms experienced.

Blood glucose testing

Finger-prick blood samples were taken using a Penlet II and analysed using a One Touch Profile pocket glucose analyser (Lifescan, High Wycombe, UK). Readings were recorded in the diet diary and stored in the analyser memory for authentication. From these readings, mean values were calculated for each subject. Data were further subdivided in the RH group in order to obtain mean values for symptomatic and asymptomatic occasions.

Prior to use, all eleven analysers were validated against the glucose oxidase method (Yellow Springs Inc., Yellow Springs, OH, USA) in a separate series of studies, using a hyperinsulinaemic clamp (DeFronzo *et al.* 1979) to generate forty blood samples of between 2·5 and 7·0 mmol/l. R^2 for the glucose oxidase method compared with individual monitors ranged from 0·893 to 0·980 (median 0·928).

Physical activity

Participants were asked to record all activities of daily living and sleep periods in a diary. This included all aspects of activity and not just formal exercise periods.

Estimates of daily physical activity, expressed as a multiple of resting energy expenditure (MET), were calculated from published tables (Ainsworth *et al.* 2000), each activity (including sleep) being given a MET value and being multiplied by the time (in hours) spent on it over the day. The total was then divided by 24 h to give an average MET value for each recording day. The habitual activity for each participant in the control group was then calculated by taking the mean of daily MET values over the whole recording period. In the RH group, average physical activity on symptomatic and non-symptomatic days was calculated. To assess variations in estimated energy balance in the control group, the MET value for the most active day and the mean of all other days was calculated and used in predicting daily energy requirements.

Diet diaries

Participants were asked to record all food intake, including snacks and drinks, in a diet diary, using household measures to estimate portion size. These were subsequently analysed using a food composition database (WISP V2; Tinuviel Software, Llarfechell, UK). To calculate habitual diet composition in the control group, a mean was taken over all 7 d of the recording period. In addition, the energy intake of controls was calculated for their most active day and a mean derived for the remaining recording days. In the RH group, mean food intake on symptomatic and non-symptomatic days was calculated. The ability of participants to match energy intake to energy requirement was assessed by a comparison of predicted energy requirement (calculated using the 'Schofield' equation (Schofield, 1985) and daily activity levels from activity diaries) and measured energy intake from diet diaries. In the RH group, comparisons were made between symptomatic and non-symptomatic days, and in the control group, the estimated energy requirement for their most active day and the mean of all other recording days was calculated and compared with the respective energy intakes.

Statistical analysis

All data were coded and analysed using SPSS version 10·0 (SPSS Inc., Chicago, USA).

Descriptive statistics were applied to compare those with and without reported symptoms of hypoglycaemia, for comparison, after exclusions had been made. For the purposes of

analysing dietary intake and physical activity, the RH group data were subdivided into days when symptoms were experienced and days when participants were asymptomatic.

For normally distributed data, comparisons between the RH group and controls were analysed using an unpaired Student's *t* test, with paired analysis being employed for comparisons between symptomatic and asymptomatic days within the RH group, and for comparisons between predicted and measured energy intake in all groups. Non-parametric data were analysed using the Mann–Whitney U test. Relationships were considered significant when $P<0{\cdot}05$.

Results

Subjects

Subjects in the RH group who did not experience symptoms during the recording period (*n* 4) and those from both groups without adequate datasets (*n* 8) were excluded from further analysis. Thus, datasets were obtained from thirty participants who reported symptoms synonymous with hypoglycaemia and eighteen non-symptomatic controls. The subjects' characteristics are shown in Table 1. The groups were matched for age ($P=0{\cdot}567$), BMI ($P=0{\cdot}883$), weight ($P=0{\cdot}753$) and mental health status ($P=0{\cdot}501$).

Blood glucose

Over the initial 7 d recording period, 169 postprandial blood glucose readings were obtained from controls and 278 from the RH group when they were not experiencing symptoms (median readings nine per subject for each group). The range of these recorded blood glucose values was similar between the two groups (2·7–7·5 mmol/l for the controls, compared with 2·7–7·6 mmol/l in the RH group). Four (2·3 %) of the postprandial blood glucose readings taken by those in the control group (one in each of four subjects) were less than or equal to 3·0 mmol/l, whereas five (1·8 %) readings taken by those in the RH group when asymptomatic (one in each of five subjects) were found to be 3·0 mmol/l or lower.

Three hours after eating, the mean blood glucose level in the RH group, when they were asymptomatic (4·7 mmol/l), was significantly lower than that of controls (5·1 mmol/l; $P=0{\cdot}005$). In the RH group, 108 symptomatic events were recorded over the 14 d recording period (median one per subject per week). The blood glucose level during these symptomatic events ranged from 2·4 to 5·4 mmol/l, fifteen (13·9 %) readings (in seven subjects) being 3·0 mmol/l or lower. Only two subjects in the RH group recorded blood glucose values less than or equal to 3·0 mmol/l both when asymptomatic and when symptoms were experienced. When the subjects were symptomatic, the mean blood glucose value in the RH group was lower (4·2 mmol/l) and occurred at an earlier time point (2·6 h) than when symptoms were not reported (4·7 mmol/l, 3·0 h; $P<0{\cdot}001$ and $P=0{\cdot}002$ respectively; Fig. 1).

Physical activity and diet analysis

The RH group was more physically active on days when symptoms were experienced than on asymptomatic days ($P=0{\cdot}005$). On symptomatic days, RH subjects had higher physical activity levels than controls ($P=0{\cdot}027$; Table 2).

The mean absolute fat and protein intakes of the RH group on symptomatic days were significantly lower than those of controls ($P=0{\cdot}027$ and $P=0{\cdot}040$, respectively). However, there was no difference in the total energy intake or in the percentage of energy derived from macronutrients between controls and the RH group on either symptomatic or asymptomatic days (Table 2).

Mean predicted energy requirements (from the Schofield equation and activity diaries) obviously reflect the differences in daily activity between the groups. Thus, the RH group had a higher energy requirement on a symptomatic day than on a day when symptoms were not experienced ($P=0{\cdot}005$), and on symptomatic days RH subjects had a higher predicted energy requirement compared with controls ($P=0{\cdot}023$). However, the difference between mean predicted energy requirement and mean energy intake in the RH group was −1431 kJ on days when symptoms were experienced ($P<0{\cdot}001$) and −765 kJ on asymptomatic days ($P=0{\cdot}46$). A trend was found for this difference between recorded and predicted intake to be higher on a symptomatic day compared with that seen on an asymptomatic day ($P=0{\cdot}070$). In the control group, the difference between mean predicted energy requirement and mean energy intake over all days was 35 kJ ($P=0{\cdot}940$). On their most active day, the difference between recorded and predicted intake in the control group was

Table 1. Characteristics of subjects
(Means with their standard errors)

	RH group (reporting symptoms attributed to hypoglycaemia)		Control group (not reporting symptoms)	
Group	Mean	SEM	Mean	SEM
Number of subjects	30		18	
Mean age (years)	27·3	1·19	28·4	1·75
Age range (years)	19–44		20–45	
Mean BMI (kg/m^2)	22·4	0·42	22·3	0·58
BMI range (kg/m^2)	17·5–26·3		18–27·0	
Mean weight (kg)	61·0	1·25	60·4	1·63
Normalised SF-36 mental health score	48·5	1·69	48·3	1·83

RH, reactive hypoglycaemia.

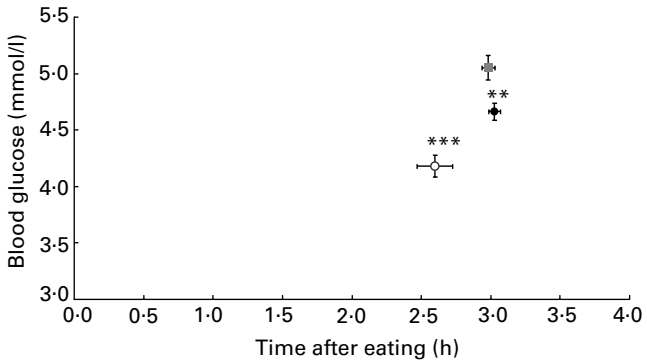

Fig. 1. Means of blood glucose readings *v.* time after eating in the reactive hypoglycaemia group when asymptomatic (●) and symptomatic (○), and in the control group (■). Standard errors of the means for blood glucose are represented as vertical bars of each datapoint and for time are represented as horizontal bars. Difference between reactive hypoglycaemia group and controls when asymptomatic $^{**}P=0{\cdot}005$, and $^{***}P<0{\cdot}001$. Difference between reactive hypoglycaemia group when asymptomatic and when symptoms were experienced $^{***}P<0{\cdot}001$.

−341 kJ ($P=0{\cdot}561$). When the mean predicted energy requirement and mean energy intake for all recording days minus the most active day in the control group were compared, the difference was 259 kJ ($P=0{\cdot}573$).

Discussion

This is the first study to investigate symptoms attributed to hypoglycaemia in a general population of the UK. Most research in this area has focused on patient groups, but, with the phenomenon reputed to be less marked in the UK (Betteridge, 1987; Snorgaard & Binder, 1990; Simpson *et al.* 2006) despite extensive coverage in the lay literature, we were interested in studying a non-referral population who reported symptoms that they attributed to hypoglycaemia.

Carbohydrate ingestion in healthy individuals is characterised by an initial rise in blood glucose that triggers the release of insulin. The effect of this hormone is to increase glucose uptake, particularly by skeletal muscle, and storage in tissues such as the liver. Initially, absorption from the gut exceeds uptake by the tissues, and blood glucose concentration rises. When absorption equals uptake, the concentration of blood glucose reaches a peak; then, as influx from the gut decreases, blood glucose falls, sometimes to below fasting levels. If the latter occurs, it triggers a release of the counterregulatory hormones (catecholamines, cortisol, glucagon, growth hormone) to restore equilibrium. These counterregulatory hormones, in particular adrenaline, elicit symptoms that have become associated in the lay literature with the condition of 'low blood sugar'. However, it remains contentious whether true, biochemical hypoglycaemia is being experienced.

Snorgaard and Binder (1990) failed to record any free-living blood glucose values below 3·3 mmol/l in their patients, who had been referred for 'functional hypoglycaemia'. In contrast, Palardy *et al.* (1989) found that although hypoglycaemia was not a common occurrence, 17 % of blood glucose readings associated with symptoms were less than 3·3 mmol/l, compared with 1·4 % in non-symptomatic controls. In the current study, there were no blood glucose values between 3·0 mmol/l and 3·3 mmol/l, so data are directly comparable with those of the Snorgaard and Palardy studies. In our non-patient cohort, we saw a pattern similar to that of the Palardy study, with a greater percentage of readings under 3·3 mmol/l being recorded by individuals when symptoms were experienced. However, only 23 % of subjects in the RH group of the current study recorded blood glucose values in this hypoglycaemic range when they were symptomatic, compared with 46 % in the Canadian patient cohort (Palardy *et al.* 1989). This may reflect the fact that the subjects in the current study were a heterogeneous non-referral group who had been selected on the basis of self-reporting symptoms that they attributed to a low blood glucose level.

The apparent absence of hypoglycaemia may, however, also be due to methodological problems. By the time symptoms

Table 2. Daily activity levels and macronutrient intake

(Means with their standard errors)

	RH group symptomatic day		RH group asymptomatic day		Control group all days		Control group most active day		Control group excluding most active day	
Group	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Physical activity (MET)	1·64	0·04*†	1·55	0·03	1·50	0·05	1·74	0·07	1·42	0·04
Predicted energy requirement (kJ)	9332	227*†	8840	180	8498	247	9892	392	8095	229
Energy intake (kJ)	7901	311	8075	335	8533	297	9551	554	8354	307
Protein (g)	65·1	2·5*	68·0	2·4	73·9	3·5				
Protein (% energy)	14·2	0·4	14·3	0·4	14·7	0·7				
Fat (g)	68·2	3·7*	70·0	3·0	78·9	3·8				
Fat (% energy)	33·1	1·0	32·9	1·1	35·2	1·4				
Carbohydrate (g)	238·9	10·1	247·3	11·1	244·6	10·8				
Carbohydrate (% energy)	51·5	1·1	51·0	1·1	48·4	1·5				
Total sugars (g)	111·6	7·6	111·1	7·9	107·1	5·8				
Total sugars (% energy)	24·0	1·3	22·7	1·3	21·2	0·9				
Starch (g)	114·0	6·6	122·5	6·2	125·9	8·5				
Alcohol (g)	11·0	2·1	16·2	3·1	13·1	3·2				

MET, multiple of resting energy expenditure; RH, reactive hypoglycaemia.
*$P<0{\cdot}05$ compared with controls (all days); †$P<0{\cdot}01$ compared with a non-symptomatic day.

have been recognised and a blood sample has been taken, blood glucose level may already be rising under the action of counterregulatory hormones, such that true blood glucose nadirs are being missed. Results from the current study show that mean blood glucose readings in the RH group, when symptoms were not being experienced, were significantly lower than those of controls at the same time point after meals. Moreover, mean blood glucose was further reduced when symptoms were being experienced. Lower blood glucose nadirs may therefore be occurring in symptomatic individuals. Periodic, ambulatory blood sampling, however, simply provides a 'snapshot' of postprandial blood glucose dynamics, and as such, more frequent glucose sampling would be required to substantiate this and would be an interesting subject for future investigation.

The prerequisite for capillary blood glucose values to be below 3·0 mmol/l when symptoms are experienced, in order for the diagnosis of hypoglycaemia to be confirmed (Service, 1989), may, however, be misleading. Although mean blood glucose readings in the current study were above this hypoglycaemic value when symptoms were experienced, the observation of significantly reduced blood glucose readings compared with controls raises questions concerning the blood glucose levels used to define hypoglycaemia in these individuals. Indeed, traditional threshold values derived from healthy volunteer studies using arterialised venous samples (Mitrakou *et al.* 1991) may not be relevant in those individuals who experience RH. Brun *et al.* (2000) demonstrated that, in individuals prone to RH, symptoms occurred at higher blood glucose readings, using venous sampling, than these threshold values. If this were reflected in our non-referral population, the symptoms they reported may have arisen as a result of 'reactive hypoglycaemia' occurring at higher glucose concentrations than were seen in the studies of hypoglycaemic thresholds carried out by Mitrakou and others.

Symptoms attributed to a low blood glucose level can, however, be equally well explained by other situations, unrelated to hypoglycaemia, but characterised by an adrenergically mediated response. Patient studies have shown higher levels of anxiety, depression and somatisation in symptomatic individuals, independent of aetiology and of whether biochemical hypoglycaemia has been demonstrated (Anthony *et al.* 1973; Berlin *et al.* 1994; Pelchat *et al.* 2004). A non-referral group of individuals may not present with such an extreme psychological profile, but an attempt has been made to standardise for this variable by selecting subjects who did not report depression and by matching both groups with regard to mental health status, as assessed by the SF-36 Health Survey.

In addition, given the media attention to RH, it is possible that participants who experience symptoms that they attribute to hypoglycaemia would have an interest in proving that their symptoms had a physiological basis. It was felt that this would be less of an issue with a non-referral group. However, all recorded readings were checked against the memory in the glucose analyser for discrepancies or omissions, and none was found. Moreover, the motivation for taking a finger-prick sample for blood glucose determination, in addition to those taken at the 3 h postprandial time point, was the experiencing of symptoms, which obviously preceded any knowledge of blood glucose value.

It is interesting to note that four participants were excluded from the study because symptoms were not experienced during the recording period, and therefore paired data were not available for comparison. However, the mean postprandial blood glucose values were similar (4·74 mmol/l) to those recorded by the RH group when asymptomatic (4·66 mmol/l; Fig. 1). It would have been useful to have had some clinical reason (e.g. headache, hunger) for the control group to take spontaneous blood glucose readings to provide paired data within controls in addition to postprandial comparisons with the RH group. However, owing to the range of symptoms that RH sufferers report, it was difficult to identify an event to use as a comparison with a symptomatic event. It is hoped that continuous glucose monitoring technology will in the future help to solve some of these drawbacks of periodic ambulatory blood glucose testing.

Exercise is known to increase insulin sensitivity (Mayer-Davis *et al.* 1998), which is largely attributable to muscle contraction-mediated increases in GLUT4 translocation (Hansen *et al.* 1998). As increased peripheral insulin sensitivity appears to be intrinsic in many individuals with reactive hypoglycaemia (Tamburrano *et al.* 1989; Brun *et al.* 1995; Brun *et al.* 2001), it is hypothesised that exercise may be a contributing factor in the development of this condition (Brun *et al.* 2001). Indeed, individuals in the RH group of the current study did report higher mean daily physical activity levels than controls on days on which they experienced symptoms. Moreover, they were more active on days when symptoms were experienced compared with a non-symptomatic day. However, the range of daily physical activity levels reported by the RH and control groups on individual days was similar (1·1–2·4 and 1·1–2·3 MET, respectively), and the range of daily physical activity levels that was reported in the RH group was identical on both symptomatic and asymptomatic days (1·1–2·4 MET).

High-carbohydrate, low-fat diets have also been implicated in the aetiology of reactive hypoglycaemia by increasing insulin sensitivity (Brun *et al.* 2000), although the effect that diets high in refined sugars have on insulin sensitivity in human subjects remains contentious (Daly, 2003). Diets high in refined sugars may still play a role in RH, independent of insulin sensitivity, by inducing greater postprandial excursions in blood glucose (Daly *et al.* 1998). This observation, together with anecdotal evidence that a low glycaemic index diet is beneficial in those with RH, supports the popular theory in the lay literature that refined carbohydrate is linked to symptoms of hypoglycaemia (Heller & Heller, 2001; Atkins, 2003). Experimentally, however, this theory has been difficult to prove, with a dietary assessment of RH patients showing no difference in intake of total sugars when compared with non-symptomatic controls (Snorgaard & Binder, 1990). Intake of total sugars in the RH group of the current study was identical, on all days, to that of controls, although, owing to reduced fat and protein consumption on symptomatic days, the percentage of energy derived from total sugars in the RH group on these days was approximately 3 % higher than that of controls. Although indicative of a trend, this finding did not, however, reach statistical significance ($P=0·070$), and data from the current study are therefore inconclusive regarding the intake of total sugars and symptoms of hypoglycaemia.

Glycaemic response can be affected by other factors, such as the fat content of the meal, with fat slowing gastric emptying and carbohydrate uptake from the gut, and reducing the

subsequent blood glucose peak. There is some suggestion, from the current study, that this may be important in the aetiology of symptoms, as reduced absolute dietary fat intake was seen in the RH group on symptomatic days when they were compared with controls, although the proportion of daily energy provided by fat in the diet did not differ.

Underreporting is a common problem with diet diary assessment of food intake (Black *et al.* 1991). However, when daily energy expenditure was predicted, no statistical difference was seen between this estimated requirement and reported energy intake (from diet diaries) in controls or in the RH group on asymptomatic days. A significant shortfall in energy intake, compared with estimated energy requirement, was recorded on days when symptoms were experienced by the RH group. This could be underreporting, commonly seen in obese subjects or those wishing to reduce their body weight (Johansson *et al.* 1998). However, as the same subjects did not appear to be underreporting on the asymptomatic days, it seems reasonable to conclude that the RH subjects did fail to match energy intake to expenditure on symptomatic days.

Reduced blood glucose levels have been demonstrated in individuals made to undertake strenuous activity while in negative energy balance, when compared with those in positive energy balance (Ainslie *et al.* 2003; Nemet *et al.* 2004). On a day on which symptoms were experienced, the mean negative energy balance and intensity of daily activity in the RH group of the current study were less than those investigated in the Ainslie and Nemet studies. However, the mean blood glucose values of the high- and low-energy intake groups reported in the literature were comparable to those of the RH group of the current study on asymptomatic and symptomatic days (respectively). Consequently, the recorded discrepancy between energy intake and estimated requirement on symptomatic days may be important in the aetiology of symptoms. This is further supported by the finding that in controls, even on their most active day, energy intake matched predicted energy requirement. Increasing energy expenditure while maintaining or decreasing energy intake is often recommended to those attempting to control their body weight. If a discrepancy between energy intake and expenditure were implicated in the development of reactive hypoglycaemia in susceptible individuals, one might expect an increased incidence in these people. To our knowledge, this has not been investigated but warrants further study.

An inherent problem in carrying out research into a health issue in human volunteers is the potential for bias that may arise as a result of only those interested in the research being motivated to participate. The possibility of the RH group being more health-conscious than the controls is therefore a potential bias to the results of this study. This is, however, unlikely in this instance as the RH group did not show convincing evidence of greater health-consciousness. The intakes of total sugars and alcohol were the same or slightly greater, and none of the differences in diet or physical activity between the RH group on asymptomatic days and controls was statistically significant or substantial in terms of trends.

In conclusion, postprandial biochemical hypoglycaemia (a blood glucose level $<3{\cdot}3$ mmol/l), as assessed by periodic capillary blood sampling and defined by counterregulatory thresholds in the literature, is a rare occurrence in otherwise healthy individuals. However, the percentage of blood glucose values below 3·3 mmol/l found in the non-referral population of the current study was similar to that seen in patient groups with RH reported in the literature. The postprandial blood glucose profile of individuals who experience symptoms that they attribute to hypoglycaemia appears to differ from that of controls and warrants further investigation. A failure to match energy intake to estimated daily energy requirement and lower fat consumption on days when symptoms of hypoglycaemia were experienced may be important in the aetiology of symptoms.

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