Oral Fatty Acid Sensitivity among Obesity Resistant and Obesity Susceptible Individuals

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Abstract

Context: While rates of global obesity are high, a substantial proportion of the population remain lean despite living in an obesogenic environment. One potential difference between obesity resistant individuals (ORIs) and obesity susceptible individuals (OSIs) is oral fatty acid sensitivity.

Objective: We compared oral fatty acid sensitivity and fat ranking ability between ORIs and OSIs.

Design and participants: Oral sensitivity to oleic acid (1.4 mM) was determined using triplicate triangle tests amongst 50 ORIs and 36 OSIs. Participants tasted three milk samples, consisting of one sample with oleic acid and two control samples without oleic acid. Hypersensitive individuals were defined as those who chose the oleic acid sample three out of three tests. Participants also ranked the fat content of custard samples containing 0%, 2%, 6% and 10% fat.

Statistics: Logistic regression models including sex, age, and percentage body fat estimated adjusted odds ratios (OR) for oral fatty acid sensitivity between ORI and OSI. Negative binomial regression adjusting for age, BMI, and height compared fat ranking scores between ORIs and OSIs.

Results: The odds of being hypersensitive to fatty acids amongst ORIs was 3.60 times that for OSIs (P=0.034). There was no evidence for an association between resistance to obesity and the ability to rank the fat levels in a food (P=0.600).

Conclusion: Hypersensitivity to oral fatty acids among ORIs may influence their dietary fat intake, and thus their body weight regulation. Future larger studies are needed to confirm this.

Keywords: Obesity resistance; Obesity susceptibility; Oral fatty acid sensitivity

Introduction

The rapid rise in obesity in recent decades is of great concern due to the associated co-morbidities and subsequent strain on healthcare [1]. Of interest are those who remain lean despite living in an obesogenic environment. Investigating the characteristics of these seemingly obesity resistant individuals may allow us to identify important factors to prevent and treat obesity. Although it is well known that the causes of obesity are complex and multi-factorial, the excessive intake of calories, including fat, is a key problem [2]. Previous research has reported

oral hypersensitivity to fat is associated with lower energy and fat intakes, BMI, and waist circumference [3, 4]. It is purported that this may be due to the fact that high fat foods are less preferred and therefore eaten less frequently among sensitive individuals [3]. This hypersensitivity may enhance preference for lower energy-dense foods and may be one mechanism whereby obesity resistant individuals (ORIs) regulate their energy intakes. Indeed it has been reported that obesity susceptible individuals (OSIs) are characterised by strong preference for palatable foods, particularly high fat foods [5]. However, it is yet to be determined

whether individuals may be predisposed to obesity on the basis of being relatively insensitive to oral fatty acids or, alternatively, whether individuals may be protected against obesity by having a heightened sensitivity to oral fatty acids. Therefore the aim of this study was to compare fatty acid sensitivity and fat ranking ability between those who are resistant and susceptible to obesity.

Method

Participants

Eighty-six participants were recruited from the general public in Dunedin, New Zealand, via flyers and advertising in local newspapers designed with specific questions to target obesity resistant and obesity susceptible individuals.

Eligible participants were healthy males aged 18-55 y and females aged 18-45 y meeting our criteria as either an ORI (remains lean with relative ease and can eat whatever they like) or an OSI (struggles to maintain their weight, despite perceived low energy intakes) as previously defined [6]. The screening questions for classification of ORI and OSI are outlined in **Table 1**. Participants were classified as an ORI if they answered positively to any of the statements outlined for ORI. Conversely, participants were classified as an OSI if they answered positively to either or both of the statements for OSI. Participants were excluded if they did not answer positively to any of the screening tool questions, had a thyroid disorder, were pregnant, lactating or menopausal, or had not been weight stable for at least 3 months.

Obesity resistant individuals (ORI) had a BMI of 16.8 to 28.1 $kg.m^{-2}$, had always been lean, and found it difficult to gain but not lose weight. In contrast, OSI had a BMI of 19.4 to 41.2 $kg.m^{-2}$, were likely to experience weight fluctuations, and found it difficult to lose but not gain weight.

Ethics

This study was approved by the Human Ethics Committee of the University of Otago, New Zealand. All participants provided written informed consent.

Prior to the tasting session participants were instructed to avoid drinking strong tea or coffee for at least 1 hour and to not wear strong perfume. Participants were also asked to avoid consuming a large meal and to come to the tasting session no more than 70-80% full.

Table 1 Screening questions for classification of participants as obesity resistant (ORIs) and obesity susceptible individuals (OSIs).

Questions for ORIs
1. I am a person who can eat whatever I like without gaining weight
2. I am a person who maintains my weight easily
3. I am a person who loses weight easily
4. I am a person who finds it difficult to put on weight
Questions for OSIs
1. I am a person who needs to eat small amounts of food to manage my weight
2. I am a person who gains weight easily

Oral fatty acid sensitivity

Oral sensitivity to oleic acid (1.4 mM) was determined by using triplicate triangle tests based on the methods by Stewart et al [4]. Participants were presented with three milk samples, consisting of one sample with oleic acid (1.4 mM, Sigma Aldrich, St Louis, MO, USA) and two control samples without oleic acid. Hypersensitive individuals were defined as those who correctly identified the oleic acid sample in all three tests (a one in 27 chance, approximately 4%, by random guessing). All other individuals were defined as hyposensitive (getting two correct by chance would occur approximately 22% of the time, one correct approximately 44% of the time, and none correct approximately 30% of the time). Participants were asked to wear nose clips during the oral fatty acid sensitivity task.

Fat ranking test

Participants performed a fat ranking test which examined their ability to differentiate the fat content of custards containing 0%, 2%, 6%, and 10% canola oil (Sunfield, Tasti Products Ltd., Auckland, New Zealand). Participants were presented with the custard in random order and asked to rank the custard samples from the highest to the lowest fat level. Participants were given a score based on their ability to rank the samples using a system based on a previous study by Stewart et al [4].

Statistics

Cronbach alpha was used to assess the internal consistency of the six binary items (screening tool) with values ≥ 0.7 considered acceptable. A 95% confidence interval for the estimated value of alpha was generated using bootstrapping (1000 replicates) to generate a bias-corrected interval. Linear regression models adjusted for sex were used to compare baseline variables between ORIs and OSIs using tests based on bootstrapped standard errors (with 1000 replicates) due to non-normality and heteroscedasticity in the model residuals that was not corrected using log-transformations and/or variance-weighted least squares. Logistic regression models for oral fatty acid sensitivity were developed with the goal of limiting the number of predictors to one for each 10 non-events and 10 events using the guidelines from Peduzzi et al. [7]. The modelling process used Greenland's [8] approach to select potential confounders in the association between being an ORI/OSI and sensitivity with variables added in a forward selection process where they changed the odds ratio (OR) by at least 10% from the previous model and with the variable changing the OR by the greatest percentage being added where multiple candidate variables were identified at a given stage. The full set of potential confounders was sex, age (in years), weight (in kilograms), height (in meters), BMI, waist circumference (in centimetres), and percentage body fat (%BF) (measured by dual-energy X-ray absorptiometry, DPX-L Scanner, Lunar Corp, Cincinnati, OH, USA). As several variables involved body composition (weight, BMI, waist circumference, and %BF) and these were expected to be correlated, once one body composition variable was added, the others were no longer considered. The Hosmer-Lemeshow test and a model specification test were used to assess goodness of fit. In a similar way, Poisson regression was used to compare fat ranking scores

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between ORIs and OSIs with negative binomial regression used where there was evidence of over-dispersion from a likelihood ratio test. The number of variables was limited to one for each ten observations for these models. For all regression models, the addition of a quadratic term for each continuous predictor was investigated to detect, and if significant model, non-linear associations. Such quadratic terms were retained if statistically significant. Stata 13.1 (Statacorp LP, College Station TX, US) was used for all statistical analyses. All statistical tests were two-sided and P<0.05 was considered statistically significant.

Results

Instrument

The six item instrument for screening ORI and OSI was completed by 172 participants as part of the recruitment phase (further details of these participants not shown here). The Cronbach alpha, after reverse coding the two ORI items, showed good internal consistency (alpha 0.86; 95% CI: 0.83, 0.88; lowest item-rest correlation 0.45) with only a very small improvement possible by removing an item (ORI item 3: I am a person who loses weight easily, alpha increased to 0.87). This provides support for the construct validity of the instrument in this population, alongside its face and content validity.

Participants

For the variables discussed here, full data was provided by all 86 participants. Their ages ranged between 19 and 55 years (with a maximum of 44 for women). Weights ranged between 44.0kg and 115.2kg and heights between 1.52m and 1.96m. BMIs were calculated to be between 16.8 and 41.2 (5 [6%] were underweight with BMI<18.5, 53 [62%] were normal weight with 18.5 ≤ BMI<25.0, 19 [22%] overweight with 25.0 ≤ BMI<30.0,

and 9 [10%] obese with 30 ≤ BMI). Body fat percentages were between 5.9% and 52.0%. Waist circumferences ranged between 59.3cm and 110.5cm. Selected characteristics of the 50 ORI and 36 OSI participants are compared in **Table 2**.

Oral fatty acid sensitivity

Among 86 participants who took part in the triplicate triangle tests, 53 participants (62% total; 56% ORIs and 69% OSIs) were defined as hyposensitive and 38% (44% ORIs and 31% OSIs) as hypersensitive. In the unadjusted model, the odds of being hypersensitive to fatty acids did not differ between ORIs and OSIs (OR=1.79, 95% CI: 0.72, 4.40; P=0.208). Confounding variables were added as follows with all these models showing statistically significantly higher odds amongst ORIs compared to OSIs: %BF (OR=3.50, 95% CI: 1.14, 10.79; P=0.029), then age (OR=4.02, 95% CI: 1.22, 13.27; P=0.022), and finally sex (OR=3.60, 95% CI: 1.11, 11.79; P=0.034) **(Table 3)**. Although the last of these models went slightly beyond the goal of one predictor per 10 non-events and 10 events (allowing 3.6 predictors for the present data), all three adjusted models produced similar interpretations and all model diagnostics indicated a lack of issues around goodness of fit.

Fat ranking test

A total of 53% (46% ORI and 64% OSI) of the cohort scored 0, 35% (36% ORIs and 31% OSIs) scored between 1 and 4, and only 12% (16% ORIs and 6% OSIs) of the cohort scored 5. There was evidence of over dispersion for all models and so negative binomial regression was used in preference to Poisson regression. There was a non-statistically significantly raised rate of scores for ORIs compared to OSIs (IRR=1.59, 95% CI: 0.80, 3.17; P=0.186) with interpretation unaffected after adding age (IRR=2.04, 95% CI: 0.99, 4.21; P=0.053), then BMI (IRR=1.53, 95% CI: 0.63, 3.71; P=0.348), and finally height (IRR=1.29, 95% CI: 0.50, 3.29;

Table 2 Characteristics of study participants.

	Obesity Resistant Individuals		Obesity Susceptible Individuals		*P*-value*
	Females	**Males**	**Females**	**Males**	
n	24	26	20	16	
Age (years)	27.1 (6.5)	29.3 (8.9)	31.2 (9.1)	38.5 (12.2)	0.002
Weight (kg)	58.7 (7.6)	71.4 (10.2)	70.3 (20.6)	88.8 (10.9)	<0.001
Height (m)	1.69 (0.06)	1.79 (0.07)	1.63 (0.06)	1.75 (0.06)	<0.001
BMI (kg.m^{-2})	20.6 (2.1)	22.3 (2.5)	26.4 (6.7)	29.1 (2.8)	<0.001
Waist circumference (cm)	68.3 (4.7)	78.8 (7.4)	79.7 (15.6)	95.2 (7.4)	<0.001
Body fat (%)	26.9 (6.6)	16.5 (6.5)	35.2 (11.4)	27.6 (7.3)	<0.001

Note: All values are means (standard deviations)
*P-value from regression analysis for obesity resistant/susceptibility type adjusted for sex

Table 3 Number (%) of obesity resistant individuals (ORIs) and obesity susceptible individuals (OSIs) hypo- and hypersensitive to fatty acids using the 3-Alternative Forced Choice tests.

	0 out of 3	1 out of 3	2 out of 3	Total hyposensitive	3 out of 3 hypersensitive	Adjusted odds ratio (95% CI)*	*P*-value
Obesity Resistant Individuals	7 (14)	10 (20)	11 (22)	28 (56)	22 (44)		
Obesity Susceptible Individuals	4 (11)	8 (22)	13 (36)	25 (69)	11 (31)	3.6 (1.11, 11.79)	0.034
Total	11 (13)	18 (21)	24 (28)	53 (62)	33 (38)		

*Odds of being hypersensitive to oral fatty acids (ORIs vs. OSIs) calculated using logistic regression models including sex, age, and percentage body fat estimated adjusted odds ratios (OR) for oral fatty acid sensitivity between the ORIs and OSIs groups.

P=0.600).

Discussion

To the best of our knowledge, this is the first study to compare oral fatty acid sensitivity and evaluate the ability to rank fat in a common food among those who self-identify as obesity resistant or susceptible. The odds of being hypersensitive to oral fatty acids was over three times higher among ORIs compared to OSIs after adjustment for potential confounders. There was, however, no evidence for an association between resistance to obesity and the ability to detect differences and rank the levels of fat in a food.

Previous studies have reported a negative association between fat sensitivity and BMI [3, 4, 9], although this finding is not unanimous [10]. We found that after controlling for %BF, those who are resistant to obesity were more likely to be hypersensitive to fat. No human studies have previously compared these two groups, but our findings are in agreement with an animal study which reported fatty acid sensitivity varied significantly between diet-induced obesity-prone and diet-induced obesity-resistant rats [11].

Our sense of taste is important in promoting either the acceptance or rejection of food. Recent research has suggested that the detection of oral fat comprises a gustatory component [12]. There appears to be inter-individual variability with reported magnitudes of four- to forty-fold for the detection of free fatty acids among adults and children [4, 13]. A number of mechanisms underlying oral fat detection have been purported, with the glycoprotein, CD36 appearing to play a key role as a prime fatty acid taste receptor, especially when concentrations are low [14]. Several researchers have shown fat sensitive people have a lower preference to high fat foods or have a lower fat intake [3, 4, 15]. Given that an acquired preference for high fat foods has been associated with obesity [16], this may indicate that ORIs are more likely to reject high fat foods. Conversely, the lower sensitivity among OSIs may mean they are more likely to accept and consume higher fat foods. This was observed by Blundell et al., where those susceptible to obesity had a higher preference for high fat foods [5]. Therefore hypersensitivity to fat may be one mechanism allowing some individuals to better regulate their body weight. However, this is a cross-sectional study, which does not allow for causal inferences. In addition, it is important to note there is large inter-individual variability in perceived intensity [17] and threshold [18] for fatty acid. A limitation of the present study was that we classified our participants as hyper- and hyposensitive to 1.4 mM of oleic acid, rather than performing a threshold test using a range of concentrations. This concentration was chosen based on the results of several studies among participants living in similar environments to those in the present study [4, 19]. Furthermore, we believe that using an empirically-derived threshold would not have altered our conclusion, as ORIs are more likely to meet the criteria for being sensitive to fatty acids compared to OSIs.

Despite our results on fat sensitivity, there was no evidence for ORIs to be better at ranking fat levels in a common food, namely custard. If indeed our ORIs, who appear more sensitive to fat, have reduced preference for high fat foods, their ability to detect different fat levels remains unclear. Further studies should assess the fat ranking ability of ORIs, using a number of different foods.

Future research could investigate the effects of changing fat sensitivity amongst those prone to obesity. Previously Stewart et al. showed consumption of a low fat diet for four weeks increased fatty acid sensitivity among both lean and overweight participants [20] suggesting that sensitivity can indeed be recalibrated. The long-term maintenance of such recalibrations would be important for interventions using this to improve weight management.

Overall it appears that those individuals resistant to obesity are more likely to be sensitive to dietary fat, which may be one mechanism whereby obesity resistant individuals remain lean despite living in an obesogenic environment.

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Authorship

The authors' contributions were as follows – RCB, RTM-C, and SLT designed the research; SLT and RTM-C conducted the research; RCB and ARG performed the statistical analyses; all authors wrote, reviewed, and approved the final manuscript.

Conflict of Interest

The authors declare that they have no conflict of interest.

Support

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