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Postprandial suppression of appetite is more reproducible at a group than an individual level: Implications for assessing inter-individual variability

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ABSTRACT

Individual differences in appetite are increasingly appreciated. However, the individual day-to-day reliability of appetite measurement is currently uncharacterised. This study aimed to assess the reliability of appetite following ingestion of mixed-macronutrient liquid meals at a group and individual level. Two experiments were conducted with identical protocols other than meal energy content. During each experiment, 10 non-obese males completed four experimental trials constituting high- and low-energy trials, each performed twice. Experiment one employed 579 kJ (138 kcal) and 1776 kJ (424 kcal) liquid meals. Experiment two employed 828 (198 kcal) and 4188 kJ (1001 kcal) liquid meals. Visual analogue scales were administered to assess appetite for 60 min post-ingestion. The typical error (standard error of measurement) of appetite area under the curve was 6.2 mm·60 min^{-1} (95%CI 4.3 −11.3 mm·60 min^{-1}), 6.5 mm (95%CI 4.5−11.9 mm·60 min^{-1}), 7.1 mm·60 min^{-1} (95%CI 4.9 −12.9 mm·60 min^{-1}) and 6.5 mm·60 min^{-1} (95%CI 4.5−11.8 mm·60 min^{-1}) with the 579, 828, 1776 and 4188 kJ meals, respectively. A systematic bias between first and second exposure was detected for all but the 4188 kJ meal. The change in appetite with high-vs. low-energy meals did not differ at a group level between first and second exposure (mean difference: -0.97 mm·60 min^{-1}; 95%CI -6.48–4.53 mm·60 min^{-1}), however, ~50% of individuals differed in their response with first vs second exposure by more than the typical error. Appetite responses are more reliable when liquid meals contain a higher-vs lower-energy content. Appetite suppression with high-vs low-energy meals is reproducible at the group- but not individual level, suggesting that multiple exposures to an intervention are required to understand true individual differences in appetite.

1. Introduction

Understanding the regulation of appetite in humans can assist in the development of strategies to prevent and/or treat disorders of energy balance such as obesity. Subjective sensations of appetite are commonly captured using visual analogue scales (VAS), typically comprised of questions attempting to assess perceptions of hunger, fullness, satisfaction and prospective food consumption (Blundell et al., 2010). The methodology of administering these scales before, and at regular intervals after the consumption of meals/beverages, is supported as a standard and accepted tool to substantiate claims relating to the effects of foods on feeling states and motivations to eat (Blundell et al., 2010). In addition to assessing the effects of meal composition on appetite (Astbury, Stevenson, Morris, Taylor, & Macdonald, 2010; Gonzalez & Stevenson, 2012, 2014; Gonzalez, Rumbold, & Stevenson, 2013; Gonzalez et al., 2015), these methods have also been applied more widely, to assess the effects of other interventions (such as acute (Alajmi et al., 2016; 2013; Deighton, Frampton, & Gonzalez; Gonzalez et al., 2013) or chronic exercise (Martins, Kulseng, King, Holst, & Blundell, 2010), food restriction (Deighton et al., 2014; Gonzalez et al., 2013) and environmental conditions (Bailey et al., 2015)) on the subjective appetite response to a standard food or beverage.

Quantifying the day-to-day variability of a measure provides greater confidence on whether an intervention is the cause of an

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observed effect, as opposed to random (biological or behavioural) variability, measurement error or systematic bias (Atkinson & Nevill, 1998; Hopkins, 2000). The day-to-day reliability of appetite perceptions in response to a meal - expressed as a coefficient of variation - has previously been reported to be in the range of 7–28%, in healthy, lean men (Flint, Raben, Blundell, & Astrup, 2000; Gonzalez, Veasey, Rumbold, & Stevenson, 2012; Raben, Tagliabue, & Astrup, 1995). The typical error (standard error of measurement) has been reported to be in the range of 8–13 mm·120 min^{-1} (Gonzalez et al., 2012).

Mixed-macronutrient liquid meals are commonly used in appetite research as "preloads" prior to ad libitum test meals, and covert manipulation of their energy content is used to assess the "sensitivity" of appetite regulation (Beaulieu, Hopkins, Blundell, & Finlayson, 2016). Moreover, liquid meals may produce more reliable appetite responses than semi-solid/solid meals (Flint et al., 2000; Gonzalez et al., 2012; Raben et al., 1995). Therefore, understanding the reliability of liquid meals with differing energy content is required in order to prescribe an appropriate preload energy content to detect subtle differences in appetite perceptions. However, it cannot necessarily be assumed that a measure shown to be reliable under one condition results in a reliable change in response to an intervention. For example, the measurement of appetite could be reproducible in response to a meal with a given energy content, but this does not provide insight into the reliability of the *suppression* of appetite with high-vs low-energy preloads.

With the growth of personalized approaches to nutrition and medicine (Betts and Gonzalez), an increasing number of studies in the area of energy balance and appetite have attempted to understand the inter-individual differences in response to an intervention (Blundell et al., 2005; Hopkins, Blundell, & King, 2014; Jebb et al., 2006; King, Hopkins, Caudwell, Stubbs, & Blundell, 2008, 2012; Parr et al., 2016). Whilst there is an increasing acknowledgement that measurement error needs to be considered in the interpretation of individual responses, there is still a common assumption that these individual responses are replicable. For example, an individual described as a "low responder" upon the first exposure to an intervention will remain a "low responder" upon repeated exposure to an intervention. It has therefore been suggested that to directly assess within-subject variability in response to an intervention, repeated exposure with an adequate washout is required (Hecksteden et al., 2015). Indeed, this appears to be relevant for appetite measurement, as the individual appetite response to a bout of exercise is not consistent enough to classify "compensators" and "non-compensators" (Unick et al., 2015). The reliability of individual appetite responses to preloads (inducing appetite suppression by nutrition) has never been documented.

The present study aimed to investigate the day-to-day reliability of appetite perceptions in response to mixed-macronutrient liquid meals differing in energy content. In addition, by capitalising on repeated exposure to high and low-energy containing meals, it was also possible to assess both inter-individual variability and within-subject variability in appetite suppression with high-energy meals.

2. Methods

2.1. Study design

The data reported in this investigation are taken from two experiments previously described (Deighton, et al., 2016), which were both conducted according to the guidelines in the Declaration of Helsinki.

Both experiments involved a preload study design to investigate the influence of ad libitum meal composition on the compensatory energy intake response to different energy preloads. Both studies followed identical procedures, other than the energy content of the preloads. Here, the individual data have been rearranged to visit order to assess the day-to-day variability in appetite responses to mixed-macronutrient meals differing in energy content but matched for macronutrient composition and ingredients used. As previously described (Deighton, et al., 2016), experiment one was conducted at the University of Bath (UK) and utilised liquid meals containing a low (579 kJ; 138 kcal) and a moderate-energy content (1776 kJ; 424 kcal). Experiment two was conducted at Leeds Beckett University (UK) and utilised liquid meals containing a low- (828 kJ; 198 kcal) and a high-energy content (4188 kJ; 1001 kcal). The use of different energy contents enabled comparisons to be made regarding the reliability of subjective appetite measures in response to liquid meals of increasing energy content. Each experiment was approved by the respective Institutional Ethics Advisory Committee for the university at which experimental testing was performed, and informed written consent was obtained from all participants.

2.2. Participants and standardisation

All participants were non-smokers, weight stable for at least six months before participation and were not dieting or taking any medication. Participants had no known history of cardiovascular or metabolic disease, were classified as unrestrained eaters (de Lauzon et al., 2004; Deighton, et al., 2016) and self-reported as recreationally active (engaging in structured exercise or sport $\geq$3 times/week). Participant characteristics have been previously reported (Deighton, et al., 2016) and are repeated for clarity. In experiment one the mean age, stature, body mass and body mass index were 22 ± 1 y, 1.80 ± 0.06 m, 81.1 ± 7.9 kg and 24.8 ± 1.6 kg/m^2, respectively. In experiment two, the mean age, stature, body mass and body mass index were 21 ± 4 y, 1.80 ± 0.05 m, 77.2 ± 6.4 kg and 24.2 ± 2.3 kg/m^2, respectively.

Diet and physical activity were standardised for 24 h prior to all trials by self-report and food diaries. Participants were asked to refrain from alcohol, caffeine and strenuous physical activity during this period. All trials commenced between 0800 and 0900 following an overnight fast ($\geq$10 h).

2.3. Experimental protocol

At each testing location, 10 healthy men completed four experimental trials in a randomized (using online software: randomizer.org), double-blind, crossover design separated by $\geq$ 72 h. The four trials consisted of the low- or moderate/high-energy liquid meals each consumed on two occasions. Anthropometric measures, screening for eating behaviours (de Lauzon et al., 2004) and self-reported habitual physical activity levels were obtained immediately before the first experimental trial.

Upon arriving at the laboratory for experimental trials, participants completed baseline visual analogue scales (VAS) to assess subjective appetite ratings before consuming the mixed-macronutrient liquid meal within a 5 min period. During the 60 min post-consumption, participants remained in the laboratory (seated and permitted to read or listen to music) whilst further VAS were administered every 15 min to assess appetite sensations. Whilst participants were not in isolation, any cues that could be seen to distort appetite perceptions were prohibited, e.g. discussions or radio/television programmes about food/appetite.

2.4. Liquid meals

Details of the mixed macronutrient liquid meals have been previously reported in detail. Briefly, each meal contained an