Use of a non-invasive acoustical monitoring system

to predict ad libitum eating events

by

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ABSTRACT

Obesity is currently a prevalent health concern in the United States. Essential to combating it are accurate methods of assessing individual dietary intake under ad libitum conditions. The acoustical monitoring system (AMS), consisting of a throat microphone and jaw strain sensor, has been proposed as a non-invasive method for tracking free-living eating events. This study assessed the accuracy of eating events tracked by the AMS, compared to the validated vending machine system used by the NIDDK in Phoenix. Application of AMS data toward estimation of mass and calories consumed was also considered. In this study, 10 participants wore the AMS in a clinical setting for 24 hours while all food intake was recorded by the vending machine. Results indicated a correlation of 0.76 between number of eating events by the AMS and the vending machine (p = 0.019). A dependent T-test yielded a p-value of 0.799, illustrating a lack of significant difference between these methods of tracking intake. Finally, number of seconds identified as eating by the AMS had a 0.91 correlation with mass of intake (p = 0.001) and a 0.70 correlation with calories of intake (p = 0.034). These results indicate that the AMS is a valid method of objectively recording eating events under ad libitum conditions. Additional research is required to validate this device under free-living conditions.

ACKNOWLEDGMENTS

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GLOSSARY

- Acoustical: Making measurements using sound, i.e. a microphone.

- Ad libitum: The Latin term for "at one's pleasure," meaning the freedom to choose remains with the individual.

- Eating event: Also known as a meal, a mass of food consumed in one discrete sitting.

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Chapter 1

INTRODUCTION

Overview

Although obesity rates have climbed to 34% among adults over 20 years of age in the United States ("Obesity and Overweight," 2011), a firm consensus has yet to be reached in the dietetics community regarding the etiology of weight gain. The dominant theory in the field is one of nutrient balance (Lee, Blair, & Allision, 2001; Ravussin & Bogardus, 2000; Spiegelman & Flier, 2001; Tataranni et al., 2003). When energy intake is greater than energy expenditure, the biological outcome is weight gain. Similarly, weight loss can only be achieved by expending more calories than one is assimilating. Hence, it is more necessary than ever for investigators to understand not only what foods individuals are eating, but also in what quantities and at what times. To date, dietary intake has been difficult to assess accurately. A device that accurately tracks food intake would be a useful tool in preventing or reversing weight gain at the individual level. This thesis presents a novel method that objectively tracks ad libitum dietary intake. Using a non-invasive strain sensor which is affixed to the skin along a participant's jaw, this technology offers a pioneering strategy for tracking dietary intake while minimizing biases and misreporting. While this study focuses on correct identification of eating events by the device, this technology could eventually progress to correctly identify mass and calories of food eaten by an individual.

Summary of Previous Research

A significant body of research has been devoted to various methods of assessing intake, a difficult task under free-living, ad libitum conditions. The simplest method is direct observation, with food selection, portion sizing, and timing of intake being recorded by an objective outside source. Many studies which focus on alternative methods of tracking dietary intake use direct observation as the "gold standard" (Jonnalagadda et al., 2000; Robert C. Klesges, Hanson, Eck, & Durff, 1988). This method produces highly accurate data regarding actual mass and caloric content of food ingested. Gittelsohn, Shankar, Pokhrel, & West (1994) found that direct observation and estimation of portion sizing has a correlation of 94% with actual weighed intake.

However, for purposes of tracking weight maintenance on a long-term basis, this method is also inherently flawed. First, it is impractical to observe eating directly over days or weeks, which would be necessary as weight changes take matters of weeks and months, not single days (Carels et al., 2008). According to the U.S. Department of Health and Human Service & U.S. Department of Agriculture (2010), the recommendation for weight loss is one pound per week if an individual is overweight, achieved by a daily reduction of 500 kilocalories from recommendations for weight maintenance. In addition, direct observation affects eating behaviors. The Hawthorne effect is a confounding factor, referring to the phenomenon in which a subject's knowledge that he or she is under observation leads to conscious or subconscious changes in eating habits (Liu, Stamler, Dyer, McKeever, & McKeever, 1978).

Self-report is also inaccurate, whether in the format of a 24-hour recall or a food frequency questionnaire. According to Lichtman et al. (1992), obese individuals were

likely to underreport their food intakes by up to 30%. This is often due to forgetfulness, underestimation of amounts, or embarrassment at food type or amount. In addition, twenty-four hour recalls are a poor reflection of usual intake, while food frequency questionnaires can lead to greater difficulties in recall (Rutishauser, 2005). Daily recording of food intake reduces the error associated with recalls, but is impacted by the Hawthorne effect, and individuals will often alter their food intake when they are asked to complete diet records (Mendez et al., 2011).

One fairly new method of tracking dietary intake that seeks to strike a balance between an objective tracking system and one that allows participants to select foods unobserved is the computerized vending machine used by researchers at the National Institutes of Health (Gluck, Venti, Salbe, & Krakoff, 2008; Gluck, Venti, Salbe, Votruba, & Krakoff, 2011; C. A. Venti, Votruba, Franks, Krakoff, & Salbe, 2010). This method of tracking intake has been validated as accurate for purposes of tracking intake in a clinical setting. The modified vending machine for use in inpatient studies is stocked with a variety of healthy and unhealthy foods, with a unit that tracks which items are selected and at what time. Participants eat alone without observation, which allows them more freedom in food selection while still maintaining an objective food record. Unfortunately, this system is still conspicuous and cannot be modified for free-living situations. The lack of accurate and unobtrusive methods for recording food intake under free-living conditions poses a difficult problem for researchers and clinicians.

Statement of Proposed Research

Until recently, little data have been collected regarding innovative technological methods of measuring the mass of dietary intake. Thus, a gap in knowledge exists for objectively tracking intake in unobserved, free-living, ad libitum conditions.

The concept of utilizing technology for diet assessment purposes has been addressed most recently by Dr. Sazonov, an engineer who developed a system to link sounds of eating to mass of food ingested (E. Sazonov et al., 2008; E. S. Sazonov, Schuckers, et al., 2010; E. S. Sazonov, Makeyev, et al., 2010; E. S. Sazonov & Fontana, 2012). Research on this system of devices, which centers around a strain sensor attached to a participant's jaw, is still in its infancy. This study examined the efficacy of the newest iteration of the device, which would eventually measure the free-living intake of individuals as mass of food ingested in free-living, unobserved conditions. Since mass of food is generally correlated with calories, measuring the grams of food ingested can help researchers predict calories ingested. Due to the established link between caloric intake and weight gain, this method of measuring intake can be used by clinicians and researchers as another tool for fighting weight gain at the individual level.

The primary purpose of this study was to compare confirmed eating events using two different methods. Actual eating events are determined using the computerized vending machine developed by researchers at the NIH. This is compared to eating events as marked by the strain sensor and acoustical monitoring system (AMS) developed by Dr. Sazonov. This relationship was tested among healthy adults of varying weights in an ad libitum, unobserved clinical setting. We hypothesize that the AMS is an accurate method of measuring eating events in ad libitum clinical settings among healthy adults of varying

weights, as measured by a high degree of correlation with the validated standard of the computerized vending machine system.

Subjects were accepted during the period of December 2011 through June 2012, as a subset of the Food Intake Phenotype (FIP) at the NIDDK in Phoenix. Subjects were healthy adults aged 18 and over, as evidenced by medical history, physical examination, and laboratory tests that include liver function tests and oral glucose tolerance tests for diabetes. Only non-diabetic individuals were included in this study. Participants were of mixed ethnic backgrounds, primarily of European, Hispanic, or Native American descent. Healthy overweight and obese participants free of chronic or acute disease were included. Recruitment occurred on an ongoing basis at NIH via advertisements for this and other studies. All participants completed written informed consent after discussing the nature and purpose of the study with one of the NIH researchers. This study was approved by the ASU Institutional Review Board as exempt, and oversight was given to the Institutional Review Board of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

One limitation of this study is the self-selection process of participants, causing a possible deviation in participant characteristics from the general population. It is possible that, due to monetary compensation, participation may be tied to lower socioeconomic status. Since this study required participants to live in a clinical setting for a significant period of time, it is also more likely that participants were unemployed when compared to the general public of Arizona. Finally, since this study occurred in a clinical inpatient setting, it can not be applied to free-living conditions yet. In-patient conditions may affect normal intake patterns in individuals tested.

This thesis will provide data on a novel method of objectively tracking dietary intake in the form of eating events. This research can then be expanded by testing the device in free-living conditions or developing methods to more accurately tie eating events to mass or calories of food ingested.

Chapter 2

BACKGROUND LITERATURE

Introduction

Research has clearly identified a rising trend of obesity in the United States, as measured by body mass index (BMI). According to the latest NHANES data, released in 2009-2010, the prevalence of obesity is currently at 35.7% of the total adult population (Ogden, Carroll, Kit, & Flegal, 2012). While researchers have yet to trace the etiology of obesity to a single variable or even cluster of variables, several factors do appear to be linked to excess adiposity. One of these factors is dietary intake, more specifically caloric intake, which depends on both the energy density and the mass of food ingested (Bray & Popkin, 1998).

This factor is a key component in the energy balance theory of weight gain, which is currently the accepted paradigm in the field (Bray & Popkin, 1998; Hill, 2006; Lee et al., 2001; Ravussin & Bogardus, 2000). By this theory, energy ingested is compared to energy burned by metabolic processes, physical activity, the thermic effect of food, and physiological stress (Donahoo, Levine, & Melanson, 2004). If energy absorbed from food and fluids ingested exceeds energy burned by the body, the result will be a tip of the balance toward intake, resulting in weight gain (Spiegelman & Flier, 2001). On the other hand, if energy intake is less than the energy burned over a particular time period, weight loss will occur.

Other factors can affect the tip of this scale as well, many of them significantly. Genetic components play a significant role in this process. According to Stunkard (1999), it is estimated that two-thirds of variation in BMI is due strictly to genetic components, as

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evidenced by studies of twins in differing environments. Furthermore, previous studies have found at least 40% of variations in BMI between individuals is linked in some way to genetic components, specifically those regulating energy intake or physical activity (Ravussin & Bogardus, 2000). Most studies on the specific genes tied to weight regulation have focused on the obesity (ob) gene, which is primarily responsible for the production of a protein associated with satiety (Feve & Bastard, 2012; Hess et al., 2013). Another strongly-supported genetic link to obesity is the FTO gene and its activation of dopaminergic receptors (Hess, et al., 2013). Finally, over 32 SNPs (single nucleotide polymorphisms) have been associated with weak but significant links to obesity status via differential macronutrient metabolism (Loos, 2012; Park et al., 2013). These include the NEGR1, TMEM18, BDNF, MC4R, and KCTD15 genes.

Closely tied to genetic influences on weight status, hormones have also been found to play a key role in regulating the energy balance equation. Leptin, responsible for satiety, and insulin, responsible for bringing glucose into cells, are linked to energy intake and expenditure (Jequier, 2002; Schwartz et al., 2003). The studies cited found that this hormonal regulation tends to favor weight gain, making it an important component to study further in the context of obesity. Ghrelin, associated primarily with sleep/wake cycles, has recently been linked to leptin levels, metabolism, and eating patterns in humans (Garcia-Garcia et al., 2012). Research has also pointed to the key role that the neurotransmitter dopamine plays in satiety signaling within the brain (Hess, et al., 2013; Wang, 2012).

Finally, foods eaten may affect either energy expenditure or energy intake beyond simple energy density of the food. For example, alcohol consumption inhibits fat

oxidation and thus slows energy expenditure, while caffeine and capsaicin raise metabolic rates (Doucet & Tremblay, 1997). A meta-analysis conducted in 2012 determined that capsaicinoids, found in peppers, raises overall metabolism by an average 50 kcal/day, raises levels of lipid oxidation, and reduces appetite (Whiting, Derbyshire, & Tiwari, 2012). Similarly, ginger increases energy expenditure and reduces appetite in men by increasing the thermic effect of food (Mansour et al., 2012). Finally, the bioactive component in Bitter Orange extract has been found to raise resting energy expenditure in human participants (Stohs, Preuss, & Shara, 2012). It is hypothesized that many of these bioactive ingredients cross-influence hormones and genetic expression in humans.

While many factors likely contribute to the etiology of obesity, dietary intake is an underlying dynamic in all of the theories presented. Truly understanding dietary intake requires knowledge of three factors in individuals: what they eat, how often they eat it, and in what quantities (Notzon et al., 1991). This study attempts to look at the second factor mentioned: how often individuals are eating. These types of studies have been taking places since Bingham's metabolic ward in the 1930s (Schoeller, 1995). Each of the methods mentioned in the following pages is used primarily to estimate caloric intake over a period of time. However, many can also be used to estimate number of eating events during a desired time period. These methods can be broken apart into self-reported and objective assessment techniques. After discussing positive and negative aspects of each tracking technique commonly in practice, the theoretical groundwork will be laid for both of the assessment techniques that will be in use for the purposes of this thesis.

This review of the current techniques used to track dietary intake seeks to illustrate the inherent flaws in the available methods. For this reason, it is important to

acknowledge the difference between reliability and validity in the context of this study. Reliability refers to the repeatability of a particular measurement or instrument: given the same set of circumstances, it is an indication of how likely that tool would be to render the same result. This term can be contrasted with validity, which refers to the instrument's ability to measure what it is intended to measure (Bernard, 2011). A valid tool will necessarily be reliable, as it is an accurate depiction of the thing being measured (Dwyer & Coleman, 1997). However, reliability alone is not enough to establish validity. In this analysis of varying techniques for recording intake, it is illuminating to consider both the reliability and validity of each technique. In addition, it should be ensured that methods of evaluation do not just assess one validity by another (Trabulsi & Schoeller, 2001).

Self-Reported Methods of Assessment

Self-reported intake tracking methods commonly used in literature include the 24-hour dietary recall, the food frequency questionnaire, and the food diary (Field et al., 1999; Macdiarmid & Blundell, 1998; Venti et al., 2010). These techniques can be subcategorized further into retrospective and prospective methods (Lennernas, 1998). The retrospective methods consist of 24-hour recalls and food frequency questionnaires, since both look backward at prior intake, while the primary prospective method is the food diary, which tracks intake in real time.

These methods of recording intake were first discussed in the literature during the 1940s, when Burke began taking diet histories from his participants (Rutishauser, 2005). Research and clinical settings typically rely on self-reported methods of recording dietary

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intake because of their cost- and time-effectiveness; in most cases, it is not feasible to directly observe participants' dietary intakes over an extended period of time, especially in free-living conditions (Martin et al., 2009). Self-reported methods are low-cost and low-effort on the part of the clinician or researcher, and while they may not be the most accurate, many argue that they are accurate enough, especially at the population level (Block, 1982).

The 24-Hour Dietary Recall

The 24-hour dietary recall consists of unobserved intake, followed by an interview with a trained professional who asks participants to verbally remember everything they have ingested over the previous 24-hour period (Martin et al., 2009). For the purposes of most clinicians or researchers, this includes quantities of all foods and beverages ingested, as well as ingredients in prepared dishes. In common practice, this recall may be simply completed for the previous day, from rising in the morning until the first meal of the next morning, regardless of when the recall is actually conducted. In the fields of nutrition research and nutrition practice, this is one of the most common methods by which trends of dietary intake are assessed (Rutishauser, 2005).

This method of recording intake owes its popularity to its ease of use, low cost, and speed (Field et al., 1998, 1999). Another advantage conferred by this method is its lack of reliance on a high degree of participant literacy, though interviewers must be highly literate and trained (Field et al., 1999). However, many researchers have questioned the accuracy of this method of gathering intake data. A single 24-hour period is rarely representative of an individual's regular pattern of intake, which decreases its insight into dietary trends (Rutishauser, 2005). Thus, while it may be accurate, it is rarely

repeatable (Lennernas, 1998). Even a single abnormal day can sway the way that an individual's food patterns appear. For this reason, it has been suggested that this tool may be better suited to studies at the group or population level, rather than at the individual level (Field et al., 1999). Several methods for improving the reliability of the 24-hour recall have been tested. For example, time periods may be lengthened to collect intake data for three days or even a week, either continuously or non-continuously (Notzon et al., 1991). However, while taking a longer view of intake patterns may provide data more closely aligned with typical eating patterns, it may also cause increasing recall difficulties (Rutishauser, 2005). It is debatable whether or not this revision is any more accurate, or if it simply changes the type of error. To bypass this tradeoff, Field suggests multiple 24-hour recalls on non-consecutive days (Field et al., 1998, 1999). However, this can be time-intensive, especially in large population studies.

Finally, as will be discussed with each self-reported method of tracking intake, there is a documented trend of underreporting. This may be due to simple recall difficulty, especially of small snacks and isolated bites of food that cannot be categorized as eating events (Livingstone & Robson, 2000; Macdiarmid & Blundell, 1998). This has been found to be especially problematic among children, aging adults, and those with lower education levels. To increase accuracy of recall, some researchers are now using a multi-pass technique (Bisogni et al., 2007; Jonnalagadda et al., 2000; Rutishauser, 2005). By this method, researchers ask for information on eating patterns over the past 24 hours with increasing detail. During the first pass, the researcher allows the participant to recount everything that was consumed from midnight of the previous day (Bisogni et al., 2007). The second pass consists of the researcher probing the participant for each of the

eating events recounted, asking for more detail on the foods and amounts. A third pass

often consists of reading back the information garnered so far while asking participants to

add any mistaken or missing details. According to Livingstone, however, research has yet

to prove that this eliminates significant underreporting (M. B. E. Livingstone & Black,

2003). A study of 35 women tested 24-hour recalls that utilized a 4-pass system and

found 16% underreporting when compared to true intake (Trabulsi & Schoeller, 2001).

This continued error may be due to the recall difficulty that even multiple-pass

dietary recalls could not overcome, or to more complex psychological phenomena. This

is a more pressing problem to researchers, as this constitutes non-random (systematic)

bias which is more likely to skew study results (M. B. Livingstone et al., 1990;

Rutishauser, 2005). While the phenomenon of underreporting, common to all self-

reported methods of recording intake, will be discussed in combination with the other

methods, several studies shed light on the extensiveness of this problem in 24-hour

recalls.

A study conducted in 2000 compared multiple-pass dietary recalls with

calculations of energy needs during periods of weight maintenance (Jonnalagadda et al.,

2000). The researchers confirmed that body weight did not change over the period of

study, and dietary intake was either self-selected or solely administered by researchers,

depending on phase of the study. The results confirmed that individuals, regardless of sex,

were likely to underestimate energy intake on a self-selected diet: men by 11% and

women by 13% of total energy. Interestingly, when given a prepared diet, men continued

to underestimate their caloric intake by 13%, while women actually overestimated by

1.3% of total energy. The results illustrate the importance of finding an unflawed method of tracking intake, especially in ad libitum circumstances.

Food Frequency Questionnaires

Food frequency questionnaires (FFQ) are a slightly less common, yet still prevalent, form of recording intake in free-living populations. Using this method, individuals answer lengthy questionnaires regarding frequency of consumption of specific foods from an extensive list of possibilities (Rutishauser, 2005). Participants mark the appropriate box for their frequency of intake of each food item listed. Typically, these time categories are daily, 3-4 times weekly, 1-2 times weekly, 1-2 times monthly, and never.

This method was designed to be self-administered and easily entered into electronic databases, which is one of the advantages conferred by this method (Rutishauser, 2005). Further, because it asks for typical intake of each food over the past month, it is a much stronger indicator of eating patterns than the 24-hour recall (Subar et al., 2001). The FFQ can also be tailored to only ask about foods with a certain characteristic, depending on the nature of the study. For example, a study about consumption of calcium-rich foods could just ask about foods that are good sources of calcium (Rutishauser, 2005).

While there is less data available on this topic, many of the limitations of this method are also common to the 24-hour recall, as both are retrospective methods of recording intake. These phenomena will shortly be discussed as a cluster, but generally pertain to underreporting of "unhealthy" foods and overreporting of "healthy" foods (Mendez et al., 2011). This may be attributed to memory error or a desire for social

acceptance. Limitations more unique to the FFQ include the less quantitative nature of this method, when compared to the 24-hour recall (Subar et al., 2001). Serving size is rarely accounted for in the questionnaire, or is broken into relative categories. The semi-quantitative nature of the FFQ can lead to large random biases in the data collected (Rutishauser, 2005). This method is not well-suited for determination of daily energy intake on an individual level. Instead, it could more practically be applied to population- or group-level studies that examine eating trends.

Finally, researchers have criticized this method for necessitating a high literacy level (Field et al., 1999). Because it is self-administered and often lengthy, the FFQ requires the ability to read and comprehend the categories of food and the time increments indicated. Thus, it raises concerns for studies involving children, as well as minority populations who may not identify English as their primary language (Field et al., 1999; Kabagambe et al., 2001). In these circumstances, the FFQ must be administered by a researcher or clinician, negating one of the original benefits of this method: self-administration. Thus far, the accuracy of this method has not been compared to an objective measure of dietary intake, only to other subjective recording methods (Kabagambe et al., 2001; M. B. Livingstone & Robson, 2000). One study comparing FFQ to multiple 24-hour recalls found that the FFQ exhibited a significantly larger magnitude of error due to underreporting (Bathalon et al., 2000). Overall, even these relative evaluations have yet to reach a clear consensus on accuracy or reliability of the FFQ.

Food Diary

Food diaries are another method that has seen a certain measure of popularity in the field. This typically requires more time and effort from the participant over a lengthier timetable than the other self-reported methods (Trabulsi & Schoeller, 2001). By this method, the individual is responsible for recording all foods and beverages ingested as they eat or drink them, weighing each item or estimating portion size (Trabulsi & Schoeller, 2001). The strongest benefit conferred by this method is that it does not rely on a participant's memory of that food or the amount consumed, thus completely eliminating recall bias (Trabulsi & Schoeller, 2001). Depending on accuracy in measuring portion sizes, this is also one of the most quantifiable methods of recording intake.

However, there are also flaws inherent to this method. As with the other self-reported measures, participants may fail to record all foods, especially if not eaten as a part of a meal. Because of the significant burden on the participant, an increase in the number of days for which participants are asked to keep records is positively correlated with the amount of missing intake data (Gersovitz, Madden, & Smiciklas-Wright, 1978).

Furthermore, interpreting these participant-recorded data into nutrient data has been shown to be expensive and labor-intensive (Field et al., 1999). Of more concern is the phenomenon among food diaries of causing changes in intake patterns. In fact, it is quite often used as a technique for promoting weight loss (Field et al., 1999; Stuart & Davis, 1972). This may be due to a desire for social acceptability, resistance to recording more foods, or increased mindfulness of intake.

As quantified by Rathje, errors in food diaries can stem from four different sources: measurement errors (either from rounding error or packaging misinformation),

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overreporting of items viewed as healthy, underreporting of items viewed as unhealthy, and recording of different foods in place of foods actually consumed (1984).

Despite this significant potential for skewing normal intake patterns, this method has been found to be an accurate tool for tracking intake. According to Bingham, et al., weighed records are roughly as accurate as the objective method of urinary nitrogen (1995), and much more accurate than food frequency questionnaires and 24-hour recalls.

A study of 30 obese men found that use of food diaries led to underreporting as well as reduced consumption, relative to normal intake patterns (Goris, Westerterp-Plantenga, & Westerterp, 2000). Measured by the doubly-labeled water technique and records of body weight, the study found 12% underrecording and a mean undereating of 26%, leading to significant weight loss. This significant confounding factor of weight loss must be accounted for when utilizing this method of recording normal intake for analysis purposes.

The Phenomenon of Underreporting

As referenced in each of the preceding sections, underreporting affects the accuracy of the self-reporting methods. Further, underreporting is extensive among participants. According to one study, 18% of men and 28% of women were classified as underreporters (Bathalon et al., 2000), which matches a similar study finding that 31% of women underreport their dietary intake (Klesges, Eck, & Ray, 1995). Recall bias, the inability to accurately remember intake, is the first source of error in the retrospective methods of the 24-hour recall and food frequency recall. This commonly takes the form of failing to mention food items eaten and/or underreporting serving sizes consumed (Schoeller, 1995). This memory loss is not a linear fading of "snapshots" over time, but a

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failure to accurately reconstruct narratives embedded disjointedly in the memory (Dwyer & Coleman, 1997). These memory errors more often take the form of omissions, but may also include errors of commission. These false memories are common in food frequency questionnaires, as the brain lacks an effective way to tally the number of times foods are eaten over a given time. Memory loss and recall bias are individualized processes which should not be oversimplified. The outcome of recall biases is often false negative study results (Livingstone et al., 1990), as the effect mutes potential relationships between dietary intake and outcome variables.

Of more concern is non-random bias. These reasons for underreporting are more complex than forgetfulness, and can lead to false positives in research by showing relationships that do not actually exist. Certain characteristics have been found to be linked to this non-random increase in underreporting. Underreporting is most strongly correlated in the literature with obesity. One study found that obese participants' reported energy intake averaged only 59% of actual intake, while the non-obese group was accurate to 81% of actual intake (Bandini, Schoeller, Cyr, & Dietz, 1990). Studies have also found that obese subjects are more likely to underreport foods that are socially unacceptable: high-fat and simple-carbohydrate foods (Mendez et al., 2011). This phenomenon creates significantly more difficulty in the assessment of potential links between dietary intake and obesity. Simple knowledge of being observed, such as during a study, can affect intake toward greater social acceptability. This is known as the Hawthorne Effect (Liu et al., 1978; Macdiarmid & Blundell, 1998).

According to the study by Lichtman et al., obese participants have differential extents of underreporting when stratified into diet resistant (not losing weight despite

reported caloric restrictions) or non-diet resistant (1992). Diet resistant individuals underreported by 46%, while non-diet resistant individuals only underestimated by 19%. This difference is not likely attributable to conscious non-compliance, according to the researchers, as the diet-resistant group reacted to the study results with surprise. Further, objective evaluation of portion sizes of various foods provided was equally accurate between both groups. Lichtman suggests that this underreporting may somehow be linked to depression, as illustrated by higher depression scores by the diet-resistant group. Similarly, independent of weight status, participants who report extremely low dietary intake are likely underreporting to a greater extent than those who report a more plausible intake. Those with the highest levels of intake are actually closest to recording their actual energy intake (M. B. Livingstone et al., 1990).

While a less common occurrence than underreporting, overreporting has also been recorded in the literature. It is most commonly reported in children (Bandini et al., 1990; Lichtman et al., 1992). In a study of elementary- and middle-school children, it was reported 5th and 6th graders were significantly less accurate on food frequency questionnaires, when compared to 7th and 8th graders (Field et al., 1999). It is hypothesized that younger children may not be able to abstractly reconstruct what they have eaten in the past, or that they mentally rely on what they consider to be standard portion sizes.

Outside of obesity, other factors have been found to be linked to more extensive underreporting. Weight-conscious individuals, highly-active individuals, athletes, and those with highly variable dietary intakes or physical activity levels have been linked to more underreporting (Barnard, Tapsell, Davies, Brenninger, & Storlien, 2002; Schoeller,

1995). As might be expected with an emerging axis of social acceptability, women, especially Caucasian women, were also more likely to underreport (Briefel, Sempos, McDowell, Chien, & Alaimo, 1997; R C Klesges et al., 1995). Both of these studies also found literacy level, smoking status, and even day of the week recorded can be correlated with underreporting.

As summed up by Bathalon, regardless of self-assessment method (7-day weighed records, 24-hour recall, or FFQ), there appears to be no significant relationship between reported energy intake and objective energy intake by doubly-labeled water (2000). While certainly not every study agrees with this conclusion, it remains that many factors must still be determined between records of dietary intake and potential confounders.

Objective Methods of Assessment

In contrast to the subjective methods discussed above, the objective methods are by definition more quantitative and independent of participant recall. This has the potential to lead to more accurate physiological information on ingestive behavior and overall intake. However, these methods are also often more expensive and labor-intensive (Livingstone & Black, 2003). Thus, they are not as practical for studies with little funding. In addition, they may require extensive training of researchers (Gittelsohn, Shankar, Pohrel, & West, 1994), as these methods necessitate more precision and often the use of specialized equipment or devices. A practical, affordable method of objectively assessing intake in free-living, ad libitum conditions would fill a gap in research, as well as in practice.

Direct Observation

Direct observation is one of the least complex methods by which to objectively measure dietary intake. It requires no special equipment and can be conducted in free-living conditions (Gittelsohn et al., 1994; Myers, Klesges, Eck, Hanson, & Klem, 1988). For example, researchers in one study surreptitiously recorded the dietary intake of college students in a student union (Myers et al., 1988). The next day, these researchers administered 24-hour recalls to the same students to determine correlation between actual and reported intake. Interestingly, significant overreporting of intake the previous day was found among this population. Another study trained 10 Nepali individuals for several months to accurately estimate others' dietary intakes and serving sizes from observations (Gittelsohn et al., 1994). When these trained individuals compared their estimations to actual serving sizes, they found a level of correlation of 0.96.

While this method is a highly accurate objective measure of intake during the interval of observation, it remains largely impractical for assessing intake patterns. First, the time investment necessary for physical observation and researcher training is often not feasible. Furthermore, while the data collected is highly accurate for the time period of observation, it cannot be generalized to overall eating patterns (Lennernas, 1998). In similar fashion to the 24-hour recall, one solution to this is extending the length of observation, which yields results that are more closely related to general eating habits. Again, however, this also increases the time demand on the researchers.

Doubly-Labeled Water

Doubly-labeled water (DLW), originally developed to calculate total daily energy expenditure, is currently considered the gold standard for total daily energy intake

(Klesges et al., 1995; Trabulsi & Schoeller, 2001). This method, as explained by Martin, et al., consists of the consumption of isotopically-modified water by participants at the beginning of a tracking period (2009). The hydrogen atoms in this water are modified to deuterium, while the oxygen atoms are converted to ^{18}O, both non-radioactive isotopes. Both deuterium and ^{18}O are eliminated as body water. However, only ^{18}O can also be converted to carbon dioxide and eliminated via exhalation as a byproduct of energy expenditure (Trabulsi & Schoeller, 2001; Weber et al., 2001). This requires that respiratory quotient, tied to macronutrient composition of dietary intake, be estimated for the participant. Once this is done, the difference in elimination rates of deuterium and ^{18}O gives an accurate estimate of energy expenditure over the course of 7-21 days (Schoeller, 1995). These levels are measured using urine samples at the beginning and end of the free-living sample period, assuming a logarithmic trend of elimination and, unless more specific information is obtained, an average respiratory quotient of 0.86 (Weber et al., 2001).

While this method biologically tracks energy expenditure, it is used primarily as a proxy for energy intake. During periods of overall energy balance, in which no weight changes occur, energy intake is assumed to equal energy expenditure by the First Law of Thermodynamics (Trabulsi & Schoeller, 2001). Since this measure is accurate over a fairly long period of weeks, energy balance can be averaged over this time (Schoeller, 1995).

The major advantage of using the doubly-labeled water method to track energy intake is its accuracy in free-living conditions. This method has been validated extensively using multiple methods in both animal and human models (Schoeller, 1995).

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When compared to the gas-exchange method of tracking energy expenditure, DLW was found to be accurate to 1%, with coefficients of variation from 2-12% (Trabulsi & Schoeller, 2001). When compared to a prescribed and pre-weighed diet, DLW was found to be an accurate measurement of dietary intake to within 5.5%, with coefficient of variation of 9% (Schoeller, 1995). Further, any identified error can be classified as unbiased measurement error, as the DLW method is independent of reporting error (Trabulsi & Schoeller, 2001). This strengthens the DLW method for use as a gold standard, especially against subjective methods of tracking intake.

However, several drawbacks prohibit this method from being utilized more often in free-living conditions. The isotopes and the equipment needed to analyze them are prohibitively costly (Rutishauser, 2005). In addition to expense, this method also fails to reveal any information about micro- or macronutrient distribution of energy intake (Martin et al., 2009). In fact, it often relies on food logs for the estimation of respiratory quotient in the individual. Thus, while it is often used to validate other methods of tracking dietary intake, it is less likely to be used to directly track intake for study purposes.

Urinary Nitrogen

The methodology behind the urinary nitrogen method of assessing intake shares much in common with that of the DLW technique. While less practical than DLW and certainly not a gold standard, the prolific use of urinary nitrogen in the literature warrants its discussion (Bingham et al., 1995; Rutishauser, 2005). This method works on the principle that the nitrogenous bases in the protein consumed by an individual are broken from the rest of the amino acids and excreted in the urine. Thus, the nitrogen content in

the foods consumed should be proportional to the nitrogen present in the urine, assuming that the body is not under metabolic stress (Bingham et al., 1995).

Since this method only captures protein intake, it is not used for tracking overall dietary intake in individuals. Instead, it is more often used to validate other methods of dietary intake, particularly self-reported methods (Bingham et al., 1995). Misreporting can be detected if nitrogen excretion does not appear to correlate with reported protein intake. The drawback of this method of tracking dietary intake is its application only as a method of validating other tracking techniques. In addition, while it is highly accurate, it provides a poor picture of habitual intake (Rutishauser, 2005). It has been suggested that collecting urine for longer periods of time (up to 8 days) would be a better indicator of intake. However, this would likely decrease compliance, as participants must collect all urine on days that are tracked. Thus, while used in many studies to validate other techniques of tracking intake, urinary nitrogen is rarely used to record intake in individuals.

Computerized Vending Machine System

The invention or modification of electronic devices has also been explored as a means by which to record dietary intake. One such strategy is the remote photography method, which relies on participant-generated photographs of foods and beverages consumed to determine intake and portions (Martin et al., 2009; Nelson, Atkinson, & Darbyshire, 1996). A buffet table in which each food option rested on a hidden scale was found to accurately record food selections and portion sizes by participants (Rising et al., 1992).

One of the focuses of this study, however, is the computerized vending machine, a validated method of tracking intake that is unique to the National Institute of Diabetes and Digestive Kidney Diseases (NIDDK) at the National Institutes of Health (NIH) in Phoenix (Venti et al., 2010). Originally designed for use in tandem with metabolic chamber studies, this device objectively measures all dietary intake in ad libitum conditions for a single individual (Pannacciulli et al., 2007; Salbe, Tschöp, DelParigi, Venti, & Tataranni, 2004). The system consists of a refrigerated vending machine containing 40 unique food items. Each of these items had been previously rated by the participant with an intermediate high hedonistic rating on the Food Preference Questionnaire. Additional condiment, spice, bread, and drink options were also offered. The participant was given ad libitum access to the eating room, which contained the vending machine, a table, chair, microwave, and toaster. Participants were not allowed to watch television while eating, and were instructed that all food consumption was to take place in the eating room, with leftover food and wrappers remaining in the room to be accounted for by the researchers. Selection of a food from the vending machine activated a time stamp, creating an objective food record with start times of eating events. Energy and macronutrient intake were analyzed for each participant using the CBORD Professional Diet Analyzer Program and the ESHA Food Processor Program. An example of the vending machine used before modification is shown in Figure 1.

Figure 1. Unmodified sample vending machine ("Ideal Vending", 2001)

This validated method of recording dietary intake has been tested for reliability, with intraclass correlation for energy intake of 0.90, (P<0.0001, Venti et al., 2010). Strengths of this method include the lack of direct observation, which minimizes the Hawthorne effect on eating patterns or food selected (Liu et al., 1978). This intake tracking method has been successfully used to track the prevalence of night eating syndrome (NES), and used as a gold standard for validifying respiratory quotients in ad libitum conditions (Gluck et al., 2011).

In fact, the only downsides of this method are the finite number of foods that can be selected, the inability to record end times of meals, and this device's inapplicability to free-living conditions. For the purposes of this study, however, the computerized vending machine serves as an excellent objective method against which to validate another method of tracking dietary intake.

Electromyography

An alternate strategy in tracking dietary intake is to start, not from the food, but from the mechanical process of eating. These consist of the biting, chewing, and swallowing of food, and the swallowing of liquid. Two methods, more common to the engineering literature than the dietary literature, are considered the gold standards of tracking the mechanics of eating: electromyography and video fluoroscopy.

Electromyography is the process of recording the electrical impulses that innervate muscle (Stalberg, 1979). Muscles are innervated when an electrical impulse from the brain is sent to the fiber bundles of the muscle, causing contraction. Electromyography was originally used to diagnose nerve disorders and paralysis, as it physiologically determines if a muscle is receiving an impulse from the brain. This used to involve inserting needles through the skin into the individual muscle fibers, where they could detect and record the electrical impulses (E. S. Sazonov, Makeyev, et al., 2010; Stalberg, 1979). Dr. Edward Sazonov, the engineer responsible for creating the AMS, was one of the pioneers of applying electromyography to ingestive behavior, specifically chewing behavior. He identified electromyography of the jaw muscles as a validated method of monitoring chewing behavior (E. S. Sazonov, Makeyev, et al., 2010). While incredibly accurate, this method of monitoring chewing behavior was never used widely, as it is highly invasive and uncomfortable, and cannot be used in free-living conditions.

More important than the device itself is the groundwork that electromyography laid for newer, less invasive devices. Surface electromyography uses electrodes placed on the participant's skin surface to record electrical activation of the muscle beneath (E. S. Sazonov & Fontana, 2012). Another device consisting of a thin sensor placed over a

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molar in the mouth senses pressure changes when the participant chews (Bousdras et al., 2006). This was the first in a series of strain sensors, in which "strain" refers to the physics term for stress placed upon a system. Another iteration of the strain sensor is used in the AMS, as will be explained below. Thus far, however, none of these devices are unobtrusive enough to be used in free-living conditions.

Videofluoroscopy

Like electromyography, videofluoroscopy has been used to evaluate the physical mechanics of ingestion. However, while the former examines chewing behavior, the latter focuses on swallowing. Essentially a moving x-ray, video fluoroscopy is often used to diagnose spinal problems such as whiplash (Makeyev, 2010; E. S. Sazonov, Makeyev, et al., 2010). However, the same technology can be applied toward quantifying mass of food ingested over time. Factors that prohibit this method from being used more extensively include high cost, lack of portability, and exposure of participants to radiation. Again, while a reliable tool for assessing swallowing behavior, videofluoroscopy's ability to validate more applicable devices is of greater importance to this study.

Another innovative family of devices sense swallowing events not by visual means, but by changes in pressure. The simplest is a pressure sensor, a small balloon-like device that sits at the base of a participant's throat. During a swallow, the participant's Adam's apple shifts and the bolus of food passes through the esophagus, causing a change in pressure on the sensor. While shown to be effective in tracking swallows in normal-weight individuals, it was found that fat deposits around the throat of obese individuals mask this pressure change, decreasing the sensitivity of the sensor. Again,

these pressure sensors are not yet considered acceptably unobtrusive for free-living conditions. Later iterations of devices for recording chewing and swallowing events are used in the current study, as will be discussed shortly.

The Mechanics of Eating

The mechanics of mastication (chewing) and deglutition (swallowing) are essential to this study, as the AMS captures these motions to track and label eating events. A Swedish study conducted in 2011 used electromyography to focus on chewing and its relationship to bite size, meal speed, and swallowing frequency (Ioakimidis et al., 2011). Eleven participants were either asked to chew gum or to eat a meal, allowing researchers to mathematically model how chewing during the course of an eating event evolves over time. Non-obese participants naturally slow their rates of consumption by the middle of their meals. This occurs not by changing rate of chewing, but by increasing length of time between bites of food. However, this rate of consumption returns to normal by the last third of the meal time (Ioakimidis et al., 2011). Obese participants showed no change in the rate of consumption over the course of the meal (Stellar & Shrager, 1985).

Another study in the field challenged the idea that obese individuals should eat more slowly to decrease consumption (Spiegel, 2000). It found that, in both obese and non-obese individuals, smaller bites of food caused overall eating rate to slow, but had no affect on total intake levels. Obese individuals were less hungry after a period of non-eating than "lean" individuals, leading them to select more high-calorie foods based off of food preferences. Eating slowly or taking small bites was found to be more indicative of the food being eaten rather than a personal characteristic. Similarly, another study

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found that eating behavior was highly influenced by palatability of the food choices and length of time since the previous eating event (Bellisle & Le Magnen, 1981). Increased palatability leads to fewer chews per swallow, and less time between bites of food (Bellisle & Le Magnen, 1981). Knowledge of eating mechanics, as related to chewing and swallowing, aids in understanding the validity and usefulness of the AMS.

Acoustical Monitoring System

This thesis attempts to validate the ability of the acoustical monitoring system (AMS) to identify eating events in ad libitum conditions. The key component of this system is the strain sensor, a flat sensor about the size of a postage stamp which attaches superficially to the jaw, just below the ear. This sensor detects changes in skin tension in this region, differentiating chewing motion from similar movements such as talking (E. S. Sazonov & Fontana, 2012). The other mechanism is the throat microphone, which sits at the base of the neck and detects vibrations associated with swallowing. Again, this device must differentiate between swallowing food/liquid and similar activities. Together with the auxiliary devices, this system is designed to correctly identify bites, chews, and swallows at the individual level, translating this information into a picture of dietary intake.

There are several other checks and balances that will be incorporated into this study. A camcorder and a "clicker" button are used for the first hour of the protocol, during the portion known as the calibration meal, to be discussed shortly. A wrist sensor and chest receiver, developed by Amft, will also be incorporated as a means by which to

measure movement of the dominant arm toward the mouth (Amft, 2009). This serves as an additional perspective from which to track intake objectively.

Software developed by Sazonov is necessary to translate the data from the AMS into identification of eating events. The current computer program is designed to create a personalized algorithm for each participant based off of the data obtained from the calibration meal. Individuals are placed in a controlled, low-noise environment for a short period of time, where they demonstrate biting, chewing, and swallowing under different conditions. This data is then manually scored by researchers as bites, chews, and swallows, information that the computer program uses to create an individualized algorithm that can rate the rest of the 24-hour period without researcher help. However, this individual rating process and algorithm creation is incredibly time-consuming and highly skilled. In the absence of an individualized algorithm, a generalized algorithm can be used, although it can be inferred that this would necessarily be less accurate.

This system's future ability to identify dietary intake is predicted to occur in three stages. The first stage of this process is the focus of the present study: eating events. However, from here, the goal proposed by Dr. Sazonov is to translate swallow information into a calculation of the mass of the ingested food and liquid (E. S. Sazonov, Schuckers, et al., 2010). It has been discussed that mass of food ingested can be inferred from eating behavior by mathematical modeling, when average mass per swallow of solid food, number of swallows per food intake period, average mass per chew, and total number of chews is known. A similar algorithm can be used for liquid intake.

While intriguing from a scientific standpoint, neither eating events nor mass of dietary intake is the final goal of this ingestion monitor. To combat obesity and fill the

knowledge gap regarding objective intake, it is necessary that this device eventually

estimate caloric intake. Indeed, the ultimate goal of this device is marketing it to the

general public as a simple, accurate method of tracking intake (Makeyev, 2010).

However, until this technology has progressed to estimation of caloric intake, preliminary

research has shown a curiously strong link between eating events and weight gain.

Stunkard found that number of swallows recorded using a simple throat sensor correlated

more closely with weight gain the following year than self-reports of caloric intake

(1999). Mass of food consumed and calories consumed are also directly related, although

caloric density is confounding.

In addition to being a predictor of weight gain and an assumption of mass

ingested, this device can also be used to diagnose eating disorders, such as night eating

syndrome (NES) and bulimia nervosa, as will be discussed below. While the ultimate

intentions of this device are to move toward caloric intake estimation, the current

generation of the AMS also holds much promise for application toward practice.

Prior Research

Prior to the invention of the current AMS, several other researchers utilized

similar technology to track dietary intake and eating behavior. The previously-cited study

on palatability and its effect on consumption rate by Bellisle was completed using a series

of strain sensors attached to both the jaw and throat regions of participants (Bellisle & Le

Magnen, 1981). An oral strain sensor that resembled a retainer was used in another study

to capture changes in eating rates associated with growing satiety during an eating event

(Stellar & Shrager, 1985). Unfortunately, neither of these devices could be easily

validated in free-living conditions, due to their obtrusiveness. For example, the oral strain

sensor required a wire to snake out of the mouth toward a receiver in the participant's pocket. Perhaps wireless technology can solve some of these issues. In the meantime, while the AMS is by no means subtle, either, it is slowly being modified toward this application.

The foundation for the current study design comes from Lopez-Meyer, who determined that a swallow sensor is an accurate way of detecting times of food ingestion (2010). Thus far, only a few studies using this device have been completed, most of them conducted by Dr. Edward Sazonov, the engineer from Alabama who originally developed this device. One of his first studies looked solely at the initial scoring of the calibration meal, in which a researcher electronically marks the bites, chews, and swallows of foods consumed during the first hour of tracking. This is done to create an individualized algorithm for accurate tracking of eating events, as distinct from baseline background noise. In this study, participants ate a meal of differing types of foods and liquids, and two different trained researchers were given the task of counting the number of each artifact (bites, chews, and swallows) for that calibration period. This preliminary study found a correlation between the two raters of 0.996 for detected bites, 0.988 for detected bites, and 0.98 for detected swallows of food during the calibration meal.(E. Sazonov et al., 2008)

Building upon this, it was found that sounds of chewing and swallowing were an accurate method of detecting ingestion information (E. S. Sazonov, Schuckers, et al., 2010). The results revealed an accuracy of over 95% of detecting eating events, 91% of identifying liquids from solids, over 91% accuracy in determining mass of solid food, and over 83% accuracy of identifying the mass of liquids ingested. Finally, Sazonov

compared two technical methods by which to extract eating sounds from background noise and speaking. This study found that the algorithm calculated from the calibration meal to determine eating events had an accuracy in detection of 84.7% when compared to weighed records (E. S. Sazonov, Makeyev, et al., 2010). This was independent of the weight of the participant, suggesting that this method is accurate for both obese and non-obese individuals. This directly contradicts research on prior devices, which suggested that swallowing events would be masked in obese participants due to excess fat deposits. This may be traced to this device's use of a microphone that detects swallowing via vibration, rather than changes in pressure due to the movement of a food bolus. It also proved that artifact sounds such as talking, moving, breathing, and food digestion could be separated and discarded from the sounds of biting, chewing, and swallowing. This makes this method of tracking ingestion much more feasible for free-living populations, where these environmental artifacts could prove to be very real barriers.

As this device has been undergoing design and testing, it has not been the only of its kind. Dr. Amft has also been developing a similar device in parallel (Amft, 2009). He has relied on similar technology, yet with a few unique features. For instance, he has developed the hand gesture monitor that tracks the movement of a participant's dominant hand to his or her mouth, providing yet another way of verifying the number of bites a person takes. In addition, Amft is developing software that would assist in eliminating the human rating portion of the protocol during the calibration meal. Collaboration has already begun to occur between these researchers, as Sazonov has incorporated the hand gesture monitor into the current protocol. The elimination of the calibration meal and development of an accurate generalized algorithm for evaluation of eating events is also

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essential, as the current requirement of individualized algorithms is prohibitively labor-intensive.

Application of Research to Free-Living Conditions

This study was undertaken to evaluate a method of tracking ad libitum energy intake under free-living conditions. However, this device is currently being studied in a research unit context. Translating clinical findings to free-living conditions has been addressed by a 1985 study, which compared ad libitum dietary intake in a clinical setting with free-living dietary intake (Obarzanek & Levitsky, 1985). First, participants kept a 4-day food diary of their free-living ad libitum intake. For the following week, participants ate all meals in the clinic, with dietary intake tracked by the researchers. Paired T-test and intraclass correlation calculations found no significant difference in the amount of food intake reported during the free-living and clinical periods of the study. Additionally, participants' weights were also recorded, with no significant differences in weight found during the two-week period. While sample size was only four men and four women, these results suggest that ad libitum consumption in a clinical environment may be translatable to free-living conditions.

Application to Eating Disorders

This study will focus primarily on identification of eating events as the next natural step in validating the AMS. An accurate method of predicting eating events is highly applicable to the field of nutrition—not only for obesity research, but also for the diagnosis of eating disorders in a free-living context. This function of objective tracking

methods has already been utilized by the modified vending machines at the NIDDK.

These researchers have successfully used the tracking of eating events to diagnose

nighttime eating syndrome (NES), an eating disorder characterized by the consumption of

large amounts of calories during the night, between approximately 11pm and 5am (Gluck

et al., 2008, 2011). By recording the times at which foods are consumed and length of

eating event, future studies may utilize the AMS in a free-living context to aid in the

diagnosis of eating disorders such as NES and even binge-eating disorder or anorexia

nervosa.

Need for Research

As identified by Lennernas, there is currently no truly objective, practical tool of

assessing dietary intake in free-living conditions (1998). The current study builds upon

previous research on the AMS. Before ultimately calculating mass and caloric content of

food ingested, the sensor system must be validated for accurate identification of eating

events. The sensor system utilized is designed to provide a comprehensive picture of

physical intake. As meal times are evolving with culture, this study fits well into a greater

cultural context. Eating events are becoming more frequent, with more calories coming

from snacks than compared to 30 years ago (Popkin & Duffey, 2010). Identification of

eating events is also diverging from the traditional 3-meal system. Participants who were

asked about their free-living dietary intake utilized conventional labels such as

"breakfast," "lunch," and dinner" only 40% of the time, using other conventional labels

such as "snack" in about 23% of cases (Bisogni et al., 2007). Adding adjectives to

conventional meals, such as "afternoon snack" occurred about 9% of the time. Finally,

completely unique meal identifiers, such as "birthday treat," were used in 28% of cases. As eating events evolve toward greater individually, the current study can aid researchers in defining eating behavior within a greater cultural context.

The AMS is less invasive and yet more objective than many currently-used methods of tracking intake. Objective methods are traditionally more accurate in recording dietary intake, but are often expensive or impractical for free-living conditions. On the other hand, self-tracking methods are prone to error, specifically underreporting. The acoustical monitoring system has broad implications for the future of measuring dietary intake and its relationship to adiposity.

Chapter 3

METHODS

Participants and Study Design

This study analyzes an existing data set, as data collection was completed prior to formal thesis proposal. However, participant selection, study design, and execution of the original study are discussed here in detail as background to the data analysis also presented.

Recruitment was completed primarily through postings on the National Institutes of Health's Clinical Trials website, http://www.clinicaltrials.gov. This study is listed as the clinical trial "The Food Intake Phenotype: Assessing Eating Behavior and Food Preferences as Risk Factors for Obesity" (NCT0342732). A copy of the recruitment page posted to the clinical trials website is included in Appendix A. Local postings on the Craigslist website (http://phoenix.craigslist.org), posters in public places, and local newspaper advertisements were also used to advertise. This study was actually a sub-study of the Food Intake Phenotype (FIP) Study, which has been ongoing since 1999. Subjects for this portion of the FIP were accepted during the period of time from December 2011 to June 2012. The only inclusion criterion was that participants were 18 years of age or older. The informed consent (see Appendix B), is a general consent form containing sections pertaining to all of the studies that are concurrently being conducted by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) in Phoenix. Within the informed consent, the current study was referred to as the "ingestive monitoring study."

After signing the informed consents, participants completed a medical history, physical examination, and laboratory tests, which included liver function tests and oral glucose tolerance tests for diabetes. Volunteers were excluded if they were under 18 years of age, not in good health, or met the criteria of diabetes. Individuals with poor health were defined as those with hyper- or hypothyroidism, those with high blood pressure (greater than 160/95), those with cardiovascular disease, or those with gallbladder disease. Possible participants were excluded if they smoked tobacco, ingested more than 2 alcoholic drinks daily, used unprescribed drugs, were pregnant, or used medications that have psychiatric side-effects, if these effects could influence the outcome or safe completion of the study. Weight and ethnicity/race were not used as exclusion criteria.

This sub-study, as designed by the NIDDK, was conducted as a quasi-experiment. Its purpose was to determine the level of correlation between the numbers of eating events recorded simultaneously using two objective monitoring systems. The first was the experimental acoustical monitoring system (AMS). This method of tracking eating events was compared to the modified vending machine system, which has been validated previously. Participants were not randomized into separate groups; rather, each participant served as his or her own "control," by having daily caloric intake monitored by both systems over the same 24-hour period. Thus, the accuracy of the AMS was compared to the vending machine system on a per-participant basis, before results were aggregated between participants.

In overview, each participant remained in the laboratory for several days to complete this study. Upon admit, participants were placed on a 3-day weight maintenance diet while

the OGTT, DEXA, and assessment of weight stability were performed. Participants then completed a supervised calibration meal, which allowed the AMS to distinguish eating events from related activities, such as talking, silently sitting, and walking. While this data was not analyzed in the previous study, it can be used for the future creation of individualized algorithms. For the next 24 hours, participants continued to reside in the clinic and were allowed to move about the area at will. All food eaten during this time was ad libitum, taken from the modified vending machine. Participants remained in the room until they were finished eating, and food wrappers and remaining food were accounted for by the facility cooks. At the conclusion of this 24-hour period, participants were discharged. The following flowchart, Figure 2, illustrates the overall timing of events during the study, on a per-participant basis:
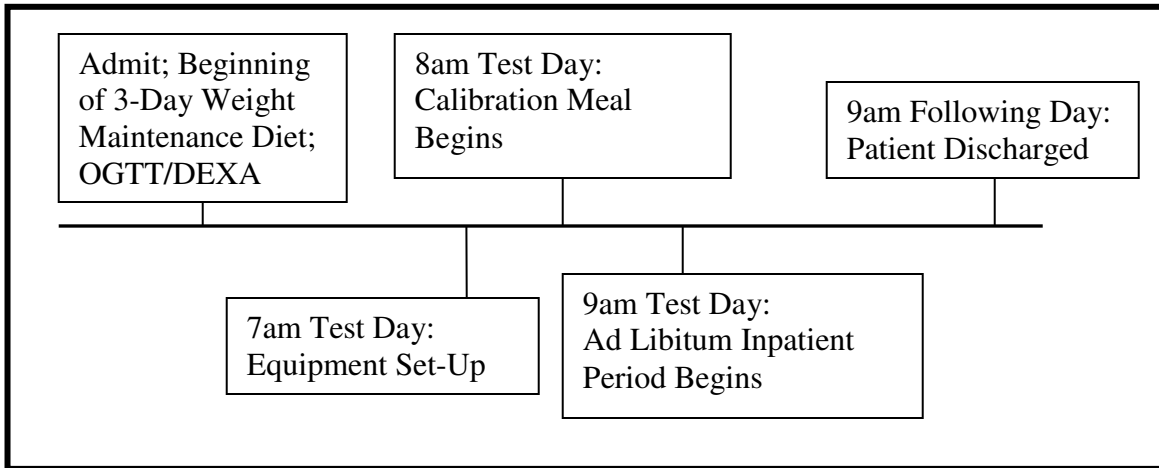
Figure 2. Participant Timeline

Acoustical Monitoring System

The monitoring system that was the focus of this study consisted of two similar set-ups of the devices: one for the calibration meal, and a more simplified version for the 24-hour ad libitum portion. The calibration meal equipment consisted of two main

sensors: a strain sensor at the jaw and a microphone at the hollow of the throat. These input devices were connected to recording devices housed in two separate Altoids tins. Ancillary devices included a hand-held clicker with removable beeping attachment, which was given to the participant for use in recording swallows. A wrist- and chest-sensor set was attached to the participant to record, via radio waves, the number of trips the dominant hand made to the mouth. Finally, a camcorder was trained on the participant during the calibration meal. All of the equipment except the camcorder were carried in two pouches that were hung around the participant's neck and/or in a fanny pack, as needed. All of these devices are shown in the following figures. Figure 3 shows the throat microphone, which was connected to a paintball collar. It also illustrates Altoids box #1, which housed the mp3 recording device that captured the microphone data, as well as a battery pack to extend the life of the mp3 recorder.
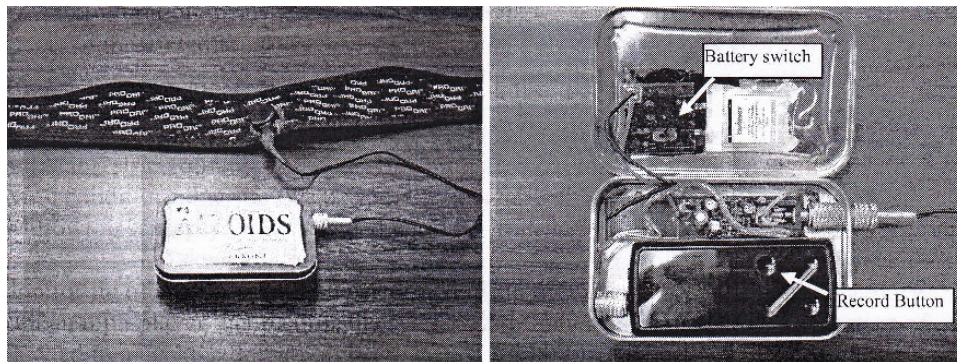
Figure 3. Altoids Box #1 and throat microphone.

Figure 4 shows the other devices used during the calibration meal, all of which plugged into Altoids box #2 for data recording. These devices included, from left, the push button, the strain sensor (shown below the Altoids box), and the chest/wrist sensor.
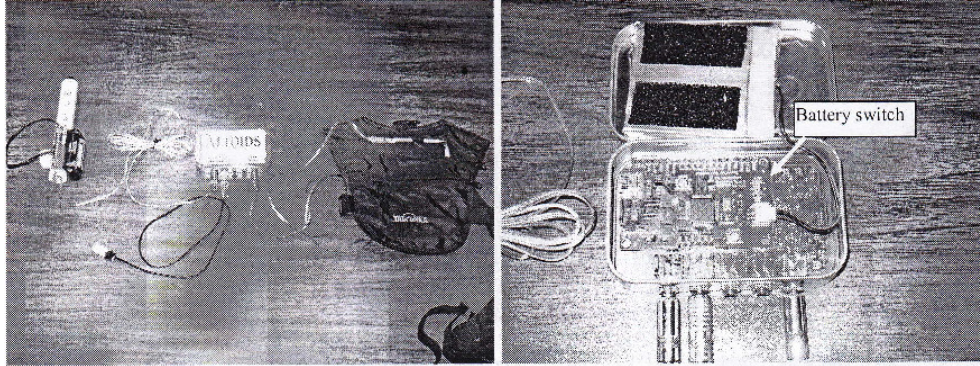
Figure 4. Altoids Box #2 and associated devices.

Once the calibration segment of the experiment was complete and the participant moved into the 24-hour ad libitum clinical segment, two of the devices were removed for ease of participant use. The camcorder was taken away, as participants were no longer under direct observation. In addition, the clicking device was removed until the end of data collection the following morning.

The only other materials used for the purposes of this study were computer programs created by Dr. Edward Sazonov and Dr. Juan Fontana at the University of Alabama's School of Engineering. These computer programs used the data obtained from the recording devices in the Altoids boxes to sync the information into a cohesive file, and to apply the created algorithm to determine the number of eating events for each participant during the trial. SPSS Statistics 19 was also used to perform statistical tests on the results of the experiment to determine significance of results.

Calibration Meal Procedures

During the course of the calibration meal, a standardized breakfast meal was administered and a timed list of different events was completed. This calibration 'trained' the devices in the various activities that will be encountered during the ad libitum period

of the experiment. This aided in the discrimination of eating events from non-eating events. Bites, chews, and swallows are highly individualized, so using the calibration meal procedure to create an individualized algorithm would theoretically lead to more accurate data. While this sub-study used a generalized algorithm, the calibration meal data can be used for a future study to determine if the device can be made more accurate. To begin the calibration period, all equipment was prepared, including spreading skin-safe glue on the strain sensor.

First, a wrist sensor to transmit hand movements during eating was attached to the participant's dominant wrist, and a chest pouch receiver was secured around the torso. The participant was given the push button to hold in his or her non-dominant hand. The throat collar microphone was attached snugly around the participant's neck. The strain sensor was attached to the skin of the participant's jaw, on the right side, just below the ear. Placement of the throat microphone and the strain sensor is shown in Figure 5:
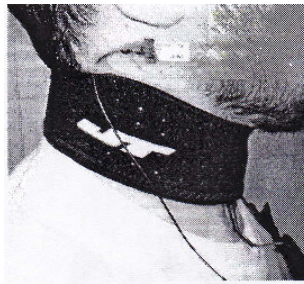
Figure 5. Placement of the strain sensor and throat microphone.

Recording was begun on the camcorder to capture the entire calibration meal, and recording on all other devices began as simultaneously as possible by starting both Altoids boxes concurrently. Once all devices were recording, the official beginning of the calibration meal was marked using the push-button device that the participant was

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holding. A removable attachment was affixed to the push-button device which makes an audible beep when the button is pressed. For the synchronization signals, the participant was asked to bring the beeper close to his or her throat microphone and press the button five times. The beeping attachment was then removed and the participant was instructed to press the button every time he or she swallows. The actual meal was called for at this time, which consisted of standardized portions of corn flakes, milk, banana slices, bacon, and yogurt. While the meal was being prepared by the kitchen, the following protocol was completed, as illustrated by Figure 6:

1. Point out to the subject the importance of using the button to indicate swallows
2. Time first quiet inactivity (10 min)
3. Call for tray of food from kitchen from nursing station
4. Time the talking period (10 min)
    a. Provide a conversation to the subject during this period
    b. Topics may be: subject's hobbies, favorite childhood toy, subject's daily schedule, current and past jobs, family
5. Serve the meal to the subject. Subject may talk while eating
6. Time second quiet inactivity (10 min)
7. Time a reading aloud period or second talking period (5 min)
8. Time a walking period (5 min) around the building.

Figure 6. Experimental protocol of calibration meal

With later participants, quiet inactivity periods, talking periods, and walking periods were abbreviated to only 5 minutes at a time to shorten the meal.

Once this procedure had been completed, the beeper attachment to the push button was reattached, and the procedure for a set of five synchronization signals was repeated before stopping the camcorder. The participant then entered the 24-hour ad libitum data collection period. The beginning of this period was signaled by a third set of synchronization signals using the beeping attachment on the push button.

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After this procedure, the clicker was completely removed and the 24-hour collection period began. The throat microphone, strain sensor, and wrist/chest sensor remained recording. During this time, the participant resided exclusively on the research floor of the NIDDK with open access to a bedroom, bathroom, recreation room, and eating room. Within the eating room was a computerized vending machine, as described in the review of literature, which allowed the participant unrestrained access to a variety of foods. Although food intake was at libitum, the participant had to eat in the dining room without any distractions (no phone calls or television). After the participant had finished eating, food wrappers and uneaten food were left in the room for the researchers to weigh and record. The machine recorded the foods vended and associated times, while participants were asked to record when eating was completed. After 24 hours had been completed (usually following breakfast), the push button and beeper were attached again and used to complete a final set of five calibration signals. All recording devices were stopped, all hardware was removed, and the patient was discharged.

Data processing

Data analysis occurred by downloading and syncing all of the information from each participant's calibration meal. This information consisted of the recorder in Altoids box #2, which held strain sensor, push button, and hand gesture data; the mp3 player, which recorded swallow data from the throat microphone; and the camcorder video. Audio files were format converted using Winamp, while strain sensor data were format converted using the custom program 'bintocsv_v2' and command prompt. The file was

downsized using the custom program 'downSample_1000to100Hz.vi.' Finally, the camcorder video was deinterlaced and compressed using "windv.exe" and Audacity.

All of the edited files were then copied to a disc and sent to researchers with the School of Engineering at the University of Alabama, who used a generalized algorithm created previously to turn the data from the strain sensor and ancillary data into a record of eating events. While the calibration meal conducted with each participant would allow for analysis using a unique algorithm, the time and labor needed by the researchers in Alabama to do so were prohibitive at this time. Once run through the generalized algorithm, each participant's AMS data consisted of a binary indication of "eating" or "not eating" for every 30-second epoch during the ad libitum period. Data from the vending machine was also broken into the same binary system of "eating" or "not eating" for the same 30 second epochs. These results were integrated into three columns in Microsoft Excel, indicating time, detection of an eating event according to the vending machine, and detection of an eating event according to the AMS. These data were then returned to the Phoenix branch of the NIDDK for further statistical analysis.

<center>Statistical analysis</center>

This was a quasi-experiment, as no randomization of participants took place and results were not blinded. Eating events, as measured by the AMS, were recorded and compared with eating events as determined by the modified vending machine for each participant. Thus, the basic data set consisted of two columns per participant, one per method of recording intake. Each column contained binary data indicating whether or not that method recorded the person as eating during that 30-second epoch. For each

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participant, the number of eating events was tallied by both methods. Number of eating events by each method among all participants was analyzed using a test for normalcy, then a correlated samples T-test. A P-value <0.05 was considered significant. All statistical analysis was conducted using SPSS Version 19 Statistics Software.

Chapter 4

RESULTS

Descriptives

Participants who completed the study consisted of 10 adults. A greater number of potential participants began the study, but were unable to complete for various reasons, among them family responsibilities and failure to meet screening criteria. Descriptives of participants who completed the study are shown in Table 1. Of the 10 participants, 7 were men and 3 were women, with a mean age of 39.8 (± 11.1) years. The body mass index (BMI) of the participants averaged 29.1 (± 7.0), with values spread over the interval 20.2-39.6. For reference, a healthy BMI is considered to be 18.5-25, with obesity status beginning at a BMI of 30 (NIH, 1998). Average percent body fat was calculated to be at 26.3% for men and 39.0% for women, with an overall percent body fat of 30.1%. At this time, research-based standards for healthy percent body fat categories are few. However, according to the American Council on Exercise, obesity is classified as body fat percentages greater than 25% body fat for men and 32% body fat for women (Bryant & Green, 2010). Weight, height, and body fat percentage were measured using a DEXA (Dual-energy X-ray absorptiometry) system.

Number of Eating Events

These results can be analyzed several different ways. Correlation of number of eating events will be examined first. Vending eating events were calculated using the records from the machine. Since participants had access to their own machine, we can be certain of times at which they withdrew each food. However, due to a lack of a

Table 1. Characteristics of participants wearing AMS device

Subject number	Age (years)	Sex	Ethnicity	Height (cm)	Weight (kg)	Body mass (BMI)	Body fat (%)	Waist (cm)
01	23.5	F	Native American	163	103.1	38.8	53.4	52.0
02	32.7	M	Caucasian/ African American	184	134.5	39.7	30.3	48.5
03	27.4	M	Caucasian	169	65.2	22.8	20.7	31.0
04	43.4	M	--	170	73.5	25.4	21.6	35.0
05	27.3	M	Native American/ Hispanic	180	70.2	21.7	18.2	32.5
06	29.8	M	Caucasian	173	86.5	28.9	30.7	38.0
07	53.5	F	Native American	159	50.6	20.0	17.7	32.0
08	50.8	M	Caucasian/ African American	175	102.9	33.6	32.5	43.0
09	43.1	M	Hispanic	182	109.9	33.2	30.3	46.0
10	50.6	F	African American	166	71.5	25.9	44.1	34.0
Mean	39.8			172.2	87.1	29.1	30.1	39.3
Min	23.5			159	50.6	20.2	17.7	31.1
Max	53.5			184	134.5	39.7	53.4	52.0
SEM	2.8			2.6	8.0	2.2	3.7	2.4
SD	11.1			8.2	25.2	7.0	11.8	7.5

mechanism for accurately defining the end of an eating event by the vending method, an estimation of 20 minutes was used for most eating events. When records of end times were kept by the participant, these numbers were used instead of the arbitrary 20-minute estimation. The AMS calculates both start and end times. However, this may be complicated by the observation that, for several participants, the battery needed for recording the strain sensor signals had run out before the end of the 24-hour ad libitum period.

Regardless, a determination of how to define eating events by AMS criteria had to be made. Complicating the data was the remnant of short meals (2-5 minutes) and short intermeal intervals (5-20 minutes). Possible methods of determining number of eating

events for the purposes of this study consisted of 1) unmodified, 2) small non-eating gaps eliminated, and 3) small non-eating gaps eliminated and small eating events eliminated.

Theoretically, the AMS should exhibit 1:1 agreement, graphed linearly with a slope of 1 (Bland & Altman, 1986). This can be contrasted with correlation, which indicates a direct relationship, but not necessarily a 1:1 relationship. However, as Figure 7 illustrates, none of the three methods of restricting the data provided a high degree of agreement, which would have appeared similar to the line of perfect agreement shown. The graph also shows degrees of correlation via R^2 values, indicating strength of a direct relationship between the vending machine and the AMS. Unrestricted data showed the lowest correlation coefficient, while the most restricted category had the highest R^2.

It was determined, derived from the precedent set by Popkin (Popkin & Duffey, 2010), that eating events spaced less than 20 minutes apart should not constitute separate events, but rather a pause in the same eating event. For this reason, eating events separated by a gap of less than 20 minutes were combined, whether this occurred in the vending machine or AMS categories. However, due to lack of precedent on setting eating event length, short eating event lengths were not eliminated. Mean number of eating events by the vending machine was 6.9 (±0.64) meals, while the mean of the AMS was 6.2 (±0.59) meals.
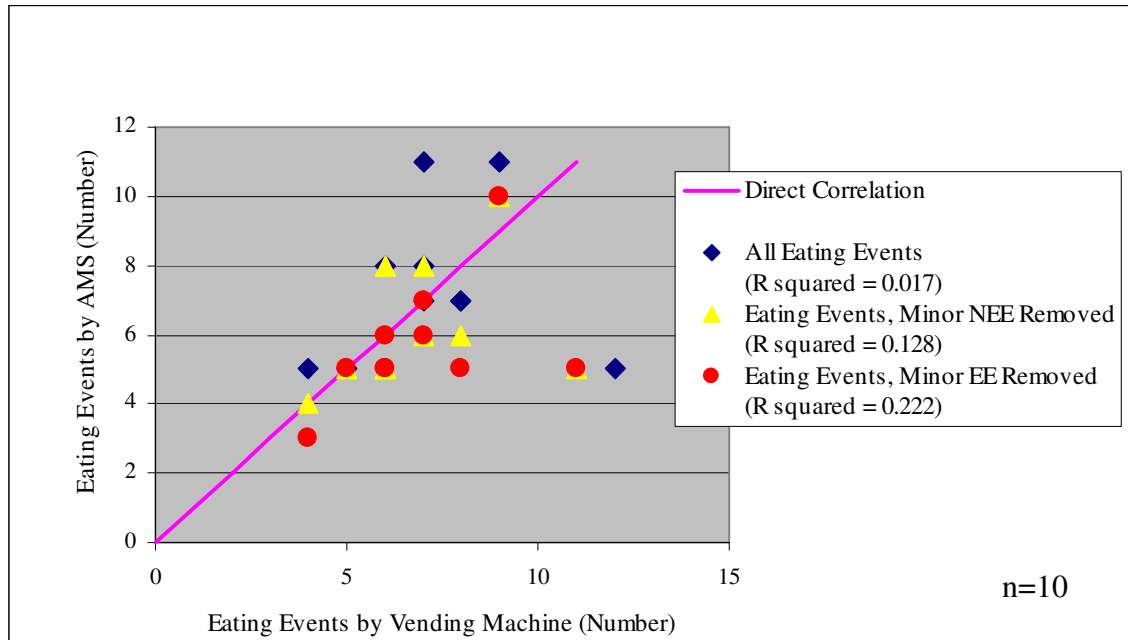
Figure 7. Comparison of eating events by method**.**
Note: NEE= Non-Eating Events, EE= Eating events.
"All eating events" shows the correlation between number of eating events by vending machine and by AMS, when no gaps are removed and no categories combined. "Eating Events (Minor NEE Removed)" shows correlation when gaps between meals of less than 20 minutes were removed. Finally, "Eating Events (Minor EE removed)" also incorporated removal of meals less than 4 minutes in length from the data set.

A paired samples correlation and paired samples t-test were conducted on the number of eating events using SPSS Version 19, as seen in Table 2. However, results were not significant. It was noted that Participant 09 appeared to be an outlier, which was defined as more than double eating events by one method (either vending or AMS) than the other method. This was not true of any other participant. For this reason, participant 09 was excluded from the data set and these tests were run again. This time, a paired samples correlation (Pearson correlation) of 0.756 was found (p = 0.019). A paired-sample T-test statistic was calculated as 0.263 (p = 0.799).

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Table 2. Participant eating episodes		
Subject number	Vending Machine EE	AMS EE
01	6	5
02	4	4
03	6	8
04	7	8
05	8	6
06	9	10
07	7	6
08	5	5
09	11	5
10	6	5

Note: EE = Eating Event

Frequency of matches between eating and non-eating data points was also compared. For each participant, all 30-second epochs were evaluated by both vending machine and AMS methods for agreement. If both methods indicated eating or both methods indicated non-eating, this was considered a matched data point. Average distribution frequency of all matching data points between participants is 0.8948, as shown in Table 3.

Table 3. Relative frequencies of matching eating epochs		
Subject number	Matching epoch frequency	Non-matching epoch frequency
01	0.866713	0.133287
02	0.984673	0.015327
03	0.927793	0.072207
04	0.895443	0.104557
05	0.838047	0.161953
06	0.841962	0.158038
07	0.860488	0.139512
08	0.908153	0.091847
09	0.827646	0.172354
10	0.995341	0.004659
Overall	0.894800	0.105200

However, this strong frequency may be partially due to the fact that the participant was not eating for long portions of the day. Since the focus of this study was

identification of eating events, matching between eating and non-eating by the vending machine and AMS was modified by recategorizing each 30-second epoch as follows: 1) both methods indicating non-eating, 2) non-agreement between methods, and 3) both methods indicating eating. Frequencies of each of these categories were calculated for each participant, then frequencies were averaged between participants. Results are shown in Figure 8.

Results were also restricted to time of day, with morning eating events, defined as <28660 seconds of ad libitum intake (roughly 8 hours), showing a greater matching percentage. This data is shown in Figure 9. Note that matched non-eating events decreased, since sleeping was largely eliminated. Meanwhile, matched eating events increased by 125% as unmatched eating events increased by only 68%.

Eating Events by Demographic

To determine is the AMS was more accurate among particular subsets of the sample, frequency of matching eating events was stratified by three different descriptive factors: gender, age, and obesity status. When participants were divided by gender, the male category had 7 participants, while the female category had 3 participants. When divided by age, the 20-39 years category had 5 participants, as did the 40-59 years category. Finally, when classified by obesity status, the non-obese (BMI<30) category contained 6 participants, while the obese category (BMI≥30) had 4 participants. The frequency of non-matching eating events was normally distributed. However, independent t-tests of each of these variables failed to show significance.

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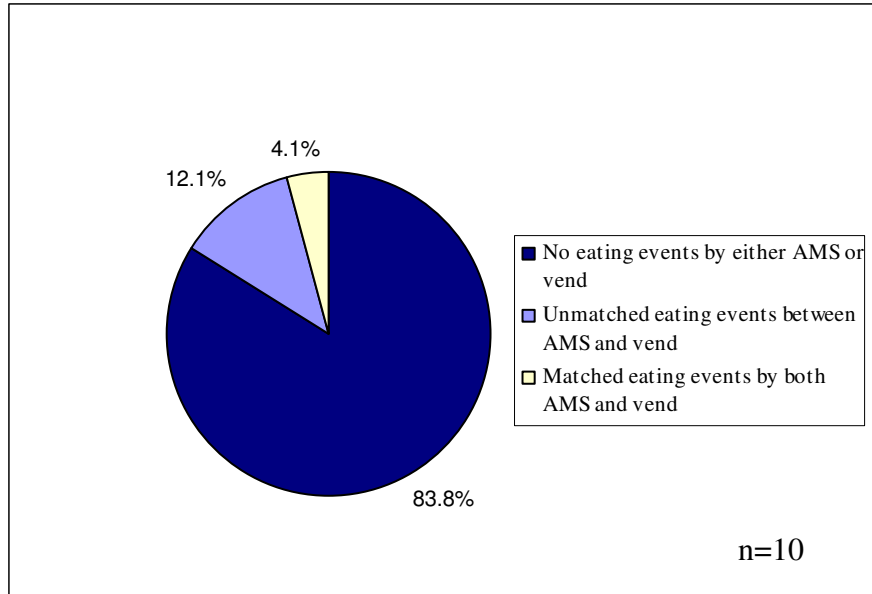
Figure 8. Percent matching eating epochs between the AMS and vending machine over 24 hours, aggregated between all participants. This figure shows that the AMS was in agreement with the vending machine for the majority of data collection, with non-agreement occurring in 12.1% of epochs.
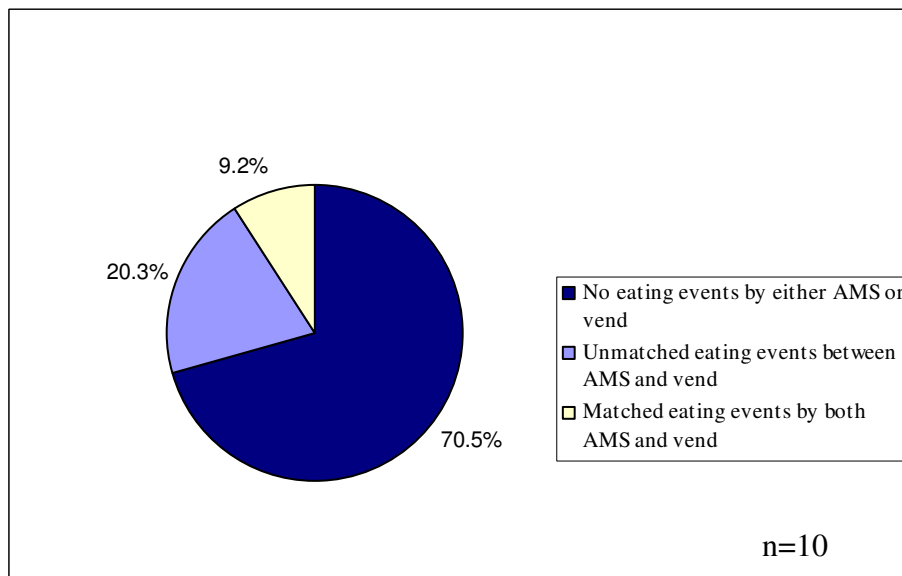
Figure 9. Percent matching eating epochs between the AMS and vending machine during the first 28660 seconds (approximately 8 hours) of data collection, aggregated between all participants. This figure shows that the AMS was in agreement with the vending machine for the majority of data collection, but that non-agreement increased when data was restricted to the first 8 hours of collection.

Mass and Caloric Estimate

The ultimate goal of the AMS or a similar device is estimation of mass of food ingested, eventually moving to caloric intake. In this study, participant intake during the ad libitum portion of the experiment was recorded as both mass and kilocalories for 9 out of 10 participants. For this reason, a calculation of correlation between AMS data and mass/caloric intake was completed. Number of eating events by the AMS did not appear to correlate with either mass or caloric intake, and was not significant. To determine if AMS eating epochs correlated significantly with either mass or caloric intake, this independent variable was first transformed from a count variable into a continuous variable. For each participant, the total number of 30-second epochs as labeled by the AMS was multiplied by 30 seconds, yielding total number of seconds labeled as eating, to an accuracy of 30 seconds. This continuous variable was highly correlated and significant with both mass (0.908, p = 0.001) and caloric intake (0.704, p = 0.034) by a Pearson correlation. This study yields preliminary results on the accuracy of the AMS, providing direction both for current application and future research opportunities.

Chapter 5

DISCUSSION

The present study was designed to evaluate the accuracy of an Auditory

Monitoring System (AMS) to identify eating events in ad libitum conditions. This system

was compared to the modified vending machine system at the NIDDK in Phoenix, a

validated method of tracking dietary intake.

This study's primary hypothesis was that the AMS is an accurate method of

measuring eating events in an ad libitum clinical setting among healthy adults of varying

weights, as measured by a high degree of correlation with the validated standard of the

computerized vending machine system. Secondary to this hypothesis was the possible

correlation of AMS data to mass or calories of intake during the same period.

The results of this study show little 1:1 agreement between the number of eating

events calculated by the vending machine and AMS methods, when examined graphically.

Data restriction was based partially off of precedence in the definition of an eating event,

and partially off of the R^2 values of the restriction options. It was also noted that

participant 09 appeared to be an outlier, so this participant's data were removed for the

determination of Pearson correlation. For the purposes of this study, an outlier was

defined as any participant in whom the number of calculated eating events by one method

was more than double the number of eating events by the other method. With the

exception of participant 09, all participants' number of eating events by the AMS was

within two meals of the vending machine's number. For this reason, participant 09 was

excluded. Pearson was used as this data was normally distributed. The results indicate a

correlation of 0.756, or 75.6% correlation in number of eating events, which was

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significant. Furthermore, the paired t-test yielded a p-value of 0.799. This p-value illustrates a lack of a significant difference between the vending and AMS methods of counting eating events. This result is highly desirable, especially when taken with the significantly high Pearson correlation, as it assists in the validation of the AMS method. Unfortunately, this result was only possible after removing one of the participants in an already small sample. Increasing sample size would be the solution to this potential shortcoming.

The degree of matching between methods of each 30-second epoch was also evaluated. A simple overall frequency of matching epochs yielded 0.895, or a frequency of 89.5%. Most of these matching data points occurred during times of not eating, which is more a function of physiological amount of time spent eating by participants than a drawback of the device. When restricted to the first 8 hours of data collection, the AMS actually became less accurate. Unmatched events increased from 12.10% of epochs to 20.31% of epochs, an overall growth rate of 68%. This likely means that the long periods of non-eating during the night, if more easily identifiable by the AMS, were inflating the matching percentage of epochs.

Demographics were not found to be a useful method of stratifying data. Stratifying for age, gender, or obesity had no significant effect on the accuracy of the AMS device. However, it is impossible to tell whether this is due to consistency of the AMS, regardless of age, gender, or obesity status, or rather to a sample size that was too small to detect differences. While this data suggests that the AMS can be used with equal accuracy across diverse populations, a larger study sample would be necessary to confirm that the small number of participants is not the cause of this lack of significance.

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Ultimately, the goal of this device is an objective method of tracking mass and/or calories of intake at the individual level. This was preliminarily studied using the food records from the vending machine. It was found that, while number of eating events by the AMS did not correlate with mass or caloric intake, seconds eating according to the AMS correlated significantly with both. Number of seconds and mass of intake had a Pearson correlation of 0.908, with a p-value of 0.001, while number of seconds and calories of intake had a Pearson correlation of 0.704, with a p-value of 0.034. The correlation between mass and time spent eating according to the AMS is strong, as hypothesized. It is logical that the correlation between time eating and calories is weaker, though still significant, as caloric density complicates the relationship between mass and calories of dietary intake.

A limitation of this study is ambiguity in length of eating events by the vending machine method. As correct identification of eating status was evaluated in 30-second epochs, the validity of this study design would be strengthened by tracking distinct endpoints by both methods. For example, if participants' meal lengths were markedly different from the 20 minutes assumed by the vending method, it is possible that more data points were matching between the vending method and AMS.

Secondly, as noted in the results, the battery responsible for recording strain sensor data did not last for the full 24-hour ad libitum period for several participants. Since the device was usually removed from the participant directly following the breakfast meal, this may have led to failure to detect this final eating event by the AMS only. This could have caused inaccuracies in both number of eating events recorded by the AMS and total period of time spent eating according to the AMS, without a

corresponding effect on the vending machine accuracy. To determine if this battery was a source of inaccuracy, it would be necessary to test this device again, with a longer-lasting battery on the device recording AMS signals.

Finally, this population may not be representative of the general population. Due to the extended periods of time for which they remain in the clinic and the significant monetary compensation, participants are more likely than the general population to be jobless or economically insecure. Economic insecurity has been linked to both food insecurity and obesity status, which can have a significant effect on unrestricted dietary intake (Sarlio-Lahteenkorva & Lahelma, 2001). These potential limitations, however, do not affect the validity of these findings with respect to the given hypotheses.

This research helps to fill the literature gap identified at the beginning of this thesis. While it remains that no truly objective measure of intake yet exists in free-living conditions, research is drawing ever closer (Lennernas, 1998). Consider this study's conclusions and implications in the context of the other studies conducted on the AMS device. Research had previously validated manual rating for algorithm development (E. Sazonov et al., 2008), illustrated the device's ability to correctly identify chews, bites, and swallows (E. Sazonov et al., 2009), and showed the high degree of accuracy with which the device could identify eating events in a controlled environment (E. S. Sazonov, Makeyev, et al., 2010). This research fills the needed next step in the validation of a free-living objective measure of intake by testing the AMS's ability to identify eating events in ad libitum conditions, looking forward to the application of this device in tracking caloric intake. Furthermore, it tests this against a validated objective measure, thus strengthening findings.

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In the greater body of research, this study strengthens the viability of devices that utilize technology in cost-effective and user-friendly ways to increase health awareness and promote healthier lifestyles. The AMS, once validated for free-living populations, could serve to curb the widespread underreporting evident in self-reported methods of recording intake (Bathalon et al., 2000; Klesges et al., 1995; Schoeller, 1995). The ability of the AMS to identify eating events could provide a standard against which to evaluate participant self-reported intake.

Once refined, the AMS could potentially give more specific information than the vending machine system currently does, as it also has the ability to mark end times of meals. Future research utilizing this device can focus on several different angles. First, design modifications could make this device more viable for free-living conditions. Adoption of a more unobtrusive design is already underway by Dr. Sazonov, aided by the elimination of the swallow sensor in the neck collar. Once the strain sensor is made wireless and disguised, this could potentially be a marketable device to the public for the purpose of assessing dietary habits and intake. As iterations of design changes occur, it will also be necessary to advance the device to more accurately detect mass consumed and, eventually, calories consumed. If applied to obesity prevention or treatment, this evolution is essential.

Finally, the development of a more accurate generalized algorithm for analysis of intake data must be continued. This device was originally designed to run on individualized algorithms, hence the need for calibration meals. However, the time-intensive need for skilled engineers to create this algorithm for each participant is prohibitive of practicality. As was seen in this study, it is not feasible to use an

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individualized algorithm, even though it likely would have led to more accurate results. Instead, designing a more accurate and sensitive generalized algorithm would be a significant step toward improving the accuracy and application of results.

This study found significant correlations between the AMS method of tracking eating events and the validated vending machine method. It also established a strong significant relationship between time spent eating, as measured by the AMS, and both mass and calories of intake. These results further the process of validating the AMS in ad libitum conditions as an objective method of tracking dietary intake.

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APPENDIX A

EXAMPLE OF RECRUITMENT PAGE

| Full Text View | Tabular View | No Study Results Posted | Related Studies |

The Food Intake Phenotype: Assessing Eating Behavior and Food Preferences as Risk Factors for Obesity

This study is currently recruiting participants.
Verified on June 2011 by National Institutes of Health Clinical Center (CC)

First Received on June 19, 2006.   Last Updated on July 19, 2011   History of Changes

Sponsor:	**National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)**
Information provided by:	National Institutes of Health Clinical Center (CC)
ClinicalTrials.gov Identifier:	NCT00342732

▶ **Purpose**

The prevalence of obesity in the United States has reached alarming proportions with 33% of adults over the age of 20 being overweight. Obesity is more than twice as prevalent, however, in the Pima Indians of Arizona. Although there have been a number of advances in our understanding of the genetics of obesity, the environmental influences on the genetic expression of obesity requires further investigation.

In an effort to understand some of the influences on the high prevalence of obesity in the Pima Indians, the present study was designed to investigate eating behaviors and food preferences, most especially the preference for high fat foods, in sib -pairs of Pima Indians who have been previously genotyped in our genomic scan for loci linked to diabetes/obesity. Most specifically, we will utilize several questionnaires and methods of assessing eating behavior and the preference for high fat foods to create a food intake phenotype. In addition, we will study Caucasians so that comparisons can be made between these two groups. We will make these evaluations by assessing eating behavior, food preferences including usual fat intake and preferences for high fat foods, body image perceptions, and energy expenditure. It is hoped that the data gathered from this study will elucidate some of the risk factors for the development of obesity among the Pima Indians.

Condition
Obesity

Study Type: Observational
Official Title: The Food Intake Phenotype: Assessing Eating Behavior and Food Preferences as Risk Factors for Obesity

Resource links provided by NLM:

Genetics Home Reference related topics: Help Me Understand Genetics

MedlinePlus related topics: Obesity

U.S. FDA Resources

Further study details as provided by National Institutes of Health Clinical Center (CC):

Estimated Enrollment: 600
Study Start Date: April 1999

Detailed Description:
The prevalence of obesity in the United States has reached alarming proportions with 33% of adults over the age of 20 being overweight. In some populations, obesity is even more prevalent. Although there have been a number of advances in our understanding of the genetics of obesity, the environmental influences on the genetic expression of obesity requires further investigation.

In an effort to understand some of the influences on the high prevalence of obesity, the present study was designed to investigate what drives how much people eat. More specifically, we will try to understand what drives food intake utilizing 1) questionnaires that assess eating behavior, 2) measurements in blood, urine or fat tissue, and 3) genotypic associations to investigate the various factors that control what and how much people eat. As food intake influences appetite-regulating hormones and vice versa, we also plan to assess the effect of short-term overfeeding on ad libitum intake and the appetite-stimulating hormone, ghrelin. Also, as the body's metabolism of carbohydrates may influence food intake, we propose to look at the effects of isocaloric high fat and high carbohydrate diets on short-term ad libitum intake. We will make these evaluations by assessing eating behavior, food preferences including usual fat intake and preferences for high fat foods, body image perceptions, and energy expenditure. It is hoped that the data gathered from this study will elucidate some of the risk factors for the development of obesity.

▶ **Eligibility**

Genders Eligible for Study: Both
Accepts Healthy Volunteers: Yes

Criteria

• INCLUSION CRITERIA:

Healthy, as determined by medical history, physical examination, and laboratory tests.

EXCLUSION CRITERIA:

Hypo or hyper thyroid

Blood pressure greater than 160/95

Cardiovascular disease

Gallbladder disease
Alcohol and/or current use of drugs (more than 2 drinks per day and regular use of drugs such as amphetamines, cocaine, heroin, or marijuana)

Psychiatric conditions or behavior that would be incompatible with safe and successful participation in this study, including claustrophobia and eating disorders such as anorexia or bulimia nervosa

Use of medications affecting metabolism and appetite

Pregnancy

Smoking

▶ **Contacts and Locations**

Please refer to this study by its ClinicalTrials.gov identifier: NCT00342732

Contacts

Contact: Susanne Votruba, Ph.D.   (602) 200-5336   votrubas@mail.nih.gov

Locations

United States, Arizona
     NIDDK, Phoenix   **Recruiting**
            Phoenix, Arizona, United States, 85014

Sponsors and Collaborators
     National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

APPENDIX B

INFORMED CONSENT

MEDICAL RECORD	CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY
	• Adult Patient or • Parent, for Minor Patient

INSTITUTE: National Institute of Diabetes and Digestive and Kidney Diseases

STUDY NUMBER: OH99-DK-NO19   PRINCIPAL INVESTIGATOR: Clifton Bogardus, M.D.

STUDY TITLE: The Food Intake Phenotype: Assessing Eating Behavior and Food Preferences as
                Risk Factors for Obesity

Latest IRB Review:
Latest Amendment Approved:

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

- Taking part in NIH research is entirely voluntary.
- You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.
- You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

PURPOSE OF THE STUDY

This study has been designed to investigate some of the causes of the high prevalence of obesity in the U.S. population. We hope to assess eating behavior, food preferences and activity level with a series of questionnaires, two taste tests, how the body uses fat and a nutrition study using vending machines. We also will collect genetic material (DNA) from volunteers so we can investigate how genetic differences may affect food intake. You may also be invited to wear a sensor around your neck and on your cheek for one day. We hope these studies will help us to better understand the factors that affect food intake and eating behavior and which may put people at risk of becoming obese and to possibly develop strategies to assist people in losing weight.

CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH
STUDY
• Adult Patient or   • Parent, for Minor Patient
NIH-2514-1 (4-97)
P.A.: 09-25-0099
File in Section 4: Protocol Consent
This Consent document is approved by the IRB through 07/26/11

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	CONTINUATION SHEET for either:
MEDICAL RECORD	NIH 2514-1, Consent to Participate in A Clinical Research Study NIH 2514-2, Minor Patient's Assent to Participate in A Clinical Research Study

OVERVIEW OF THE STUDY

You are being invited to participate in this study at the NIH in Phoenix in order to measure your eating habits, food preferences, and activity level. This study consists of eleven questionnaires, two taste tests, an overnight stay in the metabolic chamber, fat biopsies, a test using a special tracer to see how the body uses fat while in the metabolic chamber, and a nutrition study using vending machines. You may also be asked to wear a sensor around your neck and on your cheek for one day while using the vending machines. This sensor will measure when and how much you eat by counting your "chews" and "swallows."

After we have performed some screening medical tests and determined that you have no active medical problems, we will have you fill out a series of questionnaires. On the second day, the amount of fat and bone in your body will be measured by DXA (described below) and you will have a taste test and fill out a questionnaire about your normal eating behavior. On day 3, you will have another taste test. On day 4, you will have an oral glucose tolerance test to determine if you are diabetic. Day 5 will begin with 2 biopsies of the fat tissue on your stomach and thigh. On day 6, you will spend 24 hours in the metabolic chamber. You will receive a breakfast before entering the chamber containing a stable (non-radioactive) tracer of dietary fat (described below). On days 7-9, you will take food dispensed from the vending machines (described below) and have a blood draw each morning. If you choose to participate in this part of the study, on day 7 you will also wear a chewing sensor on your cheek and microphone around your neck for 24 hours (described below). On day 10, you will be discharged.

It is possible that you may not be eligible for this study based on the results from the screening tests, as detailed below. Additionally, if you have any conditions not specifically mentioned below that are deemed to be contraindicated for your participation in the study, you may be excluded from the study at the discretion of the investigators. This includes, but is not limited to, such things as not following study and unit policies and procedures, diagnosis of contraindications, and illness/infection unrelated to the study.

TESTS AND PROCEDURES

1. **Screening tests.** These tests are to make sure you are healthy enough to take part in the study. On the first day you arrive on the unit, you will have a physical exam including an EKG (a tracing of your heartbeat), blood test, and urine tests (including a pregnancy test if you are a woman). We will perform a test to determine whether you are a smoker. We will also perform certain tests to exclude people with recent or active drug use with substances such as marijuana, cocaine or amphetamines. These results will be stored as part of your permanent medical record and could potentially be available to someone having access to this record (see section on

PATIENT IDENTIFICATION	CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY (Continuation Sheet)
	• Adult Patient or • Parent, for Minor Patient NIH-2514-1 (4-97) P.A.: 09-25-0099 File in Section 4: Protocol Consent

	CONTINUATION SHEET for either:
	NIH 2514-1, Consent to Participate in A Clinical Research Study
MEDICAL RECORD	NIH 2514-2, Minor Patient's Assent to Participate in A Clinical
	Research Study

STUDY NUMBER: OH99-DK-NO19   CONTINUATION: page 3 of 10 pages

"Release of Medical Records" below). We will draw about 2 ounces of blood for these tests that will require one small needle in your vein for less than three minutes. The risks include the small chance of a bruise and slight pain from the needle.

2.   **Genetic studies**. Some of the blood drawn during screening will be used to obtain genetic material called DNA. The DNA will be taken from your white blood cells. We will grow your white blood cells in the laboratory and then freeze them so that we will have a supply of the DNA.   The DNA may be sent to other scientists who work with us on studies of diabetes, obesity and related medical problems. If we do this, the DNA will be coded and you would not be personally identified.

The results of these genetic tests will be used to attempt to find out why some people eat more than others, why they choose specific foods (for instance with more fat) and why they become overweight. We may also try to find out why some people make more insulin than others, why some respond poorly to insulin, and why some are more likely to get diabetes.

Unless there is a very good reason, we do not plan on sharing the genetic information with you.

Like other institutions, the NIH may have to release information to an insurance company if you have signed an authorization form from the insurance company.

•   Storage and confidentiality of genetic material: Any information collected or discovered about you through the study of your blood or tissue will be kept confidential. Research results about your genetic make up will be kept separately from the medical record. Occasionally, during the study of mutations of genes and DNA, identification of a condition unrelated to food intake, obesity, or diabetes may be found. In this case, you will be informed and genetic counseling or appropriate referrals will be provided.

A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. According to this law, health insurance companies or group health plans (as of May 21, 2010) cannot request your genetic information or use it to make decisions about your eligibility or premiums; and employers cannot use it in deciding to hire, promote, or fire you or in setting the terms of your employment (as of Nov 21, 2009).

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

The following link contains details on this policy:
http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfoDoc.pdf. You may ask

PATIENT IDENTIFICATION	CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY
	(Continuation Sheet)
	• Adult Patient or • Parent, for Minor Patient
	NIH-2514-1 (4-97)
	P.A.: 09-25-0099
	File in Section 4: Protocol Consent
	This Consent document is approved by the IRB through 07/26/11

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your research team for additional information or a copy of The Genetic Information Nondiscrimination Act of 2008 informational document.

3. **Pregnancy screening.** Pregnancy causes many changes in the body that may affect the tests. Because of this, and due to unknown possible risks to unborn children, a pregnancy test will be performed on all women who could bear children. You will not be allowed to undergo any of the tests if you are pregnant. However, you will be able to take part in the studies again after you have your baby and stop breast-feeding.

4. **Questionnaires** - The purpose of these questionnaires is to measure your usual food habits and to understand your food preferences. These questionnaires will be answered by you privately. There is minimal risk involved in answering these questionnaires. However, some of the questions are personal and you may not wish to respond to some of the questions. You may refuse to answer any of these questions or withdraw from this study at any time without risk of losing benefits to which you are otherwise entitled.

5. **Oral glucose tolerance test.** This test has been used for many years to diagnose diabetes. For this test, we insert a small plastic tube (an IV) into an arm vein using a small needle. You will be given a solution of glucose to drink and then we will take some blood from you over a three-hour period. There is a small risk that a black-and-blue mark or a minor infection might occur where the needle enters your vein. We will watch for these problems and treat them if they occur. The needle stick to place the plastic tube in your arm vein may be slightly painful. About 2 tablespoons of blood are drawn for this test. If you are found to have diabetes during this test, you will not be allowed to continue with the study. You will be provided with diabetes and nutrition education and referred to the appropriate services for follow-up care.

6. **DXA Scan**. The DXA is used to determine the percentage of your body that is fat tissue. During this test you will lie quietly on a table for 5-10 minutes while you are scanned. The DXA measures your body composition with a low dose of x-rays. Using a standard way of describing the radiation dose, you will receive a maximum average skin exposure of 4 mrem/year from two scans assuming two scans are required. Please be aware that this radiation exposure is necessary for this research study only and is not necessary for medical care.

The average person in the United States receives 0.3 rem per year from natural background sources, such as from the sun, outer space, and from radioactive materials found naturally in the earth's air and soil. The dose that you will receive from this research study is about the same amount you would normally receive in five days from these natural sources. If you would like more information about radiation and examples of exposure levels from other sources, please ask the investigator for a copy of the pamphlet called *An Introduction to Radiation for NIH Research Subjects*.

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One possible effect that could occur at these doses is a slight increased risk of cancer. Please be aware that the natural chance of a person getting a fatal cancer during his/her lifetime is about 1 out of 4 (25 percent). The increase in the chance of getting a fatal cancer as a result of the radiation exposure received from this research study is less than 0.0002 percent. Therefore, the total risk of fatal cancer may be estimated to increase from 25 percent to 25.0002 percent. This additional risk is too small to be measured and is general regarded as insignificant.

The Phoenix NIH Radiation Safety Committee has reviewed the use of radiation in this research study and has approved this use as involving minimal risk and necessary to obtain the research information desired. The amount of radiation you will receive is within this committee's guidelines for research subjects of 3,000 mrem to any tissue in a 13-week period and 5,000 mrem in 1 year.

If you are pregnant or breastfeeding, you will not be able to participate in this research study. It is best to avoid radiation exposure to unborn or nursing children, since they are more sensitive to radiation than adults.

7.   **Taste tests.** The purpose of these tests is to measure your responses to sweet, creamy and bitter foods. It is likely that taste preferences affect the foods that you choose to eat and we would like to determine if this is so. To determine your preference for sweetness and creaminess, you will taste 16 milkshakes with different contents of sugar and cream and rate how appealing each of the shakes is. To determine your ability to taste bitter foods, you will be asked to place a small piece of paper containing a bitter-tasting substance on your tongue for a moment and then rate your reaction to it. These procedures involve minimal risk.

8.   **Twenty-four hour metabolic rate in the metabolic chamber.** The chamber is a small room that is designed to measure how many calories you burn over a 24-hour period. You will enter the room at 8 AM and leave at 7:30 AM the following day. The room contains a sink, toilet, bed, desk, chair, color TV, telephone, radio and refrigerator. Your food will be passed to you through a small door. There are two windows facing outside and an intercom so that you can talk with people outside the chamber. At any time, you will be able to contact the nurses as well as speak to people on the outside using the telephone. The risk associated with this measurement is the feeling of being confined to a relatively small room. If you feel this way, you will be able to end the test and leave the chamber anytime if necessary. The second morning, for about 40 minutes before leaving the bed in the chamber, you will have a clear plastic hood placed over your head so that we can measure the number of calories you burn at rest. This is a large hood that you can easily see and hear through. There is minimal risk involved in this part of the test.

9.   **Blood drawing for hormone assessment** – On the morning of days 7-10, you will have 40 cc (about 8 teaspoons) of blood drawn for measuring hormones that regulate appetite. This

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requires one small needle in your vein for less than 3 minutes. The risks include a small chance of a bruise and slight pain from the needle.

10.   **Vending machine study** - For 3 days, you will be asked to choose all your food from our vending machines. These machines will provide you with a large selection of items you have indicated that you like. You will have free access to the machines, 24-hours a day, for the 3 days of the study. The purpose of using the vending machines is to allow us to see the food choices you make, as well as the timing of your meals. There is minimal risk involved in performing this test.

11.   **Fat biopsies** – We wish to obtain a sample of fat tissue. Some of this tissue will be stored but some will also be used to see how the fat cells work when isolated from the body. We first "numb up" your skin, then withdraw pieces of fat tissue with a larger needle. The fat will be obtained from your belly, around your navel, and your thigh, near the muscle biopsy site. There may be some mild pain when the skin is being "numbed." A black and blue mark may occur at the site of the biopsies and the site may be slightly tender for 1-2 days afterward. A minor infection might develop at the biopsy sites, however this is unlikely and will be treated if it occurs. There is a slight chance of blood collecting beneath the skin (a "hematoma"). This may take 2-3 weeks to resolve and may result in some tenderness at the site for several days after the biopsy. There is a remote chance of allergic reactions to the "numbing" medicine (lidocaine) or tape and wound dressings covering the biopsy site.

12. **The use of wearable sensors to estimate food intake and mass** – A group of volunteers will be asked to wear sensors to measure times and amount of food intake for one day while using the vending machine system. These sensors are a small band-aid-like device that attaches below the outer ear that monitor chewing and a microphone (on a neck strap) that detects swallowing. Volunteers that wear the sensors will be given a meal on their first day of eating from the vending machine that will be observed by a study worker and filmed in order to make sure the sensors are picking up chews and swallows. Following this meal, volunteers will continue wearing the sensors for 24 hours while using the vending machines. After 24 hours, the sensors will be removed and volunteers will continue eating from the vending machines for two more days. Except for the inconvenience of wearing the strain sensor and swallowing microphone with the band around the neck, there is no risk associated with these sensors. The devices are currently in development for scientific use only, but there may be potential for commercial development in the future.

13. ^{2}**H-palmitate tracer to measure how the body uses fat** – Prior to entering the metabolic chamber, we will ask you to provide a urine sample. You will be given a breakfast that includes a serving of Ensure which contains a dietary fat with a non-radioactive marker or tracer (^{2}H-palmitate). ^{2}H-palmitate adheres to the dietary fat as it travels through your body. We will ask you to provide urine samples while you are in the chamber and will measure the amount of 2H-

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palmitate in the urine so that we can determine how your body uses the dietary fat. There have been no reports of any signs of toxicity or abnormalities in metabolism using this tracer.

BENEFITS

This study is entirely for research purposes. You will not receive any medical benefits from this study; however, we may learn things that will benefit others, including your family and community. You will receive some information about your own health, including having a thorough physical exam, a measurement of your body fat, and a test to find out whether or not you have diabetes. The results of these tests will be given to you and your doctor if you so desire. If we find through these questionnaires that some of your behaviors are unhealthy, we will advise you of this and offer you assistance in changing these behaviors.

PAYMENT

1)	Daily payment $35/day x 10 days	$350.00
2)	Three inconvenience units for the metabolic chamber	75.00
3)	Two inconvenience units for the questionnaires	50.00
4)	One inconvenience unit for the OGTT study	25.00
5)	Three inconvenience units for the vending machine study	75.00
6)	Two inconvenience units for blood drawing	50.00
7)	Ten inconvenience units for fat biopsies	250.00
8)	One inconvenience unit for measurement of ^{2}H-palmitate	25.00
9)	One inconvenience unit for wearing chew/swallow sensors	25.00

TOTAL	$925.00
BONUS PAYMENT FOR STUDY COMPLETION	$100.00
GRAND TOTAL	$1025.00

CIRCUMSTANCES THAT APPLY TO ALL RESEARCH CONDUCTED AT THE NIH

In addition to the description of the actual research protocol, there are several general points that we want to mention to help you understand issues that are indirectly related to your participation in this study:

Family studies: During the course of this study, it is possible (although not likely) that we will obtain unanticipated information about your health or genetic background. If this information is considered to be important to your health care, we will give it to you or your doctor. It is also possible that we may learn sensitive things about your family. For example, it is possible that we might learn that a family member is not the biological child of the parents with whom he/she lives. We will not ordinarily provide this type of information to any member of the family or your doctor. However, we may make exceptions under extraordinary circumstances if this information was

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required for the medical care of the individuals involved. If we were convinced that this was necessary, we will provide the information to the doctor providing medical care to the patient. By agreeing to participate in this study, you do not waive any rights that you may have regarding access to and disclosure of your records. For further information on those rights, please contact Dr. Susanne Votruba.

Release of medical records: In the course of applying for certain types of insurance (e.g., medical insurance, life insurance, or disability insurance), people are often asked to sign forms that authorize insurance companies to obtain their medical records. If you sign such a release form at some point in the future, it is possible that the insurance company would present this signed release form to the Phoenix Indian Medical Center and/or the NIH. In that event, the hospital and the National Institutes of Health would comply with your request to provide the insurance company with your medical record. It is possible that the information contained in your medical record might affect (either favorably or unfavorably) the willingness of the insurance company to insure you.

Storage and confidentiality of genetic material: Any information collected or discovered about you through the study of your blood or tissue is strictly confidential. Research results about your genetic make up will be kept separately from the medical record. Occasionally, during the study of mutations of genes and DNA, identification of a condition unrelated to food intake, obesity, or diabetes may be found. In this case, you will be informed and genetic counseling or appropriate referrals will be provided. Information gained by studying the mutations of genes and DNA, if used outside the research context, could possibly lead to yet unknown discrimination, such as difficulty in obtaining health or life insurance. Like other institutions, the NIH may have to release information to an insurance company if you have signed an authorization form from the insurance company.

Future research: During the research study, we will obtain blood, urine and fat samples. While we can do some of our tests immediately, we may store these samples in the freezer for future studies. In addition, certain information will be stored in your medical record. In the future, it is possible that your blood, urine or fat samples or your medical records will be used for research purposes other than those specifically outlined in this consent form. Your stored samples will only be used to evaluate factors that are related to the development of obesity, diabetes and their complications. This may require sending samples or data to other places that do research for measurement of these factors. All samples are stored using only a unique code number and date of sample collection, so if your samples are used, you cannot be identified. We do keep a local record of your code number so we can identify your samples if necessary. This record is kept in a secure system that only the researchers here have access to. We will not ordinarily inform you of the results of these tests unless the results, in our judgment, clearly will help you identify, prevent, or treat a health problem. In addition, it is possible that some information obtained from these studies will be published in medical journals. However, your identity will not be included in these

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publications. Samples will be stored until used, unless you request in writing that we destroy your samples. By agreeing to participate in this study, you do not waive any rights you may have regarding access to and disclosure of your records. For further information on those rights, please contact Dr. Susanne Votruba (lead associate investigator) at 602-200-5300.

As mentioned above, samples may be sent to other places that do research for measurement of factors related to obesity and diabetes and their complications. At this time, samples or data from this study have been or will be sent to the Obesity Research Center, University of Cincinnati-Genome Research Institute in Cincinnati, OH, the Umeå Hospital, Umeå, Sweden, Unit on Growth and Obesity, National Institute of Child Health and Disease, Bethesda, MD, Clarkson University in Potsdam, NY, and University of California, Irvine, CA. It is possible that your own samples may be sent to facilities not yet listed that may be able to make measurements that may help understand how obesity and diabetes develop.

Conflict of interest: The National Institutes of Health reviews NIH employees at least yearly for conflicts of interest. The following link contains details on this process: http://ethics.od.nih.gov/forms/Protocol-Review-Guide.pdf. You may ask your research team for additional information or a copy of the Protocol Review Guide. This protocol has investigator(s) who are not NIH employees. They are expected to comply with their Institution's conflict of interest policies.

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OTHER PERTINENT INFORMATION

1. **Confidentiality.** When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

   The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or other authorized people.

2. **Policy Regarding Research-Related Injuries.** The Clinical Center will provide short-term medical for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. **Payments.** The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health.

4. **Problems or Questions.** If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Lead Associate Investigator, Dr. Susanne Votruba, phone 602-200-5314. Another researcher you may call is Dr. Joy Bunt, phone 602-200-5314. You may also call the protocol nurse coordinator, Joan Nethercutt, at 602-200-5313, or our Patient Representative, Mrs. Carol Massengill, at 602-200-5314.

5. **Consent Document.** Please keep a copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM BELOW, A or B:

A. Adult Patient's Consent I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.	**B. Parent's Permission for Minor Patient.** I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study. (Attach NIH 2514-2, Minor's Assent, if applicable.)
_____ _____ Signature of Adult Patient Date THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE THROUGH	_____ _____ Signature of Parent(s) Date _____ _____ (If Other Than Parent, Specify Relationship) Date

_____ _____	_____ _____
Signature of Investigator Date	Signature of Witness Date

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APPENDIX C

IRB APPROVAL (NATIONAL INSTITUTES OF HEALTH)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

National Institute of Diabetes and
Digestive and Kidney Diseases
Bethesda, Maryland 20892

Date: July 13, 2011

TO: Clifton Bogardus, M.D.
             Principal Investigator

FROM: Chair, NIDDK/NIAMS IRB

SUBJECT: Final and Approved Version of Protocol # OH99-DK-N019
             **The Food Intake Phenotype: Assessing Eating Behavior and Food
             Preferences as Risk Factors for Obesity**

- Your Continuing Review was approved at the May 31, 2012 IRB Meeting. Please use
  the final approved version of the protocol and consent as a guide for the next continuing
  review.

- Changes in research activity (e.g., terminations) should be reported promptly to the IRB.

- No changes, amendments or addenda may be made to the protocol or the consent form
  without IRB re-review and approval.

- If adverse consequences or unexpected side effects are encountered during the course of
  the study, or if new information becomes available which would change the perception of
  a favorable risk/benefit ratio, you are responsible for informing the IRB promptly, as well
  as institutional officials and the FDA as indicated.

- As Principal Investigator you are responsible for informing the Associate Investigators of
  the status of the project.

Howard Austin

Howard Austin

THIS PROTOCOL WILL EXPIRE ON: May 30, 2012
This protocol's next continuing review will be two months prior to this date.

APPENDIX D

IRB APPROVAL (ARIZONA STATE UNIVERSITY)

Office of Research Integrity and Assurance

To: Carol Johnston

From: Mark Roosa, Chair Soc Beh IRB

Date: 01/06/2012

Committee Action: Exemption Granted

IRB Action Date: 01/06/2012

IRB Protocol #: 1201007244

Study Title: Prediction of Ad Libitum Eating Events Using a Non-Invasive Acoustical Monitoring System

The above-referenced protocol is considered exempt after review by the Institutional Review Board pursuant to Federal regulations, 45 CFR Part 46.101(b)(4) .

You should retain a copy of this letter for your records.