THE RELATIONSHIP BETWEEN SLEEP, SWEET TASTE, AND FOOD SENSORY PERCEPTION

By

Edward J. Szczygiel

A DISSERTATION

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

Food Science—Doctor of Philosophy

2019

ABSTRACT

THE RELATIONSHIP BETWEEN SLEEP, SWEET TASTE, AND FOOD SENSORY PERCEPTION

By

Edward J. Szczygiel

Little is known about the relationship between sleep, chemosensation, and food perception. Given that sleep curtailment is a becoming more prevalent in the developed world and that short sleep duration is routinely associated with weight gain and obesity, understanding the mechanisms that drive this relationship is of great interest to public health advocates. Further, this relationship may contribute to poor test-retest reliability in food sensory studies. Therefore, the primary objective of this body of work was to characterize the relationship between sleep duration, chemosensation, and hedonic sensory perception with a focus on sweet taste perception.

In chapters 1-2, the linear relationships between chemosensation and sleep duration and architecture are assessed. A total of 56 non-obese female participants and 51 male participants who denied having diagnosed sleep disorders completed testing across the two studies. Sleep was measured for two nights using a single-channel (A_1–A_2) electroencephalogram-(EEG) (Zmachine). Sweet taste threshold and preference, as well as olfactory threshold, recognition ability, and pleasantness ratings, were evaluated. Sweet taste preference was correlated with total sleep time (TST) (Females: p=0.0074, males: p=0.0111) as well as with several individual stages of sleep. For males only, odor identification ability was positively associated with TST (P=0.0187) and REM sleep duration (P=0.0424). Participants grouped into shorter sleep groups and low REM+SWS preferred significantly greater sucrose concentrations than those in longer

and high REM+SWS groups (Females: p=0.041, 0.049, Males: p=0.0420, 0.0039, respectively). Sex differences in the effect of short sleep duration on chemosensory function overall were found to be minimal.

In chapters 3-5, a sleep curtailment intervention design was employed to assess the effect of a one night of 33% reduction in habitual sleep duration on perception of both model solution and complex food stimuli. Forty-one participants recorded a habitual and curtailed night of sleep using a single-channel electroencephalograph. After curtailment, a significant increase in preferred solution sweetener concentration ($p<0.001$ for sucrose and sucralose sweeteners) was observed. The slope of sucrose sweet liking increased after curtailment (p=0.001). The slope of sucralose liking also increased, but the effect was not significant (p=0.129). Another forty-one participants, using similar methodology, evaluated energy- and nutrient-matched solid and liquid oat products after a night of curtailed sleep. Overall (p=0.047) and flavor (p=0.017) liking slopes across measured concentrations were steeper after curtailment, suggesting that sweeter versions of the oat products were liked more after sleep curtailment. Sweet intensity perception of the was not altered by sleep curtailment in either study. Hierarchical cluster analysis was used to classify participants by sweet liking phenotype. Phenotypes were not found to moderate the effect of sleep curtailment on sweet taste, but did predict preferred sweetener concentration. These findings contribute to our understanding of biological mechanisms that drive human hedonic response to food and contribute a currently missing link in the proposed causal chain by which insufficient sleep can lead to excess energy intake

This dissertation is dedicated to
my family

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

KEY TO ABBREVIATIONS

TIB	Time in Bed
TST	Total Sleep Time
SWS	Slow Wave Sleep
REM	Rapid Eye Movement
NREM	Non-Rapid Eye Movement
LS	Light Sleep
FDR	False Discovery Rate
PSQI	Pittsburgh Sleep Quality Index
PANAS	Positive Affect Negative Affect Schedule
G-FCQ-T	General Food Cravings Questionnaire-Trait Version
G-FCQ-S	General Food Cravings Questionnaire-State Version
KSS	Karolinska Sleepiness Scale
PSS	Perceived Stress Scale
VAS	Visual Analog Scale
BMI	Body Mass Index
BF	Body Fat
PSG	Polysomnography
EEG	Electroencephalogram
SR	Sleep Rating
HRS	High REM and Slow Wave Sleep
LRS	Low REM and Slow Wave Sleep

NNS	Non-nutritive Sweetener
OFC	Orbitofrontal Cortex
SLP	Sweet Liking Phenotype

Introduction

Sleep duration for Americans has been declining over time. In the 1960s, the American Cancer Society reported modal sleep duration to be 8 h (Kripke, Garfinkel, Wingard, Klauber, & Marler, 2002). Today, nearly 40% of Americans fail to meet the recommended 7 h of sleep per night (Bonnet & Arand, 1995; Chen, Gelaye, & Williams, 2014; Hirshkowitz et al., 2015). This phenomenon is particularly prevalent in America, where the risk of obtaining less than 6 h of less per night has increased steadily over the past four decades for full-time workers (Knutson, Van Cauter, Rathouz, DeLeire, & Lauderdale, 2010). The trend for decreased sleep duration is alarming given that insufficient sleep is routinely associated with a myriad of health conditions (Ayas, White, Al-Delaimy, et al., 2003; Ayas, White, Manson, et al., 2003; Cappuccio, Cooper, D'Elia, Strazzullo, & Miller, 2011; Cappuccio, D'Elia, Strazzullo, & Miller, 2010; Cappuccio et al., 2008), including obesity. There is currently no consensus on how insufficient sleep ultimately leads to obesity (St-Onge, 2015). However, understanding the processes that drive the relationship between insufficient sleep and obesity is of great interest to scientists, the food industry, and public health advocates.

Sleep is a combination of physiological and behavioral processes involving perceptual disengagement and reduced responsiveness to the environment (Carskadon, Dement, & others, 2005). There are two distinct states of sleep, rapid eye movement (REM) and non-REM (NREM), which exist in nearly all mammals and birds studied to date (Carskadon et al., 2005; Scullin & Bliwise, 2015). The onset of sleep under ordinary circumstances in healthy humans is through NREM sleep. NREM can be subdivided into three sleep stages (N1-3) based on electroencephalogram (EEG) measurements. Stages N1 and N2 are characterized by a low threshold for awakening (Scullin & Bliwise, 2015) and will be referred to henceforth as "light

sleep" (LS). N3 sleep is also referred to as "slow wave sleep" (SWS) and is characterized by slower brain wave frequency and strong resistance to being awakened (Roth, 2009). NREM sleep usually comprises 75-80% of sleep, with 47-60% of sleep in stages 1 and 2, and 13-23% occurring in stage 3 (Chokroverty, 2017). REM sleep, occurring more frequently during the last third of the night, usually accounts for 20-25% of sleep (Carskadon et al., 2005; Chokroverty, 2017; Roth & Roehrs, 2000). The exact biological function of both REM and NREM sleep remains elusive (Cappuccio, Miller, Lockley, & Rajaratnam, 2018); however, a wide variety of physiological processes occur during sleep.

While there is no consensus on how insufficient sleep causes weight gain, sleep affects both sides of the energy balance equation: reducing energy expenditure (Dinges et al., 1997) and increasing energy intake (Karine, Esra, & Plamen, 2004). Excess energy intake, particularly from highly palatable sugary and high-fat foods, is currently the more well-supported mechanism driving the relationship between insufficient sleep and obesity (Calvin et al., 2013; M.-R. G. Silva, Silva, & Paiva, 2017). The relationship between insufficient sleep and increased energy intake is theorized to be motivated by both disrupted appetite-endocrine homeostasis (Cauter, Leproult, & Plat, 2000; Robertson, Russell-Jones, Umpleby, & Dijk, 2013; Scheen, Byrne, Plat, Leproult, & Cauter, 1996; Spiegel, Leproult, & Van Cauter, 1999; van der Lely, Tschöp, Heiman, & Ghigo, 2004) and increased brain reward sensitivity, that is, increased pleasure in response to the rewarding properties of food, especially palatable food (Bosy-Westphal et al., 2008; Calvin et al., 2013; Markwald et al., 2013; Nedeltcheva et al., 2009). While sleep-related changes in appetitive hormones likely play an important role in eating behavior, several studies have suggested that altered reward processing is the predominant mediator in the sleep-weight gain relationship (Bosy-Westphal et al., 2008; Calvin et al., 2013; Chaput & St-Onge, 2014;

Markwald et al., 2013; Nedeltcheva et al., 2009; St-Onge, 2015). Sensory attributes of food, including pleasant tastes, odors, or textures may be increasingly desired (Beaver et al., 2006) or liked (Boutelle et al., 2015) when reward sensitivity is high. Palatable food tends to be energy-dense, and therefore, consumption of highly palatable food for pleasure, also known as hedonic eating, can lead to weight gain (A. Drewnowski, 1999). Surprisingly, there are very few studies examining the effect of insufficient sleep on food sensory perception,

The few studies that have explored the effect of insufficient sleep on food sensory perception have reported contradictory findings (Furchtgott & Willingham, 1956; Hogenkamp et al., 2013; Killgore & McBride, 2006; Lv, Finlayson, & Dando, 2018; McBride, Balkin, Kamimori, & Killgore, 2006; Smith, Ludy, & Tucker, 2016; Tanaka, Hong, Tominami, & Kudo, 2018). Some studies reported differences between participants with curtailed and habitual sleep, such as increased sour (Furchtgott & Willingham, 1956) and umami intensity perception (Lv et al., 2018) and increased sweet taste preference (Smith et al., 2016). Other studies reported no changes in taste sensitivity (Tanaka et al., 2018) or sweet taste preference (Hogenkamp et al., 2013) after sleep deprivation. Finally, two studies observed differences in olfactory identification ability following one (Killgore & McBride, 2006) and two (McBride et al., 2006) days of sleep deprivation. Given the limited number of studies, the wide variety of foci (olfactory identification, taste sensitivity, and hedonics), and contradictory findings between studies, more research regarding the effect of insufficient sleep on chemosensation is merited.

Sweet taste is a particularly important taste quality due to the impact it can have on eating behavior, food choice, and eating intake. Sweetness innately elicits positive feelings of pleasure, which is not surprising considering the proposed physiological role of sweet taste: to detect energy required to sustain ourselves (Looy & Weingarten, 1992). Sweetness has been shown to

be a uniformly pleasurable taste stimulus for humans, as demonstrated by positive facial expressions upon tasting sweetness at birth in humans and primates (Desor, Maller, & Turner, 1973; Steiner, Glaser, Hawilo, & Berridge, 2001). Further, sweet taste has been shown to be an important factor in food acceptability and choice (Birch, 1999; Blundell, Rogers, & Hill, 1988). Due to the fact that sweet taste is likely to interact with reward-related brain areas thought to be affected by insufficient sleep (Rolls, 2011), and that sweetened foods tend to be more energy-dense (Adam Drewnowski, 1998), it is an ideal taste to begin to study the relationship between sleep and excess energy intake.

There are several factors which may contribute to individual differences in taste response to insufficient sleep. First, differences in brain anatomy (Luders & Toga, 2010) and sensory function (Ohla & Lundström, 2013; Paller, Campbell, Edwards, & Dobs, 2009; L. da Silva et al., 2014) between the sexes could contribute to males and females experiencing different effects of short sleep on sensory perception. Second, in adulthood, individuals display different patterns of sweetness liking (Yeomans, Tepper, Rietzschel, & Prescott, 2007). Several patterns of liking have been identified, and whether an individual is classified as a "sweet liker", individuals who show increasing hedonic response to sweet solutions as concentration of sweetener increases, or as a "sweet disliker", individuals who show decreasing hedonic response to sweet solutions as concentration increases, may influence how taste perception is altered after a night of sleep curtailment. Individual differences in patterns of sweet liking are partially determined by genetic factors and are commonly referred to as "sweet liking phenotypes" (Bachmanov et al., 2011). Finally, differences in sleep architecture, that is, the composition of sleep stages within the total sleep duration, may determine whether changes in sensory perception occur after sleep curtailment. For example, REM sleep duration may play an especially important role in

determining hedonic response to food, due to its proposed role in modulating emotional behaviors (Horne, 2015). Characterizing the effect these important factors have on the relationship between sleep duration and sensory perception will improve understanding of how sleep can lead to excess energy intake.

Therefore, the primary objective of this body of work was to characterize the relationship between sleep duration and sensory perception: from psychophysical analysis of the relationship between chemosensory function and habitual sleep to evaluation of hedonic response to complex foods after a sleep curtailment intervention. A secondary objective was to determine the role of sex, sweet liking phenotype, and sleep architecture in the relationship between insufficient sleep and sensory perception to identify relevant interactions and provide a framework for future work examining the behaviors and biological mechanisms driving sleep-related changes in sensory perception.

REFERENCES

REFERENCES

Ayas, N. T., White, D. P., Al-Delaimy, W. K., Manson, J. E., Stampfer, M. J., Speizer, F. E., … Hu, F. B. (2003). A prospective study of self-reported sleep duration and incident diabetes in women. *Diabetes Care*, *26*(2), 380–384. https://doi.org/10.2337/diacare.26.2.380.

Ayas, N. T., White, D. P., Manson, J. E., Stampfer, M. J., Speizer, F. E., Malhotra, A., & Hu, F. B. (2003). A prospective study of sleep duration and coronary heart disease in women. *Archives of Internal Medicine*, *163*(2), 205–209. https://doi.org/10.1001/archinte.163.2.205.

Bachmanov, A. A., Bosak, N. P., Floriano, W. B., Inoue, M., Li, X., Lin, C., … Beauchamp, G. K. (2011). Genetics of sweet taste preferences. *Flavour and Fragrance Journal*, *26*(4), 286–294. https://doi.org/10.1002/ffj.2074.

Beaver, J. D., Lawrence, A. D., Ditzhuijzen, J. van, Davis, M. H., Woods, A., & Calder, A. J. (2006). Individual differences in reward drive predict neural responses to images of food. *Journal of Neuroscience*, *26*(19), 5160–5166. https://doi.org/10.1523/JNEUROSCI.0350-06.2006.

Birch, L. L. (1999). Development of food preferences. *Annual Review of Nutrition*, *19*(1), 41–62.

Blundell, J. E., Rogers, P. J., & Hill, A. J. (1988). Uncoupling sweetness and calories: methodological aspects of laboratory studies on appetite control. *Appetite*.

Bonnet, M. H., & Arand, D. L. (1995). We are chronically sleep deprived. *Sleep*, *18*(10), 908–911. https://doi.org/10.1093/sleep/18.10.908.

Bosy-Westphal, A., Hinrichs, S., Jauch-Chara, K., Hitze, B., Later, W., Wilms, B., … Müller, M. J. (2008). Influence of partial sleep deprivation on energy balance and insulin sensitivity in healthy women. *Obesity Facts*, *1*(5), 266–273. https://doi.org/10.1159/000158874.

Boutelle, K. N., Wierenga, C. E., Bischoff-Grethe, A., Melrose, A. J., Grenesko-Stevens, E., Paulus, M. P., & Kaye, W. H. (2015). Increased brain response to appetitive tastes in the insula and amygdala in obese compared with healthy weight children when sated. *International Journal of Obesity*, *39*(4), 620–628. https://doi.org/10.1038/ijo.2014.206.

Calvin, A. D., Carter, R. E., Adachi, T., Macedo, P. G., Albuquerque, F. N., Walt, C. van der, … Somers, V. K. (2013). Effects of experimental sleep restriction on caloric intake and activity energy expenditure. *CHEST*, *144*(1), 79–86. https://doi.org/10.1378/chest.12-2829.

Cappuccio, F. P., Cooper, D., D'Elia, L., Strazzullo, P., & Miller, M. A. (2011). Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. *European Heart Journal*, *32*(12), 1484–1492. https://doi.org/10.1093/eurheartj/ehr007.

Cappuccio, F. P., D'Elia, L., Strazzullo, P., & Miller, M. A. (2010). Sleep duration and all-cause mortality: A systematic review and meta-analysis of prospective studies. *Sleep*, *33*(5), 585–592. https://doi.org/10.1093/sleep/33.5.585.

Cappuccio, F. P., Miller, M. A., Lockley, S. W., & Rajaratnam, S. M. W. (2018). *Sleep, Health, and Society: From Aetiology to Public Health*. Oxford University Press.

Cappuccio, F. P., Taggart, F. M., Kandala, N.-B., Currie, A., Peile, E., Stranges, S., & Miller, M. A. (2008). Meta-analysis of short sleep duration and obesity in children and adults. *Sleep, 31*(5), 619–626. https://doi.org/10.1093/sleep/31.5.619.

Carskadon, M. A., Dement, W. C., & others. (2005). Normal human sleep: An overview. *Principles and Practice of Sleep Medicine, 4*, 13–23.

Cauter, E. V., Leproult, R., & Plat, L. (2000). Age-related changes in slow wave sleep and REM sleep and relationship with growth hormone and cortisol levels in healthy men. *JAMA, 284*(7), 861–868. https://doi.org/10.1001/jama.284.7.861.

Chaput, J.-P., & St-Onge, M.-P. (2014). Increased food intake by insufficient sleep in humans: Are we jumping the gun on the hormonal explanation? *Frontiers in Endocrinology, 5*. https://doi.org/10.3389/fendo.2014.00116.

Chen, X., Gelaye, B., & Williams, M. A. (2014). Sleep characteristics and health-related quality of life among a national sample of American young adults: Assessment of possible health disparities. *Quality of Life Research, 23*(2), 613–625. https://doi.org/10.1007/s11136-013-0475-9.

Chokroverty, S. (2017). Overview of Normal Sleep. In S. Chokroverty (Ed.), *Sleep Disorders Medicine: Basic Science, Technical Considerations and Clinical Aspects* (pp. 5–27). https://doi.org/10.1007/978-1-4939-6578-6_2.

Desor, J. A., Maller, O., & Turner, R. E. (1973). Taste in acceptance of sugars by human infants. *Journal of Comparative and Physiological Psychology, 84*(3), 496.

Dinges, D. F., Pack, F., Williams, K., Gillen, K. A., Powell, J. W., Ott, G. E., … Pack, A. I. (1997). Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 hours per night. *Sleep, 20*(4), 267–277. https://doi.org/10.1093/sleep/20.4.267.

Drewnowski, A. (1999). Intense sweeteners and energy density of foods: Implications for weight control. *European Journal of Clinical Nutrition, 53*(10), 757–763. https://doi.org/10.1038/sj.ejcn.1600879.

Drewnowski, Adam. (1998). Energy density, palatability, and satiety: Implications for weight control. *Nutrition Reviews, 56*(12), 347–353. https://doi.org/10.1111/j.1753-4887.1998.tb01677.x.

Furchtgott, E., & Willingham, W. W. (1956). The effect of sleep-deprivation upon the thresholds of taste. *The American Journal of Psychology*.

Hirshkowitz, M., Whiton, K., Albert, S. M., Alessi, C., Bruni, O., DonCarlos, L., … Ware, J. C. (2015). National sleep foundation's updated sleep duration recommendations: Final report. *Sleep Health, 1*(4), 233–243. https://doi.org/10.1016/j.sleh.2015.10.004.

Hogenkamp, P. S., Nilsson, E., Chapman, C. D., Cedernaes, J., Vogel, H., Dickson, S. L., … Benedict, C. (2013). Sweet taste perception not altered after acute sleep deprivation in healthy young men. *Somnology: Sleep Research and Sleep Medicine, 17*(2), 111–114. https://doi.org/10.1007/s11818-013-0606-0.

Horne, J. A. (2015). Human REM sleep: Influence on feeding behaviour, with clinical implications. *Sleep Medicine*, *16*(8), 910–916. https://doi.org/10.1016/j.sleep.2015.04.002.

Karine, S., Esra, T., & Plamen, P. (2004). Sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. *American College of Physicians*, *141*, 846–850.

Killgore, W. D. S., & McBride, S. A. (2006). Odor identification accuracy declines following 24 h of sleep deprivation. *Journal of Sleep Research*, *15*(2), 111–116. https://doi.org/10.1111/j.1365-2869.2006.00502.x.

Knutson, K. L., Van Cauter, E., Rathouz, P. J., DeLeire, T., & Lauderdale, D. S. (2010). Trends in the prevalence of short sleepers in the USA: 1975–2006. *Sleep*, *33*(1), 37–45. https://doi.org/10.1093/sleep/33.1.37

Kripke, D. F., Garfinkel, L., Wingard, D. L., Klauber, M. R., & Marler, M. R. (2002). Mortality associated with sleep duration and insomnia. *Archives of General Psychiatry*, *59*(2), 131–136. https://doi.org/10.1001/archpsyc.59.2.131.

Looy, H., & Weingarten, H. P. (1992). Facial expressions and genetic sensitivity to 6-n-propylthiouracil predict hedonic response to sweet. *Physiology & Behavior*, *52*(1), 75–82.

Luders, E., & Toga, A. W. (2010). Chapter 1 - Sex differences in brain anatomy. In I. Savic (Ed.), *Progress in Brain Research* (pp. 2–12). https://doi.org/10.1016/B978-0-444-53630-3.00001-4.

Lv, W., Finlayson, G., & Dando, R. (2018). Sleep, food cravings and taste. *Appetite*, *125*, 210–216. https://doi.org/10.1016/j.appet.2018.02.013.

Markwald, R. R., Melanson, E. L., Smith, M. R., Higgins, J., Perreault, L., Eckel, R. H., & Wright, K. P. (2013). Impact of insufficient sleep on total daily energy expenditure, food intake, and weight gain. *Proceedings of the National Academy of Sciences*, *110*(14), 5695–5700. https://doi.org/10.1073/pnas.1216951110.

McBride, S. A., Balkin, T. J., Kamimori, G. H., & Killgore, W. D. S. (2006). Olfactory decrements as a function of two nights of sleep deprivation. *Journal of Sensory Studies*, *21*(4), 456–463. https://doi.org/10.1111/j.1745-459X.2006.00080.x.

Nedeltcheva, A. V., Kilkus, J. M., Imperial, J., Kasza, K., Schoeller, D. A., & Penev, P. D. (2009). Sleep curtailment is accompanied by increased intake of calories from snacks–. *The American Journal of Clinical Nutrition*, *89*(1), 126–133. https://doi.org/10.3945/ajcn.2008.26574

Ohla, K., & Lundström, J. N. (2013). Sex differences in chemosensation: sensory or emotional? *Frontiers in Human Neuroscience*, *7*. https://doi.org/10.3389/fnhum.2013.00607

Paller, C. J., Campbell, C. M., Edwards, R. R., & Dobs, A. S. (2009). Sex-based differences in pain perception and treatment. *Pain Medicine*, *10*(2), 289–299. https://doi.org/10.1111/j.1526-4637.2008.00558.x.

Robertson, M. D., Russell-Jones, D., Umpleby, A. M., & Dijk, D.-J. (2013). Effects of three weeks of mild sleep restriction implemented in the home environment on multiple metabolic and

endocrine markers in healthy young men. *Metabolism*, *62*(2), 204–211. https://doi.org/10.1016/j.metabol.2012.07.016

Rolls, E. T. (2011). Taste, olfactory and food texture reward processing in the brain and obesity. *International Journal of Obesity*, *35*(4), 550–561. https://doi.org/10.1038/ijo.2010.155

Roth, T. (2009). Slow wave sleep: Does it matter? *Journal of Clinical Sleep Medicine : JCSM : Official Publication of the American Academy of Sleep Medicine*, *5*(2 Suppl), S4–S5.

Roth, T., & Roehrs, T. (2000). Sleep organization and regulation. *Neurology*, *54*(1), S2.

Scheen, A. J., Byrne, M. M., Plat, L., Leproult, R., & Cauter, E. V. (1996). Relationships between sleep quality and glucose regulation in normal humans. *American Journal of Physiology - Endocrinology and Metabolism*, *271*(2), E261–E270.

Scullin, M. K., & Bliwise, D. L. (2015). Sleep, cognition, and normal aging: integrating a half century of multidisciplinary research. *Perspectives on Psychological Science*, *10*(1), 97–137.

Silva, L. da, Lin, S. M., Teixeira, M. J., Siqueira, J. de, Filho, W. J., & Siqueira, S. de. (2014). Sensorial differences according to sex and ages. *Oral Diseases*, *20*(3), e103–e110. https://doi.org/10.1111/odi.12145

Silva, M.-R. G., Silva, H.-H., & Paiva, T. (2017). Reduced sleep duration associated with consumption of higher calorie foods in young roller hockey players. *Sleep Medicine*, *40*, e307. https://doi.org/10.1016/j.sleep.2017.11.904.

Smith, S. L., Ludy, M.-J., & Tucker, R. M. (2016). Changes in taste preference and steps taken after sleep curtailment. *Physiology & Behavior*, *163*, 228–233. https://doi.org/10.1016/j.physbeh.2016.05.002.

Spiegel, K., Leproult, R., & Van Cauter, E. (1999). Impact of sleep debt on metabolic and endocrine function. *The Lancet*, *354*(9188), 1435–1439. https://doi.org/10.1016/S0140-6736(99)01376-8.

Steiner, J. E., Glaser, D., Hawilo, M. E., & Berridge, K. C. (2001). Comparative expression of hedonic impact: Affective reactions to taste by human infants and other primates. *Neuroscience & Biobehavioral Reviews*, *25*(1), 53–74.

St-Onge, M.-P. (2015). Chapter 2 - The role of sleep in the control of feeding behavior. In R. R. Watson (Ed.), *Modulation of Sleep by Obesity, Diabetes, Age, and Diet* (pp. 11–16). https://doi.org/10.1016/B978-0-12-420168-2.00002-8.

Tanaka, T., Hong, G., Tominami, K., & Kudo, T. (2018). Oral fat sensitivity is associated with social support for stress coping in young adult men. *The Tohoku Journal of Experimental Medicine*, *244*(4), 249–261.

van der Lely, A. J., Tschöp, M., Heiman, M. L., & Ghigo, E. (2004). Biological, physiological, pathophysiological, and pharmacological aspects of ghrelin. *Endocrine Reviews*, *25*(3), 426–457. https://doi.org/10.1210/er.2002-0029

Yeomans, M. R., Tepper, B. J., Rietzschel, J., & Prescott, J. (2007). Human hedonic responses to sweetness: role of taste genetics and anatomy. *Physiology & Behavior*, *91*(2–3), 264–273.

Chapter 1:

This work is published and re-used in this dissertation with permission by Elsevier. The full citation is presented below:

Szczygiel, E.J, Cho, S., & Tucker, R. M. (2018). Characterization of the relationships between sleep duration, quality, architecture and chemosensory function in non-obese females. *Chemical Senses*, *43*(4), 223–228. https://doi.org/10.1093/chemse/bjy012.

Little is known about the relationship between sleep and chemosensation. The purpose of this study was to characterize the relationship between chemosensory function and sleep duration, quality, and architecture. A total of 56 non-obese female participants who denied having diagnosed sleep disorders completed testing. Sleep was measured for two nights using a single-channel (A_1–A_2) electroencephalogram-(EEG) (Zmachine). Sweet taste threshold and preference, as well as olfactory threshold, recognition ability, and pleasantness ratings, were evaluated. Sweet taste preference was correlated with total sleep time (TST) (P=0.0074) as well as with the sum of rapid eye movement (REM) and stage N3/slow wave sleep (SWS) duration (P=0.0008). Participants who slept more than the average TST or more than the average REM+SWS time preferred lower concentrations of sweetness (P=0.041, 0.049, respectively), than those whose sleep times fell below the means. Multiple linear regression revealed that REM and SWS predicted approximately 18% of the variance of sweet taste preference. These findings suggest that scientific and consumer studies related to sweet preference might benefit from screening participants for short sleep duration prior to testing.

1. Introduction

Insufficient sleep is associated with the consumption of additional energy, especially from fats and carbohydrates, including sugar-sweetened beverages (Nedeltcheva et al. 2009, Gonnissen et al. 2013, Markwald et al. 2013, Golley et al. 2013, Patterson et al. 2014, Prather et al. 2014, Hjorth et al. 2014). Excess intake of foods and beverages high in saturated fats and refined carbohydrates has been associated with weight gain (Mozaffarian et al. 2011, Prather et al. 2014). Given that the foods we choose to consume are typically selected based on their sensory properties (Glanz and Basil 1998, Sørensen et al. 2003, Dressler and Smith 2013), and the small, but growing, body of evidence that suggests sleep changes may alter chemosensory function (McBride et al. 2006, McBride et al. 2006, Smith et al. 2016), characterizing chemosensation while objectively measuring sleep is necessary to improve our understanding of ingestive behavior.

Previous work examining chemosensory function and sleep is limited (Killgore and McBride 2006, McBride et al. 2006, Hogenkamp et al. 2013, Smith et al. 2016) but suggests that sleep deprivation or curtailment is detrimental to function. Odor identification accuracy was significantly impaired after both 24 h (Killgore and McBride 2006) and 52 h (McBride et al. 2006) of sleep deprivation. Preferred concentration of sucrose solutions increased after a night of less than 7 h of sleep in individuals who routinely slept more than 7 h per night (Smith et al. 2016). However, another study reported no differences in intensity and pleasantness ratings of yogurts with varying amounts of sucrose after a night of total sleep deprivation compared to a night of normal sleep (Hogenkamp et al. 2013). One major limitation to studies of total sleep deprivation is their questionable ecological validity for large segments of the population. Thus,

examining chemosensory function under conditions of habitual sleep may provide more insight into the relationship between sleep and chemosensation under more representative conditions.

Sleep research typically focuses on two aspects of sleep – sleep duration and sleep quality. Sleep duration refers to the amount of time spent sleeping, and researchers often explore how sleep deprivation (total sleep loss) or curtailment (sleep restriction) affect outcomes of interest. Sleep duration can be subjectively measured using participant self-report, but self-report frequently differs from objective measurements (Lauderdale et al. 2008). While the gold standard for measuring sleep is polysomnography (PSG), determination of sleep stage is typically done by technicians, and agreement is not always substantial (Wang et al. 2015). PSG also requires an overnight stay in a sleep lab with bulky equipment that inhibits natural movement; these factors contribute to the "first night effect," where sleep duration and quality can substantially differ in the laboratory setting from that typically experienced at home (Le Bon et al. 2001). At-home sleep monitors may help to address this problem by allowing participants to sleep in their own bed while maintaining sufficient agreement with PSG (Wang et al. 2015). For example, the at-home monitor used in this study, the Zmachine (General Sleep, Columbus, OH) is a single-channel (A_1–A_2) electroencephalogram (EEG) based sleep monitoring system that, when evaluated against PSG, was found to have substantial agreement in identifying wake, light sleep, slow wave sleep (SWS), and rapid eye movement sleep (REM) sleep stages (Cohen's kappa = 0.72 for all) (Wang et al. 2015). Regardless of the technique used, objective measures of duration are preferred to self-report.

Unlike sleep duration, measures of sleep quality differ across studies (Krystal and Edinger 2008). Some researchers rely on objective measures of sleep architecture, a term that refers to the pattern and duration of sleep stages across the night. These measures include the

amount of time spent in SWS or REM sleep or the percentage of time spent in these stages as a component of total sleep time (Elsenbruch et al. 1999, Naismith et al. 2004, Friese et al. 2007), as these stages are associated with physical restoration and mental function, for example, mood (Vandekerckhove and Cluydts 2010, Li et al. 2017). Others (for example, Parcell et al. 2008, Buysse et al. 2008) use self-reported measures of sleep quality, including the Pittsburgh Sleep Quality Index (PSQI), a validated tool that provides a subjective measure of habitual (past month) sleep quality and duration (Buysse et al. 1989). Scores greater than 5 on the PSQI suggest disordered sleep (Buysse et al. 1989, Smith and Wegener 2003). Unfortunately, the PSQI does not always reliably correlate to objective measures of sleep quality, suggesting that there are other factors important to perceived sleep quality that are not captured by traditional objective measures (Pilcher et al. 1997, Krystal and Edinger 2008, Buysse et al. 2008). Thus, sleep quality likely comprises aspects of both objective and subjective measures, and while there is much overlap between sleep duration, sleep architecture, and subjective sleep quality, each merit evaluation when measuring sleep.

Differences in sleep might contribute to the poor test-retest reliability that psychophysical and sensory studies can suffer from (Stevens et al. 1995, Mueller et al. 2003, Tucker et al. 2013, Satoh-Kuriwada et al. 2014). Attempts to reduce this variability by controlling for a number of variables thought to influence the chemical senses, like age (Schiffman et al. 2004) or adiposity (Pepino et al. 2010) are frequently made. There is a lack of consensus as to which factors should be controlled for, but to our knowledge, only four psychophysical or sensory studies have examined or controlled for sleep duration (Killgore and McBride 2006, McBride et al. 2006, Hogenkamp et al. 2013, Smith et al. 2016) and none for sleep quality. Whether controlling for sleep duration or quality is necessary for sensory studies is currently unknown. Therefore, the

objective of this study was to characterize the relationships between chemosensory measures and sleep duration, quality, and architecture by measuring sweet taste threshold and preference as well as odor threshold, recognition, and pleasantness. We hypothesized that shorter sleep duration, both in terms of total sleep time (TST) as well as time spent in SWS and REM sleep, and poorer subjective sleep quality would increase gustatory and olfactory thresholds, increase preferred sweetness, reduce odor recognition scores, and increase food odor pleasantness ratings.

2. Materials and methods

The study protocol was approved by the Institutional Review Board of Michigan State University (East Lansing, MI, USA). Written informed consent was obtained from all participants prior to testing.

2.1. Participants

Non-obese females (BMI < 30.0 kg/m^2) of any ethnicity between the ages of 18-55 years with no diagnosed sleep conditions were eligible to participate in the study (Table 1). Prior to testing, participants completed a demographic questionnaire and the PSQI. Height, weight, body mass index (BMI), and percent body fat (%BF) were measured using bioelectrical impedance (TBF-400, Tanita).

2.2. Sleep measures

Participants were trained in the use the Zmachine (General Sleep, Columbus, OH) ("Zmachine Insight and Insight+ Model:DT-200: Clinician instruction and service manual" 2016). In order to minimize the "first night effect", participants were asked to follow their usual

sleep schedule and wear the Zmachine for two consecutive weeknights prior to taste and smell testing, which occurred on the third day. Data collected by the Zmachine relevant to this study included TST, SWS, and REM sleep duration. Given the lack of consensus on appropriate measures of sleep quality, we examined SWS and REM sleep independently, as a combined variable, and as a percentage of total sleep time (for example, Elsenbruch et al. 1999, Naismith et al. 2004, Friese et al. 2007).

2.3. Laboratory visit

After two consecutive weeknights of sleep monitoring, participants came to the laboratory for taste and smell testing. Participants were asked not to eat or drink anything except water for an hour prior to testing. Testing occurred between 9 a.m. – 3:00 p.m. each day.

2.4. Gustatory testing

Taste-testing followed the protocol used previously (Smith et al. 2016). Briefly, sweet taste threshold testing utilized an ascending, 3-alternative forced-choice procedure with sucrose dissolved in distilled water. Sucrose concentrations spanned 0.021% - 2.1% w/v and were separated by quarter log step dilutions. Sweet taste preference testing followed the Monell forced-choice paired comparison protocol (Mennella et al. 2011). Participants were given two concentrations of suprathreshold sucrose solutions and asked to select the one they preferred. Based on their choice, additional concentrations were provided until the same solution was selected twice in a row. Concentrations included 3, 6, 12, 24, and 36% w/v sucrose solutions. The test was performed twice – once with the lower concentration presented first each time and once with the higher concentration presented first each time. The geometric

mean of each test was calculated to determine the preferred concentration. Participants wore nose clips during taste testing.

2.5. Olfactory testing

Three different olfactory tests were conducted using Sniffin' Sticks (Burghart, Wedel, Germany) (Hummel et al. 1997). Olfactory threshold testing and olfactory recognition testing followed the Sniffin' Sticks protocol provided by the manufacturer. Participants were also asked to smell four odors used in the recognition test a second time and asked to rate the pleasantness of each using a 100 mm visual analog scale with the anchors "not at all" and "extremely". Three odors, apple, pineapple, and clove were odors associated with food, while rose was used as a non-food stimulus.

2.6. Statistical analysis

Data analysis was completed using SAS version 9.4 (SAS Institute, Cary, NC., U.S.A.). Results are presented as means ± standard deviations except when presenting sensory data where standard error of the mean is presented. Simple linear regression (Proc Reg) was used to compute coefficients of determination to assess the associations between sensory measures and recorded sleep variables. Pearson correlation coefficients and R^2 from simple linear regression (Proc Corr) were computed to assess the relationship between sensory measures and measures of sleep. Multiple linear regression (Proc Reg with Collin option) analysis was used to evaluate associations while accounting for covariates and multicollinearity. Backward (step-down) selection was used to select the best model (Neter et al. 1996). Independent t-tests (Proc ttest) were used to determine significant differences between various groups. Results were considered significant when $P<0.05$.

3. Results

3.1. Participant Demographics

Participant demographics are reported in Table 1.1. A total of 56 lean or overweight females (BMI < 30.0 kg/m^2) with ages ranging from 18-44 participated in the study. Participants were primarily white, with 72% (n=40) identifying as White, 16% (n=9) identifying as Asian and 13% (n=7) identifying as Black. The mean PSQI score was below 5, indicating that the majority of participants were free from sleep disorders. There were no significant associations between PSQI scores and any demographic variables (BMI, age, %BF) ($p>0.05$).

Table 1.1. Participant demographics

Variable (n = 56)	Mean	Std. Dev
Age (y)	24.4	6.4
BMI (kg/m^2)	21.6	6.9
BF (%)	23.9	12.3
PSQI	4.09	2.2

3.2. Taste threshold

No correlations between taste threshold and demographic variables (BMI, age and %BF), objective sleep measures (TST, REM, SWS, REM+SWS), or subjective sleep measures (PSQI) were observed ($p>0.05$).

3.3. Taste preference

No significant correlations were observed between taste preference and any of the demographic variables (age, BMI, %BF) ($p>0.05$). Significant associations were observed

between objective sleep measures and preferred sweetness concentration (Table 1.2). In each case, the association between the objective sleep measure and taste preference was negative.

Table 1.2. Simple linear regression of the taste preference and various objective sleep measures

Variable	Mean±Std.Dev	Pearson's r	R-square	p-value[a]
TST (h)	6.43±1.1	-0.35	0.12	0.0074**
REM (h)	1.70±0.7	-0.41	0.16	0.0018**
SWS (h)	1.33±0.5	-0.31	0.09	0.0221*
SWS+REM (h)	3.03±1.0	-0.43	0.18	0.0008***
% total sleep time in REM	25.95±8.7	-0.34	0.12	0.0093**
% total sleep time in SWS	20.70±7.8	-0.17	0.03	0.2065
% total sleep time in REM+SWS	46.69±12.9	-0.33	0.11	0.0118*

[a] * indicates p-values are significant at the $p<0.05$ level. ** indicates p-values are significant at the $p<0.01$ level and *** indicates p-values are significant at the $p<0.001$ level

To further evaluate the impact of sleep duration on taste preference, individuals were categorized as either a long sleeper or short sleeper by whether they fell above or below the mean TST (mean ± SD [h] = 6.43 ± 1.1) for the sample population (Table 1.3). Short sleepers (n=29) and long sleepers (n=27) did not differ by age, BMI, or %BF ($p > 0.05$). There were no significant differences in demographics between the two groups (age, BMI, %BF) ($p>0.05$). Shorter sleepers preferred higher concentrations of sucrose (*M*=12.68±9.6%, SEM=1.78%) compared to longer sleepers (*M*=7.70±8.11%, SEM=1.56%) ($p=0.041$) (Figure 1.1).

Table 1.3. Summary statistics of sleep duration and architecture groups

Group	n=	Mean sucrose preference (%w/v)	Std. Dev (%)	SEM (%)
Longer Sleepers	27	7.7	8.8	1.56
Shorter Sleepers	29	12.68	9.6	1.78
HSR	29	7.95	8.37	1.55
LSR	27	12.67	9.51	1.83

To evaluate the impact of sleep architecture on taste preference, participants were classified as low REM+SWS (LRS) (n=27) and high REM+SWS (HRS) (n=29) sleepers by whether they were above or below the mean hours of REM+SWS sleep (Table 1.3) (mean ± SD [h] = 3.03 ± 1.0) for the respective night, given this was the strongest predictor of taste preference according to the results from the simple linear regression analysis (Table 1.2). The two groups did not differ by age, BMI, or %BF (P>0.05). HRS sleepers (*M*=7.95±8.37%, SEM=1.55%) preferred lower concentrations of sucrose compared to LRS sleepers (*M*=12.67±9.51%, SEM=1.83%) (p=0.049). T-tests between the long, short, HRS and LRS groups showed no significant difference for any of the taste variables (p>0.05).

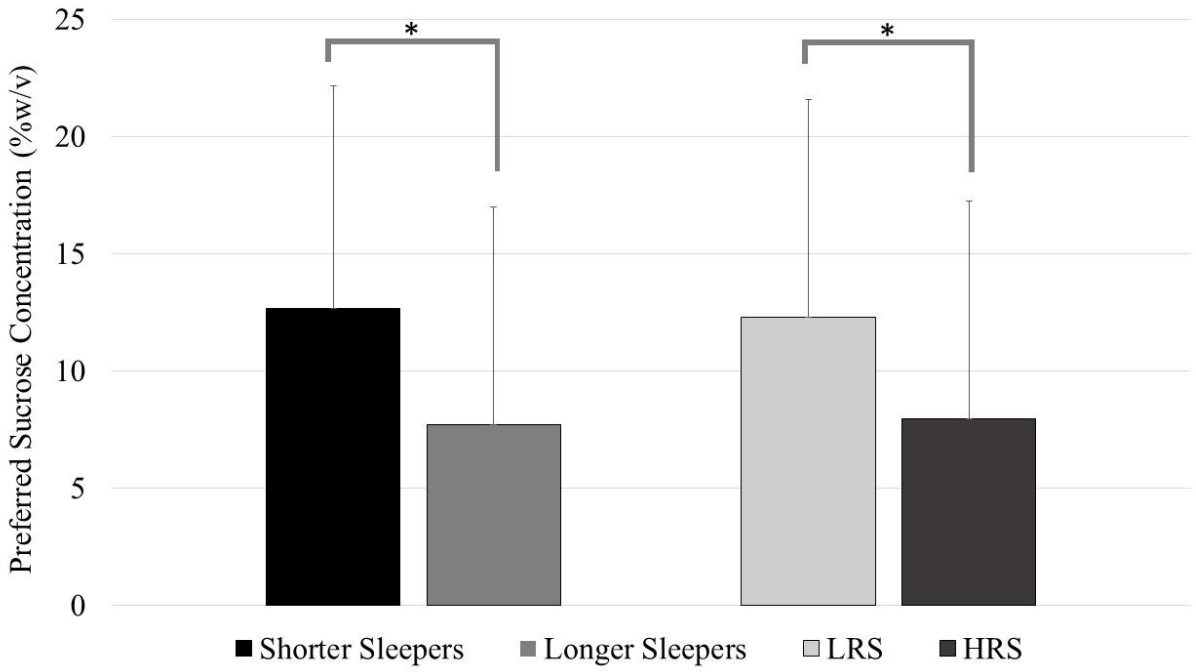

Figure 1.1. *Differences in taste preference by TST and sleep quality groups.* Significant differences between below average duration (shorter sleepers, n=29) and above-average duration (longer sleepers, n=27) (p=0.041) as well as below average REM+SWS sleepers (LRS, n=29)

Figure 1.1 Cont. and above-average REM+SWS sleepers (HRS, n=27) (p=0.049) for the night before testing. * denotes significant difference between conditions, $p<0.05$.

Multiple regression analysis was used to evaluate the best model to predict taste preference and evaluate the potential multicollinearity between TST and REM+SWS (r=0.54). Four variables (TST, REM+SWS, BMI, and age) were selected as variables of interest related to sweet taste preference. Using backwards selection, the best model contained only one variable, REM+SWS (h) and explained 18% of the variance (R^2=0.18, F (2,56) =6.58, p=0.0028). Sleep duration (TST), age and BMI were removed from the model with a partial R^2 of 0.015, 0.023, and 0.038, respectively (Table 1.4).

Table 1.4. Results of multiple linear regression model selection by backwards variable selection analysis to predict taste preference (% w/v) as a continuous variable

Multiple Regression Predicting Taste Preference					
Variable	β	Std. Err	Parm. Est.	t-value	p-value
REM+ SWS (h)	-0.43	1.10	-3.92	-3.54	0.0008

3.4. Olfactory results

Odor recognition, odor threshold, and pleasantness rating of the three food and one non-food odor were not significantly correlated with subjective sleep quality, nor with any sleep stage or TST. T-tests between the long, short, HRS and LRS groups showed no significant difference for any of the odor variables ($p>0.05$).

4. Discussion

Sleep duration and architecture were associated with aspects of chemosensory function, specifically sweet taste preference. Subjective measures of sleep quality were not associated with the measures of chemosensory function evaluated in this study. Shorter TST and REM+SWS duration correlated with increased preference for sweetness, and differences between shorter and longer sleepers as well as HRS and LRS sleepers were observed.

This is the second psychophysical study to suggest that sweet taste preferences are associated with sleep. Previously we reported that the preferred sweet taste concentration increased when individuals who reported sleeping longer than 7 h per night were asked to sleep less than their habitual duration (Smith et al. 2016). Sweet taste thresholds in that study were unchanged by sleep duration, and we also failed to observe threshold differences between shorter and longer sleepers or HRS and LRS sleepers. In contrast, Hogenkamp et al. (2013) reported no change in preferred sweetness of yogurt among 16 men who underwent sleep deprivation. Differences in the populations tested (males vs. females) and stimuli – the complex food matrix of the yogurt compared to sucrose solutions – could contribute to these discrepant findings, and future work should explore these ideas further.

The significant difference in preferred taste concentrations between shorter and longer as well as HRS and LRS sleepers suggests that controlling for sleep duration and quality when conducting sensory studies might be beneficial, especially when hedonics are involved. The two groups differed in sweet taste preference by approximately 6% w/v when comparing both shorter vs. longer and HRS vs. LRS sleepers. While few sensory scientists are likely to be able to objectively measure sleep, TST was also observed to be a significant predictor of taste preference. Future work will examine if self-reported TST the night before testing also predicts

taste preference, which would allow for quick screening of participants. It should be noted that self-reported habitual sleep duration as reported in the PSQI was not significantly associated with TST, but given that the PSQI measures sleep patterns over the past month and that some individuals experience a high degree of variability in TST from one night to the next (Clausen et al. 1974), a repeated-measures study is needed to confirm the relationship between self-report and objectively measured TST. It could be the case that the effect of sleep on preference is acute rather than chronic.

How sleep architecture might contribute to differences in taste preference is currently unknown, given that the exact functions of REM and SWS are not fully understood. Studies suggest REM is correlated with learning ability, memory, and emotional regulation (Siegel 2001, Kanda et al. 2016, Peever and Fuller 2016). Like REM, the exact role of SWS is not clearly understood (Roth 2009), but SWS appears to promote several homeostatic processes, including cerebral restoration and recovery in humans (Benington and Heller 1995); growth hormone (GH), ghrelin, and cortisol secretion (Born et al. 1988, Spiegel et al. 1999); and memory consolidation (Rasch et al. 2007). While there are no official recommendations for the amount of REM and SWS sleep a person should get, each typically comprises approximately 20% of the total sleep time in healthy sleepers (Carskadon et al. 2005). The sample population in the current study aligns with these expectations.

Despite the uncertainty of the exact mechanisms, it is clear that sleep plays a multifaceted role in biological homeostasis, particularly in the endocrine system. Sleep debt has been shown to alter cortisol levels, indicating physiological stress on the body (Spiegel et al. 1999). More specifically, there is a negative association between the amount of REM sleep and cortisol levels (Lauer et al. 1989). Increased cortisol levels have been linked to increased food consumption,

which is thought to impact weight and health (Epel et al. 2001). Conversely, SWS is positively correlated with GH and ghrelin secretion (Cauter et al. 2000). Ghrelin, often referred to as "the hunger hormone" promotes SWS in humans (Weikel et al. 2003), may stimulate appetite (van der Lely et al. 2004), and is thought to enhance food reward as part of its role in the gut-brain reward pathway (Menzies et al. 2013). Therefore, increased preference for sweetness as a result of sleep debt, specifically REM+SWS sleep debt, might play a role in stress-induced over-eating and increased appetite observed with elevated cortisol and ghrelin concentrations.

The current understanding of the homeostatic drivers of food intake outstrips our understanding of hedonic drivers. One group (Kenny 2011) has suggested that REM sleep may play an important role in developing food preferences. Brain reward circuits contained in the orbitofrontal cortex, amygdala and anterior cingulate cortex are activated during excessive consumption to palatable food, and these same areas are active during REM sleep (Kenny 2011, Horne 2015). In humans, sleep curtailment has been shown to increase neuronal response to unhealthy food in normal-weight individuals (St-Onge et al. 2014). Due to the potential impact sleep can have on reward processing (Horne 2015), it is possible that the taste-reward pathway and hedonic feeding control is modulated by sleep through changes to chemosensory function. The present findings add support to the importance of REM sleep in terms of food preference, at least acutely speaking, illustrating that sweet taste preference is directly associated with REM sleep duration, even when controlling for age, BMI, and TST. SWS appears to play a less significant role in the acute changes to sweet preference, but when used a component of what has been described as "restorative" (REM+SWS) sleep (Espiritu 2008), it strengthens the correlation.

Contrary to our hypotheses and previous reports, we observed no apparent relationship between sleep and olfactory function of any kind. Given that previous research reported that

sleep deprivation for both 24 and 52 h negatively impacted olfactory function (Killgore and McBride 2006, McBride et al. 2006), differences in findings could be due to differences in study design. The current study did not curtail or deprive participants of sleep unlike previous reports, so it could be the case that extreme sleep deprivation is needed to induce these differences, or that the effect of sleep on olfaction is less pronounced compared to sweet taste preference.

4.1. Study Strengths and Limitations

The use of the Zmachine to collect EEG habitual sleep data from participants was a major strength of this study, given that self-report suffers from significant error (Lauderdale et al. 2008). In order to eliminate confounding from obesity, sex, and age, only non-obese females between the ages of 18-55 were eligible for testing, so the ability to generalize to other groups is limited. Food intake was not recorded prior to testing, which could impact gustatory and olfactory ability (Finlayson et al. 2008). Future research should investigate whether this effect exists with other basic tastes to determine whether the effect is global or if only sweet taste is affected. In addition, this effect should be evaluated in different populations, including males and individuals with obesity. Finally, given the cross-sectional study design, future work should examine whether these differences in preference respond to nightly variations in sleep or if they are stable from night-to-night.

5. Conclusions

Decreased sleep duration and REM+SWS duration are both correlated with an increased sweet taste preference. In this study, sweet taste preference was best predicted by the sum of SWS and REM sleep. These findings suggest that sleep modulates aspects of the hedonic taste-reward

pathway, possibly by enhancing the reward of sweetness, as opposed to eliciting physiological changes in receptor function. More research is needed to clarify the role of sleep in taste perception, particularly how sleep interacts with reward pathways. While previous studies have indicated that olfactory function may be negatively impacted by sleep deprivation, our findings illustrate that gustatory processes may be more readily impacted by sleep architecture and duration Further, these results illustrate the possible need for screening or controlling for sleep habits in sensory studies due to the large amount of variation in sweet taste preference that REM+SWS deprivation can predict.

REFERENCES

REFERENCES

Benington, J. H., & Heller, H. C. (1995). Restoration of brain energy metabolism as the function of sleep. *Progress in Neurobiology*, *45*(4), 347–360.

Born, J., Muth, S., & Fehm, H. L. (1988). The significance of sleep onset and slow wave sleep for nocturnal release of growth hormone (GH) and cortisol. *Psychoneuroendocrinology*, *13*(3), 233–243. https://doi.org/10.1016/0306-4530(88)90021-2.

Buysse, D. J., Hall, M. L., Strollo, P. J., Kamarck, T. W., Owens, J., Lee, L., … Matthews, K. A. (2008). Relationships between the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and clinical/polysomnographic measures in a community sample. *Journal of Clinical Sleep Medicine*, *4*(6), 563–571.

Buysse, D. J., Reynolds III, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research*, *28*(2), 193–213. https://doi.org/10.1016/0165-1781(89)90047-4

Carskadon, M. A., Dement, W. C., & others. (2005). Normal human sleep: An overview. *Principles and Practice of Sleep Medicine*, *4*, 13–23.

Cauter, E. V., Leproult, R., & Plat, L. (2000). Age-related changes in slow wave sleep and REM sleep and relationship with growth hormone and cortisol levels in healthy men. *JAMA*, *284*(7), 861–868. https://doi.org/10.1001/jama.284.7.861.

Dressler, H., & Smith, C. (2013). Food choice, eating behavior, and food liking differs between lean/normal and overweight/obese, low-income women. *Appetite*, *65*, 145–152. https://doi.org/10.1016/j.appet.2013.01.013.

Elsenbruch, S., Harnish, M. J., & Orr, W. C. (1999). Subjective and objective sleep quality in irritable bowel syndrome. *The American Journal of Gastroenterology*, *94*(9), 2447–2452. https://doi.org/10.1016/S0002-9270(99)00430-X.

Epel, E., Lapidus, R., McEwen, B., & Brownell, K. (2001). Stress may add bite to appetite in women: a laboratory study of stress-induced cortisol and eating behavior. *Psychoneuroendocrinology*, *26*(1), 37–49.

Espiritu, J. R. D. (2008). Aging-related sleep changes. *Clinics in Geriatric Medicine*, *24*(1), 1–14. https://doi.org/10.1016/j.cger.2007.08.007

Finlayson, G., King, N., & Blundell, J. (2008). The role of implicit wanting in relation to explicit liking and wanting for food: Implications for appetite control. *Appetite*, *50*(1), 120–127. https://doi.org/10.1016/j.appet.2007.06.007.

Friese, R. S., Diaz-Arrastia, R., McBride, D., Frankel, H., & Gentilello, L. M. (2007). Quantity and quality of sleep in the surgical intensive care unit: Are our patients sleeping? *Journal of Trauma and Acute Care Surgery*, *63*(6), 1210–1214.

Glanz, K., & Basil, M. (1998). Why Americans eat what they do: Taste, nutrition, cost, convenience, and weight control concerns. *Journal of the American Dietetic Association*, *98*(10), 1118–1126..

Golley, R. K., Maher, C. A., Matricciani, L., & Olds, T. S. (2013). Sleep duration or bedtime? Exploring the association between sleep timing behaviour, diet and BMI in children and adolescents. *International Journal of Obesity*, *37*(4), 546–551. https://doi.org/10.1038/ijo.2012.212.

Gonnissen, H. K., Hursel, R., Rutters, F., Martens, E. A., & Westerterp-Plantenga, M. S. (2013). Effects of sleep fragmentation on appetite and related hormone concentrations over 24 h in healthy men. *Br J Nutr*, *109*, 748–756. https://doi.org/10.1017/S0007114512001894.

Hjorth, M. F., Quist, J. S., Andersen, R., Michaelsen, K. F., Tetens, I., Astrup, A., … Sjödin, A. (2014). Change in sleep duration and proposed dietary risk factors for obesity in Danish school children. *Pediatric Obesity*, *9*(6), e156–e159. https://doi.org/10.1111/ijpo.264.

Hogenkamp, P. S., Nilsson, E., Chapman, C. D., Cedernaes, J., Vogel, H., Dickson, S. L., … Benedict, C. (2013). Sweet taste perception not altered after acute sleep deprivation in healthy young men. *Somnology-Sleep Research and Sleep Medicine*, *17*(2), 111–114.

Horne, J. A. (2015). Human REM sleep: Influence on feeding behaviour, with clinical implications. *Sleep Medicine*, *16*(8), 910–916. https://doi.org/10.1016/j.sleep.2015.04.002

Hummel, T., Sekinger, B., Wolf, S. R., Pauli, E., & Kobal, G. (1997). 'Sniffin' Sticks': Olfactory performance assessed by the combined testing of odor identification, odor discrimination and olfactory threshold. *Chemical Senses*, *22*(1), 39–52. https://doi.org/10.1093/chemse/22.1.39.

Kanda, T., Tsujino, N., Kuramoto, E., Koyama, Y., Susaki, E. A., Chikahisa, S., & Funato, H. (2016). Sleep as a biological problem: An overview of frontiers in sleep research. *The Journal of Physiological Sciences*, *66*(1), 1–13. https://doi.org/10.1007/s12576-015-0414-3.

Kenny, P. J. (2011). Reward mechanisms in obesity: New insights and future directions. *Neuron*, *69*(4), 664–679. https://doi.org/10.1016/j.neuron.2011.02.016.

Killgore, W. D., & McBride, S. A. (2006). Odor identification accuracy declines following 24 h of sleep deprivation. *J Sleep Res*, *15*, 111–116.

Krystal, A. D., & Edinger, J. D. (2008). Measuring sleep quality. *Sleep Medicine*, *9*, S10–S17. https://doi.org/10.1016/S1389-9457(08)70011-X.

Lauderdale, D. S., Knutson, K. L., Yan, L. L., Liu, K., & Rathouz, P. J. (2008). Sleep duration: How well do self-reports reflect objective measures? The CARDIA Sleep Study. *Epidemiology (Cambridge, Mass.)*, *19*(6), 838–845. https://doi.org/10.1097/EDE.0b013e318187a7b0.

Lauer, C., Schreiber, W., Berger, M., Pirke, K.-M., Holsboer, F., & Krieg, J.-C. (1989). The effect of neuroendocrine secretion on brain morphology and EEG sleep in patients with eating disorders. *European Archives of Psychiatry and Neurological Sciences*, *238*(4), 208–212. https://doi.org/10.1007/BF00381467.

Le Bon, O., Staner, L., Hoffmann, G., Dramaix, M., San Sebastian, I., Murphy, J. R., … Linkowski, P. (2001). The first-night effect may last more than one night. *Journal of Psychiatric Research*, *35*(3), 165–172. https://doi.org/10.1016/S0022-3956(01)00019-X.

Li, W., Ma, L., Yang, G., & Gan, W.-B. (2017). REM sleep selectively prunes and maintains new synapses in development and learning. *Nature Neuroscience*, *20*(3), 427–437. https://doi.org/10.1038/nn.4479.

Markwald, R. R., Melanson, E. L., Smith, M. R., Higgins, J., Perreault, L., Eckel, R. H., & Wright, K. P., Jr. (2013). Impact of insufficient sleep on total daily energy expenditure, food intake, and weight gain. *Proc Natl Acad Sci U S A*, *110*, 5695–5700. https://doi.org/10.1073/pnas.1216951110.

McBride, S. A., Balkin, T. J., Kamimori, G. H., & Killgore, W. D. S. (2006). Olfactory decrements as a function of two nights of sleep deprivation. *Journal of Sensory Studies*, *21*(4), 456–463. https://doi.org/10.1111/j.1745-459X.2006.00080.x.

Mennella, J. A., Lukasewycz, L. D., Griffith, J. W., & Beauchamp, G. K. (2011). Evaluation of the Monell forced-choice, paired-comparison tracking procedure for determining sweet taste preferences across the lifespan. *Chemical Senses*, *36*, 345–355.

Menzies, J. R. W., Skibicka, K. P., Leng, G., & Dickson, S. L. (2013). *Ghrelin, reward and motivation*. *25*, 101–111. https://doi.org/10.1159/000346058.

Mozaffarian, D., Hao, T., Rimm, E. B., Willett, W. C., & Hu, F. B. (2011). Changes in diet and lifestyle and long-term weight gain in women and men. *N Engl J Med*, *364*, 2392–2404.

Mueller, C., Kallert, S., Renner, B., Stiassny, K., Temmel, A. F. P., Hummel, T., & Kobal, G. (2003). Quantitative assessment of gustatory function in a clinical context using impregnated" taste strips". *Rhinology*, *41*(1), 2–6.

Naismith, S., Winter, V., Gotsopoulos, H., Hickie, I., & Cistulli, P. (2004). Neurobehavioral functioning in obstructive sleep apnea: Differential effects of sleep quality, hypoxemia and subjective sleepiness. *Journal of Clinical and Experimental Neuropsychology*, *26*(1), 43–54. https://doi.org/10.1076/jcen.26.1.43.23929.

Nedeltcheva, A. V., Kilkus, J. M., Imperial, J., Kasza, K., Schoeller, D. A., & Penev, P. D. (2009). Sleep curtailment is accompanied by increased intake of calories from snacks. *Am J Clin Nutr*, *89*, 126–133. https://doi.org/10.3945/ajcn.2008.26574.

Neter, J., Kutner, M. H., Nachtsheim, C. J., & Wasserman, W. (1996). *Applied linear statistical models* (Vol. 4).

Parcell, D. L., Ponsford, J. L., Redman, J. R., & Rajaratnam, S. M. (2008). Poor sleep quality and changes in objectively recorded sleep after traumatic brain injury: A preliminary study. *Archives of Physical Medicine and Rehabilitation*, *89*(5), 843–850. https://doi.org/10.1016/j.apmr.2007.09.057.

Patterson, R. E., Emond, J. A., Natarajan, L., Wesseling-Perry, K., Kolonel, L. N., Jardack, P., … Arab, L. (2014). Short sleep duration is associated with higher energy intake and expenditure among African-American and non-Hispanic white adults. *J Nutr*, *144*, 461–466. https://doi.org/10.3945/jn.113.186890.

Peever, J., & Fuller, P. M. (2016). Neuroscience: A distributed neural network Ccontrols REM sleep. *Current Biology*, *26*(1), R34–R35. https://doi.org/10.1016/j.cub.2015.11.011.

Pepino, M. Y., Finkbeiner, S., Beauchamp, G. K., & Mennella, J. A. (2010). Obese women have lower monosodium glutamate taste sensitivity and prefer higher concentrations than do normal-weight women. *Obesity*, *18*, 959–965.

Pilcher, J. J., Ginter, D. R., & Sadowsky, B. (1997). Sleep quality versus sleep quantity: Relationships between sleep and measures of health, well-being and sleepiness in college students. *Journal of Psychosomatic Research*, *42*(6), 583–596. https://doi.org/10.1016/S0022-3999(97)00004-4.

Prather, A. A., Leung, C., Adler, N. E., Epel, E. S., Ritchie, L., & Laraia, B. (2014). Abstract P110: Short and sweet: Short sleep duration is associated with increased sugar sweetened beverage consumption in the united states. *Circulation*, *129*(Suppl 1), AP110–AP110.

Rasch, B., Büchel, C., Gais, S., & Born, J. (2007). Odor cues during slow-wave sleep prompt declarative memory consolidation. *Science*, *315*(5817), 1426–1429. https://doi.org/10.1126/science.1138581.

Roth, T. (2009). Slow wave sleep: Does it matter? *Journal of Clinical Sleep Medicine : JCSM : Official Publication of the American Academy of Sleep Medicine*, *5*(2 Suppl), S4–S5.

Satoh-Kuriwada, S., Kawai, M., Iikubo, M., Sekine-Hayakawa, Y., Shoji, N., Uneyama, H., & Sasano, T. (2014). Development of an umami taste sensitivity test and its clinical use. *PLOS ONE*, *9*(4), e95177. https://doi.org/10.1371/journal.pone.0095177.

Schiffman, S. S., Rogers, M. O., & Zervakis, J. (2004). Loss of taste, smell, and other senses with age. In *Handbook of Clinical Nutrition and Aging* (Vols. 1–Book, Section, pp. 211–289). Springer.

Siegel, J. M. (2001). The REM sleep-memory consolidation hypothesis. *Science*, *294*(5544), 1058–1063. https://doi.org/10.1126/science.1063049.

Smith, M. T., & Wegener, S. T. (2003). Measures of sleep: The Insomnia Severity Index, Medical Outcomes Study (MOS) Sleep Scale, Pittsburgh Sleep Diary (PSD), and Pittsburgh Sleep Quality Index (PSQI). *Arthritis Care & Research*, *49*(S5), S184–S196.

Smith, S. L., Ludy, M.-J., & Tucker, R. M. (2016). Changes in taste preference and steps taken after sleep curtailment. *Physiology & Behavior*, *163*, 228–233. https://doi.org/10.1016/j.physbeh.2016.05.002.

Sørensen, L. B., Møller, P., Flint, A., Martens, M., & Raben, A. (2003). Effect of sensory perception of foods on appetite and food intake: A review of studies on humans. *International Journal of Obesity*, *27*(10), 1152–1166.

Spiegel, K., Leproult, R., & Van Cauter, E. (1999). Impact of sleep debt on metabolic and endocrine function. *The Lancet*, *354*(9188), 1435–1439. https://doi.org/10.1016/S0140-6736(99)01376-8.

Stevens, J. C., Cruz, L. A., Hoffman, J. M., & Patterson, M. Q. (1995). Taste sensitivity and aging: High incidence of decline revealed by repeated threshold measures. *Chemical Senses, 20,* 451–459.

St-Onge, M.-P., Wolfe, S., Sy, M., Shechter, A., & Hirsch, J. (2014). Sleep restriction increases the neuronal response to unhealthy food in normal-weight individuals. *International Journal of Obesity (2005), 38*(3), 411–416. https://doi.org/10.1038/ijo.2013.114.

Tucker, R. M., Laguna, L., Quinn, R., & Mattes, R. D. (2013). The effect of short, daily oral exposure on non-esterified fatty acid sensitivity. *Chemosens Percept, 6*, 78–85.

van der Lely, A. J., Tschöp, M., Heiman, M. L., & Ghigo, E. (2004). Biological, physiological, pathophysiological, and pharmacological aspects of ghrelin. *Endocrine Reviews*, *25*(3), 426–457. https://doi.org/10.1210/er.2002-0029.

Chapter 2:

This work is published and re-used in this dissertation with permission from Oxford University Press. The full citation is presented below:

Szczygiel, E. J., Cho, S., Snyder, M. K., & Tucker, R. M. (2019). Associations between chemosensory function, sweet taste preference, and the previous night's sleep in non-obese males. *Food Quality and Preference, 75,* 105–112. https://doi.org/10.1016/j.foodqual.2019.02.018.

There is a growing body of evidence suggesting that sleep influences chemosensory perception. Males and females differ in neural responses to chemosensory function as well as average sleep duration, suggesting the possibility of sex differences regarding relationships between sleep and chemosensory perception. Therefore, the primary objective of this study was to characterize relationships between sleep and chemosensory function in males. A total of 51 non-obese (BMI<30.0 kg/m^2) male participants completed testing. Sleep was measured using a single-channel (A_1–A_2) electroencephalogram-(EEG) (Zmachine) and next day sensory function, including sweet taste threshold, sweet taste preference, olfactory threshold, olfactory identification ability, and odor pleasantness ratings, was evaluated. Sweet taste preference was associated with total sleep time (TST) (P=0.0111), rapid eye movement (REM) sleep (P=0.0003), stage N3/slow wave sleep (SWS) duration (P=0.0248), and the sum of REM and SWS (P=0.0088). Further, odor identification ability was positively associated with TST (P=0.0187) and REM sleep duration (P=0.0424). Participants grouped into shorter sleep groups and low REM+SWS preferred significantly greater sucrose concentrations than those in longer and high REM+SWS groups (P=0.0420, 0.0039, respectively). Multiple regression analysis indicated that REM alone was the best predictor of sweet taste preference and that TST alone

was the best predictor of odor identification score. A simple previous night's sleep quality rating measurement was associated with objective sleep measures, suggesting a possible method by which scientific and consumer studies might improve data by screening participants for poor sleep prior to testing.

1. Introduction

Excessive intake of foods and beverages high in saturated fats and simple carbohydrates is associated with insufficient sleep (Golley, Maher, Matricciani, & Olds, 2013; Gonnissen et al., 2013; Hjorth et al., 2014; Markwald et al., 2013; Nedeltcheva et al., 2009; Prather et al., 2014). This relationship is thought to be an important mechanism by which insufficient sleep is associated with weight gain and obesity (Alvarez Gonzalo G. & Ayas Najib T., 2007; Cappuccio, Cooper, D'Elia, Strazzullo, & Miller, 2011; Chapman, Benedict, Brooks, & Birgir Schiöth, 2012; St-Onge, 2017), although there is evidence of a bidirectional relationship (Vgontzas, Bixler, & Basta, 2010). Changes in chemosensory function or preferences after a night of insufficient sleep may mediate the relationship between insufficient sleep and excessive intake of these specific food types, due to the fact that food selection is frequently based primarily on the sensory properties of food (Dressler & Smith, 2013; Glanz, Basil, Maibach, Goldberg, & Snyder, 1998; Sørensen, Møller, Flint, Martens, & Raben, 2003). There is evidence that insufficient sleep may alter chemosensation, including a reduction in odor identification abilities after 24 and 52 h of sleep deprivation (Killgore & McBride, 2006; McBride, Balkin, Kamimori, & Killgore, 2006) and increased preference for sweetness with sleep curtailment (Smith, Ludy, & Tucker, 2016; Szczygiel, Cho, & Tucker, 2018). Previous work suggests that differences in sleep could account for up to 15% of the total variance in sweet taste preference in females (Szczygiel et al., 2018).

Behavioral and neurophysiological evidence suggests that there are sex differences in gustatory (Martin & Sollars, 2017) and olfactory (Brand & Millot, 2001) function and perception. Females tend to have a lower taste threshold in humans (Bartoshuk, Duffy, & Miller, 1994) and more accurate orofacial sensory perception (Silva et al., 2014) compared to males. Females surpass males in odor identification ability, regardless of familiarity or exposure to an odorant (Brand & Millot, 2001; Doty, Applebaum, Zusho, & Settle, 1985). Males and females have also been found to have differential brain activation to taste and food cues in reward centers of the brain (Cornier, Salzberg, Endly, Bessesen, & Tregellas, 2010; Haase, Green, & Murphy, 2011). Previous work has noted differences in brain structure (Wager, Phan, Liberzon, & Taylor, 2003), odor identification ability (Doty et al., 1985), neural response to food stimuli (Cornier et al., 2010), and neural processing of pleasurable odors and emotional stimuli (Royet, Plailly, Delon-Martin, Kareken, & Segebarth, 2003), lending support to the idea that the relationships between sleep and chemosensory function may be sex-specific. Additionally, behavioral differences such as sleep habits (Lauderdale et al., 2006), sweet preference (Enns, Van Itallie, & Grinker, 1979; Greene, Desor, & Maller, 1975), and food choice (Westenhoefer, 2005) indicate that males get less sleep, prefer sweeter foods, and make more unhealthy food choices, lending further support to sex differences. To date, attempts to characterize sex-specific relationships between chemosensory function and sleep has been limited (Hogenkamp et al., 2013; McNeil et al., 2017; Szczygiel et al., 2018). Further characterization of the relationships between sleep and chemosensory function and preference in males is needed.

The pattern and duration of sleep stages during sleep, known as sleep architecture, may play a role in the relationship between insufficient sleep and chemosensory function. In healthy adults, total sleep time (TST) can be divided into rapid eye movement (REM) and non-REM

(NREM) sleep. NREM sleep can be further divided into N3 or slow wave sleep (SWS) and light sleep (stage N1 and N2). Reductions in REM, SWS and stage N2 of light sleep have been associated with signs of positive energy balance (Shechter et al., 2012), suggesting that architecture plays an important role in the relationship between insufficient sleep and excessive energy intake. Sleep architecture may also be related to reward processing of food stimuli, as REM sleep restriction has been found to increase motivation for food reward (Hanlon, Andrzejewski, Harder, Kelley, & Benca, 2005; McNeil et al., 2017). Previous work has found that the sum of SWS and REM sleep may be a better predictor of changes in sweet taste preference than TST alone (Szczygiel et al., 2018). Thus, sleep architecture merits specific attention when characterizing the relationship between sleep and hedonic evaluation of chemosensory stimuli.

In a separate study carried out previously, we observed that while sleep and sweet taste acuity (detection threshold) were unrelated, an inverse relationship between sweet preference and sleep duration and various facets of sleep architecture existed in non-obese females (Szczygiel et al., 2018). Additionally, changes in olfactory function were investigated, but no associations with sleep were observed (Szczygiel et al., 2018). Therefore, using similar methodology, we aimed to characterize these olfactory and gustatory function in relation to objectively measured sleep duration and architecture in males. We hypothesized that shorter sleep time (TST) and poorer sleep quality, characterized by less time spent in REM and SWS, would be associated with increased gustatory and olfactory thresholds, reduction in ability to identify odorants, and an increase in food odor pleasantness rating. Further, considering the chemosensory, behavioral, and neural differences between males and females, we hypothesized that associations discovered between sleep and sweet taste preference using a female sample would also exist in males, but

that these relationships might be stronger given the documented differences in neural biology and behaviors. Given the similarity in protocols and the lack of associations between sleep and olfaction in our previous work, relationships between olfaction and sleep in non-obese males were not anticipated.

2. Materials and methods

The study protocol was approved by the Human Research Protection Program at Michigan State University (East Lansing, MI, USA). Written informed consent was obtained from all participants prior to testing.

2.1. Participants

Non-obese males (BMI < 30.0 kg/m^2) of any race or ethnicity between 18-55 years of age with no diagnosed sleep conditions, who considered themselves healthy and who claimed they normally slept 7-9 h per weeknight and had no taste or smell deficiencies. were eligible to participate in the study. During the initial consent visit, participants completed a demographic questionnaire and the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a validated questionnaire that measures subjective sleep quality and duration during the past month (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). PSQI scores equal to five or greater indicate possible disordered sleep (Buysse et al., 1989). Height was measured using a stadiometer (HM200P, Charder, Taichung, Taiwan) and body mass index (BMI), percent body fat (%BF), and weight, were measured using a bioelectrical impedance scale (TBF-400, Tanita, Arlington Heights, IL).

2.2. Sleep measures

Participants were trained to operate the Zmachine (General Sleep, Columbus, OH) ("Zmachine Insight and Insight+ Model:DT-200: Clinician instruction and service manual" 2016) during the consent visit. The Zmachine is a single-channel EEG that monitors sleep and provides algorithm-based sleep staging. The participant adheres Ag/AgCl surface sensors to the differential-mastoids (A_1-A_2) and a common reference electrode to the nape before attaching the EEG unit to the sensors via metal fasteners before bedtime. The Zmachine automatically uses the raw EEG signal to determine whether the participant is asleep or awake (Z-ALG) (Kaplan, Wang, Loparo, Kelly, & Bootzin, 2014). If the Z-ALG finds a participant is asleep at a given 30 sec epoch, a second algorithm (Z-PLUS) is automatically employed to stage the sleep period as "light sleep" (N1+N2), "deep sleep" (SWS, N3) or REM sleep (Wang, Loparo, Kelly, & Kaplan, 2015). The Zmachine, when evaluated against PSG, was found to have substantial agreement in identifying wake, light sleep, SWS, and REM sleep (Cohen's Kappa=0.72 for all) (Wang et al., 2015). Participants were then asked to adhere to their usual sleep schedule and wear the Zmachine for two consecutive weeknights to minimize a possible "first-night effect" (Bon et al., 2001) prior to sensory testing, which occurred on the third day. Upon arriving at the lab after a night of sleep recording, the EEG data from the previous night's sleep was immediately uploaded to the Zmachine data viewer. The participant was then asked to confirm that the data matched their own recollection of the previous night and was re-recorded if discrepancies were noted. Data collected by the Zmachine relevant to this study included time in bed (TIB), NREM, TST, SWS, and REM sleep duration. The first night of data was not used. While there is a lack of consensus on how objective sleep quality should be reported (Krystal & Edinger, 2008), SWS and REM sleep duration are independently and jointly associated with changes in

chemosensation in females (Szczygiel et al., 2018) and, therefore, were selected as the main objective sleep quality measures for this study. Additionally, participants were asked to report how well they thought they slept on a 100-mm anchored visual analog scale with "worst sleep I have ever had" at 0 and "best sleep I have ever had" at 100 (Sleep Rating (SR)).

2.3. Laboratory visit

Participants came to the laboratory between 8:00 a.m. and 3:00 p.m. each day for sensory testing after two consecutive weeknights of sleep monitoring. Participants were told not to eat or drink anything except water for one hour prior to testing and not to nap between wake time and their scheduled appointment. During each lab visit, which lasted approximately 1 h, participants tasted, on average, 14-18 sweet solutions and sniffed 35-40 odorants.

2.4. Gustatory testing

Taste-testing followed the protocol used previously (Szczygiel et al., 2018). Briefly, sweet taste threshold was measured using a 3-alternative forced-choice procedure using ¼ log step dilutions of sucrose in water ranging from 0.021%-2.1%. Participants wore nose clips during both threshold and preference taste testing. The Monell forced-choice paired comparison protocol (Mennella, Lukasewycz, Griffith, & Beauchamp, 2011) was used to evaluate sweetness preference. For this testing protocol, participants were given two concentrations of suprathreshold sweet solutions consisting of either 3, 6, 12, 24, or 36% w/v sucrose and asked to select the one they preferred. Based on their choice, two additional concentrations were provided until the participant selected the same solution twice in a row. The test was performed once with the lower concentration presented first each time and once with the higher concentration presented first each time. The geometric mean of the %w/v

preferred sucrose solution is reported as the sweet taste preference. To evaluate the impact of sleep duration on taste preference, individuals were categorized as either a long sleeper or short sleeper by whether they were in bed above or below the minimum recommended amount of sleep (7h) (Hirshkowitz et al., 2015).

2.5. Olfactory testing

Three different olfactory tests were conducted using Sniffin' Sticks (Burghart, Wedel, Germany) (Hummel et al. 1997). Olfactory threshold testing and olfactory identification testing followed the Sniffin' Sticks protocol provided by the manufacturer. Briefly, for threshold testing, participants are presented with three sticks in random order, one of which contains standard odor, and ask to select which of the three contain the odorant. If they fail, a set with a higher concentration of odorant is presented until they correctly identify the stick with odorant twice. The staircase is then reversed and they are presented with descending concentrations of odorant until they fail once. The staircase is reversed seven times and the geometric mean of the last four reversals is used as the threshold score. In addition to threshold and identification testing, participants were asked to smell four odors used in the identification test a second time and to rate the pleasantness of each using a 100 mm visual analog scale with the anchors "not at all" and "extremely". Three food odors (apple, pineapple, and clove) and one non-food odor (rose) were presented to participants for odor pleasantness evaluation.

2.6. Statistical Analyses

Data analysis was completed using SAS version 9.4 (SAS Institute, Cary, NC., U.S.A.). Simple linear regression and Pearson's correlations were used to evaluate relationships between sleep variables and sensory measures. Independent t-tests were used to compare

measures of duration and architecture between sleep groups. Results are presented as means ± standard deviations. Multiple linear regression analysis was used to evaluate associations while accounting for covariates and multicollinearity, and backward (step-down) selection was used to select the best model (Neter, Kutner, Nachtsheim, & Wasserman, 1996). An α=0.05 level of confidence was used to determine significance in all instances.

3. Results

3.1. Participant Demographics and Sleep Characteristics

Fifty-two non-obese male participants completed the study. Any participant with any objective sleep measure (TIB, TST, REM, SWS) greater than three standard deviations from the mean was considered an outlier. One participant was considered an outlier because his REM duration was 3.8 standard deviations away from the mean REM duration (1.4±0.6h) of all other participants and was subsequently removed from all further analysis. Therefore, data from a total of 51 males were used for analysis. Participants were young (mean 24.89 y ± 5.32, range 18-39) and non-obese (mean BMI: 24.36 ± 3.09, range 18-29; body fat percentage: mean 17.28±5.57, range 6-28%). While eligibility criteria included habitually getting 7-9 h of sleep per night and having no diagnosed sleep conditions, 17 participants were found to have a PSQI composite score ≥5, indicating that these participants were habitually poor sleepers. However, objective sleep measures were not significantly different between the group with ≥5 PSQI and the group with <5 PSQI scores, so all data were pooled. The mean PSQI score for the entire study population was below 5. A summary of participant sleep measures for the complete sample

is presented in Table 2.1. In terms of race, 47% (n=24) identified as White, 37% (n=19) identified as Asian, and 12% (n=6) identified as Black and with 4% (n=2) identified as more than one or none. The SR measurements were above 50 (midline, 100-mm line scale) (Table 2.1), indicating that perceived sleep quality the night before testing was slightly above average. There were no significant associations between PSQI or SR (r=-0.19, P=0.16) and any demographic or anthropometric variables (age, BMI, %BF) (P>0.05). Subjective SR was correlated with SWS (r=0.29, P=0.0397) and SWS+REM (r=0.32, P=0.0237).

Table 2.1. Summary of objective and subjective sleep measures of study participants

Variable*	Mean	Std. Dev	% of TST	Range
Time in Bed (TIB) (h)	6.7	1.7		2.8-10.2
Total Sleep Time (TST) (h)	5.5	1.6		2.0-8.7
Rapid Eye Movement (REM) (h)	1.4	0.6	25%	0.2-2.8
Slow Wave Sleep (SWS, N3) (h)	1.3	0.6	24%	0-2.7
SWS+REM (h)	2.7	1	49%	0.3-4.8
Light Sleep (LS) (N1+N2)	2.8	1.1	51%	0.9-5.3
NREM (LS+SWS)	4.1	1.1	75%	1.1-6.1
PSQI (Composite Score)	3.8	2.1		0-9
SR (0-100mm line scale)	61.9	15.6		20-85

3.2. Taste threshold

No significant correlations between taste threshold and demographic or anthropometric variables (age, BMI and %BF), objective sleep measures (TIB, TST, REM, SWS, NREM, REM+SWS), or subjective sleep measures (PSQI, SR) were observed (P>0.05).

3.3. Taste preference

Significant inverse associations were observed between TST, REM, SWS, and SWS+REM, and preferred sweetness concentration (Table 2.2) (P<0.05). NREM was not correlated with taste preference (P>0.05). No significant correlations were observed between

taste preference and any of the demographic variables (age, BMI, %BF) ($P>0.05$). Multiple regression analysis was used to identify the best model to predict taste preference. Three variables (TST, REM, SWS) were selected as variables of interest related to sweet taste preference based on previous findings in females and the presence of linear associations in the current study. Using backward selection, the best model contained only one variable, REM+SWS (h) and explained 24% of the variance ($R^2=0.24$, $F(2, 51) =15.31$, $P=0.0003$) (Table 2.3). TST and SWS were removed from the model with a partial R^2 of 0.0005, 0.0104, respectively. The same selection method and variables were used to identify the best model to predict odor identification. TST explained 10% of the variance ($R^2=0.10$, $F(2, 51) =5.92$, $P=0.0187$). REM and SWS were removed from the model with a partial R^2 of 0.0039 and 0.0059, respectively.

Table 2.2 Simple linear regression of the sleep measures and chemosensory functions

Sensory Variable	Sleep Variable* (h)	Pearson's r	R-square	P-value
Taste Preference (%w/v)	TST	-0.35	0.12	0.0111
	REM	-0.49	0.24	0.001
	SWS (N3)	-0.31	0.1	0.0248
	SWS+REM	-0.47	0.22	0.0005
	LS	-0.08	0.01	0.5998
	NREM	-0.22	0.05	0.1293
Odor Identification (score 0-16)	TST	0.33	0.1	0.0187
	REM	0.29	0.08	0.0424
	SWS	0.13	0.02	0.3515
	SWS+REM	0.25	0.06	0.0817
	LS	0.24	0.06	0.0801
	NREM	0.28	0.08	0.0451

Simple linear regressions of the taste preference, odor identification score and various objective sleep measures (Total sleep time (TST), Rapid eye movement (REM), Slow-wave sleep (SWS, N3), Light sleep (LS), NREM (Non-rapid eye movement)) of all participants. Negative correlations between taste preference and sleep variables indicate that higher preferred concentrations were associated with less sleep. Positive correlations between odor identification and sleep variables indicate that better odor identification scores were associated with more sleep.

Table 2.3. Multiple Regression Predicting Taste Preference and Olfactory Identification Score

	Variables	β	Std. Err	Parm. Est.	t value	P
Taste Preference	REM (h)	-0.49	3.29	-8.51	-3.91	0.0003
Olfactory ID	TST (h)	0.33	0.18	0.45	2.43	0.0187

Results of multiple linear regression model selection by backwards variable selection analysis to predict taste preference (% w/v) and olfactory identification (ID) score continuous variables (n=51).

Short sleepers (n=27) and long sleepers (n=24) did not differ by age, BMI, or %BF (P> 0.05). There were no significant differences in demographic or anthropometric measures

between the two groups (age, BMI, %BF) (P>0.05). The magnitude of difference in sweet taste preference between the two groups was 6%, with shorter sleepers preferring a higher concentration (*M*=15.70±11.11%) compared to longer sleepers (*M*=9.70±9.14%) (P=0.0420) (Figure 2.1).

To evaluate the impact of sleep architecture on taste preference, participants were classified as low REM+SWS (LRS) (n=25) and high REM+SWS (HRS) (n=26) sleepers by whether they were above or below the mean duration (h) of REM+SWS sleep (mean ± SD [h] = 2.7 ± 1.0) for the night before testing, given both of these stages have been suggested to play a role in sleep quality (Krystal & Edinger, 2008). The two groups did not differ by age, BMI, or %BF (P>0.05). HRS sleepers preferred lower concentrations of sucrose compared to LRS sleepers (*M*=8.7±9.14%), *M*=17.22±12.14%, respectively) (P=0.0039) (Figure 2.1). Comparisons between the long, short, HRS and LRS groups showed no significant difference for any of the other taste variables (P>0.05).

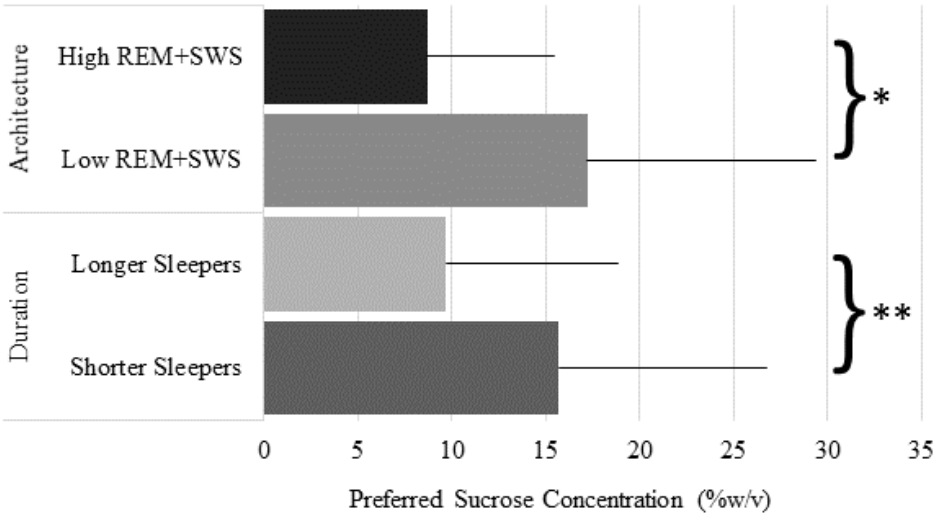

Figure 2.1. *Sweet taste preference differences between sleep architecture and total sleep duration groups.* Healthy, non-obese males who were classified as short sleepers (n=27) or had low REM+SWS sleep duration (n=25) the night before testing preferred higher concentrations of sweetness compared to those classified as longer sleepers (n=24, P=0.042) or high REM+SWS (n=26, P=0.0039). Bars represent means and error bars represent standard deviations. * indicates p-values for paired t-tests are significant at the P<0.05 level. ** indicates p-values are significant at the P<0.01 level

3.4. Olfactory results

Odor threshold and pleasantness ratings of the three food and one non-food odor were not significantly correlated with subjective sleep quality, TST, or duration of any specific sleep stage (P>0.05). Comparisons between the long, short, HRS and LRS groups showed no significant difference for any of the odor variables (P>0.05). However, significant correlations were found

between odor identification scores and both TST and REM sleep duration (Table 2.2). NREM (SWS+light sleep) was also associated with odor identification (r=0.28, P=0.0451) (Table 2.2).

4. Discussion

The primary objective of this study was to characterize the relationships between sleep and chemosensory function and preference in non-obese males. Objectively measured sleep duration and architecture were both associated with various measures of chemosensory function. TST, REM, SWS, and REM+SWS duration were all inversely associated with preference for sweetness in the sample (n=51). REM sleep duration was the best predictor of sweet taste preference, followed by the sum of REM and SWS. Odor identification ability was positively correlated with TST and REM sleep. Non-obese male HRS sleepers preferred sucrose solutions approximately 8.5% less concentrated compared to LRS sleepers and "longer" sleepers preferred sucrose solutions approximately 6.0% less concentrated compared to "shorter" sleepers. Previously published literature demonstrates that males have increased brain response to hedonic food stimuli after acute sleep deprivation (Benedict et al., 2012). Thus, one possible explanation for the observed change in sweetness preference is that total sleep duration and REM+SWS duration may mediate reward response to sweet stimuli through changes in reward processing in the brain. Insufficient sleep has been shown to increase activity in the amygdala (Gujar, Yoo, Hu, & Walker, 2011; St-Onge et al., 2012) and striatum (Norgren, Hajnal, & Mungarndee, 2006) and impair OFC function (Gujar et al., 2011), and these neurological changes are thought to coincide with amplified reward sensitivity and biased appraisal of positive experiences (Gujar et al., 2011). The observed associations with sleep duration and olfactory response may be related to impaired memory recall and recognition related to insufficient sleep (Kapur et al., 1995;

Thomas et al., 2000). These findings suggest that it may be beneficial to control for sleep duration and/or architecture in psychophysical studies, particularly when hedonics are a focus on the research.

It is currently unclear how sleep architecture contributes to sleep-related changes in chemosensory function. SWS and REM sleep have both been independently observed to play a role in regulating a variety of psychological and physiological processes, such as memory (Siegel, 2001) and physical restoration (Roth, 2009). SWS and REM sleep typically each compose roughly 20-30% of total sleep duration in healthy sleepers (Carskadon, Dement, 2005). REM and SWS composed 25% and 24% of sleep duration, respectively, in the current study sample population (Table 2.1), indicating that the sleep architecture of the participants can be considered healthy.

The specific biological role of REM sleep is not fully understood (Kanda et al., 2016). Some have speculated that REM plays a role in several psychological processes including memory consolidation (Siegel, 2001), learning ability (Curcio, Ferrara, & De Gennaro, 2006) and emotional processing (Walker & van der Helm, 2009). Additionally, REM sleep duration and cortisol levels are inversely correlated (Lauer et al., 1989), and increased cortisol is associated with excessive food consumption (Epel, Lapidus, McEwen, & Brownell, 2001), particularly in females. REM sleep, specifically, has been hypothesized to play a role in the development of food preference and has been found to activate the same areas of the brain that are active during excessive consumption of highly palatable food (Horne, 2015; Kenny, 2011). Further, there is evidence that REM sleep deprivation causes acute changes in reward processing of the brain, leading to an increased neural response to food stimuli (Benedict et al., 2012; Demos et al., 2017; Hanlon et al., 2005; Horne, 2015; Kenny, 2011). Taken together, these data

suggest that REM sleep may play a role in shaping sweet taste preference. The association between sweet taste preference and REM sleep duration does not appear to be a result of changes to chemosensory acuity, as sweet taste threshold was observed to be unrelated to any sleep variable measured.

While the exact role of SWS has also not been identified, it is thought to play a role in homeostatic feeding processes, namely, secretion of ghrelin (Cauter, Leproult, & Plat, 2000), an appetite-stimulating hormone (van der Lely, Tschöp, Heiman, & Ghigo, 2004) and may enhance food reward through its role in the gut-brain reward pathway (Menzies, Skibicka, Leng, & Dickson, 2013). However, we observed SWS to have the weakest association with sweet taste preference among the sleep variables. During normal sleep in healthy adults, NREM sleep (including SWS) usually occurs early in the night, with REM duration per sleep cycle increasing as the night progresses (Carskadon et al., 2005). SWS may disappear altogether during the second and third sleep cycles (Carskadon et al., 2005). SWS+REM sleep was the second-best predictor of taste preference in the current study and was found to be the best predictor in previous work with females (Szczygiel et al., 2018), but SWS alone was more weakly correlated with sweet taste preference than REM in both studies. It is possible that SWS does not play a direct biological role in the relationship between sleep and chemosensation, but rather is a component of healthy sleep architecture with sufficient amounts of REM sleep, which is a stronger predictor of changes in chemosensation.

Despite TST being a significant predictor of sweet taste preference in both males in the current study and females in previous literature (Szczygiel et al., 2018), the strongest sleep stage predictor varied between the sexes. SWS+REM was the best predictor of sweet taste preference for females; whereas, REM alone was the best predictor for males. However, differences

between the association of sweet taste preference with REM and SWS+REM were small for both males (REM r=-0.49, SWS+REM r=-0.47) and females (REM r=-0.41, SWS+REM r=-0.43). While it is possible that this finding is evidence that different sleep stages drive the sleep-taste relationship in males and females, it is more likely that REM and SWS+REM represent similar dimensions of this relationship. Importantly, REM, SWS, and other sleep measures are typically highly correlated; therefore, future work should endeavor to directly manipulate sleep architecture to determine the causative role of each sleep stage in chemosensory function and whether the mechanisms driving this relationship varies between the sexes.

The observations made in the current study using an entirely male sample align closely with our previous work using an all-female sample (Szczygiel et al., 2018). However, there are several minor differences between the male and female samples worth noting. While there was no statistical difference, males preferred higher sucrose concentrations (Males: 12.88±10.57 %w/v, Females: 10.27±9.18 %w/v, P=0.1925). Other studies have reported similar findings (Enns et al., 1979; Greene et al., 1975). The male sample in this study had a higher spread around the mean TST compared to the female study and had a lower average TST (Males 5.5±1.7 h, Females 6.42±1.1 h, P=0.0024). Differences of similar magnitude have been reported in a large epidemiological study (Lauderdale et al., 2006). These differences, while minor, may be useful to researchers investigating sex differences in sleep and/or food sensory studies.

The significant difference in sweet taste preference between HRS and LRS groups and between longer and shorter sleeper groups suggest that sleep may be a useful variable to control in sensory studies, particularly when sweetness liking is being assessed. However, it is typically not feasible for sensory scientists to control for objective total sleep due to the difficulty in obtaining objective sleep data from participants. Unfortunately, subjective sleep measures, such

as the PSQI, are not associated with objective sleep measures (Buysse et al., 2008); therefore, there is a need for a proxy measure for objective sleep quality that can be rapidly measured during food sensory studies. While the PSQI composite score was not related to any objective sleep measure in the current study, a simple 100-mm line scale (SR) was found to be significantly correlated with SWS and SWS+REM (n=51). However, this measure did not predict sweet taste preference directly. It is possible that this sleep rating represents a holistic evaluation of the previous night sleep, which is best predicted by the duration of SWS. Even so, given that SWS+REM is one of the strongest predictors of sweet taste preference in both males and females (Szczygiel et al., 2018), this simple 100-mm line-scale may be suitable for use in controlling sleep-related bias or screening out participants in psychophysical experiments without objectively measuring sleep. However, more research needs to be done to establish an appropriate lower-limit of previous night subjective sleep quality which can reliably be used to reduce sleep-related bias in psychophysical studies.

Contrary to what has been reported regarding female-only samples, we observed an association between objective sleep measures and olfactory function in non-obese males. Olfactory identification ability was directly correlated with TST. This is consistent with previously published literature using a primarily male sample that reported negatively impacted olfactory identification ability after 24 (Killgore & McBride, 2006) and 52 (McBride et al., 2006) h of sleep deprivation. There is growing evidence that sleep is related to memory recall and that REM and NREM sleep are thought to each play distinct roles in memory processing (Smith, 2001). REM is thought to play a major role in procedural memory ("knowing how") and NREM sleep is thought to be essential to declarative memory ("knowing what") (Smith, 2001). Odor identification is a type of memory recall task that is declarative in nature. Therefore, it is

surprising to see that REM sleep is correlated with odor identification. Evidence from rodent models suggests that both the strength and precision of odor memories is sleep-dependent and particularly associated with SWS (Barnes & Wilson, 2014). In the present study, SWS was not correlated with odor identification. However, when summed with light sleep, as NREM sleep (SWS+light), an association was observed. TST was the strongest predictor of odor identification ability, suggesting that total duration may be more important than sleep architecture in this relationship. The most likely explanation for why these associations were not observed in another study using females (Szczygiel et al., 2018) is that the male sample in this study had lower TST on average than the females (Males 5.5±1.7 h, Females 6.42±1.1 h, P=0.0024) and olfactory function associations may only become significant when sleep is "sufficiently insufficient". Previous research has hypothesized that olfactory identification ability is only inhibited when sleep is insufficient enough to impair metabolic function to the prefrontal cortex, a known consequence of sleep deprivation (Kapur et al., 1995; Thomas et al., 2000).

There is limited research studying the relationships between sleep, chemosensory function and taste preferences, the majority of which have opted to use both males and females despite the possibility of sex-differences (Furchtgott & Willingham, 1956; Hogenkamp et al., 2013; Killgore & McBride, 2006; Lv, Finlayson, & Dando, 2018; McBride et al., 2006; Smith et al., 2016; Szczygiel et al., 2018). Further, these studies vary widely in their objectives. One study investigated multiple basic tastes and found that sweet and salty thresholds were not associated with sleep duration, but that sour and umami tastes were (Lv et al., 2018). This study used a predominantly female sample (Males n=10, Females n=47). Three studies have assessed taste preferences in relation to sleep. The first (Male n=9, females n=42) found sweet taste preference was increased after curtailing sleep of habitual long sleepers (Smith et al., 2016). Another study

used a male-only sample (n=16) and found that sweet preference in yogurt was not altered after acute sleep deprivation (Hogenkamp et al., 2013). Two studies have assessed odor identification ability after sleep deprivation using mixed-sex samples (Males n=19, 22, females n=5,16, respectively) and found odor identification was altered post-sleep deprivation (Killgore & McBride, 2006; McBride et al., 2006). One study reported a direct association between sleep fragmentation and "wake after sleep onset" and odor identification ability in older adults (McSorley et al., 2017). Contrary to findings in the current study, another recent study found that partial sleep restriction reduced olfactory performance (threshold, detection, and identification) in women and increased performance in men (McNeil et al., 2017) using a mixed-sex sample (Males n=12, females n=6). Only one study has characterized sweet taste acuity, sweet taste preference, and olfactory function and found that only sweet preference was associated with objectively measured sleep duration (females only, n=56) (Szczygiel et al., 2018). Differences in methodology and objectives, such as sleep modification (curtailment or deprivation) and varying stimuli (food or model systems) make it difficult to compare findings across studies. In total, the body of work discussed here consists of 183 female and 54 male study participants, illustrating a tendency to use predominantly female samples, which may lead to results with limited generalizability. Results from this study suggest that, while there are similarities between males and females, there are important differences, such as odor identification ability, to consider.

While this is the fourth psychophysical study to suggest that sleep architecture and duration are related to sweet taste preference, this study contrasts with (Hogenkamp et al., 2013) who found no change in liking of six yogurt samples ranging in sweetness from 2-29 %w/w sucrose after total sleep deprivation using an all-male sample. However, key differences in methodology exist between the two studies. Hogenkamp used a relatively small sample (n=16)

and delivered sweetness in a complex food matrix (yogurt), using a single bite. The Monell preference test used in the present study is a different measure of the perception of sweetness, as it is designed to hone in on the preference level through repeated presentation of pairs of solutions of sucrose. These differences may explain the contradictory findings between the two studies. A second study found that sweet taste preference was higher after sleep curtailment for those who were habitual long sleepers (>7h) (Smith et al., 2016). A third study found that sweet taste preference was inversely related to TST, REM and REM+SWS duration (Szczygiel et al., 2018). All three studies discussed above, as well as the current study, found no changes in sweet threshold or intensity perception. This collection of findings suggests that insufficient sleep may induce cognitive changes that result in altered processing of chemosensory information, but that these changes are not mediated by changes to chemosensory function.

4.1. Study Strengths and Limitations

The strengths of this study include the use of the Zmachine EEG to objectively measure the sleep of participants in their habitual sleep environment. Not only is this a more reliable than self-report (Lauderdale, Knutson, Yan, Liu, & Rathouz, 2008), but it also enables objective sleep measurement to occur in the home, removing any discomfort associated with sleeping in a foreign lab environment. Further, possible confounding factors such as obesity, sex, and age were controlled for using strict recruitment criteria. Limitations of this study include food intake not being recorded or measured in any way, which could influence gustatory and olfactory acuity (Meilgaard, Carr, Civille, Carr, & Civille, 1999); although, participants were told not to consume food at least an hour before testing. Additionally, physical activity between wake-time and testing was not monitored or recorded, which could influence preference for sweetness (Horio & Kawamura, 1998). Finally, while we recruited participants who claimed to have no sleep issues

and who habitually slept 7-9 h per night, not all participants succeeded in sleeping 7h the night prior to testing and some scored ≥5 on the PSQI indicating that they may have been experiencing disordered sleep.

5. Conclusions

Non-obese male participants who had a shorter night sleep with less REM and SWS sleep preferred higher concentrations of sweetness. Participant's sweet taste preference was inversely associated with both sleep architecture and TST and was most strongly predicted by REM sleep duration. These findings are in agreement with previous research that found similar results using a female sample, indicating that this effect is not sex-specific. These findings could point toward a mechanism by which insufficient sleep and excessive food intake are related. Additionally, higher TST and REM duration was associated with improved odor identification ability, contrary to findings in previous literature using only females, suggesting a possible sex difference. Associations between sweet taste preference and olfactory identification ability appeared to be independent of differences in olfactory or gustatory thresholds, suggesting changes in hedonic perception rather than a change chemosensory function. This research corroborates our previous suggestion that it may be beneficial to control for sleep habits in sensory studies where hedonic are of interest due to the significant variation in sweet preference associated with REM & SWS. Future work should investigate if a curtailment intervention can elicit changes in hedonic perception in individuals using a repeated measures approach and investigate whether these changes are likely to cause behavioral changes such as modified, e.g., sweeter, food choices.

REFERENCES

REFERENCES

Alvarez Gonzalo G., & Ayas Najib T. (2007). The impact of daily sleep duration on health: A review of the literature. *Progress in Cardiovascular Nursing*, *19*(2), 56–59. https://doi.org/10.1111/j.0889-7204.2004.02422.x.

Barnes, D. C., & Wilson, D. A. (2014). Sleep and olfactory cortical plasticity. *Frontiers in Behavioral Neuroscience*, *8*, 134. https://doi.org/10.3389/fnbeh.2014.00134

Bartoshuk, L. M., Duffy, V. B., & Miller, I. J. (1994). PTC/PROP tasting: Anatomy, psychophysics, and sex effects. *Physiology & Behavior*, *56*(6), 1165–1171.

Benedict, C., Brooks, S. J., O'Daly, O. G., Almèn, M. S., Morell, A., Åberg, K., … Schiöth, H. B. (2012). Acute sleep deprivation enhances the brain's response to hedonic food stimuli: An fMRI study. *The Journal of Clinical Endocrinology & Metabolism*, *97*(3), E443–E447. https://doi.org/10.1210/jc.2011-2759.

Bon, O. L., Staner, L., Hoffmann, G., Dramaix, M., Sebastian, I. S., Murphy, J. R., … Linkowski, P. (2001). The first-night effect may last more than one night. *Journal of Psychiatric Research*, *35*(3), 165–172. https://doi.org/10.1016/S0022-3956(01)00019-X.

Brand, G., & Millot, J.-L. (2001). Sex differences in human olfaction: Between evidence and enigma. *The Quarterly Journal of Experimental Psychology Section B*, *54*(3), 259–270. https://doi.org/10.1080/713932757.

Buysse, D. J., Hall, M. L., Strollo, P. J., Kamarck, T. W., Owens, J., Lee, L., … Matthews, K. A. (2008). Relationships between the Pittsburgh sleep quality index (PSQI), Epworth sleepiness scale (ESS), and clinical/polysomnographic measures in a community sample. *Journal of Clinical Sleep Medicine : JCSM : Official Publication of the American Academy of Sleep Medicine*, *4*(6), 563–571.

Buysse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Research*, *28*(2), 193–213. https://doi.org/10.1016/0165-1781(89)90047-4.

Cappuccio, F. P., Cooper, D., D'Elia, L., Strazzullo, P., & Miller, M. A. (2011). Sleep duration predicts cardiovascular outcomes: A systematic review and meta-analysis of prospective studies. *European Heart Journal*, *32*(12), 1484–1492. https://doi.org/10.1093/eurheartj/ehr007.

Carskadon, M. A., Dement, W. C. (2005). Normal human sleep: An overview. *Principles and Practice of Sleep Medicine*, *4*, 13–23.

Cauter, E. V., Leproult, R., & Plat, L. (2000). Age-related changes in slow wave sleep and REM sleep and relationship with growth hormone and cortisol levels in healthy men. *JAMA*, *284*(7), 861–868. https://doi.org/10.1001/jama.284.7.861

Chapman, C. D., Benedict, C., Brooks, S. J., & Birgir Schiöth, H. (2012). Lifestyle determinants of the drive to eat: a meta-analysis–. *The American Journal of Clinical Nutrition*, *96*(3), 492–497.

Cornier, M.-A., Salzberg, A. K., Endly, D. C., Bessesen, D. H., & Tregellas, J. R. (2010). Sex-based differences in the behavioral and neuronal responses to food. *Physiology & Behavior, 99*(4), 538–543.

Curcio, G., Ferrara, M., & De Gennaro, L. (2006). Sleep loss, learning capacity and academic performance. *Sleep Medicine Reviews*, *10*(5), 323–337.

Demos, K. E., Sweet, L. H., Hart, C. N., McCaffery, J. M., Williams, S. E., Mailloux, K. A., … Wing, R. R. (2017). The effects of experimental manipulation of sleep duration on neural response to food cues. *Sleep*, *40*(11). https://doi.org/10.1093/sleep/zsx125.

Doty, R. L., Applebaum, S., Zusho, H., & Settle, R. G. (1985). Sex differences in odor identification ability: A cross-cultural analysis. *Neuropsychologia*, *23*(5), 667–672. https://doi.org/10.1016/0028-3932(85)90067-3.

Dressler, H., & Smith, C. (2013). Food choice, eating behavior, and food liking differs between lean/normal and overweight/obese, low-income women. *Appetite*, *65*, 145–152.

Enns, M. P., Van Itallie, T. B., & Grinker, J. A. (1979). Contributions of age, sex and degree of fatness on preferences and magnitude estimations for sucrose in humans. *Physiology & Behavior*, *22*(5), 999–1003. https://doi.org/10.1016/0031-9384(79)90346-9.

Epel, E., Lapidus, R., McEwen, B., & Brownell, K. (2001). Stress may add bite to appetite in women: A laboratory study of stress-induced cortisol and eating behavior. *Psychoneuroendocrinology*, *26*(1), 37–49.

Furchtgott, E., & Willingham, W. W. (1956). The effect of sleep-deprivation upon the thresholds of taste. *The American Journal of Psychology*, *69*, 111-112.

Glanz, K., Basil, M., Maibach, E., Goldberg, J., & Snyder, D. A. N. (1998). Why Americans eat what they do: Taste, nutrition, cost, convenience, and weight control concerns as influences on food consumption. *Journal of the American Dietetic Association*, *98*(10), 1118–1126.

Golley, R. K., Maher, C. A., Matricciani, L., & Olds, T. S. (2013). Sleep duration or bedtime? Exploring the association between sleep timing behaviour, diet and BMI in children and adolescents. *International Journal of Obesity*, *37*(4), 546. https://doi.org/10.1038/ijo.2012.212.

Gonnissen, H. K. J., Adam, T. C., Hursel, R., Rutters, F., Verhoef, S. P. M., & Westerterp-Plantenga, M. S. (2013). Sleep duration, sleep quality and body weight: Parallel developments. *Physiology & Behavior*, *121*, 112–116. https://doi.org/10.1016/j.physbeh.2013.04.007.

Greene, L. S., Desor, J. A., & Maller, O. (1975). Heredity and experience: Their relative importance in the development of taste preference in man. *Journal of Comparative and Physiological Psychology*, *89*(3), 279.

Gujar, N., Yoo, S.-S., Hu, P., & Walker, M. P. (2011). Sleep deprivation amplifies reactivity of brain reward networks, biasing the appraisal of positive emotional experiences. *Journal of Neuroscience*, *31*(12), 4466–4474. https://doi.org/10.1523/JNEUROSCI.3220-10.2011.

Haase, L., Green, E., & Murphy, C. (2011). Males and females show differential brain activation to taste when hungry and sated in gustatory and reward areas. *Appetite*, *57*(2), 421–434.

Hanlon, E. C., Andrzejewski, M. E., Harder, B. K., Kelley, A. E., & Benca, R. M. (2005). The effect of REM sleep deprivation on motivation for food reward. *Behavioural Brain Research*, *163*(1), 58–69. https://doi.org/10.1016/j.bbr.2005.04.017.

Hirshkowitz, M., Whiton, K., Albert, S. M., Alessi, C., Bruni, O., DonCarlos, L., … Ware, J. C. (2015). National Sleep Foundation's updated sleep duration recommendations: Final report. *Sleep Health*, *1*(4), 233–243. https://doi.org/10.1016/j.sleh.2015.10.004.

Hjorth, M. F., Quist, J. S., Andersen, R., Michaelsen, K. F., Tetens, I., Astrup, A., … Sjödin, A. (2014). Change in sleep duration and proposed dietary risk factors for obesity in Danish school children. *Pediatric Obesity*, *9*(6), e156–e159. https://doi.org/10.1111/ijpo.264.

Hogenkamp, P. S., Nilsson, E., Nilsson, V. C., Chapman, C. D., Vogel, H., Lundberg, L. S., … Schiöth, H. B. (2013). Acute sleep deprivation increases portion size and affects food choice in young men. *Psychoneuroendocrinology*, *38*(9), 1668–1674. https://doi.org/10.1016/j.psyneuen.2013.01.012.

Horio, T., & Kawamura, Y. (1998). Influence of physical exercise on human preferences for various taste solutions. *Chemical Senses*, *23*(4), 417–421.

Horne, J. A. (2015). Human REM sleep: Influence on feeding behaviour, with clinical implications. *Sleep Medicine*, *16*(8), 910–916. https://doi.org/10.1016/j.sleep.2015.04.002.

Kanda, T., Tsujino, N., Kuramoto, E., Koyama, Y., Susaki, E. A., Chikahisa, S., & Funato, H. (2016). Sleep as a biological problem: An overview of frontiers in sleep research. *The Journal of Physiological Sciences*, *66*(1), 1–13. https://doi.org/10.1007/s12576-015-0414-3.

Kaplan, R. F., Wang, Y., Loparo, K. A., Kelly, M. R., & Bootzin, R. R. (2014). Performance evaluation of an automated single-channel sleep–wake detection algorithm. *Nature and Science of Sleep*, *6*, 113–122. https://doi.org/10.2147/NSS.S71159.

Kapur, S., Craik, F. I., Jones, C., Brown, G. M., Houle, S., & Tulving, E. (1995). Functional role of the prefrontal cortex in retrieval of memories: A PET study. *Neuroreport*, *6*(14), 1880–1884.

Kenny, P. J. (2011). Reward mechanisms in obesity: New insights and future directions. *Neuron*, *69*(4), 664–679. https://doi.org/10.1016/j.neuron.2011.02.016.

Killgore, W. D. S., & McBride, S. A. (2006). Odor identification accuracy declines following 24 h of sleep deprivation. *Journal of Sleep Research*, *15*(2), 111–116. https://doi.org/10.1111/j.1365-2869.2006.00502.x.

Krystal, A. D., & Edinger, J. D. (2008). Measuring sleep quality. *Sleep Medicine*, *9*, S10–S17. https://doi.org/10.1016/S1389-9457(08)70011-X.

Lauderdale, D. S., Knutson, K. L., Yan, L. L., Liu, K., & Rathouz, P. J. (2008). Sleep duration: How well do self-reports reflect objective measures? The CARDIA Sleep Study. *Epidemiology (Cambridge, Mass.)*, *19*(6), 838–845. https://doi.org/10.1097/EDE.0b013e318187a7b0.

Lauderdale, D. S., Knutson, K. L., Yan, L. L., Rathouz, P. J., Hulley, S. B., Sidney, S., & Liu, K. (2006). Objectively measured sleep characteristics among early-middle-aged adults: The CARDIA Study. *American Journal of Epidemiology*, *164*(1), 5–16. https://doi.org/10.1093/aje/kwj199.

Lauer, C., Schreiber, W., Berger, M., Pirke, K.-M., Holsboer, F., & Krieg, J.-C. (1989). The effect of neuroendocrine secretion on brain morphology and EEG sleep in patients with eating disorders. *European Archives of Psychiatry and Neurological Sciences*, *238*(4), 208–212. https://doi.org/10.1007/BF00381467.

Lv, W., Finlayson, G., & Dando, R. (2018). Sleep, food cravings and taste. *Appetite*, *125*, 210–216. https://doi.org/10.1016/j.appet.2018.02.013.

Markwald, R. R., Melanson, E. L., Smith, M. R., Higgins, J., Perreault, L., Eckel, R. H., & Wright, K. P. (2013). Impact of insufficient sleep on total daily energy expenditure, food intake, and weight gain. *Proceedings of the National Academy of Sciences*, *110*(14), 5695–5700. https://doi.org/10.1073/pnas.1216951110.

Martin, L. J., & Sollars, S. I. (2017). Contributory role of sex differences in the variations of gustatory function. *Journal of Neuroscience Research*, *95*(1–2), 594–603. https://doi.org/10.1002/jnr.23819.

McBride, S. A., Balkin, T. J., Kamimori, G. H., & Killgore, W. D. S. (2006). Olfactory decrements as a function of two nights of sleep deprivation. *Journal of Sensory Studies*, *21*(4), 456–463. https://doi.org/10.1111/j.1745-459X.2006.00080.x.

McNeil, J., Forest, G., Hintze, L. J., Brunet, J.-F., Finlayson, G., Blundell, J. E., & Doucet, É. (2017). The effects of partial sleep restriction and altered sleep timing on appetite and food reward. *Appetite*, *109*, 48–56. https://doi.org/10.1016/j.appet.2016.11.020.

McSorley, V. E., Pinto, J., Schumm, L. P., Wroblewski, K., Kern, D., McClintock, M., & Lauderdale, D. S. (2017). Sleep and olfaction among older adults. *Neuroepidemiology*, *48*(3–4), 147–154. https://doi.org/10.1159/000479066.

Meilgaard, M. C., Carr, B. T., Civille, G. V., Carr, B. T., & Civille, G. V. (1999). *Sensory Evaluation Techniques*. CRC Press. https://doi.org/10.1201/9781439832271.

Mennella, J. A., Lukasewycz, L. D., Griffith, J. W., & Beauchamp, G. K. (2011). Evaluation of the Monell forced-choice, paired-comparison tracking procedure for determining sweet taste preferences across the lifespan. *Chemical Senses*, *36*(4), 345–355. https://doi.org/10.1093/chemse/bjq134

Menzies, J. R. W., Skibicka, K. P., Leng, G., & Dickson, S. L. (2013). Ghrelin, reward and motivation. *Endrocr Dev*, *25*, 101–111. https://doi.org/10.1159/000346058.

Nedeltcheva, A. V., Kilkus, J. M., Imperial, J., Kasza, K., Schoeller, D. A., & Penev, P. D. (2009). Sleep curtailment is accompanied by increased intake of calories from snacks. *The American Journal of Clinical Nutrition*, *89*(1), 126–133. https://doi.org/10.3945/ajcn.2008.26574.

Neter, J., Kutner, M. H., Nachtsheim, C. J., & Wasserman, W. (1996). *Applied linear statistical models* (Vol. 4). Irwin Chicago. Retrieved from https://mubert.marshall.edu/bert/syllabi/32862015011408990509712 2.pdf.

Norgren, R., Hajnal, A., & Mungarndee, S. S. (2006). Gustatory reward and the nucleus accumbens. *Physiology & Behavior*, *89*(4), 531–535. https://doi.org/10.1016/j.physbeh.2006.05.024.

Prather, A. A., Leung, C., Adler, N. E., Epel, E. S., Ritchie, L., & Laraia, B. (2014). Abstract P110: Short and sweet: Short sleep duration is associated with increased sugar sweetened beverage consumption in the United States. *Circulation*, *129*(Suppl 1), AP110–AP110.

Roth, T. (2009). Slow wave sleep: Does it matter? *Journal of Clinical Sleep Medicine : JCSM : Official Publication of the American Academy of Sleep Medicine*, *5*(2 Suppl), S4–S5.

Royet, J.-P., Plailly, J., Delon-Martin, C., Kareken, D. A., & Segebarth, C. (2003). fMRI of emotional responses to odors: Influence of hedonic valence and judgment, handedness, and gender. *NeuroImage*, *20*(2), 713–728. https://doi.org/10.1016/S1053-8119(03)00388-4.

Shechter, A., O'Keeffe, M., Roberts, A. L., Zammit, G. K., RoyChoudhury, A., & St-Onge, M.-P. (2012). Alterations in sleep architecture in response to experimental sleep curtailment are associated with signs of positive energy balance. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*, *303*(9), R883–R889. https://doi.org/10.1152/ajpregu.00222.2012.

Siegel, J. M. (2001). The REM sleep-memory consolidation hypothesis. *Science*, *294*(5544), 1058–1063. https://doi.org/10.1126/science.1063049.

Silva, L. da, Lin, S. M., Teixeira, M. J., Siqueira, J. de, Filho, W. J., & Siqueira, S. de. (2014). Sensorial differences according to sex and ages. *Oral Diseases*, *20*(3), e103–e110. https://doi.org/10.1111/odi.12145.

Smith. (2001). Sleep states and memory processes in humans: Procedural versus declarative memory systems. *Sleep Medicine Reviews*, *5*(6), 491–506. https://doi.org/10.1053/smrv.2001.0164.

Smith, S. L., Ludy, M.-J., & Tucker, R. M. (2016). Changes in taste preference and steps taken after sleep curtailment. *Physiology & Behavior*, *163*, 228–233. https://doi.org/10.1016/j.physbeh.2016.05.002.

Sørensen, L. B., Møller, P., Flint, A., Martens, M., & Raben, A. (2003). Effect of sensory perception of foods on appetite and food intake: A review of studies on humans. *International Journal of Obesity*, *27*(10), 1152.

St-Onge, M.-P. (2017). Sleep–obesity relation: Underlying mechanisms and consequences for treatment. *Obesity Reviews*, *18*(S1), 34–39. https://doi.org/10.1111/obr.12499.

St-Onge, M.-P., McReynolds, A., Trivedi, Z. B., Roberts, A. L., Sy, M., & Hirsch, J. (2012). Sleep restriction leads to increased activation of brain regions sensitive to food stimuli. *The American Journal of Clinical Nutrition*, *95*(4), 818–824. https://doi.org/10.3945/ajcn.111.027383.

Szczygiel, E., Cho, S., & Tucker, R. (2018). Characterization of the relationships between sleep duration, quality, architecture and chemosensory function in non-obese females. *Chemical Senses*, *43*(4), 223–228. https://doi.org/10.1093/chemse/bjy012.

Thomas, M., Sing, H., Belenky, G., Holcomb, H., Mayberg, H., Dannals, R., … Redmond, D. (2000). Neural basis of alertness and cognitive performance impairments during sleepiness. I.

Effects of 24 h of sleep deprivation on waking human regional brain activity. *Journal of Sleep Research*, *9*(4), 335–352. https://doi.org/10.1046/j.1365-2869.2000.00225.x.

van der Lely, A. J., Tschöp, M., Heiman, M. L., & Ghigo, E. (2004). Biological, physiological, pathophysiological, and pharmacological aspects of ghrelin. *Endocrine Reviews*, *25*(3), 426–457. https://doi.org/10.1210/er.2002-0029.

Vgontzas, A. N., Bixler, E. O., & Basta, M. (2010). Obesity and sleep: A bidirectional association? *Sleep*, *33*(5), 573–574. https://doi.org/10.1093/sleep/33.5.573.

Wager, T. D., Phan, K. L., Liberzon, I., & Taylor, S. F. (2003). Valence, gender, and lateralization of functional brain anatomy in emotion: a meta-analysis of findings from neuroimaging. *NeuroImage*, *19*(3), 513–531. https://doi.org/10.1016/S1053-8119(03)00078-8.

Walker, M. P., & van der Helm, E. (2009). Overnight therapy? The role of sleep in emotional brain processing. *Psychological Bulletin*, *135*(5), 731–748. https://doi.org/10.1037/a0016570.

Wang, Y., Loparo, K. A., Kelly, M. R., & Kaplan, R. F. (2015). Evaluation of an automated single-channel sleep staging algorithm. *Nature and Science of Sleep*, *7*, 101–111. https://doi.org/10.2147/NSS.S77888.

Westenhoefer, J. (2005). Age and gender dependent profile of food choice. *Diet Diversification and Health Promotion, 57*, 44–51. https://doi.org/10.1159/000083753.

Chapter 3:

There is great interest from both the food industry and consumers to reduce added sugar in foods. Non-nutritive sweeteners (NNS), which provide no energy, are one possible route by which sugar can be reduced in foods. However, replacing sugar with NNS in food presents many challenges, such as determining iso-sweet concentrations of NNS and sugar. While some tools exist for iso-sweet substitution of sucrose for NNS, many have only been evaluated in complex food matrices and do not use currently popular sweeteners, limiting their application in modern psychophysics and product development. Therefore, the objective of this study was to develop iso-sweet matching tools for sucralose, pure stevia-derived rebaudioside M, and a steviol glycoside blend using a wide range of sweetness levels for use in developing new food products and a modified taste-evaluation protocol. Consumer-based magnitude estimation was used to compare sweetness intensity of the sweeteners to a fixed 12% w/v sucrose reference. Power functions were developed using the data for all sweeteners and equal-sweet concentrations of sucralose and rebaudioside M were calculated for 3, 6, 12, 24, and 36% w/v sucrose. These functions may prove useful to sensory scientists studying the use of sucralose or stevia in reduced sugar foods or researchers who wish to modify existing taste evaluation protocols for use with artificial or natural NNS. However, the steviol glycoside blend had too much bitter off-taste to be evaluated effectively by consumers, rendering the power function unreliable.

1. Introduction

In response to the rise of obesity and other non-communicable diseases related to sugar consumption (Lustig, Schmidt, & Brindis, 2012), the food industry has shown great interest in reducing added sugars in food products. One strategy for reducing sugar in food products is the

use of non-nutritive sweeteners (NNS), which can replace the sweetness of sugar in the absence of energy. When developing new food products with reduced sugar, substituting sucrose with a concentration of NNS that provides the same sweetness as sucrose is key to product success. Artificial sweeteners, such as sucralose, aspartame, and saccharin, have been used for many years in a wide variety of food products (Shankar, Ahuja, & Sriram, 2013). Sucralose is one of the most widely utilized artificial sweeteners in commercial food and beverage products (Ng, Slining, & Popkin, 2012) due to its sugar-like sensory properties as well as its heat and pH stability (Binns, 2003).

Despite the wide-spread use of sucralose and other artificial sweeteners, concerns about the health effects of these sweeteners have caused consumer interest to shift towards natural NNS alternatives (Pawar, Krynitsky, & Rader, 2013). This shift has resulted in the need to replace artificial NNS with natural NNS in many food products. For example, steviol glycosides extracted from the leaf of *Stevia rebaudiana* plants, commonly referred to as "stevia sweeteners", are rapidly increasing in popularity among consumers and were included in over 14,000 new food and beverage products launched between 2011 and 2016 ("Global Food and Beverage Products with Stevia: 2011–2016 Data.," 2017).

With increased consumer and food industry interest in replacing sucrose and artificial NNS with natural NNS in food, more sensory and psychophysics researchers are investigating factors which influence sensory and hedonic response to NNS and how to optimally incorporate natural NNS into foods. However, many psychophysical sweet taste evaluation protocols are designed using sucrose dissolved in water over a wide range of sweetness levels and are not easily modified to be used with NNS. For example, the Monell sweet preference determination protocol (Mennella, Lukasewycz, Griffith, & Beauchamp, 2011), includes sucrose concentrations

ranging from 3-36% w/v sucrose, while many of the available resources for sucrose solution substitution only utilize a small range (0-9 % w/v sucrose equivalency),e.g., (Moskowitz, 1970a). One study, which used a wide range of sweetness levels excluded the current most commonly used commercial artificial NNS, sucralose, and used low purity stevia lead extracts, which are no longer the state-of-the-art (Cardello, Silva, & Damasio, 1999). Further, the limited range of sweetness studied in previous explorations of equal-sweet concentrations of NNS and sucrose are not suitable for replacing sucrose in highly sweet foods, such as frozen desserts, which generally 15-20% w/v sucrose (Goff, 2015). Several recent studies have evaluated wide ranges of sweetness in complex food matrices (e.g. (Cardoso & Bolini, 2007; De Souza et al., 2011)), but these are not applicable to model systems with prototypical tastants dissolved in water or other foods. Therefore, an updated sweetness equivalency resource for the most popular sweeteners using a wide range of sweetness levels is needed to aid in psychophysics research and new food product development.

One commonly used methodology to obtain iso-sweet concentrations of sweeteners is magnitude estimation. Magnitude estimation data can be normalized using Steven's Power Function (Moskowitz, 1970a), and the resulting equations can be used to determine iso-sweet concentrations between sweeteners. While magnitude estimation methods traditionally utilize 8-10 trained sensory panelists, recent studies have demonstrated that larger samples of 40-50 naïve consumers are equally effective at determining iso-sweet concentrations of sweeteners (Reis, De Andrade, Deliza, & Ares, 2016).

The sweet taste of stevia comes from steviol glycosides which are naturally found in stevia leaf (I. Prakash, DuBois, Clos, Wilkens, & Fosdick, 2008). Stevioside and rebaudioside A (Reb A) are the most abundant glycosides found in stevia, but they have undesirable bitter

aftertaste (Goyal, Samsher, & Goyal, 2010). While blends of different steviol glycosides have been used widely in commercial predicts, Reb M, a minor glycoside in stevia leaf, has garnered much attention as it has been shown to have higher sweetness intensity and less off-taste than other steviol glycosides (Indra Prakash, Markosyan, & Bunders, 2014). Given the differences between the sweet potency and the level of off-taste between steviol glycosides, iso-sweet evaluation of individual glycosides of interest as well as blends of glycosides is merited. Therefore, the objective of this study was to use magnitude estimation to develop iso-sweet concentrations of sucrose, sucralose, purified stevia Reb M, and a commercial blend of steviol glycosides.

2. Materials and Methods

2.1. Participants

Three-hundred and two participants between the ages of 18-65 were recruited. Nine participants were removed from the final dataset due to failure to follow instructions. The remaining 293 participants were used for all data analysis. No exclusion criteria were used.

2.2. Sensory Evaluation

Prior to tasting any stimuli, participants were provided a script that explained the procedure for evaluating the samples (Moskowitz, 1977). After familiarizing themselves with the fixed reference sample, a solution sweetened with 12% w/v sucrose, participants were provided samples to evaluate in random order. For each sample, participants rated the sweetness intensity relative to the reference sample (Moskowitz, 1977).

Sensory evaluation took place over the course of three days. Sucrose and Sucralose (Sweet Solutions, Edison, NJ) were evaluated on day one. On day two and three, 95% pure Reb M (BESTEVIA® Reb M stevia leaf sweetener, Ingredion, Westchester, IL) and a commercial steviol glycoside blend (ENLITEN® Fusion 6400, Ingredion, Westchester, IL) were evaluated, respectively. A preliminary study (n=20) revealed that participants had no difficulty evaluating six sucrose and sucralose samples. The sucrose concentrations participants tasted were 3%, 6%, 9% 12%, 24%, and 36% w/v and the sucralose concentrations were 0.005%, 0.015%, 0.03%, 0.06%, 0.08%, and 0.16% w/v. However, participants reported difficulty evaluating more than three stevia samples at a time due to bitter and lingering off-tastes, which have been reported previously for Reb A (I. Prakash et al., 2008). As there is almost no published literature. Therefore, two sets of 50 participants were recruited to evaluate three samples of stevia. The first group evaluated 0.03%, 0.12% and 0.4% w/v and the second group evaluated 0.07%, 0.24%, 0.6% %w/v Reb M and Reb blend. Power functions for each sweetener were calculated using Excel (Microsoft, Redmond, WA, U.S.)

3. Results

3.1. Participants

A summary of self-reported demographic and anthropometric variables are summarized in Table 3.1.

Table 3.1. Summary of Participants Characteristics

Sex	n
Male	93
Female	200
Anthropometrics	Mean (SD)
BMI (kg/m^2)	24.78 (5.82)
Age (y)	30 (12.4)

3.2. Magnitude estimation

Four power functions, one for each sweetener, were calculated using the magnitude estimations for a range of sweeteners compared to a fixed 12% sucrose reference (Table 3.2). For the stevia sweeteners, the set of concentrations with the higher R value (0.03%, 0.12% and 0.4% w/v.), indicating a more consistent relationship between magnitude estimation and concentration (Moskowitz, 1977), was chosen for further data analysis and the other set was discarded. The Reb blend showed a low linear correlation coefficient (0.08089) relative to the other sweeteners (0.09225-0.9868), indicating inconsistent responses as sweetener concentration increased for this sweetener. Iso-sweet concentrations of each sweetener for a range of sucrose concentrations were calculated using the power functions (Table 3.3).

Table 3.2. Slopes, Y-intercept, linear correlation coefficients and power functions

Sweetener	Slope	Y-intercept	R[a]	Power function
Sucrose	1.3090	-0.4730	0.9225	$S=0.3365\ C^{1.309}$
Sucralose	0.8413	2.1936	0.9868	$S=156.18\ C^{0.8413}$
Reb M	0.6968	1.1910	0.9461	$S=15.523\ C^{0.6968}$
Reb Blend	1.0812	1.4929	0.8089	$S=31.112\ C^{1.0812}$

[a] R = Linear correlation coefficient

Table 3.3. Iso-sweet concentration at different percentages of sucrose

Sucrose (% w/v)	Sucralose (% w/v)	Reb M (% w/v)	Reb blend (% w/v)
3	0.004	0.032	0.058
6	0.011	0.118	0.133
12	0.032	0.436	0.308
18	0.060	0.934	0.503
24	0.095	1.607	0.714
36	0.178	3.438	1.165

4. Discussion

The power function obtained for sucrose and sucralose agrees with previous power functions obtained for the sweeteners using smaller ranges (Moskowitz, 1970b). These power functions can be used to calculate the iso-sweet concentration of two sweeteners per the methods described in (Moskowitz, 1970b). While iso-sweet concentration determined using these functions may not function perfectly in all food matrices, they will serve as a useful guide to begin replacing sucrose and sucralose in highly sweet foods, such as ice-cream.

Further, these iso-sweet concentrations may be useful to psychophysics researchers who wish to determine sweet taste responses using a non-nutritive sweetener (Szczygiel, Cho, & Tucker, , 2019.). For example, the iso-sweet concentrations presented in Table 3 include the concentrations used in the commonly used Monell forced-choice paired comparison sweet preference evaluation protocol (Mennella et al., 2011).

Others have reported issues substituting sucrose with Reb A at high concentrations due to high amounts of off-taste (Cardello et al., 1999; Cardoso & Bolini, 2007). The power function and correlation coefficient observed for the steviol glycoside blend is similar to what has been reported in peach nectar using a Reb blend over a smaller range of sweetness levels (Cardoso & Bolini, 2007). The functions differed between the two stevia sweeteners, with stevia Reb M providing more sweetness at higher concentration and less sweetness at lower concentrations than the Reb blend. One limitation of this study is that the ratio of steviol glycosides in the Reb blend is unknown. However, Reb A and stevioside are the most abundant glycosides found in stevia plants (Karimi et al., 2015), and are reported to have off and bitter tastes (Goyal et al., 2010). Off tastes provided by Reb A or stevioside may have caused participants to perceive less sweetness relative to Reb M at high concentrations, where off-tastes will dominate. The inability of consumers to effectively evaluate the sweetness for the Reb blend may have altered the function such that, at low concentrations, higher concentrations for equal sweetness are calculated compared to Reb M. The more complex the total perception associated with a sweetener, the greater the variance in intensity response (Tunaley, Thomson, & Mcewan, 1987), and therefore, stevia sweeteners with high amounts of off-tasting glycosides may require specialized approaches for developing sweetness equivalency tools. Substituting sucrose with stevia sweeteners in food may be further

complicated by differences in relative quantities of steviol glycosides in stevia-based sweeteners. It may be necessary for sweetener producers to provide tools for each version of their sweeteners or to provide product developers with steviol glycoside composition to avoid extended formulation duration. Steviol glycoside composition should ideally be determined before attempting to replace sucrose.

5. Conclusions

Using a consumer-based magnitude estimation method, power functions for sucrose, sucralose, Reb M, and a Reb blend were developed. However, the Reb blend function is likely unreliable due to increased off bitter tastes reducing the ability of consumers to estimate sweetness. The functions for sucralose and Reb M may be useful for modification of psychophysical taste protocols and as a starting point for development of products with reduced sucrose.

REFERENCES

REFERENCES

Binns, N. M. (2003). Sucralose – all sweetness and light. *Nutrition Bulletin*, *28*(1), 53–58. https://doi.org/10.1046/j.1467-3010.2003.00307.x.

Cardello, H. M. a. B., Silva, M. A. P. A. D., & Damasio, M. H. (1999). Measurement of the relative sweetness of stevia extract, aspartame and cyclamate/saccharin blend as compared to sucrose at different concentrations. *Plant Foods for Human Nutrition*, *54*(2), 119–129. https://doi.org/10.1023/A:1008134420339.

Cardoso, J. M. P., & Bolini, H. M. A. (2007). Different sweeteners in peach nectar: Ideal and equivalent sweetness. *Food Research International*, *40*(10), 1249–1253. https://doi.org/10.1016/j.foodres.2007.08.004.

De Souza, V. R., Pinheiro, A. C. M., Carneiro, J. D. D. S., Pinto, S. M., Abreu, L. R., & Menezes, C. C. (2011). Analysis of various sweeteners in petit suisse cheese: Determination of the ideal and equivalent sweetness. *Journal of Sensory Studies*, *26*(5), 339–345. https://doi.org/10.1111/j.1745-459X.2011.00349.x.

Global Food and Beverage Products with Stevia: 2011–2016 Data. (2017). *Mintel Global New Products Database*. Retrieved from : www.mintel.com/global-new-products-database.

Goff, H. D. (2015). Ice cream and frozen desserts. In *Ullmann's Encyclopedia of Industrial Chemistry* (pp. 1–15). https://doi.org/10.1002/14356007.a13_563.pub2.

Goyal, S. K., Samsher, G. R., & Goyal, R. K. (2010). Stevia (Stevia rebaudiana) a bio-sweetener: A review. *Int J Food Sci Nutr*, *61*(1), 1–10.

Karimi, M., Ahmadi, A., Hashemi, J., Abbasi, A., Tavarini, S., Guglielminetti, L., & Angelini, L. G. (2015). The effect of soil moisture depletion on Stevia (Stevia rebaudiana Bertoni) grown in greenhouse conditions: Growth, steviol glycosides content, soluble sugars and total antioxidant capacity. *Scientia Horticulturae*, *183*, 93–99. https://doi.org/10.1016/j.scienta.2014.11.001.

Lustig, R. H., Schmidt, L. A., & Brindis, C. D. (2012). Public health: The toxic truth about sugar. *Nature*, *482*(7383), 27.

Mennella, J. A., Lukasewycz, L. D., Griffith, J. W., & Beauchamp, G. K. (2011). Evaluation of the Monell Forced-Choice, Paired-Comparison Tracking Procedure for determining sweet taste preferences across the lifespan. *Chemical Senses*, *36*(4), 345–355. https://doi.org/10.1093/chemse/bjq134.

Moskowitz, H. R. (1970a). Ratio scales of sugar sweetness. *Perception & Psychophysics*, *7*(5), 315–320. https://doi.org/10.3758/BF03210175.

Moskowitz, H. R. (1970b). Sweetness and intensity of artificial sweeteners. *Perception & Psychophysics*, *8*(1), 40–42. https://doi.org/10.3758/BF03208930.

Moskowitz, H. R. (1977). Magnitude estimation: Notes on what, how, when, and why to use it. *Journal of Food Quality*, *1*(3), 195–227. https://doi.org/10.1111/j.1745-4557.1977.tb00942.x.

Ng, S. W., Slining, M. M., & Popkin, B. M. (2012). Use of caloric and noncaloric sweeteners in US consumer packaged foods, 2005-2009. *Journal of the Academy of Nutrition and Dietetics*, *112*(11), 1828-1834.e6. https://doi.org/10.1016/j.jand.2012.07.009.

Pawar, R. S., Krynitsky, A. J., & Rader, J. I. (2013). Sweeteners from plants—with emphasis on Stevia rebaudiana (Bertoni) and Siraitia grosvenorii (Swingle). *Analytical and Bioanalytical Chemistry*, *405*(13), 4397–4407.

Prakash, I., DuBois, G. E., Clos, J. F., Wilkens, K. L., & Fosdick, L. E. (2008). Development of rebiana, a natural, non-caloric sweetener. *Food and Chemical Toxicology*, *46*(7, Supplement), S75–S82. https://doi.org/10.1016/j.fct.2008.05.004.

Prakash, Indra, Markosyan, A., & Bunders, C. (2014). Development of next generation stevia sweetener: Rebaudioside M. *Foods*, *3*(1), 162–175. https://doi.org/10.3390/foods3010162.

Reis, F., De Andrade, J., Deliza, R., & Ares, G. (2016). Comparison of two methodologies for estimating equivalent sweet concentration of high-intensity sweeteners with untrained assessors: Case study with orange/pomegranate juice. *Journal of Sensory Studies*, *31*(4), 341–347. https://doi.org/10.1111/joss.12217.

Shankar, P., Ahuja, S., & Sriram, K. (2013). Non-nutritive sweeteners: Review and update. *Nutrition*, *29*(11), 1293–1299. https://doi.org/10.1016/j.nut.2013.03.024

Szczygiel, E. J., Cho, S., & Tucker, R. M. (2019). Multiple dimensions of sweet taste perception altered after sleep curtailment. *Nutrients, Under Review*.

Tunaley, A., Thomson, D. M. H., & Mcewan, J. A. (1987). Determination of equi-sweet concentrations of nine sweeteners using a relative rating technique. *International Journal of Food Science & Technology*, *22*(6), 627–635. https://doi.org/10.1111/j.1365-2621.1987.tb00530.x.

Chapter 4:

Short sleep duration increases preferences for high-carbohydrate and high-fat foods. It is unclear if insufficient sleep-induced changes in food preference are mediated by changes in taste perception and if these changes are related to sweetener type (sucrose or sucralose) or sweet liking phenotype. The primary objective of this study was to determine if sleep curtailment results in changes in sweet taste perception after sleep curtailment. Forty participants used a single-channel electroencephalograph to record both a habitual and curtailed night (33% reduction) of sleep at home. The following morning, multiple dimensions of sweet taste perception were measured, including preferred sweetener concentrations, patterns of sweet liking, and intensity perception over a range of concentrations. After curtailment, a significant increase in preferred concentration for both sucrose and sucralose ($p<0.001$ for both) was observed. The slope of sucrose sweet liking increased after curtailment ($p=0.001$). The slope of sucralose liking also increased, but this was not significant ($p=0.129$). Intensity perception of the sweeteners was not altered by curtailment. Hierarchical cluster analysis was used to classify participants by sweet liking phenotype. Phenotypes were found to predict preferred sweetener concentration. These findings illustrate a possible need to control for sleep in food sensory studies and suggest a potential mechanism by which insufficient sleep can lead to excess energy intake.

1. Introduction

Nearly 40% of US adults report habitually sleeping less than the recommended 7 h per night (Chen, Gelaye, & Williams, 2014), a proportion that has been steadily rising across all age groups since the 1980s (Ford, Cunningham, & Croft, 2015). Short sleep duration has routinely

been associated with excess energy intake, weight gain, and obesity (Patel Sanjay R. & Hu Frank B., 2012). The relationship between insufficient sleep and excess energy intake is hypothesized to be motivated by both homeostatic (Cauter, Leproult, & Plat, 2000; Robertson, Russell-Jones, Umpleby, & Dijk, 2013; Scheen, Byrne, Plat, Leproult, & Cauter, 1996; Spiegel, Leproult, & Van Cauter, 1999; van der Lely, Tschöp, Heiman, & Ghigo, 2004) and hedonic (Greer, Goldstein, & Walker, 2013; Hanlon, Andrzejewski, Harder, Kelley, & Benca, 2005; McNeil et al., 2017; Thomas et al., 2000) drives to eat. However, several recent studies suggest that hedonic drivers of food intake may predominate when sleep is insufficient (Bosy-Westphal et al., 2008; Calvin et al., 2013; Chaput & St-Onge, 2014; Markwald et al., 2013; Nedeltcheva et al., 2009). For example, experiments using an *ad libitum* feeding paradigm have demonstrated that sleep curtailment increases energy intake, even when appetite-stimulating hormones are not elevated (Chaput, 2014; Marie-Pierre St-Onge, 2013), suggesting that the relationship between insufficient sleep and excess energy intake is driven more by hedonic rather than homeostatic factors (Chaput & St-Onge, 2014). Because hedonic evaluation of foods and beverages is based on sensory input from gustatory, olfactory, and somatosensory systems (Meilgaard, Carr, Civille, Carr, & Civille, 1999), altered sensory perception after short sleep may contribute to changes in food choice. Based on previous observational work reporting correlations between sleep duration and sweetness perception (Szczygiel, Cho, & Tucker, 2018; Szczygiel, Cho, Snyder, & Tucker, 2019), the primary objective of the current study was to determine if sleep curtailment resulted in changes in sweet taste preference and sweet taste intensity perception after sleep curtailment.

Sweetness is an ideal taste to begin to study the relationship between sleep and taste function for several reasons. First, nutritive sweeteners, such as sucrose, can contribute to excess energy intake and the development of obesity (Lean, Astrup, & Roberts, 2018). Second, sweet

taste represents a palatable taste that will interact with brain reward systems; reward systems that are altered by insufficient sleep (Leigh & Morris, 2018). Brain imaging studies have demonstrated that insufficient sleep results in amplified reward from positive experiences (Gujar, Yoo, Hu, & Walker, 2011) and increased positive hedonic perception of food cues (Benedict et al., 2012; Demos et al., 2017; Greer et al., 2013; Hanlon et al., 2005; M-P St-Onge, Wolfe, Sy, Shechter, & Hirsch, 2014). These studies suggest that insufficient sleep results in increased reward sensitivity, which could lead to increased consumption of palatable food for pleasure (hedonic eating). Highly palatable food tends to be energy dense, and therefore, increased hedonic eating can lead to excess energy intake (Drewnowski, 1999). While it is unclear if sleep-related changes in the hedonic perception of food are mediated by changes in taste perception, the preponderance of available evidence (Furchtgott & Willingham, 1956; Lv, Finlayson, & Dando, 2018; Smith, Ludy, & Tucker, 2016; Szczygiel et al., 2018; Szczygiel et al., 2019; Tanaka, Hong, Tominami, & Kudo, 2018) suggests that insufficient sleep influences both taste function (Furchtgott & Willingham, 1956; Lv et al., 2018) and taste preference (Smith et al., 2016; Szczygiel et al., 2018; Szczygiel et al., 2019). Altered sweet taste perception after a night of insufficient sleep may contribute to the link between insufficient sleep and excess energy intake, but more research is needed to confirm this.

While sweetness is palatable, individuals differ in their hedonic responses as concentrations increase (Yeomans, Tepper, Rietzschel, & Prescott, 2007). Three fundamental patterns of sweet liking have been repeatedly identified across studies (Iatridi, Hayes, & Yeomans, 2018, 2019; Yeomans et al., 2007): sweet likers, who show an increase in liking as sweetener concentration increases; sweet dislikers, who show a decrease in liking as sweetener concentration increases; and "inverted U-shape" responders, who like sweetness up to a certain

concentration and then begin to dislike subsequently higher concentrations, such that the pattern appears as an inverted U-shape. Additionally, a fourth phenotype has been reported, where the pattern of liking is stable over a range of concentrations (Iatridi et al., 2019); however, many studies do not report observing this phenotype (for example: (Asao et al., 2015; Kim, Prescott, & Kim, 2014, 2017)). These fundamental patterns are referred to as sweet liking phenotypes, due to the fact that they are determined by both genetic and environmental factors (Bachmanov et al., 2011; Keskitalo et al., 2007; Mennella, Pepino, & Reed, 2005). The sweet liker phenotype has been found to be a meaningful predictor of several behaviors and traits, such as predicting the extent to which sweet taste from saccharin would condition hedonic response to a novel odorant when tasted together in solution (Yeomans, Prescott, & Gould, 2009), predicting the strength of positive emotional response to highly sweet samples (Kim et al., 2017), or predicting the risk of alcohol related problems (Lange, Kampov-Polevoy, & Garbutt, 2010). These behaviors, taken together with genetic evidence (Bachmanov et al., 2011; Keskitalo et al., 2007), suggest that sweet liking phenotype is an indicator of heritable dysfunction of the brain reward system (Kampov-Polevoy, Alterman, Khalitov, & Garbutt, 2006; Kampov-Polevoy et al., 2014). Increased brain reward system activity is one proposed mechanism by which insufficient sleep can lead to excess energy intake (St-Onge et al., 2014). Therefore, insufficient sleep may differentially increase brain reward function in sweet likers compared to other phenotypes. No study to date has investigated whether there is a relationship between insufficient sleep and sweet liking phenotype (SLP).

Due to reported differences in brain reward processing of sucrose compared to non-nutritive sweeteners (NNS) (Frank et al., 2008). sweetener type is an important factor to consider when examining the effect of sleep on hedonic response to sweet taste. While nutritive and NNS

activate the same taste pathways in the brain, NNS have been shown to activate key reward centers (anterior insula, striatum and anterior cingulate) less than sucrose and fail to activate dopaminergic midbrain areas at all (Frank et al., 2008). Given that increased brain reward sensitivity is a well-supported mechanism by which insufficient sleep is linked to increased energy intake, it stands to reason that insufficient sleep may differentially impact taste perception of nutritive and NNS sweeteners. Further, individual differences in hedonic response to sweet taste from NNS may not align with hedonic response to sucrose and, therefore, must also be considered separately. In addition, the effects of sweetener type on SLP have been explored almost exclusively by using nutritive sweeteners (e.g., (Asao, Luo, & Herman, 2012; Kim et al., 2014, 2017; Yeomans et al., 2009), so it is unclear if NNS will also show distinct liking phenotypes. To our knowledge, only one study has examined SLPs using a NNS and reported similar phenotypes in stevia (Oleson & Murphy, 2017). Others have reported that roughly-equal sweet concentrations of NNS and sucrose are preferred similarly in healthy people (Bobowski & Mennella, 2017), and that sweet tastes, whether from nutritive or NNS, stimulate higher order reward regions of the brain (Green & Murphy, 2012). Therefore, it is likely, though unconfirmed, that sweet liking phenotypes extend to other sweeteners.

The primary objective of the current study was to determine if sleep curtailment resulted in changes in sweet taste preference and sweet taste intensity perception of sucrose and sucralose after sleep curtailment. A secondary objective was to determine if there is a relationship between SLP and insufficient sleep. Sucralose was selected as a representative NNS due to having a similar taste profile compared to sucrose and less off flavor compared to other NNS (Binns, 2003; Wiet & Beyts, 1992). Given the current psychophysical and behavioral evidence, it was hypothesized that insufficient sleep would result in an increase in sucrose preference and an

increase in sucrose sweet liking at each sweetness level over a range of concentrations. While we expected similar findings for sucralose, we also hypothesized that the increase in liking after curtailment would be less pronounced in sucralose given the differences in brain response between the two sweeteners. Further, it was hypothesized that fundamental SLP classification would exist for sucralose, and that sweet likers would be more susceptible to changes in sweet taste perception compared to other SLPs.

2. Materials and Methods

The study protocol was approved by the Human Research Protection Program at Michigan State University (East Lansing, MI, USA). Written informed consent was obtained from all participants prior to testing.

2.1. Participants

Non-obese participants (BMI < 30.0 kg/m^2) of any race or ethnicity between the ages of 18-45 with no diagnosed sleep conditions who normally slept 7-9 h per weeknight and had a regular weekday bedtime were eligible to participate in the study. Additionally, each participant was provided with a sample of the highest concentration of sucralose (0.094 %weight/volume (% w/v)) to screen for bitterness sensitivity. While sucralose does not typically display high levels of bitterness (Wiet & Beyts, 1992), individuals who are highly sensitive to bitterness (Mennella et al., 2005) may find it difficult to evaluate sucralose samples for sweetness. Participants who reported tasting any bitterness were not eligible for the study. Three people who were otherwise eligible were excluded for this reason.

2.2. Study Timeline

Participants were required to attend an initial consent visit where the study administrator confirmed that each participant met the eligibility criteria for the study. After the consent visit, each participant visited the sensory laboratory for testing twice, once after a habitual night of sleep and once after a curtailed night of sleep, with at least 7 days between each visit. The second laboratory visit was required to take place on the same weekday and time (±30 min) as the first visit. Participants were randomly assigned to the sleep condition (habitual or curtailed) they would undergo first. Sleep time was centered to split the curtailment equally; that is, if the curtailment was 2 h, the participant was instructed to go to bed 1 h later and wake up 1 h earlier. Centering the curtailment was designed to minimize circadian rhythm effects while still inducing sleepiness (Dinges et al., 1997). Curtailment was based on participants' self-reported habitual bed and wake times. Partial sleep curtailment was selected because it represents a modest reduction in sleep that is more representative of free-living conditions compared to total sleep deprivation (Dinges et al., 1997). Participants selected an available 1 h testing slot between 7:00 - 10:00 a.m. on any weekday (Monday-Friday) for sensory testing. These time slot options were selected to accommodate a range of possible habitual bed and wake times.

2.2.1 Consent Visit

During the initial consent visit, eligible participants completed the Pittsburgh Sleep Quality Index (PSQI), Perceived Stress Scale (PSS), and the General Food Craving Questionnaire –Trait version (G-FCQ-T) and demographic questions. The PSQI (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989), PSS (Cohen, Kamarck, & Mermelstein, 1983), and G-FCQ-T (Cepeda-Benito, Gleaves, Williams, & Erath, 2000) are validated questionnaires that were selected to assess subjective sleep, perceived stress, and general food craving traits,

respectively. The PSQI measures subjective sleep quality and duration during the past month, and PSQI scores equal to five or greater indicate possible disordered sleep (Buysse et al., 1989). PSQI scores were measured to screen out participants with disrupted sleep in the past month who may not believe or be aware that they have disrupted sleep. The PSS measures perceptions of stress during the past month (Cohen et al., 1983). Chronic stress is associated with undesirable changes in sleep architecture (Cheeta, Ruigt, van Proosdij, & Willner, 1997). PSS was measured to confirm that participants were not experiencing unusual chronic stress. The G-FCQ-T is a 21-item questionnaire which involves participants indicating the degree to which each item is generally true for them on a 6-point Likert scale ranging from 1 (never or not applicable) to 6 (always). These items are divided into subscales which measure nine dimensions of food cravings (Nijs, Franken, & Muris, 2007). Food craving traits were measured as they may moderate reward sensitivity (Meule & Kübler, 2014), and thus may aid in interpretation of findings. Height was measured using a stadiometer (HM200P, Charder, Taichung, Taiwan) and weight, body mass index (BMI), and percent body fat (%BF), were assessed using a bioelectrical impedance scale (TBF-400, Tanita, Arlington Heights, IL). Anthropometrics were measured to serve as evidence that participants were healthy, non-obese individuals.

Participants were also trained to operate the Zmachine (General Sleep, Columbus, OH) during the consent visit, The Zmachine records a single channel (A_1-A_2) of electroencephalography (EEG) and uses an automated scoring algorithm to differentiate between light sleep (LS), slow wave sleep (SWS), rapid eye movement (REM) sleep and waking states. When the performance of the Zmachine was compared to PSG, an overall kappa agreement of 0.72, indicating substantial agreement, was reported (Kaplan, Wang, Loparo, Kelly, & Bootzin, 2014). Participants were told to wear the Zmachine at least 30 min before the predetermined

bedtime to ensure compliance with the assigned protocol. Finally, participants were instructed to not eat or drink anything other than water between their wake time and their scheduled sensory testing appointment.

2.2.2 Laboratory Visits

The procedure for each of the two test visits was identical. Upon arriving at the lab after a night of sleep recording, the EEG data from the previous night's sleep was immediately uploaded to the Zmachine data viewer, and the participant was asked to confirm that the data matched their own recollection of the previous night. If there was substantial data loss or disagreement with the participant's recollection, the recording was reattempted after 7 days. Prior to beginning sensory testing, participants were asked to take a "Hydrogen Breath Test" by blowing into a metalized bag with a valve to ensure they had fasted. This procedure was a strategy used to encourage participants to adhere to the fasting instructions. The samples were not analyzed, and participants were told the true purpose of the "Hydrogen Breath Test" after completion of the study.

Prior to tasting any stimuli, participants self-administered a series of questionnaires including the Karolinska Sleepiness Scale (KSS), the Positive Affect-Negative Affect Schedule (PANAS), the General Food Craving Questionnaire-State version (G-FCQ-S), and a simple 100 mm visual analog scale (VAS) to measure hunger with "Extremely Hungry" (0) and "Extremely Full" (100) labels. The KSS (Kaida et al., 2006), PANAS (Watson, Clark, & Tellegen, 1988), and G-FCQ-S (Cepeda-Benito et al., 2000) are validated questionnaires used to measure sleepiness, affect, momentary food cravings, respectively. KSS is a 10-point category scale ranging from "Extremely alert" (1) to "Extremely sleepy, can't keep awake" (10) (Shahid, Wilkinson, Marcu, & Shapiro, 2012). The KSS was used to determine the effectiveness of the

curtailment treatment. The PANAS assessed affect changes across the treatment conditions and is scored between 10-50 for both positive and negative affect separately (50 being more negative or more positive) (Watson et al., 1988). Affect has been found to shift after a night of insufficient sleep (Franzen, Siegle, & Buysse, 2008) and, therefore, was measured to aid in the interpretation of findings. The G-FCQ-S contains 15 items which participants indicate on a 5 point Likert scale, ranging from " Strongly disagree" (1) to "Strongly Agree" (5), the extent to which they agree with each item "*right now, at this very moment*". The G-FCQ-S can be subdivided into 5 subscales which represent different dimensions of momentary food craving (Nijs et al., 2007). Craving states have been found to be associated with sleep duration (Lv et al., 2018) and, therefore, were measured to aid in the interpretation of findings. The VAS used to measure hunger has been shown to be a sensitive measure of hunger (Merrill, Kramer, Cardello, & Schutz, 2002) and was used to assess whether fasting was effective in controlling for hunger.

To assess subjective sleep quality, participants answered four questions regarding their recollection of the previous night's sleep. There are currently no validated questionnaires available for assessing previous night's subjective sleep quality. Therefore, questions were developed to measure some dimensions of subjective sleep quality for the purpose of assessing whether the curtailment or Zmachine altered subjective sleep quality. The four questions were: "How much sleep did you obtain last night?" (1: Far less than I needed, 5: Far more than I needed), "How deeply did you sleep last night?" (1: Extremely shallow, 5: Extremely deep), "How would you rate the quality of your sleep last night?" (1: Poor, 5: Excellent), and "Compared to an average night of sleep, how comfortable were you when sleeping last night?" (1: Far less than an average night, 5: Far more than an average night). Additionally, a composite score of these questions was used to represent overall subjective sleep quality.

2.3. Development of Iso-Sweet Stimuli

While several studies have developed iso-sweet stimuli between sucrose and non-nutritive sweeteners, none have extended into the concentration range needed to assess typical human sweetness preference with sucralose (Moskowitz, 1970; Reis, De Andrade, Deliza, & Ares, 2016). To compare hedonic response to sweetness across sweeteners, it was necessary to ensure that the concentrations of the two sweeteners were comparable. Thus, a preliminary study aimed at identifying iso-sweet concentrations of sucralose and sucrose was conducted per the methods of Reis, et al. (Reis et al., 2016). Briefly, 100 participants assessed the relative sweetness of a range of concentrations of sucralose (0.005% w/v-0.16% w/v, n=50) and sucrose (3% w/v-36% w/v, n=50) using magnitude estimation with a fixed reference (12% sucrose). From these data, Steven's power functions were produced and used to select concentrations of sucralose equivalent to the 3%, 6%, 12%, 18%, and 24% w/v sucrose. These concentrations were adapted from the Monell forced choice paired comparison protocol (Mennella, Lukasewycz, Griffith, & Beauchamp, 2011) used in the preference testing portion of the experiment (see below). Equivalent sucralose concentrations were found to be 0.004%, 0.011%, 0.032%, 0.06% and 0.094% w/v, respectively.

2.4. Sensory Evaluation

All sensory data was collected using RedJade Sensory Software (RedJade, Redwood Shores, CA, USA) at the Michigan State University sensory laboratory. All samples were served at room temperature in 10 mL quantities using 30 mL plastic soufflé cups. Participants wore nose-clips during all tastings. Additionally, participants were instructed to taste the whole sample and expectorate. The sensory evaluation consisted of two tasks; preference testing and liking evaluation. The two tasks were carried out first with sucrose solutions and then again with

sucralose solutions of equal sweetness. This was done to reduce any possible effect of lingering sucralose aftertaste on sucrose taste perception (Wiet & Beyts, 1992).

2.4.1 Preference testing

A modified version of the Monell forced choice paired comparison protocol (Mennella et al., 2011) was used for preference testing. While the original Monell procedure used a wider range (3%-36% w/v) of sucrose concentrations, at concentrations of sucralose equivalent to 36% sucrose, the risk of bitter taste impairing sweetness evaluation increases (Moskowitz, 1970). However, in order to measure preference using a forced choice paired comparison, it is necessary to have at least five clearly distinguishable levels of sweetness while maintaining a mid-point that is close to the average sweetness liking seen in healthy populations (Mennella et al., 2011). If the range is too small, sweet likers could select the highest sweetness level every time, making it impossible to measure changes. Thus, the two highest concentrations from the Monell protocol, 24%, and 36% w/v, were reduced to 18% and 24% w/v. In a preliminary triangle test (n=15), participants were able to discriminate 18% and 24% w/v sucrose ($p<0.05$). The modification allowed for the avoidance of off tastes at high concentrations while maintaining the efficacy of the protocol. Aside from the modifications to the range of sweetness, the Monell protocol was followed. Participants were given two concentrations of suprathreshold sweetener and asked to point to the solution which they liked more. Participants rinsed with purified water between tasting each solution in the pair and between each set of pairs. Based on their selection, a second pair containing the concentration they previously selected and an adjacent concentration were presented until they selected the same solution twice in a row. The protocol was repeated twice, first with the lower concentration presented first and second with the higher concentration

presented first. The geometric mean of the % w/v preferred sweetener concentration is reported as the "sweet taste preference".

2.4.2 Evaluation of Sweetness Liking

Sweetness liking was assessed by presenting a range of different concentrations of sweetener solutions identified with three-digit blinding codes in random order. Due to interest in changes in liking slope and SLP, eight increasing concentrations were used to ensure patterns of liking would be unambiguous. The sweetener concentrations included 3%, 6%, 9%, 12%, 15%, 18%, 21% and 24% w/v sucrose and 0.004%, 0.011%, 0.020%, 0.032%, 0.045%, 0.060%, 0.075%, 0.094% w/v sucralose. Participants were asked to rate their liking of each solution on a 15 cm VAS scale with anchors at 0 (dislike extremely), 7.5 (neutral) and 15 (like extremely). Additionally, participants were asked to rate how intensely they perceived the sweetness to be on a 15 cm VAS scale with anchors at 0 (not at all intense) and 15 (extremely intense). Following the tasting of a solution, there was a 45 second forced wait period in which the participant was required to rinse three times with purified water.

2.5. Statistical Analysis

Data analysis was completed using SAS version 9.4 (SAS Institute, Cary, NC., U.S.A.). Findings were considered statistically significant if $p<0.05$ in all analyses, and data are presented as the mean±standard deviation unless otherwise stated. Liking scores were plotted against sweetener concentration, and the best fit linear function was calculated in Excel (Microsoft, Redmond, WA, U.S.) and used to determine the "Liking Slope" variable used throughout the study.

A mixed model was used to compare the main effects of sleep curtailment and the interaction effects between SLP (n=2, sweet likers and non-likers, see "*sweet liking phenotypes*"

section below), sweetener type (n=2, sucrose and sucralose) and sleep curtailment (n=2, habitual and curtailed sleep) on preferred sweetener concentration and sweet liking slope. Participant and interactions between participant and the main effects were included as random factors. Sequence (curtailed or habitual night first) and period (first or second visit) were initially included to determine whether there were significant carry-over effects. No significant sequence or period effects were observed and therefore were not used in any further analysis. Tukey's correction was used for multiple mean comparisons in all cases. Paired data collected from participants after a habitual or curtailed night's sleep, such as PANAS scores or hunger rating, were analyzed using paired t-tests and corrected for multiple comparisons using false discovery rate (FDR) with a threshold of q=0.05, which has been used previously to reduce the risk of type-1 error in psychophysical studies (Glickman, Rao, & Schultz, 2014; E. J. Szczygiel et al., 2019). To provide additional evidence regarding comparisons between the sweeteners, associations between the preferred sweetness concentration of the two sweeteners were assessed using Pearson correlations. Pearson correlations were also used to assess the relationship between participant baseline and preferred sweetness concentration (see participants below). Hierarchical cluster analysis (HCA), an objective strategy for determining SLPs that is recommended as the standard for sweet liking classification (Iatridi et al., 2019), was conducted in XLstat (Addinsoft, Paris, France) using the eight liking scores across the range of concentrations of each sweetener in order to classify participants into SLPs (Iatridi et al., 2018). In order to compare sucrose and sucralose preference, sucralose preference (% w/v) was converted to sucrose preference equivalents using the power functions discussed above to produce a single dependent variable.

3. Results

3.1. Participants

Participant demographics are reported in Table 4.1. Forty participants without obesity completed the study. Participants were majority white (n=26) and female (n=27). Both BMI and percent body fat (BF%) values were considered healthy. All participants had a PSQI score ≤5. ANOVA was used to assess interactions between sleep treatment and sex. Sex did not show a significant main effect and there was no significant interaction between sex and sleep treatment for any sensory measure ($p>0.05$). Data for both sexes were therefore pooled. Anthropometric measurements as well as PSQI, G-FCQ-T and PSS scores were in not correlated with preferred sucrose or sucralose preference and therefore were not utilized in further analysis ($p>0.05$)

Table 4.1. Anthropometric and Demographic Summary

Sex	n	%
Male	13	32%
Female	27	67%
Race	**n**	**%**
White	26	65%
Asian	12	30%
Other/More than 1	2	5%
Anthropometrics	**Mean±SD**	**Range**
Body mass index (kg/m^2)	22.9±3.0	18.5-29.7
Body fat (%)	22.3±7.9	9.9-35.5
Age (y)	23.8±4.6	18-37
Traits/Habits (score)	**Mean±SD**	**Range**
General food craving questionnaire-trait version	51.3±17.2	22-89
Perceived stress scale	11.3±4.4	3-21
Pittsburgh Sleep Quality Index	3.3±1.4	0-5

3.2. Summary of Curtailment

Table 4.2. Summary of Objective and Subjective Sleep Measures

		Habitual	Curtailed	% Reduction	p-value	q-value
Objective Sleep Measures (h)	Time in bed	8.2±0.7	5.3±0.7	35.30%	<0.001	<0.001
	Total sleep time	7.0±0.8	4.5±0.8	36.00%	<0.001	<0.001
	Light sleep	3.6±0.7	2.0±0.6	44.20%	<0.001	<0.001
	REM sleep	1.9±0.5	1.1±0.3	40.40%	<0.001	<0.001
	Slow wave sleep	1.6±0.3	1.3±0.4	16.70%	<0.001	<0.001
Sleepiness (10pt)	Karolinska Sleepiness scale	3.9±1.6	5.5±1.8		<0.001	<0.001
Subjective Previous Night's Sleep Measures (5pt)	Subjective Sleep Composite	12.8±2.1	10.9±2.6		<0.001	<0.001
	How much sleep did you obtain last night?	2.9±0.6	1.5±0.6		<0.001	<0.001
	How deeply did you sleep?	3.7±0.9	2.6±0.9		0.491	0.534
	How would you rate the quality of your sleep	3.4±0.7	3.1±1.3		0.209	0.256
	Compared to an average night, how comfortable were you when sleeping last night?	2.8±0.6	2.7±0.7		0.711	0.711

All objective sleep measures were significantly reduced after sleep curtailment. Karolinska Sleepiness Scale (KSS) (for which greater scores indicate decreased alertness) was significantly higher and composite subjective previous night's sleep score was significantly lower after sleep curtailment, indicating that the curtailed night of sleep were perceived by participants to be of shorter length compared to a habitual night, resulting in decreased alertness the following morning. FDR correction did not change the significance of any comparisons. .

Sleep curtailment resulted in expected changes in sleep architecture, sleepiness, and subjective evaluation of the previous night's sleep. A 35.3% reduction in TIB resulted in reductions in TST, LS, REM and SWS duration ($p \leq 0.001$ for all) (Table 4.2). These changes in

sleep architecture and duration resulted in an increase in sleepiness, as evidenced by the increase in KSS score ($p<0.001$). Participants rated the previous night's sleep as less than needed after curtailment but did not perceive the "deepness", "quality" or "comfort" to be significantly different than the habitual night. Sleep quality was rated slightly above "about average" on both the habitual and curtailed nights.

3.3. Summary of Affect, Cravings, and Hunger

Curtailment did not result in changes in hunger, food cravings, or negative affect (Table 4.3). Curtailment resulted in a decrease in positive affect.

Table 4.3. Summary of State-Dependent Measures

Measure	Factor	Habitual	Curtailed	p-value	q-value
Hunger	Hunger (100 mm VAS)	66.0±15.6	69.6±15.1	0.193	0.248
G-FCQ-S (0-15 per factor)	Total	42.9±10.8	46.3±10.8	0.071	0.159
	F1-Desire to Eat	8.3±3.0	9.0±3.1	0.189	0.248
	F2-Anticipation to positive reinforcement	8.8±3.2	10.0±3.1	0.022	0.099[a]
	F3-Anticipation to negative reinforcement	9.8±2.9	10.5±2.3	0.104	0.188
	F4-Obsessive preoccupation	6.4±2.2	6.8±2.5	0.347	0.390
	F5-Craving as a physiological state	9.7±2.5	10.0±2.9	0.534	0.534
PANAS	Positive Affect	23.8±8.7	20.5±7.1	0.005	0.040
	Negative Affect	13.8±5.3	15.0±6.0	0.050	0.150

Positive affect was significantly decreased after sleep curtailment; whereas, hunger, food craving, and negative affect were not. Larger numbers indicate a greater response. For example, positive affect is higher (23.8) after a habitual night compared to a curtailed night (20.5). [a]FDR correction resulted in the comparison between F2 of the G-FCQ-S before and after sleep curtailment no longer being significant. Abbreviations: VAS: Visual Analog Scale, G-FCQ-S: General Food Craving Questionnaire State Version, PANAS: Positive Affect Negative Affect Schedule, F1-5: General Food Craving Questionnaire State Version Factors 1-5.

3.4. Sweet Liking Phenotypes

Hierarchical cluster analysis revealed three fundamental clusters of SLPs for both sucrose and sucralose after habitual sleep (Table 4.4). After a habitual night's sleep, each cluster presented a distinct pattern of liking (Figures 4.1 and 4.2). Members of cluster 1, the largest cluster, increasingly liked the stimuli ("likers") until leveling off at approximately 18% w/v sucrose or 0.06% w/v sucralose. Cluster 2 members displayed an inverted U-shape of liking ratings with maximum liking occurring at approximately 15% w/v for sucrose and 0.02% w/v for sucralose ("inverted U-shaped"). Members of cluster 3 rated increasing concentrations as decreasingly liked ("dislikers") until leveling off at approximately 18% w/v sucrose or 0.06% w/v sucralose. Due to the small sample size, clusters 2 and 3 were combined for use within the "SLP" two level factor (sweet likers and sweet non-likers) in mixed models analysis.

Table 4.4. Distribution of members between sweet liking phenotypes

Sweetener	Sleep Status	Sweet Likers (n)	Sweet Non-likers (n)	
			Inverted U-shape	Sweet Dislikers
Sucrose	Habitual	25	6	9
	Curtailed	28	4	8
Sucralose	Habitual	24	10	6
	Curtailed	29	3	8

Sweet liking phenotype cluster membership distribution did not differ between the sweeteners.

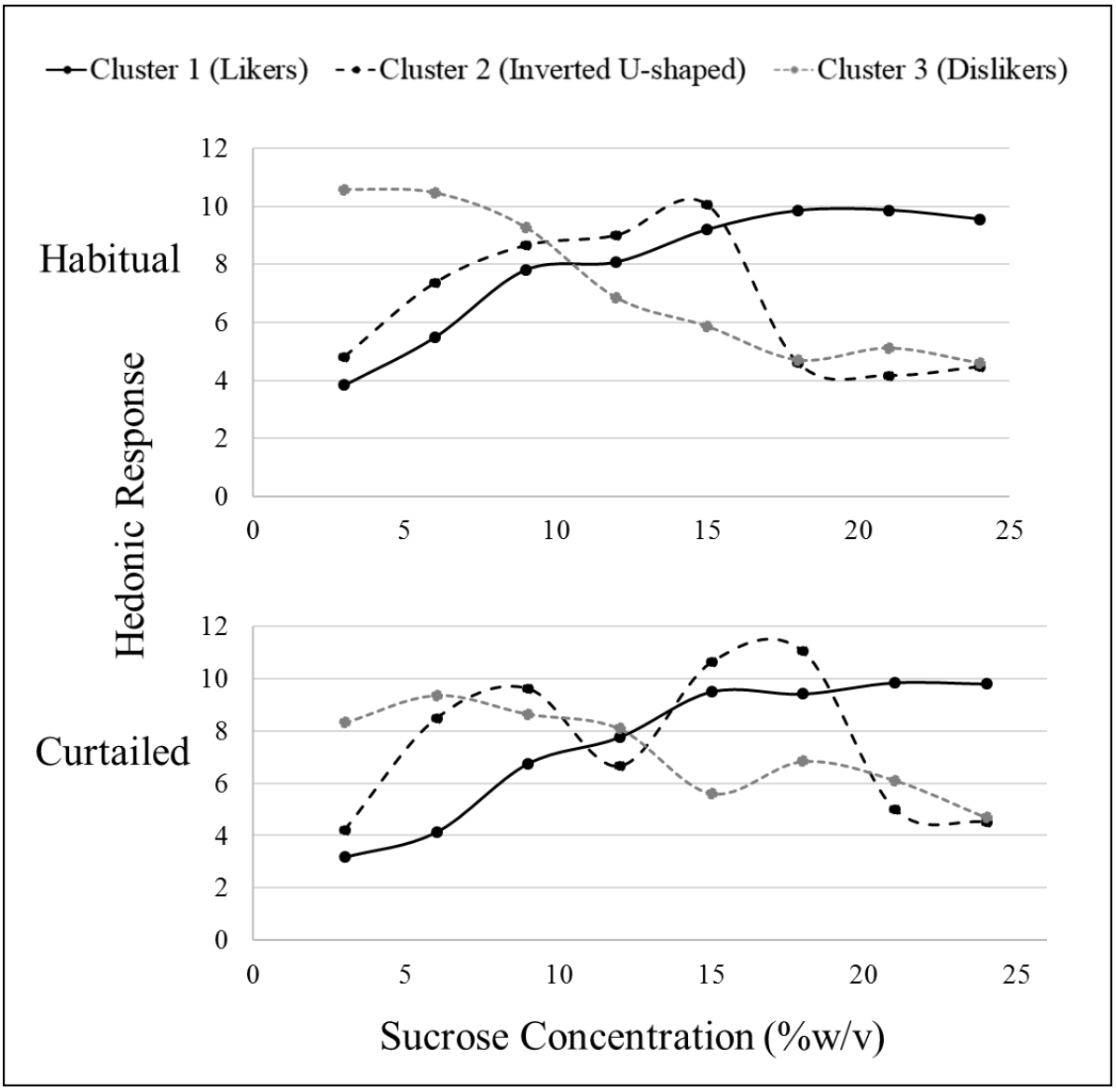

Figure 4.1. *Sucrose sweet liking hierarchical cluster analysis classifications after a habitual and curtailed night of sleep.* After the habitual night, cluster 1 (n=25), cluster 2 (n=6), and cluster 3 (n=9) demonstrated the fundamental phenotypes of sweet liking. After the curtailed night, cluster 1 (n=28) and cluster 3 (n=8) retained the familiar fundamental patterns of liking; whereas, cluster 2 (n=4) had a distorted pattern.

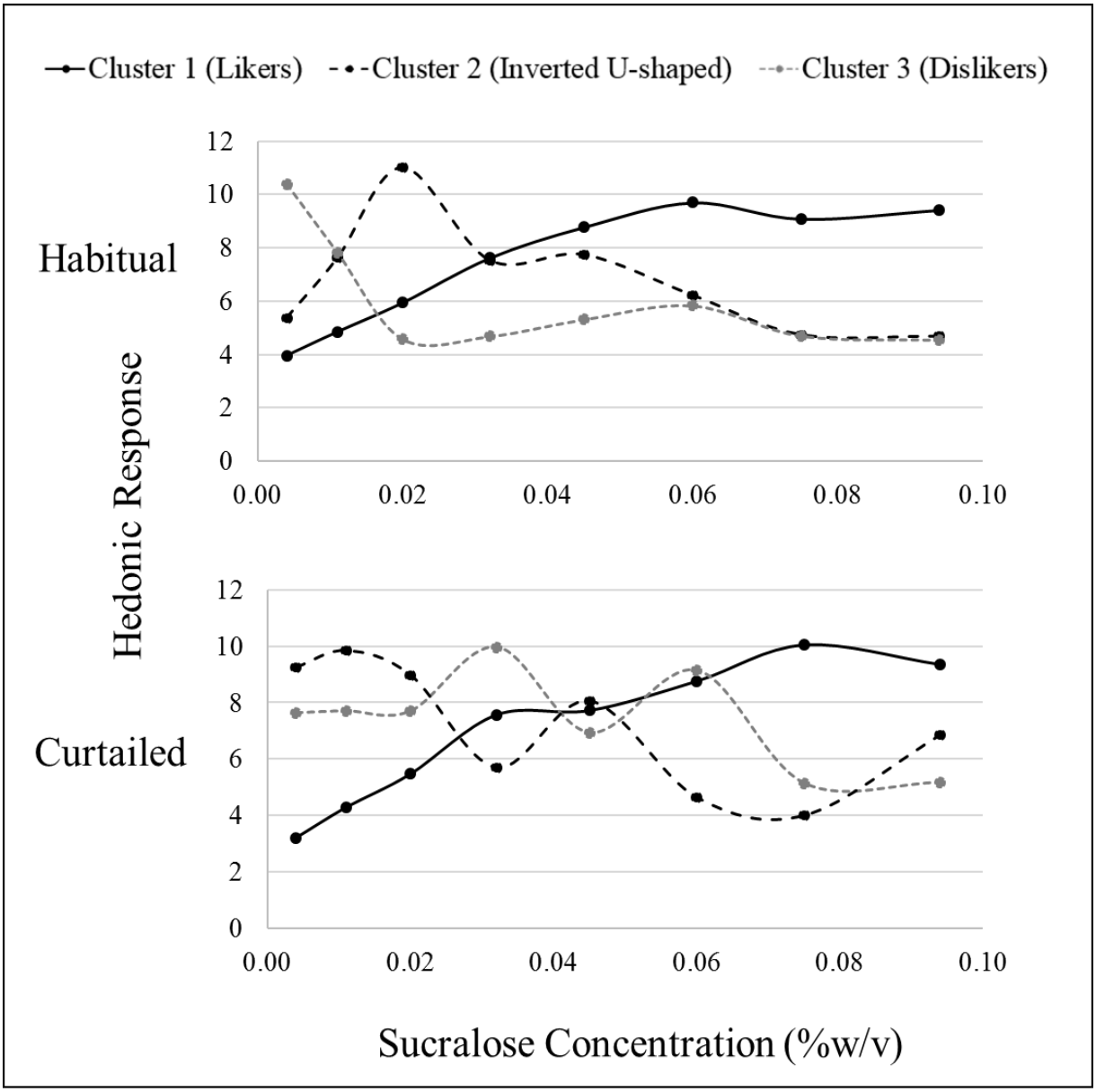

Figure 4.2. *Sucralose sweet liking hierarchical cluster classifications after a habitual and curtailed night of sleep*. After the habitual night, cluster 1 (n=24), cluster 2 (n=10), and cluster 3 (n=6) demonstrated the fundamental phenotypes of sweet liking. After the curtailed night, cluster 1 (n=29) retained the familiar fundamental pattern of liking; whereas, cluster 2 (n=3,) and cluster 3 (n=8) had distorted patterns.

After a curtailed night of sleep, the fundamental phenotypes observed after a habitual night of sleep became less distinct. For sucrose, cluster 1 still showed an increase in liking until leveling off at the 18% w/v concentration and cluster 3 still showed a decrease in liking as concentration decreased. Cluster 2 no longer displayed a clear, fundamental pattern of response (Figure 4.1). For sucralose, cluster 1 still showed an increase in liking until leveling off at the 0.060% w/v. Clusters 2 and 3 lost the fundamental SLPs with patterns becoming distorted after sleep curtailment. The formerly inverted U-shaped pattern displayed in cluster 2 showed a bimodal pattern with vertices above and below the midpoint, and cluster 3, formerly displaying a disliking pattern, displayed a bimodal pattern in the opposite direction (Figure 4.2). After a habitual night's sleep, 75% of participants had matching (i.e., in the same cluster) sucrose and sucralose liking phenotypes. After a curtailed night of sleep, 83% of participants had matching sucrose and sucralose liking phenotypes. The distribution of participants among the clusters, or how many participants were placed into each cluster, was not significantly different between the sweeteners, nor was member distribution between the clusters significantly modified after a curtailed night of sleep (Kolmogorov-Smirnov, $p>0.05$).

3.5. Sweet Preference

A model with sleep condition, sweetener type, SLP, and all interactions up to the tertiary level was used to analyze preferred sweetener concentration. Interaction terms between sleep condition and both sweetener type ($F(1,38)=0.24$, $p=0.62$) and SLP ($F(1,38)=2.0$, $p=0.164$) were not significant, indicating the effect of sleep on preferred sweetness level were not related to SLP or sweetener types. The interaction between SLP and sweetener type was not significant ($F(1,38)=0.02$, $p=0.898$), indicating that the difference in preferred sweetener concentration between the SLPs was not specific to either sweetener. The main effect of sleep condition on

preferred sweetener concentration ($F(1,38)=130.8$, $p< 0.001$) was significant, indicating a difference in preferred sweetness concentration after sleep curtailment (sucrose (M (difference)=5.4 % w/v, SD=6.5); sucralose (M (difference)=5.7 % w/v sucrose equivalencies, SD=6.7) (Figure 4.3). The sweetener main effect for preferred sweetener concentration ($F(1,38)=3.1$, $p=0.086$) was not significant, indicating that preferred sweetener concentration was

Table 4.5. Comparison of preferred sweet liking concentration after a habitual and curtailed night of sleep for each sweet liking phenotype (determined after a habitual night of sleep)

Habitual Cluster		Preferred Concentration (% w/v)			
		Sucrose		Sucralose	
		Habitual	Curtailed	Habitual	Curtailed
"Sweet Likers"	1 (Likers)	14.9±4.4*	17.5±4.4*	0.05±0.02*	0.08±0.02*
"Sweet Non-Likers"	Non-likers Total	6.8±4.1	11.4±2.9	0.02±0.02	0.03±0.02
	2 (Inverted U-shape)	8.4±5.3	12.4±3.8	0.03±0.03	0.04±0.02
	3 (Dislikers)	5.1±2.8	10.0±1.9	0.01±0.01	0.03±0.02

The main effect of sweet liking phenotype (SLP) for sweet preference was significant, indicating that sweet likers had a significantly higher preferred concentration for both sweeteners regardless of sleep status (*$p<0.001$) compared to sweet non-likers. The *SLP by sweetener type* for sweet taste preference was not significant, indicating that preferred sweetness concentration did not differ by sweetener type. The *SLP by sleep condition* interaction was not significant, indicating that sweet taste preference was not differentially effected by sleep curtailment.

not different between the sweeteners, regardless of SLP or sleep condition; that is, preferred sucralose concentration (as sucrose equivalents) was not significantly different from preferred sucrose concentration after both habitual (12.7 sucrose % w/v vs. 11.7 % w/v sucrose equivalents for sucralose) and curtailed sleep (18.1 Sucrose % w/v vs. 17.4 % w/v sucrose equivalents for sucralose). Sucrose and sucralose sweet taste preferences were strongly and positively correlated ($r=0.8356$, $p<0.001$). The SLP main effect was significant for sweet taste preferences

(F(1,38)=37.62, p<0.001), indicating that preferred sweetener concentration differed between sweet likers and sweet non-likers (Table 4.5).

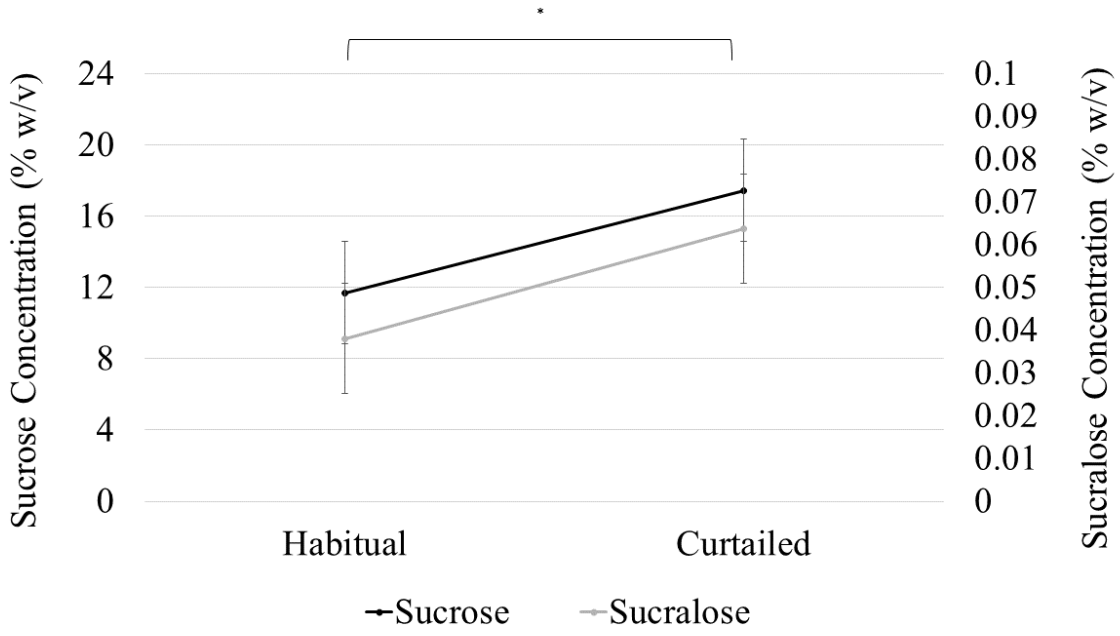

Figure 4.3. *Sucrose and sucralose preferred concentration increased significantly (p<0.001) after sleep curtailment.* Points represent preferred concentration and error bars represent standard error of the mean.

3.6. Sweet Intensity

A model with sleep condition, sweetener type, sweetener concentration, and all interactions up to the tertiary level was used to analyze explicit sweet intensity. Changes in sweet intensity perception at each concentration level for both sweeteners after sleep curtailment were assessed using the interaction terms between sleep condition, sweetener, and concentration level. SLP was excluded from this model, as there is no theoretical basis for including hedonic factors

in the intensity model. The interaction term between sleep condition and concentration level was not significant (F(7,1245)=0.47, p=0.8546), indicating sleep curtailment did not alter intensity perception at any sweetener concentration. Further, the interaction term between sweetener concentration and sweetener type was not significant (F(7, 1245)=0.74, p=0.640), indicating that the intensity of two sweeteners were not different at any concentration level (Figure 4.4).

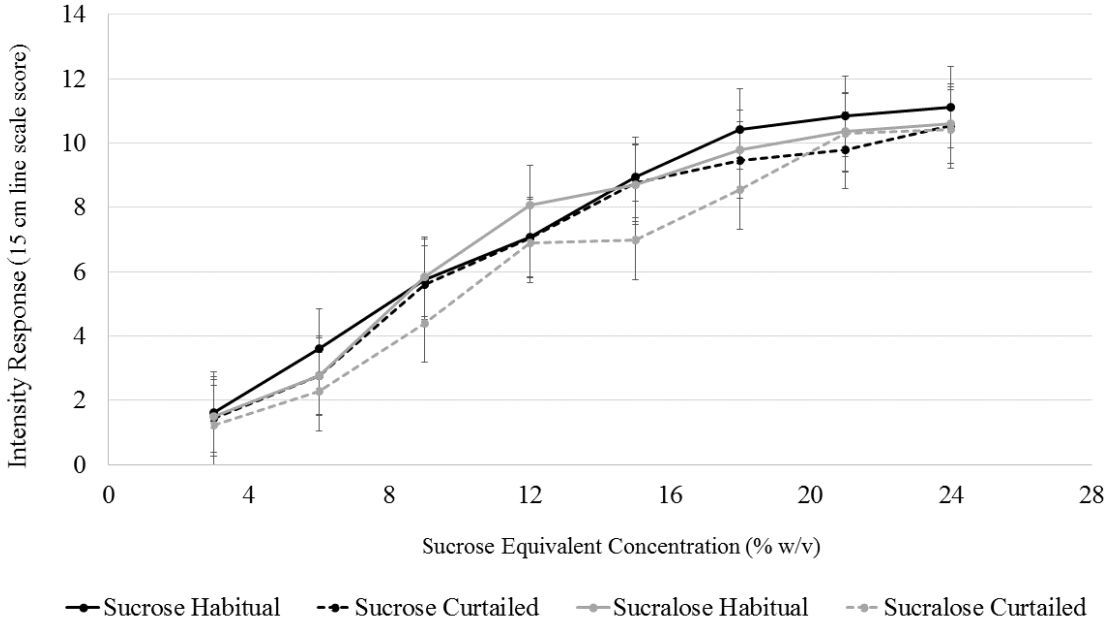

Figure 4.4. *Comparison of intensity perception of sucrose and sucralose (in sucrose equivalents) after a habitual and curtailed night of sleep.* No significant differences between the sweeteners after either sleep condition (p>0.05). Error bars represent standard error of the mean.

3.7. Sweet Liking

A model with sleep condition, sweetener type, sweetener concentration, SLP, and all interactions up to the tertiary level was used to analyze sweet liking responses. The interaction term between sleep condition and sweetener concentration was significant for sweet liking (F(1,

1245)=2.1, p=0.046), indicating that some comparisons between sweetness levels were significant after sleep curtailment. However, comparisons between like concentrations (for example, the comparisons between 3% liking after a habitual and curtailed sleep) were not found to be significant during post-hoc testing ($p>0.05$). Further, neither the sleep condition and sweetener type interaction ($F(1, 1217)=0.17$, $p=0.677$), nor the tertiary sleep condition, sweetener type and sweetener concentration interaction ($F(7,1245)=0.59$, $p=0.762$) were significant, indicating no difference in liking after sleep curtailment between the two sweeteners after sleep curtailment.

A model with sleep condition, sweetener type, SLP, and all interactions up to the tertiary level was used to analyze sweet liking slope. The interaction term between sleep condition and sweetener type was significant ($F(1,38)=4.97$, $p=0.032$), indicating a differential effect of sleep curtailment on the two sweeteners. Post-hoc testing revealed a significant increase in the steepness of sucrose liking slope ($p=0.001$) (Figure 5) but not sucralose liking ($p=0.129$) (Figure 4.5). Sucrose liking slope shifted from 0.08 to 0.19 increase in hedonic response per 1% increase in sucrose concentration after sleep curtailment; whereas, sucralose slope moved from 0.11 to 0.18 sucrose equivalent rate of change.

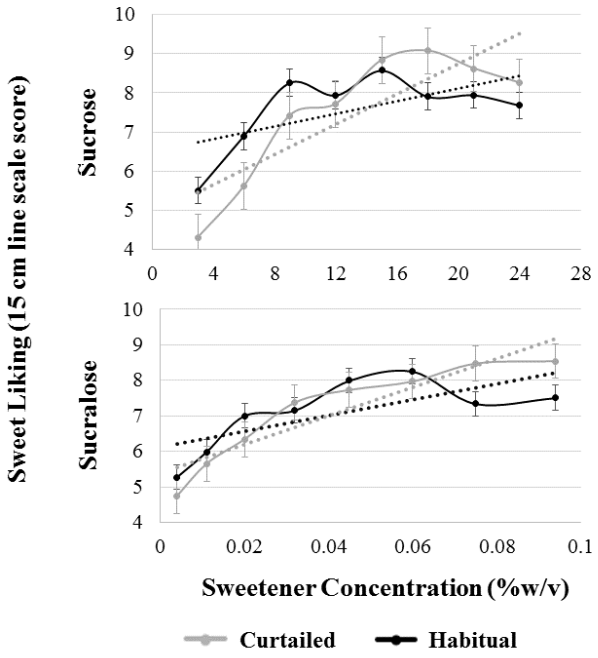

Figure 4.5. *Comparison of patterns of sweet liking of sucrose and sucralose after a habitual and curtailed night of sleep for all participants.* Black dotted lines represent the best fit linear slope for the pattern of liking after the habitual night; gray dotted lines represent the best fit linear slope for the pattern of liking after the curtailed night. The habitual liking slope and curtailed liking slope are significantly different for sucrose (p=0.001), but not sucralose (p=0.129). Error bars represent standard error of the mean.

4. Discussion

The primary objective of this study was to characterize the impact of modest sleep curtailment on chemosensory function and hedonic perception of sweetness from sucrose and sucralose. It was hypothesized that a 33% reduction in sleep duration would result in a shift toward increased liking and preference for sweetness from sucrose and, to a lesser degree, from sucralose. Sleep curtailment resulted in the hypothesized increase in sweet taste preference in

both sucrose and sucralose. However, sleep curtailment did not result in a clear shift towards increased liking of all levels of sweetness. Rather, a complex series of changes in hedonic perception of sweetness that resulted in a steeper pattern of liking as sweetness increased in sucrose, and no significant difference, but a similar pattern, in sucralose liking was observed. Further, it was hypothesized that changes in liking would occur independently of changes in taste intensity perception. In agreement with our hypothesis, no changes in sucrose or sucralose intensity perception were observed after sleep curtailment. Finally, it was hypothesized that SLPs would remain stable after sleep curtailment, and that fundamental SLPs would exist for sucralose. Participants were grouped by SLPs using HCA. Sucrose phenotypes were similar to sucralose phenotypes after a habitual night of sleep, with 75% of participants belonging to the same SLP for both sucrose and sucralose after the habitual night, and commonly reported (so-called "fundamental") phenotypes were present.

To our knowledge, this is the second attempt to classify sweet liking patterns using a non-nutritive sweetener (Oleson & Murphy, 2017), and the first using sucralose. Whether a participant was classified as a liker (cluster 1) or a non-liker (clusters 2 and 3) was predictive of sweet taste preference for both sweeteners. While almost all of the work exploring sweet liking phenotypes has been done using sucrose, that these phenotypes are also present when sucralose is used as the stimulus and when stevia is used (cite) suggests that these classifications extend to other sweeteners. While there appears to be some cases of individual variability, where a sucrose disliker was not a sucralose disliker, in general, the phenotypes were relatively stable across sweeteners.

While it was hypothesized that there would be a shift in liking so that all levels of sweetness would show an increased hedonic response after a night of sleep curtailment, the

findings suggest a more complex relationship where the pattern of liking was altered so that the slope of the best-fit linear function of the hedonic response-concentration plot became significantly steeper after sleep curtailment. The change in pattern suggests a shift in hedonic responses so that higher concentrations of sweetness are more liked and lower concentrations are less liked after sleep curtailment, which, taken together with reported changes in desire for sweet and high-carbohydrate foods (Calvin et al., 2013; Nedeltcheva et al., 2009), could contribute to the association between insufficient sleep and excess energy intake. The notion that higher concentrations of sweetness are more liked after sleep curtailment is further supported by the significant increase in preferred concentration of sweetness for both sweeteners. The increase in steepness of the slope may also be driven partially by a decrease in liking of lower concentrations of sucrose. The significant shift in slope of the liking function suggests that low concentrations are generally less liked after a curtailed night of sleep. Given that sleep deprivation has been associated with increased neural and behavioral reactivity to both negative and positive experiences (Gujar et al., 2011) it is possible that an increase in liking of highly sweet solutions and a decrease in liking of less sweet solutions occurs simultaneously.

The two sweeteners were not perceived as differently intense or pleasurable. Under normal conditions, adults have been shown to prefer approximately equally sweet concentrations of sucrose and sucralose (Bobowski & Mennella, 2017), which is in agreement with the data presented in the current study. Importantly, average sweetness intensity for both sweeteners was not significantly different from one another at any of the sweetness levels, indicating that, at each level of sweetness, the two sweeteners were approximately iso-sweet, as designed. Despite previous research suggesting that sucralose and sucrose may differentially stimulate reward processing centers in the brain (Frank et al., 2008), participants in the current study preferred

equivalent concentrations of sweetness between the two sweeteners (as measured by sucrose equivalency). However, the change in participants' sucralose liking over the range of concentrations after curtailment, while similar in shape to sucrose, was not significant. While not statistically significant, the similarities in the shapes of the two curves after curtailment suggests that a similar modification of patterns of sweet liking may be occurring, albeit to a lesser degree, as hypothesized. Other than the magnitude of the change in slope, sleep curtailment generally did not appear to differentially impact sweet taste perception of the two sweeteners. However, we cannot conclude that the two sweeteners were equally affected by sleep curtailment due to the lack of statistically significant change in the slope of sucralose liking.

A preferential increase in sucrose liking after sleep curtailment compared to sucralose could have important dietary implications. Sucrose preference might be increased by insufficient sleep due to alteration in dopaminergic midbrain function; whereas, preference for a NNS, such as sucralose, may be less affected due to sucralose's lack of midbrain interaction (Frank et al., 2008). If this is the case, sleep curtailment could increase the palatability of sucrose while leaving sucralose palatability unchanged. However, the increase in palatability of high concentrations of sucrose may lead to excess energy intake, suggesting that sucralose might be a better sweetener option for habitually short sleepers. Alternatively, sucralose may be relatively sub-optimal at satisfying sweet cravings compared to sucrose in individuals who had an insufficient previous night's sleep, driving increased consumption. Therefore, more work is needed to assess differences in hedonic response between nutritive and NNS after sleep curtailment and how these changes influence dietary intake, if at all.

While it was hypothesized that sweet likers might be more susceptible to changes in sweet liking after sleep curtailment, the data did not support this hypothesis. Both sweet likers

and non-likers showed an increase in preferred sweetness concentration for both sweeteners after sleep curtailment. However, it should be noted that the absolute increase in preferred sucrose concentration is similar for all of the clusters; therefore, having a low habitual sweetness preference may be still be protective against the effects of sleep curtailment when considering how these changes may manifest to alter food choice. For example, a sweet liker, who, after sleep curtailment, prefers sucrose concentrations as large as 17% w/v, may be at higher risk for selecting a high calorie sweetened foods compared to a non-liker who still only prefers between 10-12% w/v sweetener concentration after sleep curtailment. However, sweet taste perception is not always predictive of dietary intake (Tan & Tucker, 2019), and therefore, the effects of these perceptual changes on food choice cannot yet be determined until more is understood about how momentary taste preferences inform eating behaviors.

Sleep curtailment resulted in a significant decrease in positive affect and no change in negative affect. Positive affect can be defined as a state of pleasurable engagement with the environment that elicits feelings, such as happiness or joy (Ong, Kim, Young, & Steptoe, 2017). Negative affect can be defined as a state of unpleasant engagement with the environment that elicits feelings, such as anxiety or anger (Stringer, 2013). Positive and negative affect are thought to be statistically independent (Stringer, 2013). In agreement with our findings, previous literature has reported a decrease in positive affect without changes in negative affect after a night of sleep curtailment (Lo, Ong, Leong, Gooley, & Chee, 2016; Rossa, Smith, Allan, & Sullivan, 2014; Steptoe, O'Donnell, Marmot, & Wardle, 2008). It is important to note that changes in negative affect are have been reported when participants were totally sleep deprived, but not after partial sleep curtailment, (Minkel et al., 2012) and that the modest curtailment used in the current study may not have been large enough to elicit changes in negative affect. The

difference in positive affect between the sleep conditions may play a role in the differences in hedonic response to the sweet stimuli. One study reported that positive affect was associated with increased acceptance of generally less preferable flavors, suggesting that less-preferable stimuli become more acceptable when in a state of high positive affect [82]. Higher positive affect after a habitual night of sleep may partially explain the shift in the sweet liking slope, as sweet likers with higher positive affect may rate less preferable low concentrations more favorably. However, our participants were clearly not in a "state of high positive affect", given the mean (23.8) is lower than normative momentary positive affect measured using the PANAS (29.7) (Watson et al., 1988). It is not clear if increased liking of less preferable flavors is linearly associated with positive affect or if increased liking only occur after a threshold of positive affect is reached.

4.1. Strengths and Limitations

The strengths of this study include the randomized crossover design with testing sessions held one week apart on the same day within 30 minutes of the previous session under fasted conditions. Another strength is the use of the Zmachine EEG to collect objective at-home sleep data from participants. The Zmachine allowed for the confirmation of adherence to the prescribed sleep curtailment. Limitations of this study include possible fatigue effects from the large sample tasting load per lab visit. To minimize this, breaks between trials were instituted. Further, the range of sweetness levels used may not have been large enough to fully capture changes in sweet taste preference after sleep curtailment, as evidenced by participants who selected the highest level of sweetness after a habitual (sucrose n=4, sucralose n=4) or curtailed night of sleep (sucrose: n=11, sucralose n=12) in at least one of the two trials during sweet preference testing. Finally, sweet taste alone was measured using prototypical tastants in water,

and therefore, it is unclear how these sleep curtailment-induced changes manifest, if at all, when complex foods with multiple sensory attributes are consumed.

5. Conclusions

Healthy participants who were not obese had increased preference for sweetness and fundamental SLPs were distorted after a night of modestly curtailed sleep. These findings suggest that increased energy intake related to insufficient sleep may be moderated by altered hedonic and chemosensory perception. While the shift in the slope of the liking of sucralose was similar in appearance to sucrose, there was, statistically, no change in sucralose liking slope, which could be related to differential brain processing of the two sweeteners after sleep curtailment. Finally, significant changes in sweet taste perception after modest sleep curtailment suggest that it may be necessary to control for sleep in food sensory studies. However, future work is needed to determine whether perception of more complex food stimuli is altered after a curtailed night of sleep.

REFERENCES

REFERENCES

Asao, K., Luo, W., & Herman, W. H. (2012). Reproducibility of the measurement of sweet taste preferences. *Appetite*, *59*(3), 927–932. https://doi.org/10.1016/j.appet.2012.09.002.

Asao, K., Miller, J., Arcori, L., Lumeng, J. C., Han-Markey, T., & Herman, W. H. (2015). Patterns of sweet taste liking: A pilot study. *Nutrients*, *7*(9), 7298–7311. https://doi.org/10.3390/nu7095336.

Bachmanov, A. A., Bosak, N. P., Floriano, W. B., Inoue, M., Li, X., Lin, C., … Beauchamp, G. K. (2011). Genetics of sweet taste preferences. *Flavour and Fragrance Journal*, *26*(4), 286–294. https://doi.org/10.1002/ffj.2074.

Benedict, C., Brooks, S. J., O'Daly, O. G., Almèn, M. S., Morell, A., Åberg, K., … Schiöth, H. B. (2012). Acute sleep deprivation enhances the brain's response to hedonic food stimuli: An fMRI study. *The Journal of Clinical Endocrinology & Metabolism*, *97*(3), E443–E447. https://doi.org/10.1210/jc.2011-2759.

Binns, N. M. (2003). Sucralose – all sweetness and light. *Nutrition Bulletin*, *28*(1), 53–58. https://doi.org/10.1046/j.1467-3010.2003.00307.x

Bobowski, N., & Mennella, J. A. (2017). Personal variation in preference for sweetness: Effects of age and obesity. *Childhood Obesity*, *13*(5), 369–376. https://doi.org/10.1089/chi.2017.0023

Bosy-Westphal, A., Hinrichs, S., Jauch-Chara, K., Hitze, B., Later, W., Wilms, B., … Müller, M. J. (2008). Influence of partial sleep deprivation on energy balance and insulin sensitivity in healthy women. *Obesity Facts*, *1*(5), 266–273. https://doi.org/10.1159/000158874

Buysse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research*, *28*(2), 193–213. https://doi.org/10.1016/0165-1781(89)90047-4

Calvin, A. D., Carter, R. E., Adachi, T., Macedo, P. G., Albuquerque, F. N., Walt, C. van der, … Somers, V. K. (2013). Effects of experimental sleep restriction on caloric intake and activity energy expenditure. *CHEST*, *144*(1), 79–86. https://doi.org/10.1378/chest.12-2829

Cauter, E. V., Leproult, R., & Plat, L. (2000). Age-related changes in slow wave sleep and REM sleep and relationship with growth hormone and cortisol levels in healthy men. *JAMA*, *284*(7), 861–868. https://doi.org/10.1001/jama.284.7.861

Cepeda-Benito, A., Gleaves, D. H., Williams, T. L., & Erath, S. A. (2000). The development and validation of the state and trait food-cravings questionnaires. *Behavior Therapy*, *31*(1), 151–173. https://doi.org/10.1016/S0005-7894(00)80009-X

Chaput, J.-P. (2014). Sleep patterns, diet quality and energy balance. *Physiology & Behavior*, *134*, 86–91. https://doi.org/10.1016/j.physbeh.2013.09.006

Chaput, J.-P., & St-Onge, M.-P. (2014). Increased food intake by insufficient sleep in humans: Are we jumping the gun on the hormonal explanation? *Frontiers in Endocrinology*, *5*. https://doi.org/10.3389/fendo.2014.00116

Cheeta, S., Ruigt, G., van Proosdij, J., & Willner, P. (1997). Changes in sleep architecture following chronic mild stress. *Biological Psychiatry, 41*(4), 419–427. https://doi.org/10.1016/S0006-3223(96)00058-3

Chen, X., Gelaye, B., & Williams, M. A. (2014). Sleep characteristics and health-related quality of life among a national sample of American young adults: Assessment of possible health disparities. *Quality of Life Research, 23*(2), 613–625. https://doi.org/10.1007/s11136-013-0475-9

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior*, *24*(4), 385–396. https://doi.org/10.2307/2136404

Demos, K. E., Sweet, L. H., Hart, C. N., McCaffery, J. M., Williams, S. E., Mailloux, K. A., … Wing, R. R. (2017). The effects of experimental manipulation of sleep duration on neural response to food cues. *Sleep*, *40*(11). https://doi.org/10.1093/sleep/zsx125

Dinges, D. F., Pack, F., Williams, K., Gillen, K. A., Powell, J. W., Ott, G. E., … Pack, A. I. (1997). Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 hours per night. *Sleep, 20*(4), 267–277. https://doi.org/10.1093/sleep/20.4.267

Drewnowski, A. (1999). Intense sweeteners and energy density of foods: Implications for weight control. *European Journal of Clinical Nutrition*, *53*(10), 757–763. https://doi.org/10.1038/sj.ejcn.1600879

Ford, E. S., Cunningham, T. J., & Croft, J. B. (2015). Trends in self-reported sleep duration among US adults from 1985 to 2012. *Sleep*, *38*(5), 829–832.

Frank, G. K. W., Oberndorfer, T. A., Simmons, A. N., Paulus, M. P., Fudge, J. L., Yang, T. T., & Kaye, W. H. (2008). Sucrose activates human taste pathways differently from artificial sweetener. *NeuroImage*, *39*(4), 1559–1569. https://doi.org/10.1016/j.neuroimage.2007.10.061

Franzen, P. L., Siegle, G. J., & Buysse, D. J. (2008). Relationships between affect, vigilance, and sleepiness following sleep deprivation. *Journal of Sleep Research*, *17*(1), 34–41. https://doi.org/10.1111/j.1365-2869.2008.00635.x

Furchtgott, E., & Willingham, W. W. (1956). The effect of sleep-deprivation upon the thresholds of taste. *The American Journal of Psychology, 69*, 111-112.

Glickman, M. E., Rao, S. R., & Schultz, M. R. (2014). False discovery rate control is a recommended alternative to Bonferroni-type adjustments in health studies. *Journal of Clinical Epidemiology*, *67*(8), 850–857. https://doi.org/10.1016/j.jclinepi.2014.03.012

Green, E., & Murphy, C. (2012). Altered processing of sweet taste in the brain of diet soda drinkers. *Physiology & Behavior*, *107*(4), 560–567. https://doi.org/10.1016/j.physbeh.2012.05.006

Greer, S. M., Goldstein, A. N., & Walker, M. P. (2013). The impact of sleep deprivation on food desire in the human brain. *Nature Communications*, *4*, ncomms3259. https://doi.org/10.1038/ncomms3259

Gujar, N., Yoo, S.-S., Hu, P., & Walker, M. P. (2011). Sleep deprivation amplifies reactivity of brain reward networks, biasing the appraisal of positive emotional experiences. *Journal of Neuroscience*, *31*(12), 4466–4474. https://doi.org/10.1523/JNEUROSCI.3220-10.2011

Hanlon, E. C., Andrzejewski, M. E., Harder, B. K., Kelley, A. E., & Benca, R. M. (2005). The effect of REM sleep deprivation on motivation for food reward. *Behavioural Brain Research*, *163*(1), 58–69. https://doi.org/10.1016/j.bbr.2005.04.017

Iatridi, V., Hayes, J. E., & Yeomans, M. R. (2018). Reconsidering the classification of sweet taste liker phenotypes: A methodological review. *Food Quality and Preference*. https://doi.org/10.1016/j.foodqual.2018.09.001

Iatridi, V., Hayes, J. E., & Yeomans, M. R. (2019). Quantifying sweet taste liker phenotypes: Time for some consistency in the classification criteria. *Nutrients*, *11*(1), 129. https://doi.org/10.3390/nu11010129

Kaida, K., Takahashi, M., Åkerstedt, T., Nakata, A., Otsuka, Y., Haratani, T., & Fukasawa, K. (2006). Validation of the Karolinska sleepiness scale against performance and EEG variables. *Clinical Neurophysiology*, *117*(7), 1574–1581. https://doi.org/10.1016/j.clinph.2006.03.011

Kampov-Polevoy, A. B., Alterman, A., Khalitov, E., & Garbutt, J. C. (2006). Sweet preference predicts mood altering effect of and impaired control over eating sweet foods. *Eating Behaviors*, *7*(3), 181–187. https://doi.org/10.1016/j.eatbeh.2005.09.005

Kampov-Polevoy, A., Lange, L., Bobashev, G., Eggleston, B., Root, T., & Garbutt, J. C. (2014). Sweet-liking is associated with transformation of heavy drinking into alcohol-related problems in young adults with high novelty seeking. *Alcoholism: Clinical and Experimental Research*, *38*(7), 2119–2126. https://doi.org/10.1111/acer.12458

Kaplan, R. F., Wang, Y., Loparo, K. A., Kelly, M. R., & Bootzin, R. R. (2014). Performance evaluation of an automated single-channel sleep–wake detection algorithm. *Nature and Science of Sleep*, *6*, 113–122. https://doi.org/10.2147/NSS.S71159

Keskitalo, K., Tuorila, H., Spector, T. D., Cherkas, L. F., Knaapila, A., Silventoinen, K., & Perola, M. (2007). Same genetic components underlie different measures of sweet taste preference. *The American Journal of Clinical Nutrition*, *86*(6), 1663–1669. https://doi.org/10.1093/ajcn/86.6.1663

Kim, J.-Y., Prescott, J., & Kim, K.-O. (2014). Patterns of sweet liking in sucrose solutions and beverages. *Food Quality and Preference*, *36*(Supplement C), 96–103. https://doi.org/10.1016/j.foodqual.2014.03.009

Kim, J.-Y., Prescott, J., & Kim, K.-O. (2017). Emotional responses to sweet foods according to sweet liker status. *Food Quality and Preference*, *59*, 1–7. https://doi.org/10.1016/j.foodqual.2017.01.013

Lange, L. A., Kampov-Polevoy, A. B., & Garbutt, J. C. (2010). Sweet Liking and High Novelty Seeking: Independent Phenotypes Associated with Alcohol-related Problems. *Alcohol and Alcoholism*, *45*(5), 431–436. https://doi.org/10.1093/alcalc/agq040

Lean, M. E. J., Astrup, A., & Roberts, S. B. (2018). Making progress on the global crisis of obesity and weight management. *BMJ*, *361*, k2538. https://doi.org/10.1136/bmj.k2538

Leigh, S.-J., & Morris, M. J. (2018). The role of reward circuitry and food addiction in the obesity epidemic: An update. *Biological Psychology*, *131*, 31–42. https://doi.org/10.1016/j.biopsycho.2016.12.013

Lo, J. C., Ong, J. L., Leong, R. L. F., Gooley, J. J., & Chee, M. W. L. (2016). Cognitive performance, sleepiness, and mood in partially sleep deprived adolescents: The need for sleep study. *Sleep*, *39*(3), 687–698. https://doi.org/10.5665/sleep.5552

Lv, W., Finlayson, G., & Dando, R. (2018). Sleep, food cravings and taste. *Appetite*, *125*, 210–216. https://doi.org/10.1016/j.appet.2018.02.013

Markwald, R. R., Melanson, E. L., Smith, M. R., Higgins, J., Perreault, L., Eckel, R. H., & Wright, K. P. (2013). Impact of insufficient sleep on total daily energy expenditure, food intake, and weight gain. *Proceedings of the National Academy of Sciences*, *110*(14), 5695–5700. https://doi.org/10.1073/pnas.1216951110

McNeil, J., Forest, G., Hintze, L. J., Brunet, J.-F., Finlayson, G., Blundell, J. E., & Doucet, É. (2017). The effects of partial sleep restriction and altered sleep timing on appetite and food reward. *Appetite*, *109*, 48–56. https://doi.org/10.1016/j.appet.2016.11.020

Meilgaard, M. C., Carr, B. T., Civille, G. V., Carr, B. T., & Civille, G. V. (1999). *Sensory Evaluation Techniques*. https://doi.org/10.1201/9781439832271

Mennella, J. A., Lukasewycz, L. D., Griffith, J. W., & Beauchamp, G. K. (2011). Evaluation of the Monell forced-choice, paired-comparison tracking procedure for determining sweet taste preferences across the lifespan. *Chemical Senses*, *36*(4), 345–355. https://doi.org/10.1093/chemse/bjq134

Mennella, J. A., Pepino, M. Y., & Reed, D. R. (2005). Genetic and environmental determinants of bitter perception and sweet preferences. *Pediatrics*, *115*(2), e216–e222. https://doi.org/10.1542/peds.2004-1582

Merrill, E. P., Kramer, F. M., Cardello, A., & Schutz, H. (2002). A comparison of satiety measures. *Appetite*, *39*(2), 181–183. https://doi.org/10.1006/appe.2002.0496

Meule, A., & Kübler, A. (2014). Double trouble. Trait food craving and impulsivity interactively predict food-cue affected behavioral inhibition. *Appetite*, *79*, 174–182. https://doi.org/10.1016/j.appet.2014.04.014

Minkel, J. D., Banks, S., Htaik, O., Moreta, M. C., Jones, C. W., McGlinchey, E. L., … Dinges, D. F. (2012). Sleep deprivation and stressors: Evidence for elevated negative affect in response to mild stressors when sleep deprived. *Emotion*, *12*(5), 1015–1020. https://doi.org/10.1037/a0026871

Moskowitz, H. R. (1970). Sweetness and intensity of artificial sweeteners. *Perception & Psychophysics*, *8*(1), 40–42. https://doi.org/10.3758/BF03208930

Nedeltcheva, A. V., Kilkus, J. M., Imperial, J., Kasza, K., Schoeller, D. A., & Penev, P. D. (2009). Sleep curtailment is accompanied by increased intake of calories from snacks–. *The American Journal of Clinical Nutrition*, *89*(1), 126–133. https://doi.org/10.3945/ajcn.2008.26574

Nijs, I. M. T., Franken, I. H. A., & Muris, P. (2007). The modified Trait and State Food-Cravings Questionnaires: Development and validation of a general index of food craving. *Appetite*, *49*(1), 38–46. https://doi.org/10.1016/j.appet.2006.11.001

Noel, C., & Dando, R. (2015). The effect of emotional state on taste perception. *Appetite*, *95*, 89–95. https://doi.org/10.1016/j.appet.2015.06.003

Oleson, S., & Murphy, C. (2017). Prediction of Stevia liking by sucrose liking: Effects of beverage background. *Chemosensory Perception*, *10*(3), 49–59. https://doi.org/10.1007/s12078-017-9225-7

Ong, A. D., Kim, S., Young, S., & Steptoe, A. (2017). Positive affect and sleep: A systematic review. *Sleep Medicine Reviews*, *35*, 21–32. https://doi.org/10.1016/j.smrv.2016.07.006

Patel Sanjay R., & Hu Frank B. (2012). Short sleep duration and weight Ggain: A systematic review. *Obesity*, *16*(3), 643–653. https://doi.org/10.1038/oby.2007.118

Reis, F., De Andrade, J., Deliza, R., & Ares, G. (2016). Comparison of two methodologies for estimating equivalent sweet concentration of high-intensity sweeteners with untrained assessors: Case study with orange/pomegranate juice. *Journal of Sensory Studies*, *31*(4), 341–347. https://doi.org/10.1111/joss.12217

Robertson, M. D., Russell-Jones, D., Umpleby, A. M., & Dijk, D.-J. (2013). Effects of three weeks of mild sleep restriction implemented in the home environment on multiple metabolic and endocrine markers in healthy young men. *Metabolism*, *62*(2), 204–211. https://doi.org/10.1016/j.metabol.2012.07.016

Rossa, K. R., Smith, S. S., Allan, A. C., & Sullivan, K. A. (2014). The effects of sleep restriction on executive inhibitory control and affect in young adults. *Journal of Adolescent Health*, *55*(2), 287–292. https://doi.org/10.1016/j.jadohealth.2013.12.034

Scheen, A. J., Byrne, M. M., Plat, L., Leproult, R., & Cauter, E. V. (1996). Relationships between sleep quality and glucose regulation in normal humans. *American Journal of Physiology - Endocrinology and Metabolism*, *271*(2), E261–E270.

Shahid, A., Wilkinson, K., Marcu, S., & Shapiro, C. M. (2012). Karolinska Sleepiness Scale (KSS). In A. Shahid, K. Wilkinson, S. Marcu, & C. M. Shapiro (Eds.), *STOP, THAT and One Hundred Other Sleep Scales* (pp. 209–210). https://doi.org/10.1007/978-1-4419-9893-4_47

Smith, Ludy, M.-J., & Tucker, R. M. (2016). Changes in taste preference and steps taken after sleep curtailment. *Physiology & Behavior*, *163*, 228–233. https://doi.org/10.1016/j.physbeh.2016.05.002

Spiegel, K., Leproult, R., & Van Cauter, E. (1999). Impact of sleep debt on metabolic and endocrine function. *The Lancet*, *354*(9188), 1435–1439. https://doi.org/10.1016/S0140-6736(99)01376-8

Steptoe, A., O'Donnell, K., Marmot, M., & Wardle, J. (2008). Positive affect, psychological well-being, and good sleep. *Journal of Psychosomatic Research*, *64*(4), 409–415. https://doi.org/10.1016/j.jpsychores.2007.11.008

St-Onge, Marie-Pierre. (2013). The role of sleep duration in the regulation of energy balance: effects on energy intakes and expenditure. *Journal of Clinical Sleep Medicine: JCSM: Official Publication of the American Academy of Sleep Medicine*, *9*(1), 73.

St-Onge, M-P, Wolfe, S., Sy, M., Shechter, A., & Hirsch, J. (2014). Sleep restriction increases the neuronal response to unhealthy food in normal-weight individuals. *International Journal of Obesity (2005)*, *38*(3), 411–416. https://doi.org/10.1038/ijo.2013.114

Stringer, D. M. (2013). Negative affect. In M. D. Gellman & J. R. Turner (Eds.), *Encyclopedia of Behavioral Medicine* (pp. 1303–1304). https://doi.org/10.1007/978-1-4419-1005-9_606

Szczygiel, E.J , Cho, S., & Tucker, R. M. (2018). Characterization of the relationships between sleep duration, quality, architecture and chemosensory function in non-obese females. *Chemical Senses*, *43*(4), 223–228. https://doi.org/10.1093/chemse/bjy012

Szczygiel, E. J., Cho, S., Snyder, M. K., & Tucker, R. M. (2019). Associations between chemosensory function, sweet taste preference, and the previous night's sleep in non-obese males. *Food Quality and Preference*, *75*, 105–112. https://doi.org/10.1016/j.foodqual.2019.02.018

Tan, S.-Y., & Tucker, R. M. (2019). Sweet taste as a predictor of dietary intake: A systematic review. *Nutrients*, *11*(1), 94. https://doi.org/10.3390/nu11010094

Tanaka, T., Hong, G., Tominami, K., & Kudo, T. (2018). Oral fat sensitivity is associated with social support for stress coping in young adult men. *The Tohoku Journal of Experimental Medicine*, *244*(4), 249–261.

Thomas, M., Sing, H., Belenky, G., Holcomb, H., Mayberg, H., Dannals, R., … Redmond, D. (2000). Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. *Journal of Sleep Research*, *9*(4), 335–352. https://doi.org/10.1046/j.1365-2869.2000.00225.x

van der Lely, A. J., Tschöp, M., Heiman, M. L., & Ghigo, E. (2004). Biological, physiological, pathophysiological, and pharmacological aspects of ghrelin. *Endocrine Reviews*, *25*(3), 426–457. https://doi.org/10.1210/er.2002-0029

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology*, *54*(6), 1063–1070. http://dx.doi.org.proxy1.cl.msu.edu/10.1037/0022-3514.54.6.1063

Wiet, S. G., & Beyts, P. K. (1992). Sensory characteristics of sucralose and other high intensity sweeteners. *Journal of Food Science*, *57*(4), 1014–1019. https://doi.org/10.1111/j.1365-2621.1992.tb14345.x

Yeomans, M. R., Prescott, J., & Gould, N. J. (2009). Acquired hedonic and sensory characteristics of odours: Influence of sweet liker and propylthiouracil taster status. *The*

Quarterly Journal of Experimental Psychology, *62*(8), 1648–1664. https://doi.org/10.1080/17470210802557793

Yeomans, M. R., Tepper, B. J., Rietzschel, J., & Prescott, J. (2007). Human hedonic responses to sweetness: role of taste genetics and anatomy. *Physiology & Behavior*, *91*(2–3), 264–273.

Chapter 5:

It is currently unclear if changes in sweet taste perception of model systems after sleep curtailment extend to complex food matrices. Therefore, the primary objective of this study was to use a novel solid food and beverage stimulus, sweetened with sucralose, to assess changes in taste perception after sleep curtailment. Forty-one participants recorded a habitual and curtailed night of sleep using a single-channel electroencephalograph. The next morning, overall, sweetness, flavor, and texture liking responses to energy- and nutrient-matched oat products across five concentrations of sweetness were measured. Overall ($p=0.047$) and flavor ($p=0.017$) liking slopes across measured concentrations were steeper after curtailment, suggesting that sweeter versions of the oat products were liked more after sleep curtailment. Additionally, hierarchical cluster analysis was used to classify sweet likers and non-likers. While the effect of sleep curtailment on sweet liking was not moderated by sweet liking classification, sleep curtailment resulted in decreased texture liking in the solid oat crisps for sweet non-likers ($p<0.001$), but not in the liquid oat beverage. These findings illustrate the varied effects of sleep on hedonic response in complex food matrices and possible mechanisms by which insufficient sleep can lead to sensory-moderated increases in energy intake.

1. Introduction

There is a growing body of evidence that insufficient sleep can alter taste perception. Several recent psychophysical studies have reported that short sleep duration is associated with increased preferred sucrose concentration (Smith, Ludy, & Tucker, 2016; Szczygiel, Cho, & Tucker, 2018; Szczygiel, Cho, Snyder, & Tucker, 2019) and increased perceived intensity of sour and umami taste (Lv, Finlayson, & Dando, 2018). Insufficient sleep-induced changes in

taste perception may partially moderate the well-supported relationship between short sleep duration, increased dietary intake of highly palatable high-carbohydrate and high-fat foods, and weight gain (Markwald et al., 2013; Nedeltcheva et al., 2009; Simon, Field, Miller, DiFrancesco, & Beebe, 2015). Brain imaging research suggests that insufficient sleep results in increased neural sensitivity to the reward properties of food (Benedict et al., 2012; Demos et al., 2017; Greer, Goldstein, & Walker, 2013; Hanlon, Andrzejewski, Harder, Kelley, & Benca, 2005; St-Onge, Wolfe, Sy, Shechter, & Hirsch, 2014). This heightened sensitivity may increase consumption of palatable food for pleasure, also known as hedonic eating. Hedonic eating is thought to promote weight gain, as highly palatable food tends to be energy dense (A. Drewnowski, 1999). Sweetness is commonly associated with the palatability of food (Adam Drewnowski, Mennella, Johnson, & Bellisle, 2012) and, when tasted, initiates brain reward processes (Yamamoto, 2003); therefore, sweet taste is of particular interest when exploring relationships between insufficient sleep and hedonic eating. Given that nearly 40% of the US adult population is reported to sleep less than the recommended 7 h per night (Chen, Gelaye, & Williams, 2014) and nearly 40% of American adults suffer from obesity (Hales, Carroll, Fryar, & Ogden, 2017), understanding the mechanisms by which insufficient sleep can lead to weight gain is of importance to scientists, the food industry, and public health advocates.

Very few studies utilize complex food when examining the effect of insufficient sleep on taste function (Hogenkamp et al., 2013; Lv et al., 2018). Instead, nearly all existing sleep-taste research has been conducted using model systems — prototypical tastants dissolved in deionized water — and evaluated while wearing nose clips (Lv et al., 2018; Smith et al., 2016; Szczygiel et al., 2018; Szczygiel et al., 2019; Szczygiel, Cho, & Tucker, 2019.; Tanaka, Hong, Tominami, & Kudo, 2018). Results from previous psychophysical studies examining the effects of sleep on

taste perception need to be replicated in more complex food matrices as findings in model systems do not always align with findings using complex foods (Adam Drewnowski, Shrager, Lipsky, Stellar, & Greenwood, 1989; Huber, 1974; Mazur, Drabek, & Goldman, 2018; Tan & Tucker, 2019). The simplicity of model systems allows participants to evaluate taste with minimal distraction from other sensory inputs like texture or aroma, but affective judgments of foods and beverages are determined using all senses, including the appearance, mouthfeel, auditory characteristics, geometry, and physical state of food (Dhillon, Running, Tucker, & Mattes, 2016).. Thus, further efforts are needed to assess the generalizability of taste-related findings from psychophysical studies to complex food matrices.

In addition to the general issues discussed above regarding translating findings from model systems to food, there are particular reasons to believe that the generalizability of findings from model stimuli to complex foods under conditions of insufficient sleep could be especially problematic. In the context of complex food, research suggests two important effects of insufficient sleep that could alter perception: impaired sensory neural processing (Gujar, Yoo, Hu, & Walker, 2011; Krause et al., 2017) and increased somatosensory sensitivity (Kamiyama et al., 2019). First, given that the orbitofrontal cortex (OFC), often described as the neural control center for food (Schloegl, Percik, Horstmann, Villringer, & Stumvoll, 2011), is impaired after sleep curtailment, the ability to interpret multimodal information may be compromised (Gujar et al., 2011; Krause et al., 2017). Under normal conditions, processing of specific attributes within multimodal sensory information is already limited. For example, when consuming complex foods, the ability of participants to separate perceived sweet taste liking from perceived flavor or overall liking may be diminished due to sensory interactions (Auvray & Spence, 2008). Thus, after sleep curtailment, impairment of OFC activity may result in further differences between

perception in controlled systems and complex food systems (Auvray & Spence, 2008). The second concern about the generalizability of findings from model systems to more complex food matrices under insufficient sleep conditions stems from documented changes in somatosensory perception. Sleep curtailment has been implicated in acute reward system-mediated hyperalgesia — an increased sensitivity to pain (Roehrs, Hyde, Blaisdell, Greenwald, & Roth, 2006) — and increased oro-facial somatosensory sensitivity, particularly in the tongue (Kamiyama et al., 2019). While speculative, increased hyperalgesia and increased oro-facial sensitivity might decrease acceptability of the texture of crispy or crunchy solid foods and increase preference for softer foods that require less oral processing. In summary, organization of sensory information, reward processing of that information, and changes in oral sensory sensitivity all represent opportunities for insufficient sleep to affect hedonic food perception.

Individual differences in hedonic response to taste make it challenging to study the relationship between insufficient sleep and gustatory perception. Despite being an innately palatable taste at birth (Barr et al., 1999), liking responses to sweet taste as the concentration of sweetness increases differ across individuals. Three fundamental patterns of liking over a range of sweetness levels have been identified previously: sweet likers, who display a rise in liking as sweetener concentration increases; inverted U-shape responders, who show an increasing liking pattern up until a certain concentration before beginning show a decrease; and dislikers, who display a reduction in liking as concentration increases (Iatridi, Hayes, & Yeomans, 2018, 2019; Yeomans, Tepper, Rietzschel, & Prescott, 2007). Additionally, a fourth pattern where hedonic response to sweetness is the same regardless of sweetness concentration has been reported (Iatridi et al., 2019), but others have reported not observing this phenotypes (Asao et al., 2015; J.-Y. Kim, Prescott, & Kim, 2014). These fundamental patterns of liking are partially determined

by genetic factors (Bachmanov et al., 2011; Mennella, Pepino, & Reed, 2005), and thus, they are commonly described as "sweet liking phenotypes" (SLP). Sweet likers differ in expressed behaviors compared to the other phenotypes, including increased intake of sugar and sugar-sweetened beverages (Garneau, Nuessle, Mendelsberg, Shepard, & Tucker, 2018; Holt, Cobiac, Beaumont-Smith, Easton, & Best, 2000). These behavioral traits suggest that sweet liking phenotypes are heritable indicators of general brain reward processing dysfunction. Given that the central hypothesis of this research is that insufficient sleep-induced reward processing dysfunction may influence hedonic perception of food, individual differences in response to sweet taste are an important factor to consider, as these baseline differences in reward processing may be reduce effects of insufficient sleep on the brain reward processing. While our previous work found that preferred sweetener concentration was similarly increased across sweet liking phenotypes after sleep curtailment (Szczygiel et al., 2019), this relationship has not been evaluated in complex foods. Therefore, the question of whether SLP is an important factor moderating the effect of sleep curtailment merits further investigation in the context of complex foods.

In order to sweeten complex foods across a wide range of sweetness levels, high-intensity non-nutritive sweeteners, such as sucralose (Binns, 2003), can be used to minimize collinear changes in texture (Cheer & Lelievre, 1983), aroma (van Boekel, 2006), and appearance (Ashoor & Zent, 1984) that could occur if iso-sweet quantities of sucrose were used. In a previous study, the effect of sleep curtailment on hedonic response to sucrose and sucralose solutions was determined (Szczygiel et al., 2019). Sleep curtailment resulted in an increase in preferred sweetener concentration for both sucrose and sucralose. However, while the effect of sleep curtailment on the slope of sweet liking across a range of sweetness concentrations increased for

both sweeteners, the increase was only significant for sucrose. This difference suggests that sucralose perception may be affected by sleep curtailment to a lesser extent than sucrose. This discrepancy may be due to reduced reactivity of brain reward centers in response to non-nutritive sweeteners (NNS) (Frank et al., 2008). However, the advantage of controlling the non-taste sensory properties in order to isolate taste changes, the main purpose of this study, outweighs potential differences in reward processing between nutritive and NNS. In addition, sucralose is used widely and increasingly in the developed world food supply (Sylvetsky & Rother, 2016), which means a large portion of the population is exposed to it on a daily basis.

The main objective of this study was to evaluate changes in hedonic response to sucralose solutions and two complex foods across a range of sweetness levels after a habitual and curtailed night of sleep. It was hypothesized that hedonic perception in the model system would change in accordance with our previous findings (Szczygiel et al., 2019); preferred sucralose solution concentration would increase and a non-significant increase in steepness of the slope of liking over a range of concentration would be observed. For the food products, it was expected that patterns of sweet liking in food products as sweetness concentration increased would, in agreement with model systems, show a non-significant increase in slope steepness after sleep curtailment. It was also expected that broader hedonic measures, such as a flavor and overall liking, would show increases corresponding with increasing sweetness after sleep curtailment, as these terms have the potential to capture changes in multisensory perception unique to complex foods. Further, it was hypothesized that texture liking would be decreased in a solid food, but not a liquid food, after sleep curtailment. A secondary objective was to assess if food form and SLP interact with sleep curtailment to alter sensory perception of complex foods. Although SLP was not found to differentially moderate changes in hedonic perception in model systems under

conditions of insufficient sleep, we sought to confirm this finding in complex foods. It was expected that SLP would not moderate changes in hedonic perception of food after sleep curtailment in accordance with previous work (Szczygiel et al., 2019).

2. Materials and Methods

The protocol for this study was approved by the Michigan State University Human Research Protection Program (East Lansing, MI, USA). Written informed consent was obtained from all participants.

2.1. Participants

Participants between the ages of 18-45, without obesity (BMI < 30.0 kg/m^2) or diagnosed sleep conditions, who typically slept 7-9 h per weeknight, and who had a consistent weekday bedtime were eligible to participate in the study. Participants were pre-screened using two criteria. First, each participant sampled both the oat "beverage" and oat "crisp" products (see Development of Stimuli section, below) evaluated in the study (sweetened with sucralose at the middle 0.032% w/v level) and asked to rate their overall liking of each on a 9-point hedonic scale (extremely dislike (1) to extremely like (9)). Participants who rated either sample < 6 (like slightly) were not eligible for the study. Second, each participant sampled the highest concentration of sucralose in water (0.094% w/v) used in the study and asked to report if they tasted any bitterness. Sucralose does not ordinarily display high levels of bitterness (Wiet & Beyts, 1992). Even so, participants who are extremely sensitive to bitterness (Mennella et al., 2005) may find it challenging to evaluate sweetness in sucralose solutions. To avoid this, participants who tasted bitterness in the highly sweet sucralose sample were excluded from the

study. Three individuals who were otherwise eligible were excluded due to tasting bitterness, and two were excluded due to dislike of the oat beverage.

2.2. Development of Stimuli

Sucralose was selected as the sweetener for this study due to its sensory and functional properties. Sucralose has a taste profile with similar character to sucrose and has low bitter and off-tastes compared to other high-intensity sweeteners (Wiet & Beyts, 1992). Sucralose requires very small amounts to achieve the same sweetness as sucrose (M.-Y. Kim et al., 2005). This property of sucralose enabled formulation of complex food products that varied in sweetness while minimizing changes in other sensory attributes, such as texture. A preliminary study was carried out to assess iso-sweet concentrations of sucralose compared to sucrose using the magnitude estimation methods of Reis et. al. 2016 (Reis, De Andrade, Deliza, & Ares, 2016). Sucralose concentrations of 0.004%, 0.011%, 0.032%, 0.060%, and 0.094%w/v were selected based on the magnitude estimation data. These concentrations are equal in sweetness to 3%, 6%, 12%, 18%, and 24% w/v sucrose, respectively.

To assess the effect of sleep curtailment on patterns of liking of complex food matrices, two energy and macronutrient-matched oat-based products were developed. The first product, an oat "beverage", was developed to assess the effect of sleep curtailment on hedonic perceptions of liquid food, and the second product, an oat "crisp", was developed to assess the effect of sleep curtailment on hedonic perceptions of solid food. The two products contained the same ingredients: whole grain rolled quick oats (Quaker Oats Company, Chicago, IL), pure sucralose powder (Sweet Solutions, Edison, NJ), and filtered water (Besco, Battle Creek, MI). In both products, sucralose was added to water at the concentrations discussed previously and used to produce five differently sweet versions of both products. Proximate analysis was performed by

Great Lakes Scientific (Stevensville, MI) using the Association of Analytical Chemists (AOAC) method. A breakdown of the macronutrient content per 100 kcal is displayed in Table 5.1. The two products were matched on macronutrients per kcal. The only difference between the two products was the moisture content, as designed.

Table 5.1. Macronutrient Composition of Oat Products

	Oat Beverage	Oat Crisp
Macronutrient	100 kcal	100 kcal
Fat	2 g	2 g
Carbohydrates	18 g	17 g
Protein	3 g	3 g
Crude Fiber	<1 g	<1 g
Moisture	189 g	1 g
Ash	<1 g	<1 g

Stimuli were matched for energy and macronutrient composition. Moisture content differed due to the physical state of the stimuli.

Oat beverage was produced by creating an oat slurry by blending (Nutribullet, NutriLiving, Northridge, CA) 240 g of sucralose-sweetened water and 50 g of rolled oats (Quaker Oat Company, Chicago, IL) for 10 s. The slurry was filtered through a 100 μm steel mesh to produce a smooth, milk-like beverage. The oat beverage was stored in glass bottles at 4° C for no more than 48 h after production.

Oat crisps were prepared using a 1200 W microwave (General Electric, Boston, MA) to dehydrate an oat slurry, which was produced by mixing oats and sucralose-sweetened water in the same procedure as the oat beverage. Differently sweetened oat slurries were microwaved in a 200 mm x 200 mm glass pan for 15 min. The semi-dry oat sheet was then flipped and a 12.7 mm circular cutter was used to cut crisps out of the sheet. The cut crisps were then microwaved for an additional 2 min. The oat crisps were weighed to insure each crisp weighed 1.2 ± 0.1 g. The

crisps were then cooled in air for 15 min before being vacuum-sealed in plastic and stored at room temperature until served.

2.3. Study Timeline

After an initial consent visit to confirm eligibility for the study, participants visited the sensory lab twice: once after a habitual night and once after a curtailed night of sleep. The lab visits occurred at least one week apart on the same weekday and time (± 30 min). Sensory testing transpired during 1 h timeslots between the hours of 7:00 - 10:00 a.m. on weekdays. The sleep condition sequence was randomly assigned during the consent visit. A sleep curtailment of 33% was determined by centering the self-reported habitual sleep duration and equally reducing bed and wake time in order to minimize circadian rhythm effects while still inducing sleepiness (Dinges et al., 1997). For example, if the curtailment was 2 h, the participant was required to go to bed 1 h later and wake up 1 h earlier. The study was designed to assess change in hedonic perception under free-living conditions, and therefore, partial sleep curtailment was utilized in place of total sleep deprivation (Dinges et al., 1997).

2.3.1. Consent Visit

Participants completed several validated questionnaires during the consent visit. The Pittsburgh Sleep Quality Index (PSQI) (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989), Perceived Stress Scale (PSS)(Cohen, Kamarck, & Mermelstein, 1983), and the General Food Craving Questionnaire –Trait version (G-FCQ-T) (Cepeda-Benito, Gleaves, Williams, & Erath, 2000) were used to determine subjective sleep, perceived stress, and general food craving traits, respectively. A relationship between food cravings and reward sensitivity has been reported previously (Meule & Kübler, 2014) and, thus, food cravings were measured to aid in

interpretation of findings. Participants may not have been aware that their sleep habits were abnormal, and thus, the PSQI scores were used to confirm that participants met the criteria for the study. Anthropometrics were also measured for use as covariates. Body mass index (BMI) and percent body fat (% BF) were measured using bioelectrical impedance (TBF-400, Tanita, Arlington Heights, IL).

Objective sleep measures were collected using the Zmachine (General Sleep, Columbus, OH). Participants were trained on how to use the Zmachine at the consent visit. The Zmachine records a single channel (A_1-A_2) of electroencephalography (EEG) and uses a scoring algorithm to discriminate between light sleep (LS), slow wave sleep (SWS), REM sleep, and waking states. The Zmachine has been reported to have significant agreement with polysomnography (PSG) (Kaplan, Wang, Loparo, Kelly, & Bootzin, 2014). To ensure participants complied with the assigned protocol, they were instructed to wear the Zmachine 30 min before the predetermined bedtime assigned to them.

To ensure that participants would be fasted after both sleep conditions, they were told to not eat or drink anything other than water between their wake time and their laboratory visit. Additionally, they were told that they would be required to take a "Hydrogen Breath Test", the results of which would inform the study administrator if they did not follow the fasting instructions. This deceptive procedure was employed to increase compliance with the fasting instructions. The samples were discarded after testing and participants were made aware of the deceit during debriefing.

2.3.2. Laboratory Visits

The testing procedure used was the same for both laboratory visits. EEG data from the previous night's sleep was promptly uploaded to the Zmachine data viewer upon arrival to the lab. The participant was asked to confirm that the data matched their own recollection of the previous night. If there were any discrepancies between the participant's memory and the recorded sleep data or significant data loss, participants returned to the lab no fewer than seven days later with a new sleep recording. Participants then completed the "Hydrogen Breath Test".

Before tasting any stimuli, participants completed several validated questionnaires, including: the Karolinska Sleepiness Scale (KSS) (Kaida et al., 2006), the Positive Affect-Negative Affect Schedule (PANAS) (Watson, Clark, & Tellegen, 1988), and the General Food Craving Questionnaire-State version (G-FCQ-S) (Cepeda-Benito et al., 2000). These tools were used to measure sleepiness, affect, and food craving state, respectively. Additionally, a 100mm visual analog scale (VAS) was used to measure hunger with "Extremely Hungry "(0) and "Extremely Full" (100) serving as anchors (Merrill, Kramer, Cardello, & Schutz, 2002). The KSS was used along with objective sleep measure to determine the efficacy of the sleep curtailment. The PANAS was used to measure affect changes between the habitual and curtailed sleep conditions to help interpret findings, as changes in affect have been reported to change with sleep curtailment (Franzen, Siegle, & Buysse, 2008) and influence taste perception (Noel & Dando, 2015). Craving states have been found to be associated with sleep duration (Lv et al., 2018); therefore, G-FCQ-S data was collected to help aid in interpretation of findings in the case that cravings were significantly increased by curtailment. Hunger was measured to confirm fasting protocol was effective.

To assess self-perception of the previous night's sleep quality, participants answered four questions regarding their recollection of the previous night's sleep (Szczygiel et al., 2019). The four questions were: "How much did sleep did you obtain last night?", "How deeply did you sleep last night?", "How would you rate the quality of your sleep last night?", and "Compared to an average night of sleep, how comfortable were you when sleeping last night?" The sum of the scores from each of these four questions was used as a measure of overall subjective sleep quality.

2.4. Sensory Evaluation

RedJade Sensory Software (RedJade, Redwood Shores, CA, USA) was used to manage sensory data collection. All data collection took place at the Michigan State University sensory laboratory. Participants were required to wear nose-clips during sucralose solution tastings but not when consuming oat products. For the sucralose-in-water tasting, participants were instructed to taste the whole cup (10 ml of sample) and expectorate all samples. For the oat product evaluation, the amount served was normalized to 5 kcal; that is, oat crisps were always served in 1.2±0.1 g quantities (5 kcal) and oat beverage was always served in 10 ml quantities (5 kcal). Oat beverage was served cool at 7° C and while oat crisps and sucralose solutions were served at room temperature (23° C). Participants did not expectorate oat products. The sensory evaluation consisted of hedonic evaluation of the sucralose solutions and sweet preference testing followed by evaluation of the oat beverage and oat crisps in random order.

The solutions and products were assessed by presenting a range of five different concentrations of sweetness of each product identified with three-digit blinding codes in random order. For the sucralose solutions, participants rated their liking of each solution on a 15 cm VAS scale with anchors at 0 (dislike extremely), 7.5 (neutral) and 15 (like extremely). For the oat

products, participants rated their overall liking, sweetness liking, flavor liking and texture liking on an identical 15 cm line scale, in that order. In food acceptance tests, it is typical for participants to rate the overall liking of a product, followed by rating a series of product attributes, such as flavor and texture (Popper, Rosenstock, Schraidt, & Kroll, 2004). Additionally, participants were asked to rate how intensely they perceived the sweetness to be on a 15 cm VAS scale with anchors at 0 (not at all intense), 7.5 (no label) and 15 (extremely intense) for both sucralose solutions and oat products. Following the tasting of a sample, there was a 45 s forced wait period in which the participant was required to rinse three times with filtered water. There were three, two-minute breaks after every five samples. In total, participants tasted between 10-15 sucralose solutions, 5 oat beverages, and 5 oat crisps at each testing visit.

A modified version of the Monell forced choice paired comparison protocol (Mennella, Lukasewycz, Griffith, & Beauchamp, 2011) was used for preference testing per the methods previously described in Szczygiel et al. 2019 (Szczygiel et al., 2019). This version of the protocol reduces the two highest concentrations from the Monell protocol— 24% and 36% w/v—to 18% and 24% w/v. respectively. The modification to the original protocol was made in order to reduce the possibility of off tastes in high concentrations of sucralose.

2.5. Statistical Analysis

SAS version 9.4 (SAS Institute, Cary, NC., U.S.A.) was used to analyze data. In all analyses, findings were treated as statistically significant if $p<0.05$ and data are presented as the mean±standard deviation unless stated otherwise. Overall and attribute liking and intensity scores were plotted against sweetener concentration. The best fit linear functions for each plot

were calculated in Excel (Microsoft, Redmond, WA, U.S.) and the slope of that function became the "Slope" variables used in several analyses.

Hierarchical cluster analysis (HCA) was conducted in XLstat (Addinsoft, Paris, France) using the five liking scores for each concentration of sucralose in water in order to classify participants into sweet liking phenotype (Iatridi et al., 2018). HCA is recommended as an objective strategy for classifying study participants into sweet liking phenotypes (Iatridi et al., 2019). Three clusters were identified. Due to limited sample size, the inverted U-shape responders and sucralose dislikers were grouped into a single "non-liker" group to be used as a fixed factor in further analysis.

A mixed-model was used to determine differences in liking and intensity responses. Sucralose concentration (n=5, 0.004% w/v-0.094% w/v), sleep treatment (n=2, curtailed and habitual) food form (n=2, oat beverage and oat crisp), and SLP (n=2, likers and non-likers) were the main fixed factors used throughout the analysis. Participant and interactions between the main fixed factors were included as random factors in all models. No significant sex, sequence or period effects were observed in the initial models. Therefore, the data for both sexes were pooled and neither sequence nor period were used in any further analysis. Data collected after both nights of sleep, such as PANAS scores or hunger rating, were analyzed using paired t-tests and corrected for multiple comparisons using false discovery rate (FDR) with a threshold of q=0.05, which is a strategy used to minimize the risk of type-1 error (Glickman, Rao, & Schultz, 2014; Szczygiel et al., 2019).

3. Results

3.1. Participants

Demographics and anthropometrics for the participants are reported in Table 5.2. Forty-one non-obese participants finished the study. Participants were primarily white (n=27) and female (n=26). Anthropometric measures as well as G-FCQ-T, PSS, and PSQI scores were not correlated with sucralose preference and therefore were not used in any further analysis ($p>0.05$).

Table 5.2. Anthropometric and Demographic Summary

Sex	n	%
Male	15	37%
Female	26	63%
Race		
White	27	66%
Asian	13	32%
Other/More than 1	1	2%
Anthropometrics	Mean±SD	Range
BMI (kg/m^2)	23.1±3.0	16.4-29.2
BF (%)	24.8±11.8	9.1-35.5
Age (y)	24.1±5.0	18-41
Traits/Habits		
G-FCQ-T (Score)	52.5±18.5	23-117
PSS (Score)	12.1±4.6	3-23
PSQI (Score	3.9±1.1	1-5

Abbreviations: BMI: body mass index, BF: body fat, G-FCQ-T: General Food Craving Questionnaire Trait version, PSS: Perceived Stress Scale, PSQI: Pittsburgh Sleep Quality Index, SD: standard deviation.

3.2. Summary of Curtailment

A 34.9% reduction in TIB resulted in restriction of TST, LS, and REM ($p=<0.001$ for all) but not SWS (Table 5.3). Sleepiness was significantly increased after sleep curtailment, as evidenced by the KSS score increase ($p<0.001$). Participants reported that the previous night's

sleep was shorter than needed and of reduced quality ($p<0.001$). While curtailment reduced perceived sleep quality ($p<0.001$), sleep was rated "about average" or higher after both sleep treatments. Participants did not perceive a difference in "deepness" or "comfort" between the two nights.

Table 5.3. Summary of Objective and Subjective Sleep Measures

		Habitual	Curtailed	% Reduction	p-value	q-value
Objective Sleep Measures (h)	Time in Bed	8.3±0.7	5.4±0.7	34.90%	<0.001	<0.001
	Total Sleep Time	7.2±0.7	4.5±1.0	37.50%	<0.001	<0.001
	Light Sleep	3.8±0.5	2.0±0.8	47.40%	<0.001	<0.001
	REM Sleep	1.9±0.5	1.2±0.4	36.90%	<0.001	<0.001
	Slow Wave Sleep	1.5±0.4	1.4±0.4	6.70%	0.043[a]	0.053
Sleepiness (10pt)	Karolinska Sleepiness Scale	3.5±1.4	5.7±1.6		<0.001	<0.001
Subjective Previous Night's Sleep Measures (5pt)	Subjective Sleep Total	13.5±2.0	10.3±2.4		<0.001	<0.001
	How much sleep did you obtain last night?	3.1±0.4	1.5±0.5		<0.001	<0.001
	How deeply did you sleep?	3.6±0.9	3.3±1.0		0.243	0.268
	How would you rate the quality of your sleep	3.8±0.8	2.6±1.0		<0.001	<0.001
	Compared to an average night, how comfortable were you when sleeping last night?	3.0±0.7	2.9±1.0		0.593	0.593

All objective sleep measures were significantly reduced after sleep curtailment. The Karolinska Sleepiness Scale measures sleepiness on a 10 point scale where 1 is "extremely alert" and 10 is "extremely sleepy". Sleepiness was significantly higher after sleep curtailment. Subjective previous night's sleep quality was measured using four questions, and the total score was used to represent general subjective sleep quality. Curtailment resulted in a significantly lower total subjective sleep score. P-values were obtained from paired t-tests, and q-values were obtained by correcting p-values for false discovery rate. [a]After false discovery rate correction, the difference between SWS after a habitual and curtailed night is no longer significant.

3.3. Summary of Affect, Cravings, and Hunger

Curtailment did not result in changes in hunger, negative affect, or food cravings— neither the composite score nor any of the five factors (Table 5.4). However, curtailment resulted in a decrease in positive affect ($p<0.001$).

Table 5.4. Summary of State-Dependent Measures

Measure	Factor	Habitual	Curtailed	p-value	q-value
Hunger	Hunger (100 mm VAS)	67.1±10.2	65.5±10.3	0.916	0.916
G-FCQ-S (0-15 per factor)	Total	44.2±9.7	46.2±12.3	0.429	0.687
	F1-Desire to Eat	6.1±2.0	6.1±2.2	0.948	0.916
	F2-Anticipation to positive reinforcement	8.9±2.0	9.5±2.7	0.232	0.618
	F3-Anticipation to negative reinforcement	11.2±1.8	11.1±2.6	0.859	0.916
	F4-Obsessive preoccupation	6.6±2.4	7.4±3.0	0.124	0.496
	F5-Craving as a physiological state	9.1±2.0	9.4±2.7	0.405	0.687
PANAS	Positive Affect	23.6±2.0	17.6±6.4	<0.001	<0.001
	Negative Affect	12.8±3.9	13.2±4.3	0.539	0.719

Positive affect was significantly decreased after sleep curtailment; whereas, hunger, food craving, and negative affect were not. Larger numbers indicate a greater response. For example, positive affect is higher after a habitual night compared to a curtailed night. FDR correction, shown as q-values, did not change the significance of any comparisons. Abbreviations: VAS: Visual Analog Scale, G-FCQ-S: General Food Craving Questionnaire State Version, PANAS: Positive Affect Negative Affect Schedule, F1-5: General Food Craving Questionnaire State Version Factors 1-5.

3.4. Sweet Liking Phenotypes

Three sweet liking phenotypes (SLP) were identified by hierarchical cluster analysis (HCA) using the hedonic response to five concentrations of the model system (sucralose-sweetened water) after the habitual night. Members of cluster 1 (n=24), the largest cluster, increasingly liked the stimuli as concentration increased until leveling off at 0.032% w/v ("likers"). Members of cluster 2 (n=10) displayed an inverted U-shape of liking ratings which

began to decrease after 0.032% w/v (“inverse U-shape”). Members of cluster 3 (n=8), the smallest cluster, liked solutions less as concentration increased (“dislikers”). After curtailment, there were 26 likers, 11 inverse U-shape, and 4 dislikers. The number of members in each cluster did not significantly differ after sleep curtailment (Kolmogorov-Smirnov, $p>0.05$); however, this obscures the fact that the SLPs were not entirely stable, as nine participants (22%) changed cluster after sleep curtailment. Seven participants moved from either the inverse U-shape or disliker to the liker cluster and two moved from the liker to the disliker cluster. Due to the small number of participants belonging to clusters 2 and 3 based on the model sucralose solutions after the habitual night, these clusters were combined will henceforth be referred to as “non-likers” (n=17).

3.5. Sweetness Perception in the Model System

Sucralose solution data was analyzed separately from the oat products using a mixed model containing sleep condition, SLP, and the interaction term between the two factors.

3.5.1. Model System Sweet Preference

Preferred concentration from the model system was analyzed to confirm the previously reported SLP-independent increase in preferred sucralose concentration after sleep curtailment and to assess whether the SLPs showed differences in preferred concentration. For preferred sucralose concentration, the sleep condition by SLP interaction was not significant, indicating no difference in the effect of sleep curtailment on preferred sucralose concentration between the SLPs ($F(1,39)=3.08$, $p=0.087$). A main effect of the sleep condition on the preferred concentration of sucralose in solution was noted ($F(1,39)=42.24$, $p<0.001$), signifying an increase in preferred concentration after sleep curtailment regardless of SLP, (0.042±0.028% w/v

habitual night and 0.063±0.025% w/v curtailed night). Regardless of sleep condition, sweet likers had a higher preferred concentration (M: 0.067% w/v SD: 0.022) compared to non-likers (M: 0.031% w/v SD: 0.021) (main effect for SLP on the preferred concentration of sucralose in solution ($F(1,39)=43.53$, $p<0.001$)),

3.5.2. Model System Sweet Liking Slopes

Model system sweet liking slopes were analyzed to assess whether sleep curtailment resulted in a change in slope of liking across the sweetener concentrations and whether changes were independent of SLP. For liking slope, neither the sleep condition by SLP interaction ($F(1,39)=0.0$, $p=0.953$) nor the main effect of sleep condition were significant ($F(1,39)=2.6$, $p=0.115$), indicating that sucralose slope did not significantly increase in steepness after sleep curtailment, regardless of SLP (habitual slope M: 2.4 liking score/0.1% w/v sucralose, curtailed slope M: 3.6 liking score/0.1% w/v sucralose). A main effect for SLP was observed ($F(1,39=89.84$, $p<0.001$), confirming the difference in slopes between sweet likers (M: 6.9 liking score/0.1% w/v sucralose) and sweet non-likers (M: -2.5 liking score/ 0.1% w/v sucralose).

3.5.3. Model System Sweet Liking by Concentration

To assess whether liking varied at specific concentrations or overall (across all concentrations) after sleep curtailment, sucralose concentration was added as a five-level fixed factor to the model. No tertiary interactions were observed ($p>0.05$). Sleep curtailment did not result in significant changes in sweet liking by concentration for sucralose solutions, as evidenced by neither the interaction terms nor the main effects for sleep condition showing significance in the model ($p>0.05$). Differences in sweetness liking between the SLPs depended on sucralose concentration (sucralose concentration by SLP interaction, $F(4, 156)=37.09$,

p<0.001) (Figure 5.1). Regardless of sleep condition, sweet likers reported lower sweet liking ratings for the two lowest concentrations (0.004% w/w, 0.011% w/v, p<0.001 for both) and higher sweet liking ratings for the two highest concentrations of model sucralose solutions (0.06% w/v, 0.094% w/v p<0.001 for both), with no difference in liking ratings for the middle concentration (0.032%w/v), compared to sweet non-likers, confirming significant differences in hedonic responses between likers and non-likers at low and high concentrations.

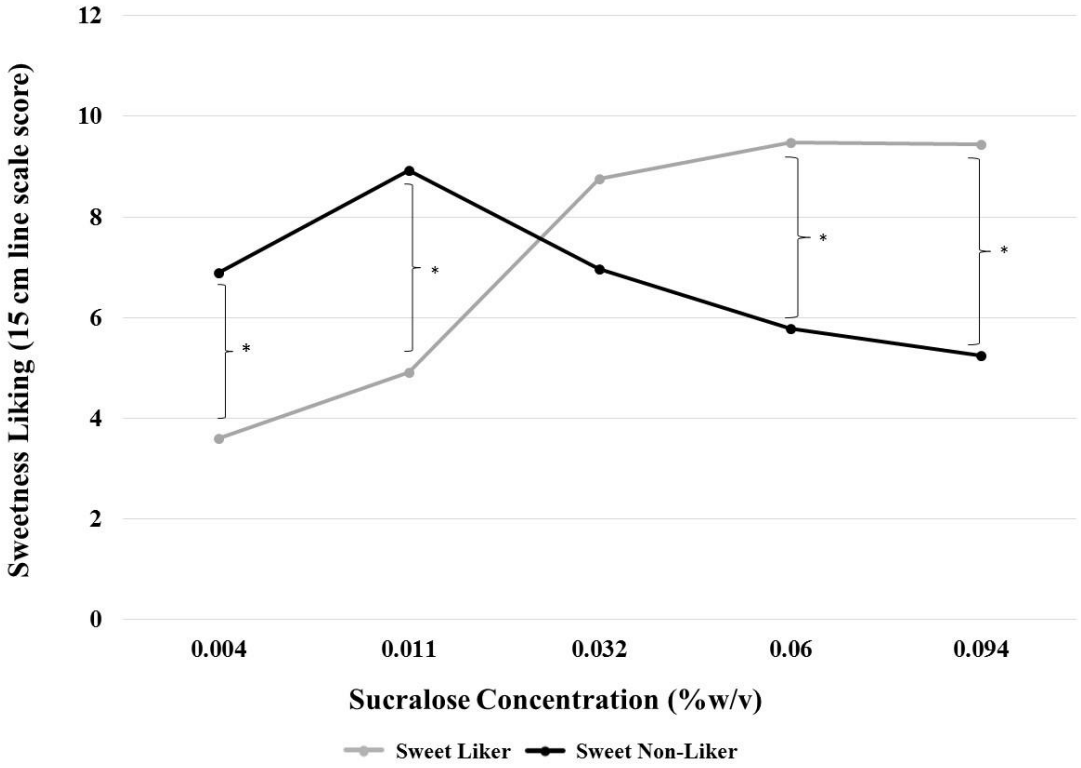

Figure 5.1. *Comparison of sweet liking response, averaged across both sleep conditions, by sweet liking phenotype (sweet likers and non-likers) determined using hierarchical cluster analysis based on liking scores over the range of sucralose solutions after a habitual night of sleep.* Likers and non-likers showed distinct patterns of liking with sweet likers showing higher

sweetness liking at 0.06% and 0.094% w/v sucralose and lower sweetness liking at 0.004% and 0.011% w/v sucralose, regardless of sleep condition. (*$p<0.001$ for all).

3.6. Hedonic Response in the Oat Product Systems

A four-factor mixed model containing sleep condition, food form, sucralose concentration, and SLP and interactions up to the tertiary level was used to test the primary hypotheses. No tertiary interactions were observed for any oat product models ($p>0.05$).

3.6.1. Oat product Sweetness Intensity

Sweetness intensity was measured to confirm previous findings that sleep curtailment does not increase sweet taste intensity perception and to assess whether the products were perceived as iso-sweet at each sucralose concentration across the systems used. It was confirmed that sweet intensity perception was not altered after sleep curtailment, as evidenced by neither the interaction terms nor the main effects for sleep condition showing significance in the model ($p>0.05$). The second concern, whether iso-sweetness between the products was achieved, was assessed by adding sucralose solution intensity scores to the food form factor and testing the sucralose concentration by food form interaction term in the mixed model. This term was not significant ($F(4,156)=1.8$, $p=0.126$), confirming that differences in intensity were similar across the sweetener levels for the food forms and the sucralose (Figure 2). Further, intensity perception did not differ between the SLPs at each sucralose concentration (SLP by sucralose concentration, $F(4,12)=0.69$, $p=0.614$), regardless of sleep condition and food form. However, there was a significant main effect of food form effect on sweetness intensity ($F(1, 40)=75.1$, $p<0.001$), signifying that sweetness was more intense for oat beverage compared to oat crisps regardless of sucralose concentration (Figure 5.2).

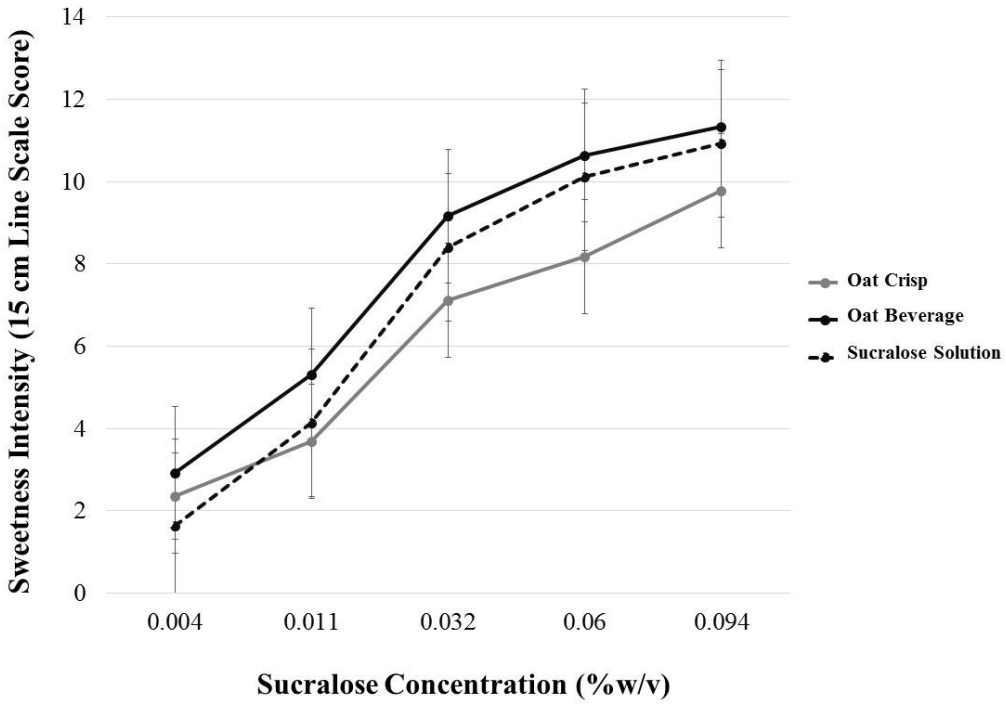

Figure 5.2. *Sweet intensity perception over the range of sucralose concentrations for sucralose solutions, oat beverage, and oat crisps.* Sweetness intensity was perceived as higher in oat milk compared to oat crisps, regardless of degree of sweetness ($p<0.001$). Errors bars represent standard error of the mean.

3.6.2. Oat Product Liking Slopes

Oat product liking slopes were analyzed to assess whether sleep curtailment resulted in changes in patterns of hedonic response across a range of sweetness levels. Liking slopes for sweetness liking, flavor liking, and overall liking were analyzed using a mixed model containing sleep condition, food form, and SLP and interactions up to the tertiary level. No tertiary interactions were observed ($p>0.05$). No significant binary interactions were observed between

the factors for overall, sweetness, or flavor slopes ($p>0.05$). The lack of interactions indicates that main effects are independent of one another. Several main effects were observed. First, a main effect of sleep was present for flavor liking slope ($F(1,39)=11.38$, $p=0.017$) and overall liking slope ($F(1,39)=4.21$, $p=0.047$), but not for sweetness liking slope, which demonstrated that overall and flavor liking slopes were steeper after sleep curtailment (Figure 3). The main effect of food form on slope for overall ($F(1,40)=5.34$, $p=0.026$) and sweetness liking $F(1,40)=9.72$, $p=0.003$) indicated steeper overall and sweetness liking slopes for the oat crisps compared to the oat beverage regardless of sleep condition. A main effect of food form on slope of flavor liking was not observed. The main effect of SLP on liking slopes was significant for slopes of overall ($F(1,39)=9.9$, $p=0.003$), sweetness liking ($F(1,39)=12.7$, $p=0.001$), and flavor ($F(1,39)=7.78$, $p=0.008$), meaning that positive and negative sweet liking slopes for sweet likers and non-likers, respectively extended to both flavor and overall liking for the oat products.

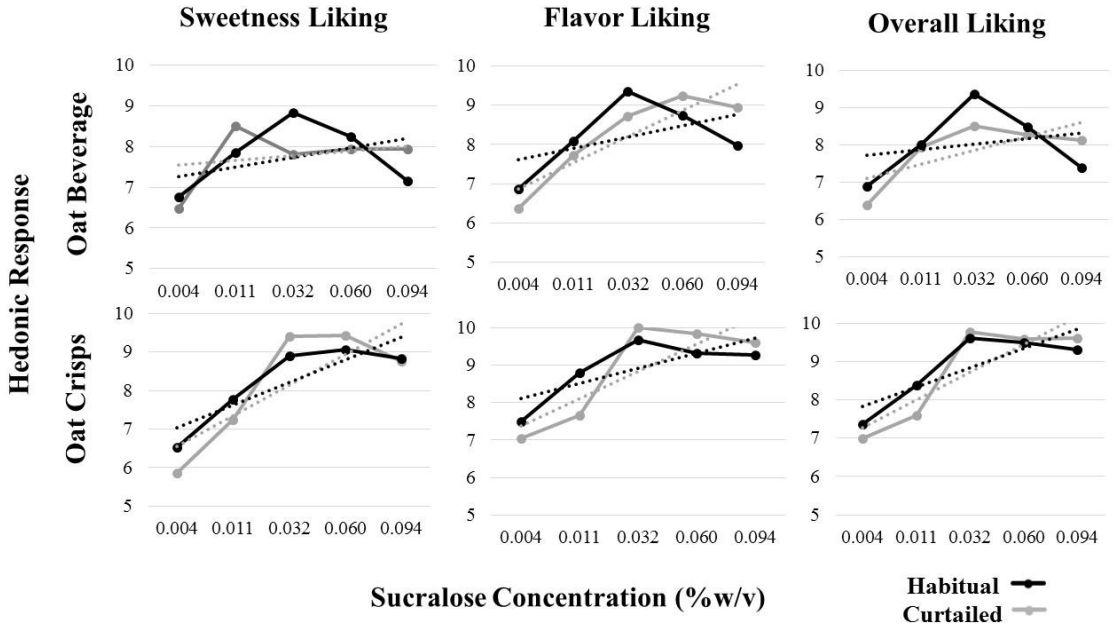

Figure 5.3. *Comparisons between liking responses for different hedonic measurements assessed with a 15 cm visual analog scale for the oat crisp and oat beverage.* A significant main effect of sleep was observed for both flavor (p=0.017) and overall liking slopes (p=0.047), indicating overall and flavor liking slopes were significantly steeper after curtailment for both oat products. No effect was observed for sweetness. No interaction between sleep condition and food form was observed. A significant food form effect on overall (p=0.026) and sweetness liking (p=0.003) slope was observed, indicating a steeper slope for oat crisps compared to oat beverage regardless of sleep condition.

3.6.3. Oat Product Liking by Concentration

The main hypothesis tested by the full model was whether oat product liking varied at specific concentrations or overall (average across all concentrations) after sleep curtailment. The

sleep condition by SLP interaction was not significant, signifying that the effect of sleep curtailment did not depend on SLP. A sleep condition by food form interaction was observed for texture ($F(4,156)=7.5$, $p=0.006$), but not for any other aspect of liking (sweetness, flavor, overall) ($p>0.05$); indicating that sleep curtailment resulted in a decrease in texture liking for oat crisps only, regardless of concentration and SLP . Texture liking data for the two oat products were separated and texture liking after a curtailed and habitual night were compared using a two-way mixed model containing sleep condition and SLP as factors. For the oat beverage, no significant effects of sleep curtailment were observed. For oat crisps, an interaction between texture liking and SLP was observed ($F(1,39)=21.16$, $p<0.001$). Further analysis revealed a decrease in texture liking in sweet non-likers after sleep curtailment (Habitual: M: 10.5, SD 3.2, Curtailed: M: 9.1, SD: 3.4, $p=0.021$), but not for sweet likers (Habitual: M: 8.4 SD 2.9, Curtailed: M: 8.8, SD: 3.0, $p>0.05$).

4. Discussion

The primary objective of this study was to determine whether sleep curtailment influences hedonic perception of complex foods, with a focus on sweet taste. The secondary objective was to assess whether these changes are moderated by food form or SLP. Hedonic responses to multiple dimensions of sucralose solutions and sucralose-sweetened liquid and solid oat products were assessed after both a night of habitual and curtailed sleep. Results from the model solution system were in agreement with our previous findings (Szczygiel et al., 2019); preferred sucralose concentration increased, and a non-significant increase in liking slope was observed. For the oat products, it was hypothesized that sleep curtailment would result in a similar non-significant increase in sweet liking slope, but that broader terms such as flavor and

overall liking would show significant increases corresponding with sweetness level. The data supported this hypothesis; in oat products, while sweetness liking slope showed a non-significant increase in sweet liking slope, flavor liking and overall liking showed an increase in slope steepness corresponding with increasing sucralose concentration after sleep curtailment. This suggests participants felt the products with greater sweetness were holistically preferable to less sweet oat products. Finally, sleep curtailment reduced texture liking of the oat crisps, but not the oat beverage, for sweet non-likers. This finding suggests an effect of sleep on oral somatosensory perception which may only affect sweet non-likers in a solid food model.

The observed increase in flavor and overall liking of the sweeter versions of each food products may play a role in determining food choice and intake after a night of insufficient sleep. The increase in steepness of the slope of flavor and overall liking suggest that sweeter products were preferable to less sweet products after sleep curtailment. Given that flavor is a primary determinant of food choice (MacFie & Meiselman, 2012), and that the increase in steepness of the flavor liking slope occurred in tandem with a similar shift in overall liking slope, insufficient sleep likely shapes both food choice and food intake. While preferred sweetener concentration was not measured in the oat products, the increase in model system preferred concentration and oat product overall liking slope, taken together, suggest that participants would have, in most cases, selected sweeter versions of the product to consume. The current study did not test the effects of sucrose in the food systems, but our previous work in model systems suggested that the effects of insufficient sleep are more pronounced for sucrose compared to sucralose, as sweet liking slope increased significantly after curtailment for sucrose but not sucralose (Szczygiel et al., 2019). This discrepancy between the two sweeteners could be due to differential neural processing of nutritive and non-nutritive sweeteners (Frank et al., 2008; Szczygiel et al., 2019),

which makes hedonic evaluation of sucralose less susceptible to the effect of sleep curtailment. While both sucrose and sucralose activate higher order brain reward centers in the brain (Green & Murphy, 2012), the magnitude of this activation is greater with sucrose exposure (Frank et al., 2008). Thus, we are likely underestimating the effects of insufficient sleep on sweet taste hedonic responses where nutritively sweetened foods are concerned. In the case of sucrose-sweetened foods, as sleep-curtailed individuals select sweeter foods, these foods tend to be more energy dense (A. Drewnowski, 1999) and more likely to promote weight gain. Thus, the observed change in hedonic perception of complex food in this study may contribute to explaining the well-supported relationship between short sleep and obesity (Cappuccio et al., 2008).

Due to the fact that the two oat products were not perceived as iso-sweet, directly comparing the two products, especially in the context of hedonic responses over a range of sweetness levels, is not recommended. The oat beverage was perceived as more sweet compared to the oat crisp regardless of sweetness level; although, the differences are much lower than what has been previously reported in similar comparisons between model and complex food systems (Alley & Alley, 1998; Adam Drewnowski et al., 1989), where sweetness intensity perception differed by nearly double. The difference in sweetness intensity perception between the products is likely a result of differences in oral processing of liquid and solid food. Liquids are able to fully and rapidly coat the tongue and, therefore, contact greater numbers of taste receptors; whereas, solids must be masticated and may be swallowed before being fully tasted (Alley & Alley, 1998).

Sleep curtailment negatively affected texture liking but only for oat crisps and only among non-likers. Sleep curtailment may have decreased texture liking of the oat crisps due to

increased oro-facial somatosensory sensitivity after sleep curtailment (Roehrs et al., 2006), which may make beverages, semi-solid, or "soft" foods more appealing after sleep curtailment compared to "hard" solid foods. Previous reports have demonstrated that sleep restriction increases nociceptor reactivity (Kundermann, Spernal, Huber, Krieg, & Lautenbacher, 2004) and oral somatosensory sensitivity (Kamiyama et al., 2019). While mechanoreceptors in the mouth are likely the primary contributors to the sense of texture, nociceptors also play an important role, particularly in the instance of "intense pressure," which may be experienced when consuming foods which shatter or fracture during mastication (Engelen & Bilt, 2008), as with the oat crisps. Beverages and softer foods require less oral processing time and, therefore, decrease satiety compared to foods that necessitate more oral processing, which may lead to excess energy intake and weight gain (de Graaf, 2011; James, 2018). Therefore, food form could be one factor that mediates the relationship between insufficient sleep and weight gain.

Why the change in texture liking was restricted to sweet non-likers is not known. However, it could be the case that these individuals have increased attention towards the texture of food. Sweet liking patterns might be a single component within a multifaceted collection of attribute liking patterns which determine an individual's overall liking of a complex food. Overall liking has been described as a function comprised of interactions between hedonic response to individual sensory attributes which are each weighted differently across individuals (de Kermadec, Durand, & Sabatier, 1997; Moskowitz & Krieger, 1995). For example, in one study, while most individuals weighted taste most heavily when considering overall liking, others placed the most importance on texture (Moskowitz & Krieger, 1995). It is possible that sweet likers weigh sweetness as a more important factor when considering overall liking and, therefore, focus less on other attributes such as texture. This finding suggests that hedonic

response to sweet taste may predict hedonic response to other sensory attributes. For example, one study illustrated that a portion of consumers who preferred sweeter chocolate also preferred less cocoa flavor (de Kermadec et al., 1997). Further, individual differences in importance placed on specific sensory attributes may moderate the effect of sleep curtailment on food perception, as sleep curtailment affected texture liking for the oat crisps but not the oat beverage. In summary, while SLP does not directly moderate the effect of sleep curtailment on sweet taste, these findings suggest that SLP may be an indicator of other sensory preferences that could be related to changes in food choice after sleep curtailment.

4.1. Strengths and Limitations:

The strengths of this study include the use of novel oat products and sucralose to deliver varying levels of sweetness while minimizing non-sweet sensory differences. The randomized crossover design with a one-week washout period and testing sessions held within 30 minutes of the previous session on the same day under fasted conditions were also strengths. Additionally, the use of the Zmachine EEG to non-intrusively collect at-home sleep data from participants provided an objective measurement of each sleep condition and confirmation of participant adherence to the prescribed sleep treatment. Limitations of this study include possible fatigue effects from the large sample tasting load per lab visit. Two-minute breaks were instituted between every five samples to minimize fatigue effects. Another limitation was the use of sucralose as the sweetener, as opposed to the commonly employed nutritive sweetener, sucrose. Our findings can only be generalized to foods sweetened with sucralose, which might not represent the primary contributors to weight gain after sleep curtailment. Finally, the majority of participants in this study were sweet likers; whereas, sweet non-likers (comprised of sweet U-shape responders and sweet dislikers) were not well represented. Therefore, it was not possible to

compare sweet non-liking phenotypes. A larger sample of sweet U-shape and disliking phenotypes is needed to determine whether these two groups are differentially effected by sleep curtailment.

5. Conclusions

Changes in hedonic responses to both sucralose solutions and sucralose-sweetened oat products were observed after sleep curtailment. In solutions, sweet liking slope was unchanged, but preferred sucralose concentration was increased after sleep curtailment. In oat products, in agreement with the solution data, sweetness liking slope did not change, but the slopes of the flavor and overall liking functions were steeper after sleep curtailment. Given that sucralose concentration and, therefore, sweetness, was the only difference between the products, the difference in flavor and overall liking slope suggests participants felt the oat products with greater sweetness were preferable. The two SLPs used in this study, likers and non-likers, showed similar changes in hedonic response after sleep curtailment, suggesting that sleep does not differentially affect hedonic responses by phenotype; however, there was one exception. After sleep curtailment, texture liking for sweet non-likers was decreased in oat crisps only, which may point to altered oral somatosensory sensitivity and particular texture salience in sweet non-likers. These findings represent possible mechanisms by which insufficient sleep leads to weight gain and obesity and signify a possible need to control for the previous night's sleep quality in affective food sensory studies.

REFERENCES

REFERENCES

Alley, R. L., & Alley, T. R. (1998). The Influence of physical state and color on perceived sweetness. *The Journal of Psychology*, *132*(5), 561–568. https://doi.org/10.1080/00223989809599289.

Asao, K., Miller, J., Arcori, L., Lumeng, J. C., Han-Markey, T., & Herman, W. H. (2015). Patterns of sweet taste liking: A Pilot Study. *Nutrients*, *7*(9), 7298–7311. https://doi.org/10.3390/nu7095336.

Ashoor, S. H., & Zent, J. B. (1984). Maillard browning of common amino acids and sugars. *Journal of Food Science*, *49*(4), 1206–1207. https://doi.org/10.1111/j.1365-2621.1984.tb10432.x.

Auvray, M., & Spence, C. (2008). The multisensory perception of flavor. *Consciousness and Cognition*, *17*(3), 1016–1031. https://doi.org/10.1016/j.concog.2007.06.005.

Bachmanov, A. A., Bosak, N. P., Floriano, W. B., Inoue, M., Li, X., Lin, C., … Beauchamp, G. K. (2011). Genetics of sweet taste preferences. *Flavour and Fragrance Journal*, *26*(4), 286–294. https://doi.org/10.1002/ffj.2074.

Barr, R. G., Pantel, M. S., Young, S. N., Wright, J. H., Hendricks, L. A., & Gravel, R. (1999). The response of crying newborns to sucrose: Is it a "Sweetness" effect? *Physiology & Behavior*, *66*(3), 409–417. https://doi.org/10.1016/S0031-9384(98)00294-7.

Benedict, C., Brooks, S. J., O'Daly, O. G., Almèn, M. S., Morell, A., Åberg, K., … Schiöth, H. B. (2012). Acute sleep deprivation enhances the brain's response to hedonic food stimuli: An fMRI study. *The Journal of Clinical Endocrinology & Metabolism*, *97*(3), E443–E447. https://doi.org/10.1210/jc.2011-2759.

Binns, N. M. (2003). Sucralose – all sweetness and light. *Nutrition Bulletin*, *28*(1), 53–58. https://doi.org/10.1046/j.1467-3010.2003.00307.x.

Buysse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Research*, *28*(2), 193–213. https://doi.org/10.1016/0165-1781(89)90047-4.

Cappuccio, F. P., Taggart, F. M., Kandala, N.-B., Currie, A., Peile, E., Stranges, S., & Miller, M. A. (2008). Meta-Analysis of short sleep duration and obesity in children and adults. *Sleep*, *31*(5), 619–626. https://doi.org/10.1093/sleep/31.5.619.

Cepeda-Benito, A., Gleaves, D. H., Williams, T. L., & Erath, S. A. (2000). The development and validation of the state and trait food-cravings questionnaires. *Behavior Therapy*, *31*(1), 151–173. https://doi.org/10.1016/S0005-7894(00)80009-X.

Cheer, R. L., & Lelievre, J. (1983). Effects of sucrose on the rheological behavior of wheat starch pastes. *Journal of Applied Polymer Science*, *28*(6), 1829–1836. https://doi.org/10.1002/app.1983.070280602.

Chen, X., Gelaye, B., & Williams, M. A. (2014). Sleep characteristics and health-related quality of life among a national sample of American young adults: Assessment of possible health disparities. *Quality of Life Research*, *23*(2), 613–625. https://doi.org/10.1007/s11136-013-0475-9.

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior*, *24*(4), 385–396. https://doi.org/10.2307/2136404.

de Graaf, C. (2011). Why liquid energy results in overconsumption. *Proceedings of the Nutrition Society*, *70*(2), 162–170.

de Kermadec, F. H., Durand, J. F., & Sabatier, R. (1997). Comparison between linear and nonlinear PLS methods to explain overall liking from sensory characteristics. *Food Quality and Preference*, *8*(5), 395–402. https://doi.org/10.1016/S0950-3293(97)00026-8.

Demos, K. E., Sweet, L. H., Hart, C. N., McCaffery, J. M., Williams, S. E., Mailloux, K. A., … Wing, R. R. (2017). The effects of experimental manipulation of sleep duration on neural response to food cues. *Sleep*, *40*(11). https://doi.org/10.1093/sleep/zsx125.

Dhillon, J., Running, C. A., Tucker, R. M., & Mattes, R. D. (2016). Effects of food form on appetite and energy balance. *Food Quality and Preference*, *48*, 368–375. https://doi.org/10.1016/j.foodqual.2015.03.009.

Dinges, D. F., Pack, F., Williams, K., Gillen, K. A., Powell, J. W., Ott, G. E., … Pack, A. I. (1997). Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 hours per night. *Sleep*, *20*(4), 267–277. https://doi.org/10.1093/sleep/20.4.267.

Drewnowski, A. (1999). Intense sweeteners and energy density of foods: Implications for weight control. *European Journal of Clinical Nutrition*, *53*(10), 757–763. https://doi.org/10.1038/sj.ejcn.1600879.

Drewnowski, Adam, Mennella, J. A., Johnson, S. L., & Bellisle, F. (2012). Sweetness and food preference. *The Journal of Nutrition*, *142*(6), 1142S-1148S. https://doi.org/10.3945/jn.111.149575.

Drewnowski, Adam, Shrager, E. E., Lipsky, C., Stellar, E., & Greenwood, M. R. C. (1989). Sugar and fat: Sensory and hedonic evaluation of liquid and solid foods. *Physiology & Behavior*, *45*(1), 177–183. https://doi.org/10.1016/0031-9384(89)90182-0.

Engelen, L., & Bilt, A. V. D. (2008). Oral physiology and texture perception of semisolids. *Journal of Texture Studies*, *39*(1), 83–113. https://doi.org/10.1111/j.1745-4603.2007.00132.x.

Frank, G. K. W., Oberndorfer, T. A., Simmons, A. N., Paulus, M. P., Fudge, J. L., Yang, T. T., & Kaye, W. H. (2008). Sucrose activates human taste pathways differently from artificial sweetener. *NeuroImage*, *39*(4), 1559–1569. https://doi.org/10.1016/j.neuroimage.2007.10.061.

Franzen, P. L., Siegle, G. J., & Buysse, D. J. (2008). Relationships between affect, vigilance, and sleepiness following sleep deprivation. *Journal of Sleep Research*, *17*(1), 34–41. https://doi.org/10.1111/j.1365-2869.2008.00635.x.

Garneau, N. L., Nuessle, T. M., Mendelsberg, B. J., Shepard, S., & Tucker, R. M. (2018). Sweet liker status in children and adults: Consequences for beverage intake in adults. *Food Quality and Preference, 65*, 175–180.

Glickman, M. E., Rao, S. R., & Schultz, M. R. (2014). False discovery rate control is a recommended alternative to Bonferroni-type adjustments in health studies. *Journal of Clinical Epidemiology, 67*(8), 850–857. https://doi.org/10.1016/j.jclinepi.2014.03.012.

Green, E., & Murphy, C. (2012). Altered processing of sweet taste in the brain of diet soda drinkers. *Physiology & Behavior*, *107*(4), 560–567. https://doi.org/10.1016/j.physbeh.2012.05.006

Greer, S. M., Goldstein, A. N., & Walker, M. P. (2013). The impact of sleep deprivation on food desire in the human brain. *Nature Communications, 4*, ncomms3259. https://doi.org/10.1038/ncomms3259.

Gujar, N., Yoo, S.-S., Hu, P., & Walker, M. P. (2011). Sleep deprivation amplifies reactivity of brain reward networks, biasing the appraisal of positive emotional experiences. *Journal of Neuroscience, 31*(12), 4466–4474. https://doi.org/10.1523/JNEUROSCI.3220-10.2011.

Hales, C. M., Carroll, M. D., Fryar, C. D., & Ogden, C. L. (2017). *Prevalence of obesity among adults and youth: United States, 2015–2016*.

Hanlon, E. C., Andrzejewski, M. E., Harder, B. K., Kelley, A. E., & Benca, R. M. (2005). The effect of REM sleep deprivation on motivation for food reward. *Behavioural Brain Research, 163*(1), 58–69. https://doi.org/10.1016/j.bbr.2005.04.017.

Hogenkamp, P. S., Nilsson, E., Chapman, C. D., Cedernaes, J., Vogel, H., Dickson, S. L., … Benedict, C. (2013). Sweet taste perception not altered after acute sleep deprivation in healthy young men. *Sleep Research and Sleep Medicine, 17*(2), 111–114. https://doi.org/10.1007/s11818-013-0606-0.

Holt, S. H. A., Cobiac, L., Beaumont-Smith, N. E., Easton, K., & Best, D. J. (2000). Dietary habits and the perception and liking of sweetness among Australian and Malaysian students: A cross-cultural study. *Food Quality and Preference, 11*(4), 299–312. https://doi.org/10.1016/S0950-3293(99)00076-2.

Huber, J. (1974). The psychophysics of taste: Perceptions of bitterness and sweetness in iced tea. *ACR North American Advances, NA-01*. Retrieved from http://acrwebsite.org/volumes/5710/volumes/v01/NA-01.

Iatridi, V., Hayes, J. E., & Yeomans, M. R. (2018). Reconsidering the classification of sweet taste liker phenotypes: A methodological review. *Food Quality and Preference*. https://doi.org/10.1016/j.foodqual.2018.09.001.

Iatridi, V., Hayes, J. E., & Yeomans, M. R. (2019). Quantifying sweet taste liker phenotypes: Time for some consistency in the classification criteria. *Nutrients, 11*(1), 129. https://doi.org/10.3390/nu11010129.

James, B. (2018). Oral processing and texture perception influences satiation. *Physiology & Behavior, 193*, 238–241. https://doi.org/10.1016/j.physbeh.2018.03.015.

Kaida, K., Takahashi, M., Åkerstedt, T., Nakata, A., Otsuka, Y., Haratani, T., & Fukasawa, K. (2006). Validation of the Karolinska Sleepiness Scale against performance and EEG variables. *Clinical Neurophysiology*, *117*(7), 1574–1581. https://doi.org/10.1016/j.clinph.2006.03.011.

Kamiyama, H., Iida, T., Nishimori, H., Kubo, H., Uchiyama, M., Laat, A. D., … Komiyama, O. (2019). Effect of sleep restriction on somatosensory sensitivity in the oro-facial area: An experimental controlled study. *Journal of Oral Rehabilitation*, *46*(4), 303–309. https://doi.org/10.1111/joor.12758.

Kaplan, R. F., Wang, Y., Loparo, K. A., Kelly, M. R., & Bootzin, R. R. (2014). Performance evaluation of an automated single-channel sleep–wake detection algorithm. *Nature and Science of Sleep*, *6*, 113–122. https://doi.org/10.2147/NSS.S71159.

Kim, J.-Y., Prescott, J., & Kim, K.-O. (2014). Patterns of sweet liking in sucrose solutions and beverages. *Food Quality and Preference*, *36*, 96–103. https://doi.org/10.1016/j.foodqual.2014.03.009.

Kim, M.-Y., Cho, H.-Y., Park, J.-Y., Lee, S.-M., Suh, D.-S., Chung, S.-J., … Kim, K.-O. (2005). Relative sweetness of sucralose in beverage systems and sensory properties of low Ccalorie Beverages Containing Sucralose. *Korean Journal of Food Science and Technology*, *37*(3), 425–430.

Krause, A. J., Simon, E. B., Mander, B. A., Greer, S. M., Saletin, J. M., Goldstein-Piekarski, A. N., & Walker, M. P. (2017). The sleep-deprived human brain. *Nature Reviews Neuroscience*, *18*(7), 404.

Kundermann, B., Spernal, J., Huber, M. T., Krieg, J.-C., & Lautenbacher, S. (2004). Sleep deprivation affects thermal pain thresholds but not somatosensory thresholds in healthy volunteers. *Psychosomatic Medicine*, *66*(6), 932–937.

Lv, W., Finlayson, G., & Dando, R. (2018). Sleep, food cravings and taste. *Appetite*, *125*, 210–216. https://doi.org/10.1016/j.appet.2018.02.013.

MacFie, H. J. H., & Meiselman, H. L. (2012). *Food Choice, Acceptance and Consumption*. Springer Science & Business Media.

Markwald, R. R., Melanson, E. L., Smith, M. R., Higgins, J., Perreault, L., Eckel, R. H., & Wright, K. P. (2013). Impact of insufficient sleep on total daily energy expenditure, food intake, and weight gain. *Proceedings of the National Academy of Sciences*, *110*(14), 5695–5700. https://doi.org/10.1073/pnas.1216951110.

Mazur, J., Drabek, R., & Goldman, A. (2018). Hedonic contrast effects in multi-product food evaluations differing in complexity. *Food Quality and Preference*, *63*, 159–167. https://doi.org/10.1016/j.foodqual.2017.06.016.

Mennella, J. A., Lukasewycz, L. D., Griffith, J. W., & Beauchamp, G. K. (2011). Evaluation of the Monell forced-choice, paired-comparison tracking procedure for determining sweet taste preferences across the lifespan. *Chemical Senses*, *36*(4), 345–355. https://doi.org/10.1093/chemse/bjq134.

Mennella, J. A., Pepino, M. Y., & Reed, D. R. (2005). Genetic and environmental determinants of bitter perception and sweet preferences. *Pediatrics*, *115*(2), e216–e222. https://doi.org/10.1542/peds.2004-1582.

Merrill, E. P., Kramer, F. M., Cardello, A., & Schutz, H. (2002). A comparison of satiety measures. *Appetite*, *39*(2), 181–183. https://doi.org/10.1006/appe.2002.0496.

Meule, A., & Kübler, A. (2014). Double trouble. Trait food craving and impulsivity interactively predict food-cue affected behavioral inhibition. *Appetite*, *79*, 174–182. https://doi.org/10.1016/j.appet.2014.04.014.

Moskowitz, H. R., & Krieger, B. (1995). The contribution of sensory liking to overall liking: An analysis of six food categories. *Food Quality and Preference*, *6*(2), 83–90. https://doi.org/10.1016/0950-3293(95)98552-T.

Nedeltcheva, A. V., Kilkus, J. M., Imperial, J., Kasza, K., Schoeller, D. A., & Penev, P. D. (2009). Sleep curtailment is accompanied by increased intake of calories from snacks–. *The American Journal of Clinical Nutrition*, *89*(1), 126–133. https://doi.org/10.3945/ajcn.2008.26574

Noel, C., & Dando, R. (2015). The effect of emotional state on taste perception. *Appetite*, *95*, 89–95. https://doi.org/10.1016/j.appet.2015.06.003.

Popper, R., Rosenstock, W., Schraidt, M., & Kroll, B. J. (2004). The effect of attribute questions on overall liking ratings. *Food Quality and Preference*, *15*(7), 853–858. https://doi.org/10.1016/j.foodqual.2003.12.004.

Reis, F., De Andrade, J., Deliza, R., & Ares, G. (2016). Comparison of two methodologies for estimating equivalent sweet concentration of high-intensity sweeteners with untrained assessors: case study with orange/pomegranate juice. *Journal of Sensory Studies*, *31*(4), 341–347. https://doi.org/10.1111/joss.12217.

Roehrs, T., Hyde, M., Blaisdell, B., Greenwald, M., & Roth, T. (2006). Sleep loss and REM sleep loss are hyperalgesic. *Sleep*, *29*(2), 145–151. https://doi.org/10.1093/sleep/29.2.145.

Schloegl, H., Percik, R., Horstmann, A., Villringer, A., & Stumvoll, M. (2011). Peptide hormones regulating appetite—focus on neuroimaging studies in humans. *Diabetes/Metabolism Research and Reviews*, *27*(2), 104–112.

Simon, S. L., Field, J., Miller, L. E., DiFrancesco, M., & Beebe, D. W. (2015). Sweet/dessert foods are more appealing to adolescents after sleep restriction. *PLOS ONE*, *10*(2), e0115434. https://doi.org/10.1371/journal.pone.0115434.

Smith, S. L., Ludy, M.-J., & Tucker, R. M. (2016). Changes in taste preference and steps taken after sleep curtailment. *Physiology & Behavior*, *163*, 228–233. https://doi.org/10.1016/j.physbeh.2016.05.002.

St-Onge, M.-P., Wolfe, S., Sy, M., Shechter, A., & Hirsch, J. (2014). Sleep restriction increases the neuronal response to unhealthy food in normal-weight individuals. *International Journal of Obesity (2005)*, *38*(3), 411–416. https://doi.org/10.1038/ijo.2013.114.

Sylvetsky, A. C., & Rother, K. I. (2016). Trends in the consumption of low-calorie sweeteners. *Physiology & Behavior*, *164*, 446–450. https://doi.org/10.1016/j.physbeh.2016.03.030.

Szczygiel, E., Cho, S., & Tucker, R. (2018). Characterization of the relationships between sleep duration, quality, architecture and chemosensory function in non-obese females. *Chemical Senses*, *43*(4), 223–228. https://doi.org/10.1093/chemse/bjy012.

Szczygiel, E. J., Cho, S., Snyder, M. K., & Tucker, R. M. (2019). Associations between chemosensory function, sweet taste preference, and the previous night's sleep in non-obese males. *Food Quality and Preference*, *75*, 105–112. https://doi.org/10.1016/j.foodqual.2019.02.018.

Szczygiel, E. J., Cho, S., & Tucker, R. M. (2019). Multiple dimensions of sweet taste perception altered after sleep curtailment. *Nutrients, Under Review*.

Tan, S.-Y., & Tucker, R. M. (2019). Sweet taste as a predictor of dietary intake: A systematic review. *Nutrients*, *11*(1), 94. https://doi.org/10.3390/nu11010094.

Tanaka, T., Hong, G., Tominami, K., & Kudo, T. (2018). Oral fat sensitivity is associated with social support for stress coping in young adult men. *The Tohoku Journal of Experimental Medicine*, *244*(4), 249–261.

van Boekel, M. A. J. S. (2006). Formation of flavour compounds in the Maillard reaction. *Biotechnology Advances*, *24*(2), 230–233. https://doi.org/10.1016/j.biotechadv.2005.11.004.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology*, *54*(6), 1063–1070. http://dx.doi.org.proxy1.cl.msu.edu/10.1037/0022-3514.54.6.1063.

Wiet, S. G., & Beyts, P. K. (1992). Sensory characteristics of sucralose and other high intensity sweeteners. *Journal of Food Science*, *57*(4), 1014–1019. https://doi.org/10.1111/j.1365-2621.1992.tb14345.x.

Yamamoto, T. (2003). Brain mechanisms of sweetness and palatability of sugars. *Nutrition Reviews*, *61*(suppl_5), S5–S9. https://doi.org/10.1301/nr.2003.may.S5-S9.

Yeomans, M. R., Tepper, B. J., Rietzschel, J., & Prescott, J. (2007). Human hedonic responses to sweetness: Role of taste genetics and anatomy. *Physiology & Behavior*, *91*(2–3), 264–273.

Conclusions

The data presented in this dissertation demonstrate that insufficient sleep can elicit changes in sensory perception of prototypical tastants dissolved in water and complex food matrices. Additionally, several novel observations which merit future work were made throughout this investigation. The most important findings are listed below:

- Participants who had a short (<7 h) previous night's sleep preferred sweeter solutions
- Total sleep and REM sleep duration were inversely associated with sweet taste preference
- No sleep measures were associated with chemosensory thresholds (sensitivity)
- Modest sleep curtailment resulted in increased sweet taste preference for both sucrose and sucralose
- Modest sleep curtailment resulted in altered patterns of sweetness liking across a range of sweetened sucrose solutions, but not sucralose solutions.
- Modest sleep curtailment resulted in altered patterns of flavor liking over a range of increasingly sweet liquid and solid oat-based food products
- Modest sleep curtailment resulted in decreased texture liking of a cracker-like oat-based food stimulus

The studies presented in chapters one and two of this dissertation demonstrate a relationship between sleep duration and architecture and several aspects of next-day chemosensory perception. Males and females both displayed an inverse linear correlation between sleep duration and sweet taste preference. Further, when males and females were

divided into short and long sleep duration groups, those with short sleep duration were more likely to prefer higher concentrations of sucrose in water the following day. No relationship between sleep and chemosensory thresholds was observed, suggesting altered sweet taste sensitivity was not involved in the observed relationship between sweet taste preference and sleep. Additionally, males and females who had short REM+SWS duration the previous night preferred higher concentrations of sucrose the next morning, suggesting that duration of specific sleep stages may play a role in next-morning changes in chemosensation. Of the sleep stages measured (LS, SWS, and REM sleep), REM sleep was most strongly associated with sweet taste preference. While the biological function of REM sleep is not currently known, it is thought to play a role in the formation of food preferences (Hanlon, Andrzejewski, Harder, Kelley, & Benca, 2005; James A. Horne, 2015). The findings from the data presented in chapters 1 and 2 of this dissertation suggest that REM sleep duration may influence food preferences partially through changes in preferred level of sweetness.

When comparing the effect of short sleep between males and females, two primary differences were observed: the odor identification ability and the best sleep stage predictor of sweet taste preference. Males who had a shorter sleep duration the previous night showed a lower odor identification ability the next morning; whereas, odor identification ability did not differ by sleep duration for females. However, the decrease in odor identification ability observed in males did not survive false discovery rate correction, and the male sample had a lower total average sleep time compared to the female sample. Therefore, the observed decreased odor identification ability might be a false positive or be related to the previous night's sleep duration of the participants, which differed between males and females, rather than sex. No relationship between sleep and pleasantness of odors or olfactory threshold was observed in

either sex. The best predictor for next morning sweet taste preference was the sum of REM and SWS sleep for females and REM sleep alone for males. Again, these differences could be related to differences in sleep duration between the two studies. Similar differences in sleep duration between the sexes have been reported previously (Lauderdale et al., 2006). To summarize, sex differences in the effect of short sleep duration on chemosensory function overall were found to be minimal.

In chapter three of this dissertation, a magnitude estimation method for determination of equal-sweet concentrations of sweeteners using naïve participants was used to generate power functions which later were used to substitute sucralose for sucrose in psychophysical sleep-taste experiments (Moskowitz, 1977; Reis, De Andrade, Deliza, & Ares, 2016). Out of the four sweeteners tested (Sucrose, sucralose, stevia Reb M, and stevia Reb blend), power functions only showed acceptable linear regression coefficients for sucrose, sucralose, and stevia Reb M. The stevia Reb blend had a strong bitter taste that prevented participants from assessing relative sweetness at the high sweetness levels used. However, sweetness at high concentrations could be evaluated when tasting purified stevia Reb M, which suggests that Reb M would be ideal for sucrose substitution in food products with high amounts of sucrose. The power functions for each sweetener are helpful tools for substituting sucrose with iso-sweet concentrations of NNS in psychophysical model systems used to evaluate taste function or as a starting point for sucrose-substitution during new food product development

In chapters four and five, a randomized cross-over study design was utilized to evaluate whether a 33% sleep curtailment elicited changes in sensory perception in both model and complex food systems. In both studies, participants recorded a night of both habitual and curtailed sleep and returned for sensory evaluation the morning following each sleep condition.

The modest sleep curtailment treatment was selected to mimic free-living conditions, improving the ecological validity of the two studies. Further, the cross-over study design allowed participants to serve as their own control, reducing individual bias. After a night of sleep curtailment, participants preferred a higher concentration of both sucrose and sucralose compared to after a habitual night of sleep. Further, patterns of sweet liking, as represented by the slope of the best-fit linear function of hedonic response plotted against sweetener concentration, were found to be steeper after a night of sleep curtailment. Taken together, these findings suggest that modest sleep curtailment can elicit changes in sweet taste preference and alter patterns of sweet liking such that sweeter tastes are more pleasurable. However, the increase in slope steepness was not significant when sucralose was used, suggesting that the effect of sleep curtailment on hedonic response to sweetness is less when sweetness comes from sucralose. After grouping participants by patterns of hedonic response to sweet taste using hierarchical cluster analysis, an increase in preferred sweetener concentration was observed after sleep curtailment for all sweet liking phenotypes suggesting that the effect of sleep on sweet taste preference is not mediated partially by genetic phenotypes (Bachmanov et al., 2011). In both of these two studies, the majority of participants were sweet likers and, therefore, these changes may effect a large segment of the population. However, due to low statistical power, these findings need to be replicated using a larger sample size.

In an effort to assess whether findings from model systems using sweeteners dissolved in water represent changes in perception of complex food matrices, five variations of two oat-based products which varied only in sweetness (oat crisp and oat milk) were developed. When participants consumed these products, they were asked to rate overall, sweetness, flavor, and texture liking. After sleep curtailment, participants showed steeper patterns of flavor liking, but

not sweetness liking, despite the fact that only sweetness varied between the five variations of each product. In addition, patterns of overall liking were also steeper in the oat milk after sleep curtailment. These findings suggest that participants found the sweeter products to be preferable overall after a night of sleep curtailment. Therefore, modest sleep curtailment could result in individuals seeking sweetener, higher energy foods, partially explaining the relationship between sleep and excess energy intake. After a night of sleep curtailment, non-sweet liking participants also showed decreased liking of texture of the oat crisps. Sleep curtailment may increase oral somatosensory sensitivity (Kamiyama et al., 2019), resulting in decreased liking of hard, crispy or crunchy foods which have the potential to shatter in the mouth and apply intense pressure. Changes in texture perception after a night of sleep curtailment may explain sleep-related changes in food choice, such as increased consumption of sugar-sweetened beverages (Prather et al., 2014).

Beyond the major findings from this research, there were several notable findings that merit future attention. While the primary objective of this research was to assess the effect of sleep on taste perception, several interesting observations unrelated to sleep are discussed. The most pressing directions for future research are discussed below.

1. Future Directions

While changes in sensory perception were observed the day following a night of insufficient night of sleep, it is not clear if this effect accumulates over repeated nights of insufficient sleep, if there is a refractory period needed before sensory perception returns to normal, or if sensory perception remains altered until a night of sufficient sleep is achieved. Two weeks of sleep curtailment has been shown to cause cumulative, dose-dependent deficits in

cognitive performance, suggesting that awakeness has a neurobiological accumulating "cost" (Van Dongen, Maislin, Mullington, & Dinges, 2003). While recovery sleep after sleep restriction has been shown to have a dose-response relationship with the return of cognitive ability, some deficits remain after a week of chronic sleep restriction (Banks, Van Dongen, Maislin, & Dinges, 2010). Therefore, it is possible that changes in sensory perception persist after a night of sleep curtailment and that these changes may not immediately reverse after "sleep debt" is paid. More work is needed to establish how long effect of insufficient sleep on taste perception lasts and if changes in taste perception can be corrected after recovery sleep.

While teasing out the relative contribution of individual sleep stages is potentially problematic due to the cyclic nature of the stages and the fact that NREM sleep acts partially as a gate-keeper REM sleep (Carskadon, Dement, & others, 2005), understanding the contribution of NREM and REM sleep may aide in determining the biological mechanisms behind changes in sensory perception after sleep curtailment. Further, by determining the role of the stages, it may help clarify the otherwise elusive exact biological role of REM and NREM (Scullin & Bliwise, 2015). REM sleep can be selectively inhibited with certain pharmaceuticals, such as monoamine oxidase inhibitors (Cohen et al., 1982), and thus it may be possible to determine of the role of REM sleep in determining sweet taste.

There is evidence that insufficient sleep can influence visual sensory perception, but no research to date has assessed if sleep curtailment can alter visual hedonic response to food. It is often said that we taste with our eyes first, due to the fact that food appearance is a critical factor when choosing and purchasing food (Meilgaard, Carr, Civille, Carr, & Civille, 1999; van der Laan, de Ridder, Viergever, & Smeets, 2011). There is limited evidence that insufficient sleep may alter visual sensory function which could alter food preference. Changes in visual sensory

perception previously observed after insufficient sleep include deterioration in visual field (Rogé & Gabaude, 2009), a rightward shift in spatial awareness (Manly, Dobler, Dodds, & George, 2005), and reduced activation within visual processing centers in the brain, resulting in poorer performance in visual-spatial tasks (Chuah, Venkatraman, Dinges, & Chee, 2006; Killgore, 2010). These changes, occurring together, may result in sleep-restricted individuals showing greater hedonic response to foods with visual defects, off colors, or signs of decay compared to rested individuals. If such an effect existed, it could potentially result in an increase hedonic response to foods with visual abnormalities or signs of decay and reduce the reliability of appearance sensory data when making food product development decisions.

Very little is known regarding the effect of insufficient sleep and auditory sensory function (Killgore, 2010). One study found that sleep deprivation reduced auditory temporal resolution (the responsiveness in detecting overlapping sounds) (Babkoff, Zukerman, Fostick, & BEN-ARTZI, 2005). However, as with other sensory effects of sleep, the effect of sleep on auditory performance may be related to attention deficits, rather than changes in perception (J. A. Horne, Anderson, & Wilkinson, 1983). Audition is an often underappreciated sense when consuming food, but plays an important role in determining hedonic response to texture, or, more directly, such as in the case of a potato chip where sound can be directly associated with food liking (MacFie & Meiselman, 2012). Insufficient sleep may interact with hedonic auditory response through development of increased sensitivity to loudness (phonophobia). Insufficient sleep is reported to induce headaches which cause sensitivity to loud sounds (Rains & Poceta, 2012). Thus, sleep-restricted individuals are likely to show negative hedonic responses to foods with significant auditory components. Further, these types of food may be avoided in the diet of

chronically sleep-deprived individuals who may fear loud sounds could trigger headaches (Rains & Poceta, 2012).

The difference in texture observed in chapter 5 of this dissertation creates a multitude of questions. Primarily, what senses are driving the observed change: differences in mechanical responses to hardness or chewiness, geometric differences perception of size or shape, or moisture and fat-related factors, such as lack of moistness or oiliness? Similar to sweet liking phenotypes, individual differences in texture liking have been observed. Qualitative research in the food industry has revealed four types of "texture likers" which researchers more commonly describe as "mouth behaviors" (Dar & Light, 2014): "Smooshers" who like to crush food on the palate of the mouth; "Crunchers" who prefer hard foods that fracture in the mouth and chew vigorously; "Chewers", who prefer soft food which can be easily chewed without vigor; and "Suckers" who like to suck on food until it dissolves in the mouth (Dar & Light, 2014). In chapter five, an inexplicable difference between sweet likers and non-likers on texture liking after sleep curtailment was observed. It is possible that sleep liking phenotypes and texture-related mouth behaviors are related in some way, or that mouth behavior is partially determined by previous night sleep (See below: Identify perceptual and behavioral traits associated with sweet liking phenotype).

There are a wide variety of well-documented sensory interactions when consuming food, the most notable of which include color-taste and taste-taste interactions (MacFie & Meiselman, 2012). The interaction between fat content and sweet taste, which varies across oral phenotypes, is one example of synergy between sensory perceptions that may play an important role in the sleep-taste relationship (Hayes & Duffy, 2008). Short sleep duration is routinely associated with an increased preference (Imaki, Hatanaka, Ogawa, Yoshida, & Tanada, 2002; Nishiura &

Hashimoto, 2010; Shi et al., 2008; Simon, Field, Miller, DiFrancesco, & Beebe, 2015) for fatty foods as well as increased intake (Brondel, Romer, Nougues, Touyarou, & Davenne, 2010; Marie-Pierre St-Onge et al., 2011). For example, one study found that, after sleep curtailment, "unhealthy" foods (e.g., pizza, doughnuts) caused increased neural response in hedonic processing centers of the brain, such as the insula and prefrontal cortex, compared to "healthy" foods (e.g., carrots, yogurt) (M-P St-Onge, Wolfe, Sy, Shechter, & Hirsch, 2014). However, it is not clear if a change in fat perception is involved in altered response to foods containing high amounts of fat. Sweet taste and fat "taste" may interact to produce larger increases in hedonic response to food after sleep curtailment. Therefore, future work should assess whether foods with certain macronutrient compositions, such as combinations of sweet carbohydrates and fat, or sensory properties are especially likely to elicit a highly positive hedonic response after sleep curtailment. Further, after determining the effect of sleep curtailment on visual hedonics, it may be beneficial to explore the role of sleep in color-taste interactions.

While the data presented in this dissertation suggest that insufficient sleep could, in certain contexts, play a role in determining results of affective food sensory tests, we did not directly assess this. However, now that it is clear that sleep partially determines hedonic response to oat-products, it is critical that the magnitude of this effect on consumer affective studies be assessed. Consumer affective tests often determine if a new food product is suitable for launch, and therefore, characterizing the effect of sleep on findings stands to save significant time, money, and energy (Sidel & Stone, 1993). However, given that self-report is unreliable as a measure of objective sleep (Lauderdale, Knutson, Yan, Liu, & Rathouz, 2008), it may be necessary to determine a suitable tool for rapidly assessing objective sleep duration before these effort are undertaken. In chapter 2, we noted that a simple 100 mm line scale was associated with

objective sleep duration, and therefore, the effectiveness of this and other similar tools may be an optimal place to begin to search for a rapid objective sleep measure.

Sweet liking phenotype was a significant source of individual variation in hedonic response to sweet liking in solutions, as would be expected. While solution-based phenotypes were not a good predictor of hedonic responses in food, some significant comparisons, particularly at low sweetness level, between solution-based sweet likers and non-likers were observed for oat-products. Further, differences as large as three points on the fifteen point scale, while not statistically significant, may still influence findings in consumer affective tests. Yet, sweet liking phenotype is not commonly controlled for in sensory experiments, even when sweet liking is central to the hypothesis (for example (Cliff, Dever, Hall, & Girard, 1995; Tuorila, Keskitalo-Vuokko, Perola, Spector, & Kaprio, 2017)). Given that the typical random samples vary widely in distribution of sweet liking phenotype, with some reporting majority sweet likers and others reporting majority non-likers, lack of control for SLP is serious concern. However, differences in classification method may play a role in differences in distribution between studies; although, there are currently efforts to standardize SLP classification methods (Iatridi, Hayes, & Yeomans, 2018). Future work should aim to directly quantify the impact that SLP can have on consumer affective studies. It may be necessary to develop a series of representative foods which can be used to assess food sweet liking phenotypes. For example, a company specializing in baked goods may benefit from developing a brownie- or cake-based sweet liking phenotype test. The effectiveness of food specific phenotyping merits investigation, asit may be a more reliable tool than solution phenotyping in many research and food industry scenarios.

Sweet liking patterns might be a single trait within a broad collection of associated behaviors, which could be a result of genetic or environmental factors (Mennella, Pepino, &

Reed, 2005). Several studies have reported specific behaviors associated with sweet likers, such as high novelty seeking and risk for alcoholism (Lange, Kampov-Polevoy, & Garbutt, 2010). Very little is known about what traits (other than disliking patterns of sweet liking) are specific to non-liker SLPs. Sweet non-likers also were the primary drivers of the difference in texture liking of the oat crisps observed after sleep curtailment, but it not clear why this is was case. Further, after a habitual night, oat product phenotype predicted one another; whereas, solution phenotype was not predictive of oat crisp or milk phenotypes. While the distribution of membership in the clusters was the same across food type, individuals who were solution sweet dislikers were not necessarily oat product dislikers, with nearly half of participants showing a different phenotype in the solutions and oat products. These discrepancies demonstrate that extreme caution is merited when interpreting the practical impact of sweet liking phenotype on sensory perception in complex foods. Understanding how sweet liking phenotypes related to other perceptual and behavioral traits will allow for better interpretations of findings related to SLPs.

2. Concluding Remarks

The findings from these experiments provide the groundwork for future nutrition and sensory studies which aim to study the relationship between insufficient sleep. Primarily, this investigation demonstrates that sleep is related to multiple dimensions of sensory perception. Further, this work identifies important moderating factors in the sleep-sensory relationship in the context of food. Finally, this research evaluated hedonic perception after sleep curtailment in both psychophysical model systems and complex food systems, which provides a better understanding of how psychophysical findings can generalize to food perception. Overall, these

experiments contribute to our understanding of biological mechanisms that drive human hedonic response to food and contribute a currently missing link in the proposed causal chain by which insufficient sleep can lead to excess energy intake. Beyond the broader scientific gains, the findings from these studies have practical applications for food sensory scientists who generally strive to exclude participants who may have compromised taste ability to improve repeatability (Moskowitz, Muñoz, & Gacula Jr, 2008).

REFERENCES

REFERENCES

Babkoff, H., Zukerman, G. I. L., Fostick, L., & BEN-ARTZI, E. (2005). Effect of the diurnal rhythm and 24 h of sleep deprivation on dichotic temporal order judgment. *Journal of Sleep Research*, *14*(1), 7–15.

Bachmanov, A. A., Bosak, N. P., Floriano, W. B., Inoue, M., Li, X., Lin, C., … Beauchamp, G. K. (2011). Genetics of sweet taste preferences. *Flavour and Fragrance Journal*, *26*(4), 286–294. https://doi.org/10.1002/ffj.2074

Banks, S., Van Dongen, H. P. A., Maislin, G., & Dinges, D. F. (2010). Neurobehavioral Dynamics Following Chronic Sleep Restriction: Dose-Response Effects of One Night for Recovery. *Sleep*, *33*(8), 1013–1026. https://doi.org/10.1093/sleep/33.8.1013

Brondel, L., Romer, M. A., Nougues, P. M., Touyarou, P., & Davenne, D. (2010). Acute partial sleep deprivation increases food intake in healthy men–. *The American Journal of Clinical Nutrition*, *91*(6), 1550–1559.

Carskadon, M. A., Dement, W. C., & others. (2005). Normal human sleep: an overview. *Principles and Practice of Sleep Medicine*, *4*, 13–23.

Chuah, Y. M. L., Venkatraman, V., Dinges, D. F., & Chee, M. W. L. (2006). The Neural Basis of Interindividual Variability in Inhibitory Efficiency after Sleep Deprivation. *Journal of Neuroscience*, *26*(27), 7156–7162. https://doi.org/10.1523/JNEUROSCI.0906-06.2006

Cliff, M. A., Dever, M. C., Hall, J. W., & Girard, B. (1995). Development and evaluation of multiple regression models for prediction of sweet cherry liking. *Food Research International*, *28*(6), 583–589. https://doi.org/10.1016/0963-9969(95)00041-0

Cohen, R. M., Pickar, D., Garnett, D., Lipper, S., Gillin, J. C., & Murphy, D. L. (1982). REM sleep suppression induced by selective monoamine oxidase inhibitors. *Psychopharmacology*, *78*(2), 137–140. https://doi.org/10.1007/BF00432251

Dar, Y. L., & Light, J. M. (2014). *Food Texture Design and Optimization*. John Wiley & Sons.

Hanlon, E. C., Andrzejewski, M. E., Harder, B. K., Kelley, A. E., & Benca, R. M. (2005). The effect of REM sleep deprivation on motivation for food reward. *Behavioural Brain Research*, *163*(1), 58–69. https://doi.org/10.1016/j.bbr.2005.04.017

Hayes, J. E., & Duffy, V. B. (2008). Oral sensory phenotype identifies level of sugar and fat required for maximal liking. *Physiology & Behavior*, *95*(1), 77–87. https://doi.org/10.1016/j.physbeh.2008.04.023

Horne, J. A., Anderson, N. R., & Wilkinson, R. T. (1983). Effects of Sleep Deprivation on Signal Detection Measures of Vigilance: Implications for Sleep Function. *Sleep*, *6*(4), 347–358. https://doi.org/10.1093/sleep/6.4.347

Horne, James A. (2015). Human REM sleep: influence on feeding behaviour, with clinical implications. *Sleep Medicine*, *16*(8), 910–916. https://doi.org/10.1016/j.sleep.2015.04.002

Iatridi, V., Hayes, J. E., & Yeomans, M. R. (2018). Reconsidering the classification of sweet taste liker phenotypes: a methodological review. *Food Quality and Preference*. https://doi.org/10.1016/j.foodqual.2018.09.001

Imaki, M., Hatanaka, Y., Ogawa, Y., Yoshida, Y., & Tanada, S. (2002). An epidemiological study on relationship between the hours of sleep and life style factors in Japanese factory workers. *Journal of Physiological Anthropology and Applied Human Science*, *21*(2), 115–120.

Kamiyama, H., Iida, T., Nishimori, H., Kubo, H., Uchiyama, M., Laat, A. D., … Komiyama, O. (2019). Effect of sleep restriction on somatosensory sensitivity in the oro-facial area: An experimental controlled study. *Journal of Oral Rehabilitation*, *46*(4), 303–309. https://doi.org/10.1111/joor.12758

Killgore, W. D. S. (2010). Effects of sleep deprivation on cognition. In G. A. Kerkhof & H. P. A. van Dongen (Eds.), *Progress in Brain Research* (Vol. 185, pp. 105–129). https://doi.org/10.1016/B978-0-444-53702-7.00007-5

Lange, L. A., Kampov-Polevoy, A. B., & Garbutt, J. C. (2010). Sweet Liking and High Novelty Seeking: Independent Phenotypes Associated with Alcohol-related Problems. *Alcohol and Alcoholism*, *45*(5), 431–436. https://doi.org/10.1093/alcalc/agq040

Lauderdale, D. S., Knutson, K. L., Yan, L. L., Liu, K., & Rathouz, P. J. (2008). Sleep duration: how well do self-reports reflect objective measures? The CARDIA Sleep Study. *Epidemiology (Cambridge, Mass.)*, *19*(6), 838–845. https://doi.org/10.1097/EDE.0b013e318187a7b0

Lauderdale, D. S., Knutson, K. L., Yan, L. L., Rathouz, P. J., Hulley, S. B., Sidney, S., & Liu, K. (2006). Objectively Measured Sleep Characteristics among Early-Middle-Aged AdultsThe CARDIA Study. *American Journal of Epidemiology*, *164*(1), 5–16. https://doi.org/10.1093/aje/kwj199

MacFie, H. J. H., & Meiselman, H. L. (2012). *Food Choice, Acceptance and Consumption*. Springer Science & Business Media.

Manly, T., Dobler, V. B., Dodds, C. M., & George, M. A. (2005). Rightward shift in spatial awareness with declining alertness. *Neuropsychologia*, *43*(12), 1721–1728.

Meilgaard, M. C., Carr, B. T., Civille, G. V., Carr, B. T., & Civille, G. V. (1999). *Sensory Evaluation Techniques*. https://doi.org/10.1201/9781439832271

Mennella, J. A., Pepino, M. Y., & Reed, D. R. (2005). Genetic and Environmental Determinants of Bitter Perception and Sweet Preferences. *Pediatrics*, *115*(2), e216–e222. https://doi.org/10.1542/peds.2004-1582

Moskowitz, H. R. (1977). Magnitude Estimation: Notes on What, How, When, and Why to Use It. *Journal of Food Quality*, *1*(3), 195–227. https://doi.org/10.1111/j.1745-4557.1977.tb00942.x

Moskowitz, H. R., & Krieger, B. (1995). The contribution of sensory liking to overall liking: An analysis of six food categories. *Food Quality and Preference*, *6*(2), 83–90. https://doi.org/10.1016/0950-3293(95)98552-T

Moskowitz, H. R., Muñoz, A. M., & Gacula Jr, M. C. (2008). *Viewpoints and controversies in sensory science and consumer product testing*. John Wiley & Sons.

Nishiura, C., & Hashimoto, H. (2010). A 4-year study of the association between short sleep duration and change in body mass index in Japanese male workers. *Journal of Epidemiology*, 1008030183–1008030183.

Prather, A. A., Leung, C., Adler, N. E., Epel, E. S., Ritchie, L., & Laraia, B. (2014). Abstract P110: Short And Sweet: Short Sleep Duration Is Associated With Increased Sugar Sweetened Beverage Consumption In The United States. *Circulation*, *129*(Suppl 1), AP110–AP110.

Rains, J. C., & Poceta, J. S. (2012). Sleep-related headaches. *Neurologic Clinics*, *30*(4), 1285–1298.

Reis, F., De Andrade, J., Deliza, R., & Ares, G. (2016). Comparison of Two Methodologies for Estimating Equivalent Sweet Concentration of High-Intensity Sweeteners with Untrained Assessors: Case Study with Orange/Pomegranate Juice. *Journal of Sensory Studies*, *31*(4), 341–347. https://doi.org/10.1111/joss.12217

Rogé, J., & Gabaude, C. (2009). Deterioration of the Useful Visual Field with Age and Sleep Deprivation: Insight from Signal Detection Theory. *Perceptual and Motor Skills*, *109*(1), 270–284. https://doi.org/10.2466/pms.109.1.270-284

Scullin, M. K., & Bliwise, D. L. (2015). Sleep, cognition, and normal aging: integrating a half century of multidisciplinary research. *Perspectives on Psychological Science*, *10*(1), 97–137.

Shi, Z., McEvoy, M., Luu, J., & Attia, J. (2008). Dietary fat and sleep duration in Chinese men and women. *International Journal of Obesity*, *32*(12), 1835.

Sidel, J. L., & Stone, H. (1993). The role of sensory evaluation in the food industry. *Food Quality and Preference*, *4*(1), 65–73. https://doi.org/10.1016/0950-3293(93)90314-V

Simon, S. L., Field, J., Miller, L. E., DiFrancesco, M., & Beebe, D. W. (2015). Sweet/Dessert Foods Are More Appealing to Adolescents after Sleep Restriction. *PLOS ONE*, *10*(2), e0115434. https://doi.org/10.1371/journal.pone.0115434

St-Onge, Marie-Pierre, Roberts, A. L., Chen, J., Kelleman, M., O'Keeffe, M., RoyChoudhury, A., & Jones, P. J. (2011). Short sleep duration increases energy intakes but does not change energy expenditure in normal-weight individuals. *The American Journal of Clinical Nutrition*, *94*(2), 410–416. https://doi.org/10.3945/ajcn.111.013904

St-Onge, M-P, Wolfe, S., Sy, M., Shechter, A., & Hirsch, J. (2014). Sleep restriction increases the neuronal response to unhealthy food in normal-weight individuals. *International Journal of Obesity (2005)*, *38*(3), 411–416. https://doi.org/10.1038/ijo.2013.114

Tuorila, H., Keskitalo-Vuokko, K., Perola, M., Spector, T., & Kaprio, J. (2017). Affective responses to sweet products and sweet solution in British and Finnish adults. *Food Quality and Preference*, *62*, 128–136. https://doi.org/10.1016/j.foodqual.2017.06.021

van der Laan, L. N., de Ridder, D. T. D., Viergever, M. A., & Smeets, P. A. M. (2011). The first taste is always with the eyes: A meta-analysis on the neural correlates of processing visual food cues. *NeuroImage*, *55*(1), 296–303. https://doi.org/10.1016/j.neuroimage.2010.11.055

Van Dongen, H. P. A., Maislin, G., Mullington, J. M., & Dinges, D. F. (2003). The Cumulative Cost of Additional Wakefulness: Dose-Response Effects on Neurobehavioral Functions and

Sleep Physiology From Chronic Sleep Restriction and Total Sleep Deprivation. *Sleep*, *26*(2), 117–126. https://doi.org/10.1093/sleep/26.2.117

Babkoff, H., Zukerman, G. I. L., Fostick, L., & BEN-ARTZI, E. (2005). Effect of the diurnal rhythm and 24 h of sleep deprivation on dichotic temporal order judgment. *Journal of Sleep Research*, *14*(1), 7–15.

Bachmanov, A. A., Bosak, N. P., Floriano, W. B., Inoue, M., Li, X., Lin, C., … Beauchamp, G. K. (2011). Genetics of sweet taste preferences. *Flavour and Fragrance Journal*, *26*(4), 286–294. https://doi.org/10.1002/ffj.2074

Banks, S., Van Dongen, H. P. A., Maislin, G., & Dinges, D. F. (2010). Neurobehavioral Dynamics Following Chronic Sleep Restriction: Dose-Response Effects of One Night for Recovery. *Sleep*, *33*(8), 1013–1026. https://doi.org/10.1093/sleep/33.8.1013

Brondel, L., Romer, M. A., Nougues, P. M., Touyarou, P., & Davenne, D. (2010). Acute partial sleep deprivation increases food intake in healthy men–. *The American Journal of Clinical Nutrition*, *91*(6), 1550–1559.

Carskadon, M. A., Dement, W. C., & others. (2005). Normal human sleep: an overview. *Principles and Practice of Sleep Medicine*, *4*, 13–23.

Chuah, Y. M. L., Venkatraman, V., Dinges, D. F., & Chee, M. W. L. (2006). The Neural Basis of Interindividual Variability in Inhibitory Efficiency after Sleep Deprivation. *Journal of Neuroscience*, *26*(27), 7156–7162. https://doi.org/10.1523/JNEUROSCI.0906-06.2006

Cliff, M. A., Dever, M. C., Hall, J. W., & Girard, B. (1995). Development and evaluation of multiple regression models for prediction of sweet cherry liking. *Food Research International*, *28*(6), 583–589. https://doi.org/10.1016/0963-9969(95)00041-0

Cohen, R. M., Pickar, D., Garnett, D., Lipper, S., Gillin, J. C., & Murphy, D. L. (1982). REM sleep suppression induced by selective monoamine oxidase inhibitors. *Psychopharmacology*, *78*(2), 137–140. https://doi.org/10.1007/BF00432251

Dar, Y. L., & Light, J. M. (2014). *Food Texture Design and Optimization*. John Wiley & Sons.

Hanlon, E. C., Andrzejewski, M. E., Harder, B. K., Kelley, A. E., & Benca, R. M. (2005). The effect of REM sleep deprivation on motivation for food reward. *Behavioural Brain Research*, *163*(1), 58–69. https://doi.org/10.1016/j.bbr.2005.04.017

Hayes, J. E., & Duffy, V. B. (2008). Oral sensory phenotype identifies level of sugar and fat required for maximal liking. *Physiology & Behavior*, *95*(1), 77–87. https://doi.org/10.1016/j.physbeh.2008.04.023

Horne, J. A., Anderson, N. R., & Wilkinson, R. T. (1983). Effects of Sleep Deprivation on Signal Detection Measures of Vigilance: Implications for Sleep Function. *Sleep*, *6*(4), 347–358. https://doi.org/10.1093/sleep/6.4.347

Horne, James A. (2015). Human REM sleep: influence on feeding behaviour, with clinical implications. *Sleep Medicine*, *16*(8), 910–916. https://doi.org/10.1016/j.sleep.2015.04.002

Iatridi, V., Hayes, J. E., & Yeomans, M. R. (2018). Reconsidering the classification of sweet taste liker phenotypes: a methodological review. *Food Quality and Preference*. https://doi.org/10.1016/j.foodqual.2018.09.001

Imaki, M., Hatanaka, Y., Ogawa, Y., Yoshida, Y., & Tanada, S. (2002). An epidemiological study on relationship between the hours of sleep and life style factors in Japanese factory workers. *Journal of Physiological Anthropology and Applied Human Science*, *21*(2), 115–120.

Kamiyama, H., Iida, T., Nishimori, H., Kubo, H., Uchiyama, M., Laat, A. D., … Komiyama, O. (2019). Effect of sleep restriction on somatosensory sensitivity in the oro-facial area: An experimental controlled study. *Journal of Oral Rehabilitation*, *46*(4), 303–309. https://doi.org/10.1111/joor.12758

Killgore, W. D. S. (2010). Effects of sleep deprivation on cognition. In G. A. Kerkhof & H. P. A. van Dongen (Eds.), *Progress in Brain Research* (Vol. 185, pp. 105–129). https://doi.org/10.1016/B978-0-444-53702-7.00007-5

Lange, L. A., Kampov-Polevoy, A. B., & Garbutt, J. C. (2010). Sweet Liking and High Novelty Seeking: Independent Phenotypes Associated with Alcohol-related Problems. *Alcohol and Alcoholism*, *45*(5), 431–436. https://doi.org/10.1093/alcalc/agq040

Lauderdale, D. S., Knutson, K. L., Yan, L. L., Liu, K., & Rathouz, P. J. (2008). Sleep duration: how well do self-reports reflect objective measures? The CARDIA Sleep Study. *Epidemiology (Cambridge, Mass.)*, *19*(6), 838–845. https://doi.org/10.1097/EDE.0b013e318187a7b0

Lauderdale, D. S., Knutson, K. L., Yan, L. L., Rathouz, P. J., Hulley, S. B., Sidney, S., & Liu, K. (2006). Objectively Measured Sleep Characteristics among Early-Middle-Aged AdultsThe CARDIA Study. *American Journal of Epidemiology*, *164*(1), 5–16. https://doi.org/10.1093/aje/kwj199

MacFie, H. J. H., & Meiselman, H. L. (2012). *Food Choice, Acceptance and Consumption*. Springer Science & Business Media.

Manly, T., Dobler, V. B., Dodds, C. M., & George, M. A. (2005). Rightward shift in spatial awareness with declining alertness. *Neuropsychologia*, *43*(12), 1721–1728.

Meilgaard, M. C., Carr, B. T., Civille, G. V., Carr, B. T., & Civille, G. V. (1999). *Sensory Evaluation Techniques*. https://doi.org/10.1201/9781439832271

Mennella, J. A., Pepino, M. Y., & Reed, D. R. (2005). Genetic and Environmental Determinants of Bitter Perception and Sweet Preferences. *Pediatrics*, *115*(2), e216–e222. https://doi.org/10.1542/peds.2004-1582

Moskowitz, H. R. (1977). Magnitude Estimation: Notes on What, How, When, and Why to Use It. *Journal of Food Quality*, *1*(3), 195–227. https://doi.org/10.1111/j.1745-4557.1977.tb00942.x

Moskowitz, H. R., & Krieger, B. (1995). The contribution of sensory liking to overall liking: An analysis of six food categories. *Food Quality and Preference*, *6*(2), 83–90. https://doi.org/10.1016/0950-3293(95)98552-T

Moskowitz, H. R., Muñoz, A. M., & Gacula Jr, M. C. (2008). *Viewpoints and controversies in sensory science and consumer product testing*. John Wiley & Sons.

Nishiura, C., & Hashimoto, H. (2010). A 4-year study of the association between short sleep duration and change in body mass index in Japanese male workers. *Journal of Epidemiology*, 1008030183–1008030183.

Prather, A. A., Leung, C., Adler, N. E., Epel, E. S., Ritchie, L., & Laraia, B. (2014). Abstract P110: Short And Sweet: Short Sleep Duration Is Associated With Increased Sugar Sweetened Beverage Consumption In The United States. *Circulation*, *129*(Suppl 1), AP110–AP110.

Rains, J. C., & Poceta, J. S. (2012). Sleep-related headaches. *Neurologic Clinics*, *30*(4), 1285–1298.

Reis, F., De Andrade, J., Deliza, R., & Ares, G. (2016). Comparison of Two Methodologies for Estimating Equivalent Sweet Concentration of High-Intensity Sweeteners with Untrained Assessors: Case Study with Orange/Pomegranate Juice. *Journal of Sensory Studies*, *31*(4), 341–347. https://doi.org/10.1111/joss.12217

Rogé, J., & Gabaude, C. (2009). Deterioration of the Useful Visual Field with Age and Sleep Deprivation: Insight from Signal Detection Theory. *Perceptual and Motor Skills*, *109*(1), 270–284. https://doi.org/10.2466/pms.109.1.270-284

Scullin, M. K., & Bliwise, D. L. (2015). Sleep, cognition, and normal aging: integrating a half century of multidisciplinary research. *Perspectives on Psychological Science*, *10*(1), 97–137.

Shi, Z., McEvoy, M., Luu, J., & Attia, J. (2008). Dietary fat and sleep duration in Chinese men and women. *International Journal of Obesity*, *32*(12), 1835.

Sidel, J. L., & Stone, H. (1993). The role of sensory evaluation in the food industry. *Food Quality and Preference*, *4*(1), 65–73. https://doi.org/10.1016/0950-3293(93)90314-V

Simon, S. L., Field, J., Miller, L. E., DiFrancesco, M., & Beebe, D. W. (2015). Sweet/Dessert Foods Are More Appealing to Adolescents after Sleep Restriction. *PLOS ONE*, *10*(2), e0115434. https://doi.org/10.1371/journal.pone.0115434

St-Onge, Marie-Pierre, Roberts, A. L., Chen, J., Kelleman, M., O'Keeffe, M., RoyChoudhury, A., & Jones, P. J. (2011). Short sleep duration increases energy intakes but does not change energy expenditure in normal-weight individuals. *The American Journal of Clinical Nutrition*, *94*(2), 410–416. https://doi.org/10.3945/ajcn.111.013904

St-Onge, M-P, Wolfe, S., Sy, M., Shechter, A., & Hirsch, J. (2014). Sleep restriction increases the neuronal response to unhealthy food in normal-weight individuals. *International Journal of Obesity (2005)*, *38*(3), 411–416. https://doi.org/10.1038/ijo.2013.114

Tuorila, H., Keskitalo-Vuokko, K., Perola, M., Spector, T., & Kaprio, J. (2017). Affective responses to sweet products and sweet solution in British and Finnish adults. *Food Quality and Preference*, *62*, 128–136. https://doi.org/10.1016/j.foodqual.2017.06.021

van der Laan, L. N., de Ridder, D. T. D., Viergever, M. A., & Smeets, P. A. M. (2011). The first taste is always with the eyes: A meta-analysis on the neural correlates of processing visual food cues. *NeuroImage*, *55*(1), 296–303. https://doi.org/10.1016/j.neuroimage.2010.11.055

Van Dongen, H. P. A., Maislin, G., Mullington, J. M., & Dinges, D. F. (2003). The Cumulative Cost of Additional Wakefulness: Dose-Response Effects on Neurobehavioral Functions and

Sleep Physiology From Chronic Sleep Restriction and Total Sleep Deprivation. *Sleep*, *26*(2), 117–126. https://doi.org/10.1093/sleep/26.2.117