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Daytime sleepiness affects prefrontal regulation of food intake☆

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ABSTRACT

The recent epidemic of obesity corresponds closely with the decline in the average number of hours of sleep obtained nightly. While growing research suggests that sleep loss may affect hormonal and other physiological systems related to food intake, no studies have yet explored the role that sleepiness may play in reducing prefrontal inhibitory control over food intake. Because evidence suggests that women may be more prone to obesity and eating disorders, as well as more likely to suffer from sleep problems, we examined the relation between general daytime sleepiness, brain responses to food stimuli, and self-reported overeating separately for men and women. Thirty-eight healthy adults (16 women; 22 men) aged 18 to 45 underwent functional magnetic resonance imaging (fMRI) while viewing pictures of high- and low-calorie foods. Subjects completed the Epworth Sleepiness Scale (ESS) and provided a rating to the query "how often do you eat more than you intend to." Contrast images comparing brain activation derived from the high- versus low-calorie conditions were correlated voxel-wise with scores from the ESS in a second-level regression model, the output of which was used to predict self-reported overeating. As hypothesized, daytime sleepiness correlated with reduced activation in the ventromedial prefrontal cortex during perception of high- versus low-calorie food images. Moreover, activation within this cluster predicted overeating, but only for women. Findings suggest that normal fluctuations in sleepiness may be sufficient to affect brain regions important for regulating food intake, but that these effects may differ between men and women.

Introduction

Over the past several decades there has been an alarming increase in the rate of excessive weight gain in Western societies (Flegal et al., 2002), with over one in three adults in the United States now meeting criteria for obesity (Ogden et al., 2012). While there are many factors that have arguably contributed to this trend, it is hard to ignore the fact that obesity rates have closely paralleled the decline in average nightly sleep during the latter portion of the 20th century. Evidence suggests that during the 1960s, Americans were sleeping between 8.0 and 8.9 h per night (Kripke et al., 1979). By the mid 1990s, average sleep had declined to about 7.0 h (Gallup Organization, 1995), and recent data from 2005 suggest that most Americans are now sleeping less than 7 h per night (National Sleep Foundation, 2005). In fact, a 2012 report by the Center for Disease Control and Prevention (CDC) found that one in three workers now report that they routinely sleep six or fewer hours nightly (Center for Disease Control and Prevention, 2012). Shorter sleep duration is related to a variety of health problems including obesity (Patel et al., 2008). Moreover, short sleep duration earlier in life is related to increased risk of weight gain later in life (Gangwisch et al., 2005; Hasler et al., 2004; Patel, 2009). The relation between sleep and weight gain is poorly understood, but may prove crucial to stopping or even reversing the current trends.

Notably, the epidemic of obesity has particularly affected women. Epidemiological studies suggest that for the past few decades, women have shown significantly higher rates of obesity compared to men (Ogden et al., 2012), and extreme levels of obesity (i.e., Body Mass Index > 40) are more than twice as prevalent among women than men (Ogden et al., 2006). It has also long been known that women tend to be at much greater risk for developing a number of different eating related problems and clinical eating disorders relative to men (Lewinsohn et al., 2002; Striegel-Moore and Bulik, 2007; Striegel-Moore et al., 2009). While the reasons for the gender differences in eating disorders are not fully understood, some evidence suggests that there may be some cognitive and behavioral differences in responses to food, with women more frequently reporting a greater perception of loss of control over the amount of food consumed during meals (Striegel-Moore et al., 2009). Functional neuroimaging studies have also suggested that there may be sex differences in responses of key appetite regions to images of food (Killgore and Yurgelun-Todd, 2010). Interestingly, the reported sex differences in food consumption

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also appear to be mirrored in the frequency of some sleep-related complaints and disorders. For instance, a recent meta-analysis of studies of insomnia showed that women were over 1.4 times more likely to suffer from insomnia compared to men (Zhang and Wing, 2006). Although sleep apnea is more common among middle to older age men (O'Connor et al., 2000), general non-respiratory sleep complaints such as poor sleep quality, longer sleep onset latency, and difficulty with sleep maintenance tend to be more common among women in the same age range (Middelkoop et al., 1996). A recent poll by the National Sleep Foundation reported that 67% of women experience sleep problems at least a few nights each week and 46% report that they suffer from sleep problems every night (National Sleep Foundation, 2007). Thus, over the past few decades, sleep duration has declined while obesity has increased, and these problems appear to be particularly common among women.

Most studies linking insufficient sleep to excess food consumption and weight gain have emphasized the effects of sleep loss on physiological variables such as reduced energy expenditure and alterations in the hormones leptin and ghrelin, which are key regulators of appetite (Knutson et al., 2007; Patel and Hu, 2008). However, lack of sleep can affect other systems that play a role in food intake as well. For instance, sleep loss is associated with altered functional activity within a number of brain regions. Of particular relevance to food consumption is the prefrontal cortex, particularly the ventromedial prefrontal cortex (vmPFC), a complex brain region that is particularly important for evaluating the reward value of objects (Paulus and Frank, 2003), regulating emotional responses (Hariri et al., 2003), and controlling behavior (Blasi et al., 2006; Ridderinkhof et al., 2004). Sleep loss is associated with a number of changes in the vmPFC, including reduced glucose metabolism (Thomas et al., 2000; Wu et al., 2006), altered functional responses during risky decision-making (Venkatraman et al., 2007) and judgments of economic value (Libedinsky et al., 2011; Venkatraman et al., 2011), as well as reduced functional connectivity with other brain regions important for self-referential and emotional processing (De Havas et al., 2012; Killgore et al., 2012c; Samann et al., 2010; Yoo et al., 2007). When sleep is lacking, these prefrontal changes appear to contribute to deficits in decision-making and inhibitory control (Drummond et al., 2006; Harrison and Horne, 2000; Killgore, 2010). Interestingly, recent data suggest that general daytime sleepiness is associated with reduced gray matter volume within the vmPFC (Killgore et al., 2012b). Some of these same sleep-sensitive prefrontal systems have previously been shown to be critical in responding to the caloric content of visually presented food stimuli (Killgore and Yurgelun-Todd, 2005b; Killgore et al., 2003) and may even relate to greater body mass index (BMI) (Killgore and Yurgelun-Todd, 2005a). Thus, evidence suggests that insufficient sleep alters functioning in key brain regions that are particularly responsive to the caloric content of food and which are important for regulating and inhibiting behavior.

The goal of the present study was to examine the relation between self-reported general daytime sleepiness and prefrontal cortex responses to the calorie content of food images. Based on the neuroimaging and behavioral literature outlined above, we hypothesized that greater general daytime sleepiness would be associated with reduced functional responsiveness of the vmPFC to high- versus low-calorie food images, and that the magnitude of responsiveness within this inhibitory region would predict self-reported problems with overeating. Furthermore, given the sex differences in the current rates of obesity, eating disorders, and sleep complaints, we also hypothesized that the relationships would be stronger in women than in men.

Methods

Participants

Thirty-eight healthy right-handed adults, ranging in age from 18 to 45 years (16 women, 22 men), were recruited via flyers and internet advertisements posted around Boston, MA, and the surrounding areas. Participants were thoroughly screened by a trained research technician during a semi-structured interview. Based on this screening, enrolled participants were deemed to be free of any evidence or history of severe medical conditions, head injury, loss of consciousness >30 min, brain tumors, seizures, neurologic conditions, symptoms consistent with Axis I psychopathology, or drug or alcohol treatment. Additionally, potential participants were excluded for current or recent use of any psychoactive medications or illicit substances, or excessive alcohol intake. Table 1 provides basic demographic information for the women and men separately. Body mass index (BMI) ranged from normal (19.80) to moderately obese (34.78) for the sample as a whole ($M=24.60$, $SD=3.75$), but this did not differ between women and men (see Table 1). Each participant completed detailed logs of all food consumed on the day of the scan. Two independent raters used the food logs to calculate each participant's calorie consumption during the hours preceding the scan via a primary web-based resource for determining calorie content from foods (http://ndb.nal.usda.gov), and relied on a secondary resource when a definitive answer could not be obtained from the first (http://caloriecount.about.com). Inter-rater reliability in calorie scoring was extremely high (ICC = 0.97, CI = 0.95–0.98), and the independent ratings were averaged for each participant to obtain a final estimate of total calorie consumption. On the whole, participants consumed an average of 327.8 calories ($SD=243.6$) during the hours leading up to the scan, with no significant difference between women and men in calorie intake (see Table 1). Overall, typical caffeine use was modest, ranging from 0 to 444 mg per day ($M=104.08$, $SD=117.65$), and did not differ between women and men. Similarly, caffeine use on the day of the scan was not significantly different for the women and men. Participants reported generally normal amounts of weeknight ($M=7.36$, $SD=0.88$ h) and weekend sleep ($M=7.71$, $SD=1.32$ h), as well as normal amounts of sleep the night before the scan ($M=7.04$,

Table 1
Demographic and performance variable information for participants.

	Men (n = 22)		Women (n = 16)			
	M	SD	M	SD	t (df = 36)	sig.
Age (years)	31.50	9.30	28.25	7.48	1.19	ns
BMI (weight [kg]/height [m]^2)	24.24	3.60	25.08	4.01	−0.68	ns
Pre-scan calories consumed	358.8	236.7	285.1	254.1	0.92	ns
Typical caffeine use (mg/day)	101.94	127.48	107.02	106.64	−0.13	ns
Study day caffeine use (mg)	73.96	122.17	88.91	106.27	−0.39	ns
Weeknight sleep (h)	7.36	0.94	7.36	0.81	0.02	ns
Weekend sleep (h)	7.82	1.31	7.56	1.38	0.58	ns
Last night sleep (h)	6.91	0.97	7.22	0.93	−0.99	ns
ESS	5.77	3.74	5.31	3.18	0.40	ns
Current hunger (1–7)	4.64	1.33	5.00	1.41	−0.81	ns
Typical appetite (1–10)	6.18	1.40	6.63	1.45	−0.95	ns
Eat more than intend to (1–10)	3.55	2.61	5.06	2.14	−1.90	ns
Flower picture ratings	1.00	0.16	1.01	0.04	−0.80	ns
Low-calorie picture ratings	3.63	1.35	3.83	1.36	−0.44	ns
High-calorie picture ratings	4.33	1.26	4.13	1.19	0.49	ns
Low-calorie picture memory	0.75	0.15	0.80	0.07	−1.19	ns
High-calorie picture memory	0.77	0.14	0.84	0.10	−1.76	ns

The table shows that there are no differences between men and women on demographic and performance variables. BMI = Body Mass Index; ESS = Epworth Sleepiness Scale; Current Hunger was rated on a 7-point scale (1 = not at all hungry; 7 = extremely hungry); Typical Appetite was rated on a 10-point scale (1 = never hungry; 10 = always hungry); Eat More than Intend to was rated on a 10-point scale (1 = never; 10 = always). Ratings refer to post-scan ratings taken for each image shown in the scanner. Participants responded to the question "how much you would like to eat each item right now" (1 = do not want to eat it; 7 = strongly desire to eat it). Memory scores indicate the proportion of correct recognition responses for each category of images (i.e., previously seen versus new foils) shown during the post-scan recognition test.