Abstract

Background: Emerging findings from neuroimaging studies investigating brain activity associated with dietary behavior are illuminating the interaction of biological and behavioral mechanisms that have implications for obesity prevention. Globally, 1.9 billion adults are overweight and 650 million are obese. Obesity/overweight are major risk factors for chronic illness and death. Behaviorally based health interventions have had limited success in curbing the obesity epidemic. Greater understanding of brain responses to food cues will contribute to new knowledge and shape public health efforts in obesity prevention. However, an integration of this knowledge for obesity prevention education has not been published.

Aim: This study links evidence generated by brain imaging studies generated in response to diet and food images and highlights educational recommendations for nurses engaged in obesity prevention and weight-loss education.

Method: An integrative review of the literature was conducted using the MeSH key words "magnetic resonance imaging" and "diet" and "food images" in PubMed, MEDLINE Complete, CINAHL and Cochrane databases from their first appearance in 2006 through March 2018. Studies published in English and using fMRI to measure brain response to diet and food images were initially identified. Animal models, those whose primary focus was a specific disease and intervention studies were excluded.

Results: Of the 159 studies located, 26 met inclusion criteria. Findings from neuroimaging studies may help explain the relationship between brain mechanisms and behavioral aspects of dietary choice and inform patient education in obesity prevention. Awareness of this evidence is applicable within nursing educational efforts. This review contributes several recommendations which should be purposefully considered by nurses providing individualized weight-loss education and obesity prevention. Keywords: obesity, prevention, patient education, evidence-based practice, neurology, nutrition.

Introduction

Considered the most significant emerging health problem worldwide, individuals living with obesity have tripled since 1975 (World Health Organization (WHO), 2018). Obesity/overweight are risk factors for chronic illness and death (WHO, 2018). Dietary risk contributes to being obese/overweight and involves complex relationships among physiological, social, and environmental factors (Hemmingsson, 2014). Behaviorally focused public health interventions have had limited success in curbing the obesity epidemic (Hung et al., 2015). Advances in neuroimaging are contributing to a scientific understanding of the obesity puzzle (Brooks, Cedernaes, and Schioth, 2013). Functional magnetic resonance imaging (fMRI) (Figure 1) is a neuroimaging technique that uses the differential magnetic properties of oxygenated (and deoxygenated) blood flow to determine which brain region(s) are more/less active when performing mental task(s). The greater the oxygenated blood flow to a given brain region, the more engaged in task performance this area is deemed to be (Huettel, et al., 2014). The blood oxygenation level dependent (BOLD) response is a relative activation measure between task activity and activation obtained during a control/baseline condition (Figure 2). The spatial resolution of fMRI is very high (approximately one millimeter) but its temporal resolution is relatively low (seconds). Studies using fMRI in response to visually presented food images are helping to build an understanding of both the neural and biobehavioral contributions to obesity risk (Collins & Riley, 2016). Moreover, elucidation of brain activation during exposure to diet and food images holds promise for advancing personalized approaches to obesity treatment and prevention. However, the literature has not yet linked findings from fMRI to education in obesity prevention. The PICO question for this review is "In an adult or adolescent population, how does research on behavioral responses to food images from fMRI data inform obesity education and prevention?"

Methodology and Appraisal

The published steps for conducting an integrative review (see Whittemore & Knafle, 2005) guided our approach. The integrative research review is a rigorous technique that allows for the inclusion of studies with varying methodologies, with the goal of summarizing research on a specific topic, and thus contributing to evidence-based insights (Brown, 2018). The aim of this review was to link the evidence generated from fMRI studies measuring brain activations in response to diet and food images to obesity education and prevention.

The search strategy was conducted in consultation with a research librarian. Articles published in CINAHL, MEDLINE Complete, PubMed, Cochrane databases were searched from their first appearance in the literature (2006) through March 2018 using the MeSH headings "magnetic resonance imaging," and "diet," and "food images". Original, peer-reviewed studies with human participants and written in English were included; animal models, disease specific and intervention focused studies were excluded.

Study inclusion was independently appraised by four researchers. To assess study quality, the AMSTAR 2 criteria was applied to two studies identified as a systematic review and/or meta-analysis. The remainder of the studies were assessed using a data extraction worksheet adapted from the CONSORT 2010 checklist for research methods and reporting. Each study was independently evaluated for adequacy of the following criteria: 1) study title, description of study background, aims and objectives; 2) study methods/design, statistical analysis, results, and findings specific to our study question, and 3) the adequacy of the description of the brain activation reported in response to diet and food images. Overall study strengths/limitations were recorded, and level of evidence was assigned using a published evidence hierarchy (Melnyk, Fineout-Overholt, 2011).

Results

Initially, 157 articles were identified through the search strategy, two were located through bibliographic mining, and nine duplicates were removed. The remaining 150 records were screened. One hundred twenty-four did not meet study inclusion criteria. Twenty-six studies comprised the final sample. Findings from the literature searches, screening, and selection processes were recorded using the PRISMA Diagram in Figure 1.

The results of this review suggest important differences in brain activation in lean as compared to overweight/obese individuals (Bruce, et al, 2014; Cornier, et al., 2013; Martin, et al., 2010; Pursey, et al., 2014; Tregalias, et al., 2011). Unique activation patterns were also observed in individuals across the weight loss/gain continuum when exposed to food images with high appeal and reward value (Brooks, Cedernaes, & Schioth, 2013; English, et al., 2017; Stice & Yokum, 2012; Yokum, Ng, & Stice, 2011). Additionally, a number of moderating metabolic and physiologic conditions were associated with activation of different brain regions (Alonso-Alonso, et al., 2011; Born, et al., 2011; Crabtree, Chambers, Hardwick & Blannin, 2014; Cornier, et al., 2010; Griffioen-Roose, et al., 2014; He, et al., 2014; Kahathuduwa, Boyd, Davis, O'Boyle & Binks, 2016; Kilgore, et al., 2013; Killgore & Yurgelun-Todd, 2006; Leidy, Lepping, Savage & Harris, 2011; Lundgren, et al., 2013; Luo, et al., 2014; Melhorne, et al., 2016; Sayer, et al., 2016; Varley-Campbell et al., 2017; Wallner-Liebmann, et al., 2010; Wagner, Boswell, Kelley & Heatherton, 2012). The results from the neuroimaging studies included in this review help explain the relationship between brain activations and behavioral aspects of dietary choice to inform patient education for obesity prevention and provides preliminary evidence for consideration by nurses when developing individualized weight-loss educational plans with patients. Table 1 summarizes the study authors, sample size/design, whole brain and/or region of interest activations, behavioral measures and a summary of key study observations. Table 2 highlights educational recommendations for consideration by nurses engaged in patient education for obesity prevention.

This integrative review has a number of limitations. The neuroimaging and behavioral metrics used were methodologically diverse (see Table 1). Most studies were small (average N = 28) with the majority using female participants as compared to males or mixed gender samples. Subjects ranged in age from 7 – 56 years with a mean age of 17. Seven of the 26 studies used children under age 18 exclusively. The majority of studies used non-random, single-site, convenience-sampling methods generating mid-range to lower level evidence. Two were categorized as systematic review/meta-analysis, producing level 1 evidence; however, independent application of the AMSTAR 2 critical domains by two reviewers suggests a moderate-low overall confidence in results.

Brain activations in overweight and obese individuals in comparison to lean individuals, in response to food images was the focus of numerous studies. In a review of 66 studies investigating brain activation response to visual food cues according to weight status, Pursey et al. (2014) found differences in obese, healthy-weight, and weight-loss groups. Across studies, motivational state (fasted/satiated) affected brain activation. Compared to healthy-weight individuals, overweight/obese participants had greater brain activation in response to food as compared to non-food images in regions associated with food cue processing.

Likewise, Bruce et al, 2014 studied weight status and brain responses in hungry/fed states before/after surgical and behavioral interventions. Compared to the bariatric group, behavioral dieters in the hungry, pre-meal condition, showed greater neural activation in the right medial prefrontal cortex and left precuneus following weight loss. In the fed state, the bariatric group had increased activation bilaterally in the temporal cortex following weight loss. These findings are consistent with the literature suggesting a link between regions of brain activation and weight loss method (Ochner, et al., 2011).

In comparison, brain responses to food cues in obesity-resistant (OR) as compared to obesity-prone (OP) individuals was examined by Cornier et al. (2013). Fasting increased brain activation in the insula, somatosensory cortex, parietal cortex, and visual cortex in both groups. Individuals at risk for weight gain had brain activation differences in regions playing a prominent role in weight regulation compared to those resistant to weight gain/obesity. Neural attenuation of brain regions in the acute fed state of OR compared to OP individuals suggests the former have alterations in brain activity contributing to excess energy intake. Obesity prone individuals, compared to OR participants, showed greater brain activation intensity in the medial and anterior prefrontal cortex, areas reported as playing a role in memory and decision-making and suggest a relationship between excessive caloric intake and obesity in OP versus OR individuals (Euston, Gruber & McNaughton, 2013).

Similarly, brain activations in lean to obese subjects and the motivational impact of caloric density was investigated by Martin et al. (2010). Increased brain activation in the limbic and paralimbic regions were found when viewing high caloric foods. These findings are consistent with the literature suggesting individuals with high motivation for energy-dense foods show lower activation in brain regions responsible for inhibition (Jensen et al., 2017). Some individuals find it difficult to inhibit impulses related to food consumption and thus educational intervention strategies targeting impulse control would be beneficial.

Brain activation in reduced-obese to lean status has been studied on the brain default network (DN; Tregellas et al., 2011). Activations in the DN (interacting brain regions thought to reflect “readiness)” were used to compare reduced-obese (RO) to lean individuals’ subjects. Increased activity of the DN in overfeeding conditions of RO subjects compared to the obese suggests hyperactivation of this network plays a pivotal role in appetite and weight status. Nurses should consider the importance of personalized patient education interventions that cultivate internal awareness for dietary adherence and self-care.

Unique activation patterns were observed in individuals across the weight loss/gain continuum when exposed to food cue images with high appeal and reward value . The addictive response to food cues in lean to obese subjects was studied in a meta-analysis conducted by Brooks, Cedernaes, and Schioth (2013). Brain activation in obese individuals was linked to areas associated with evaluation of reward and increased in individuals with obesity as compared to healthy weight controls in these regions. In obese subjects, activation of the prefrontal cortex was strongly associated with reward stimuli. Obese subjects had reduced activation in brain areas linked to cognitive control, awareness of bodily sensations, along with under-sensitivity to signals of satiety and fullness, suggesting all are contributing factors to overeating.

Similarly, Stice, Burger, & Yokum (2013) examined the effects of caloric deprivation on attentional and reward responsivity to food cue images. Caloric deprivation was found to heighten brain activation in areas related to attention, reward, and motivation. The clinical implications are important for weight loss treatment and behavioral dieting. Individuals trying to lose weight through long periods of restricted eating may have their efforts derailed by heightened sensitivity to the reward value of food and subsequently induce unhealthy food choices. Thus, *not* using caloric deprivation approaches to weight loss interventions should be part of nursing recommendations during patient education.

Comparatively, the response to caloric content and portion size in lean to obese subject was investigated by Yokum, Ng and Stice (2011), whose findings suggest overweight is related to attentional biases to food cues in individuals who showed elevated reward circuitry. The association of brain activity and BMI reported by Yokum and colleagues (2011) align with studies suggesting differences in attentional bias to food cues as critical and support the need for *personalized* approaches to obesity-prevention and weight loss (Hendrikse, et al., 2015).

The response to high-energy versus low-energy food cues in children was studied by English et al (2017). Large portion sizes were associated with decreased activation in the inferior frontal gyrus, while low-energy versus high-energy food cues were associated with increased brain activation in the caudate, cingulate and precentral gyrus and decreased activation in the insula and superior temporal gyrus pointing to the utility of interventions targeting decision-making skills to control moderate overeating.

The majority of studies tested brain activation during moderating metabolic and physiological conditions. Killgore et al. (2013) examined brain activation changes considering sex, high versus low-calorie foods, and motivational status. The long-term weight status of women was associated with their response to high-calorie food cues. Similarly, Alonso-Alonso et al. (2011) investigated women's brain response to food images during early/late follicular phase of the menstrual cycle in fasting/feeding conditions. Differences in inferior frontal and fusiform gyri brain activation during visualization of food produced greater activation in the fed versus fasting states, but only during the late follicular state when estradiol concentration was high. An inverse correlation was obtained with changes in estradiol concentration and activation of the fusiform gyrus in the fasting compared to fed conditions. Sex and estradiol (stress hormone) may play a role in diminishing brain activation to food cues during energy deprivation during hormonal changes across the menstrual cycle. Cornier et al. (2010) and Varley-Campbell, Fulfor, Moore, & Williams (2017) examined sex-based differences in response to food images. Cornier, et al report women had increased dorsolateral prefrontal cortex activation in response to food cues and greater sensitivity to hunger and satiety responses than men. Likewise, Varley-Campbell et al. (2017) examined adolescent girls and boys in fed and fasted conditions. Girls had significantly greater brain activation than boys in regions associated with decision-making, executive functioning, working memory and self-awareness when satiated state was not considered. When fasting or fed states were examined separately, boys showed increased brain activation in executive function, self-awareness, and decision-making. Food-related cues were associated with activation of regions known to be important for energy intake regulation and hold implications for sex-differentiation in designing fasting interventions.

The effects of moderating high-intensity exercise were tested by Crabtree et al. (2014) who found increased central reward system (nucleus accumbens) activation in response to low calorie images after exercise. Brain activation significantly increased in the dorsolateral prefrontal cortex and decreased in the orbitofrontal cortex (OFC) and hippocampus in the exercise group compared to resting controls after viewing high-calorie foods. Post exercise, viewing of lower-caloric food images resulted in increased activation in the insula and putamen and reduced activation in the OFC as compared to rest and correlated with thirst. Results suggest exercise-induced changes are linked to appetite regulation and hydration, which is consistent with literature supporting the role of exercise in decreasing appetite (Howe, Hand, & Manore, 2014).

Another moderating condition affecting obesity is evening hyperphagia (EH; consumption of 25% of total daily calories after the evening meal). Brain activation in obese subjects with EH compared to obese individuals without EH was studied by Lundgren et al. (2013). Individuals with EH demonstrated a decrease in brain activation in areas associated with inhibition and increased activation in areas related to visual attention after a mid-day meal. It is not known if a mid-day meal acts to disrupt dietary restraint. The possibility of a mechanistic role for circadian rhythm in delayed eating in obese adults with EH is raised by this study and suggests further research is needed.

Protein status has also been studied as a moderating variable. Griffioen-Roose et al. (2014) examined females viewing food cues including flavor (sweet/savory) and protein content (low/high), food preference, and intake. Findings suggest protein status modulates brain activation and preference for savory foods in reward areas, offering insight to the role of protein consumption. Similarly, Sayer et al. (2016) investigated dietary protein and fiber consumption at breakfast in overweight adults. The amount of fiber and protein consumed at breakfast did not influence postprandial appetite or ad libitum energy intake at lunch. Leidy et al. (2011) examined changes in brain activation in conjunction with breakfast consumption in overweight adolescent girls. The addition of a protein-rich breakfast reduced activation of neural areas related to food motivation and reward centers. Findings suggests regularly skipping breakfast as a means of weight loss may in fact, increase the risk being overweight/obese and has implications for nurses engaged in obesity education and prevention.

Wallner-Lieberman et al. (2010) used obese adolescents to examine insulin levels and hippocampal activation, the latter being a component of the limbic system involved with learning, memory, and emotional behavior in response to high-calorie food images. A positive correlation between fasting plasma insulin levels, waist circumference and right hippocampal activation was observed following the viewing of high-caloric food images. In contrast, negative associations were found between exposure to high-calorie food images and plasma levels of insulin and medial right gyrus frontalis and left thalamus activation suggesting the importance of regulatory control in circulating insulin via the hippocampus.

The influence of induced negative affect and reward value of appetizing foods in dieters was examined by Wagner et al. (2012). Distress occurred with negative mood induction and diminished participant's self-esteem. These findings suggest a neural connection between negative affect and disinhibited eating. Killgore and Yurgelum-Todd (2006) explored positive/negative ratings and regional cerebral responses to high- and low-calorie foods. Findings point to a possible involvement of a neurobiological substrate connecting cravings for calorie-dense foods with negative affective mood states and further suggest that mood is an important variable to consider in weight-loss management strategies. Luo et al. (2013) examined brain responses to high-caloric food images in Hispanic women. High calorie food images produced heightened brain activation and increased appetite drive and additional studies would be worthwhile.

The impact of high versus low hypothalmus-pituitary-adrenal axis (HPA) activation related to liking/wanting was investigated by Born et al. (2012). Elevated HPA activation interrupted and redirected brain signaling during liking/wanting. Low-liking task-related brain signaling (TRS) in the anterior insula before a meal predicted behavioral liking in response to food images; low HPA TRS in several brain regions before a meal predicted behavioral wanting. During high HPA activity, these associations were not found before the meal, although after-meal behavioral liking was predicted by activation of the nucleus accumbens and liking by the caudate nucleus. In the 21st century environment, characterized by pervasive food cues and high stress levels, a connection between HPA signaling and the neural systems related to reward and motivation are clearly areas for additional research.

In a study using monozygotic twins, Melhorn et al (2016) examined brain responses to high-caloric food cues before-after meals. Findings were consistent with heritable trait research suggesting an association among phenotype, diet and food choices (Barron et al., 2016). The neurophysiological evidence on brain response to food stimuli during short and long-term caloric restriction were reviewed by Kahathuduwa, Boyd, Davis, O'Boyle, & Binks (2016). Their findings suggest increased brain activation in fasting states. Fasting was associated with increased food-cue reactivity. He et al. (2014) studied the role three neural systems play in the inability to resist rewarding foods and the development of less healthy eating habits. The habitual system activation (right striatum) is dopamine-dependent and critical to motivation effects of natural/non-natural rewards (e.g. drugs) adding to the evidence suggesting a food-addiction model of obesity. Future research aimed at the neurophysiological mechanisms engaged when restrained eaters violate diet conditions and increasing caloric consumption should be considered.

Observations highlighting key aspects for nursing when developing patient educational experiences can be ascertained (see Table 2). Knowledge from this growing body of evidence should be useful to nurses providing educational efforts with this population. Important considerations for nurses when educating patients include: 1) regularly eating breakfast to attain weight loss, 2) long periods of restricted eating have a negative result on weight loss, 3) the role of exercise in appetite regulation and hydration and 4) awareness of mood, motivational, and internal state plays a role in weight-loss management strategies. While additional research is needed in a number of areas to build the body of evidence in this growing field, each of these should be seriously considered when developing an individualized weight-loss educational experience.

The relationship between biobehavioral mechanisms engaged during diet review and brain activations in response to food images was not readily attainable until the development of advanced neuroimaging techniques. The findings from this review suggest important differences in brain activation in overweight/obese individuals as compared to those who are lean. Food cues with high reward or appeal produce unique patterns of brain activation as do a number of moderating conditions. Given the power of such food images to stimulate the brain and activate differing cognitive strategies, the use of food images as an intervention tool should be given strong consideration. However, replication of the fMRI findings is needed and should include both whole-brain and region of interest analyses. Standardization of nutrition variables is needed for direct comparisons across studies. The capacity to develop personalized approaches to obesity prevention and treatment using innovative technologies should be a priority for nursing research and education. Integrating the use of neuroscience technologies in conjunction with behavioral, environmental and contextual social systems holds significant potential for nursing research (Collins & Riley, 2016), and the clinical insights provided to nurses working in intra-professional teams will contribute immensely to patient care and obesity prevention.

Linking Evidence to Action

Nurses engaged in patient education for obesity prevention should consider:

- Personalized interventions that cultivate internal awareness for dietary adherence, self-care, exercise, hydration and mood state
- Avoid using caloric deprivation approaches to weight loss interventions
- Avoidance of skipping breakfast as a means of weight loss
- Importance of individualized obesity prevention and weight-loss education

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