

Neuroimaging of Goal-Directed Behavior in Midlife Women

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Background: Motivational interventions to improve health behaviors based on conventional cognitive and behavioral theories have been extensively studied; however, advances in neuroimaging technology make it possible to assess the neurophysiological basis of health behaviors, such as physical activity. The goals of this approach are to support new interventions to achieve optimal outcomes.

Objectives: This study used functional magnetic resonance imaging (fMRI) to assess differences in brain responses in healthy weight to obese midlife women during a goal-directed decision task.

Methods: Thirty nondiabetic, midlife (age 47–55 years) women with body mass index (BMI) ranging from 18.5 to 40 kg/m² were recruited. A descriptive, correlational design was used to assess the relationship between brain activations and weight status. Participants underwent a goal-directed behavior task in the fMRI scanner consisting of a learning and implementation phase. The task was designed to assess both goal-directed and habitual behaviors. One participant was omitted from the analysis because of excessive motion (>4 mm), and six were omitted because of fewer than 50% correct responses on the exit survey. Four participants developed claustrophobia in the scanner and were disqualified from further participation. The remaining 19 participants were included in the final analysis.

Results: Brain responses while participants learned goal-directed behavior showed a positive correlation with BMI in the dorsomedial prefrontal cortex (dmPFC) and a negative correlation with BMI in the insula. During the implementation of goal-directed behavior, brain responses in the dorsolateral prefrontal cortex (dlPFC) negatively correlated with BMI.

Discussion: These results indicate that overweight women activate regions associated with cognitive control to a greater degree than healthy weight women during goal-directed learning. The brain regions activated (dmPFC, dlPFC, insula) are associated with cognitive control and self-regulation. On the other hand, healthy weight women activate regions associated with emotion processing, planning, and self-regulation (lateral orbitofrontal cortex, anterior insula) to a greater degree than overweight women during goal-directed learning and implementation of goal-directed behavior. Overweight women activate cognitive control regions while learning associations between actions and outcomes; however, this is not the case during the implementation phase—which may make it more difficult to transform goals into action (e.g., maintain physical activity over time). Overall, these results indicate that overweight midlife women respond differently during learning and implementation of actions that lead to positive outcomes during a general test of goal-directed behavior. Future study is needed to assess the transfer of goal-directed and habitual behavior to specific aspects of energy balance to improve health outcomes.

Key Words: fMRI • health behavior • neuroimaging • neurophysiology • obesity • women's health

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Midlife women are a critical focus for lifestyle interventions. A marked increase in the prevalence of biomarkers of cardiometabolic risk was found in

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perimenopausal midlife women—independent of other factors, such as hormonal changes (Janssen, Powell, Crawford, Lasley, & Sutton-Tyrrell, 2008). Without intervention, cardiometabolic disease progresses to diabetes and doubles the risk of cardiovascular disease morbidity and mortality (Roger et al., 2011). This is also significant because the total cost and the indirect mortality cost estimates for cardiovascular disease alone are higher than for any other major diagnostic group. This trend is expected to continue over the next 20 years, as real total direct healthcare costs of cardiovascular disease are projected to triple, from \$272.5 billion to \$818.1 billion (Heidenreich et al., 2011). Furthermore, the 2012 Economic Costs of Diabetes study showed that, in the United States alone, cost estimates of diagnosed diabetes have risen to \$245 billion, including \$176 billion in direct medical costs and \$69 billion in indirect medical costs (American Diabetes Association, 2013). This

does not take into account the personal burden associated with chronic cardiometabolic conditions or the multiple comorbidities, including stroke and kidney disease. Modifying lifestyle behaviors is demanding, and many midlife women are unable to meet the lifestyle recommendations to reduce their risk without support from their healthcare providers.

Conventional cognitive and behavioral theoretical approaches based on the constructs of social cognitive theory (SCT) have been extensively studied to guide health behavior change. Specifically, motivational interventions to improve physical activity (PA) have received considerable research attention but found sizeable variability and only modest effects on outcomes (Conn et al., 2007; Conn, Hafdahl, & Mehr, 2011; Conn, Hafdahl, Moore, Nielsen, & Brown, 2009; Conn, Phillips, Ruppert, & Chase, 2012). The primary SCT constructs for health behavior change involve self-control that can be achieved through goal-directed behavior, monitoring, and rewards for goal achievement. The main cognitive resources used in SCT are skills and self-efficacy or the capability to perform the behavior (Bandura, 1977, 2004; Baranowski, Cullen, Nicklas, Thompson, & Baranowski, 2003; Bowers, 1980).

Neuroimaging of health behavior offers a complementary approach to conventional SCT to provide insight into the underlying neural mechanisms to predict and explain health behavior. This translational approach also holds promise to improve the validity of instruments developed to measure these constructs as well as to provide an organizing framework, thereby increasing the fidelity of health behavior interventions (Borrelli et al., 2005; Bosak, Pozehl, & Yates, 2012).

Dual System Framework

The dual system framework has been used to explain the neurophysiology of behavior (de Wit, Barker, Dickinson, & Cools, 2011; de Wit, Corlett, Aitken, Dickinson, & Fletcher, 2009) and guides the analytic plan of this study. Dual system frameworks are useful for understanding human judgment, decision making, and behavior, as well as the emotion processing involved in integrating affect and cognition (Cushman, 2013). The current approach includes the goal-directed and the habit-based systems in the brain. The semiautomated habit-based system is relatively more efficient than the goal-directed system—which also requires consideration of goals and outcomes (Adams, 1982; Dickinson, 1985). On the basis of the dual system, participants who are more successful with goal-directed behavior are also more successful in developing habitual behavior—such as PA concurrently over time (de Wit et al., 2009)—resulting in improved health outcomes.

Previous Neuroimaging Studies of Goal-Directed Behavior

Functional magnetic resonance imaging (fMRI) is a noninvasive, indirect measure of brain responses that can be used to examine the brain regions associated with a variety of cognitive functions, including goal-directed behavior. fMRI can

enhance our understanding of the cognitive processes involved in lifestyle interventions by providing insight into decision making that may guide the development of more effective interventions in the future. In previous studies, goal-directed behavior was associated with reward processing, as goals tend to consist of some form of reward. In the case of lifestyle interventions, these rewards included increasing PA, fitness, and losing weight. In order to reach these goals, individuals must first evaluate the potential reward, plan actions to gain the reward, and update these reward values based on feedback.

Goal-directed behavior involves brain regions associated with evaluating whether stimuli are rewarding. Cognitive control regions are associated with inhibiting a response, and self-regulation regions integrate the reward and response information to guide goal-directed behavior (Bari & Robbins, 2013). De Wit et al. (2009) tested the dual system framework and showed that engagement of the goal-directed system during learning was associated with increased activity in the ventromedial prefrontal cortex (vmPFC; de Wit et al., 2009). In a previous lifestyle intervention study, brain activations in the vmPFC and dorsolateral prefrontal cortex (dlPFC)—while participants made decisions about food—were shown to correlate with weight loss (Hare, Camerer, & Rangel, 2009; Weygandt et al., 2013). These results indicate that vmPFC activity is a probable index of goal-directed behavior.

A preliminary study focusing on food motivation showed differential fMRI activations in healthy weight participants, compared to obese participants (Martin et al., 2010). Processing motivating stimuli—such as images of food—is associated with goal-directed behaviors in that people tend to direct their long-term goals to some sort of reward, such as living a healthier lifestyle.

Few studies have used general tasks with fMRI to test goal-directed behaviors or to explain and predict lifestyle behaviors, such as PA as in the current study. A general task of goal-directed behavior has the advantage of being translated to a variety of lifestyle interventions (e.g., PA, diet, smoking, alcohol intake) to improve health outcomes. This general task was used in previous studies to describe problematic behavior. Overreliance on habit—or an imbalance between goal-directed and habitual behavior—was found to be involved in impulsivity and related conditions underlying overeating and substance abuse disorders (de Wit et al., 2012; Gillan et al., 2011).

Objectives

The current study used a goal-directed decision task to elicit goal-directed behavior and characterize the associated brain activations in nondiabetic midlife women ranging from healthy weight (body mass index [BMI] 18.5–25 kg/m²) to overweight or obese (BMI 25–40 kg/m²) with increased cardiometabolic risk. Specifically, this research study used fMRI to assess brain responses during training and implementation of goal-directed behaviors. This study has the potential to contribute to the

existing paradigm of health behavior change. The growing interest in examining brain activations in specific cognitive control and self-regulation areas has the potential to alter the dominant cognitive behavioral approaches that are used to base interventions in this field.

METHODS

Participants

This study was approved by the Human Subjects Committee, the Institutional Review Board for the University of Kansas Medical Center. All participants provided written consent to participate. Thirty nondiabetic, healthy weight (BMI 18.5–25 kg/m²) to overweight and obese (BMI 25–40 kg/m²) women, aged 47–55 years with no routine exercise program, were recruited from a patient list generated from the electronic health record of an urban academic-affiliated internal medicine clinic.

This study was limited to midlife women because coronary heart disease morbidity and mortality continue to increase in women—with a marked increase during the transition to menopause (Janssen et al., 2008; Roger et al., 2011). Consistent with the guidelines for reporting an fMRI study (Poldrack et al., 2008), the following exclusion criteria were used: Potential participants were excluded if they reported serious medical illness unsuitable for the MRI scanner based on best clinical judgment, including any neurological or psychiatric disorder, diabetes, known heart disease, high blood pressure, thyroid conditions, significant visual impairment, seizure disorder, anorexia nervosa or bulimia, currently taking psychotropic or cardiovascular medication, and any history of alcohol or other substance dependence or current abuse. Diagnoses and medications were verified in the electronic health record for all study participants prior to scheduling the fMRI scan.

Goal-Directed Decision Task by fMRI

Participants completed a 2-hour testing session consisting of self-report measures and fMRI. The decision task based on de Wit et al. (2009) tests goal-directed and habitual behavior. The task consists of three conditions: (a) cue–outcome congruent, (b) cue–outcome incongruent, and (c) cue–outcome unrelated control trials. According to de Wit et al. (2009), congruent trials can be solved by either the goal or the habit-based systems because the cues always match the outcomes, and there is only one response associated with the cues. Incongruent trials can only be solved by the habit system because the cue and outcome do not match, and participants must learn which response is associated with the cue–outcome pair. The cue–outcome unrelated control trials are easily solved by the goal system because these stimuli only have one response associated with the outcomes (Figure 1).

Participants received a demonstration of the task prior to going into the scanner. Following the demonstration, participants

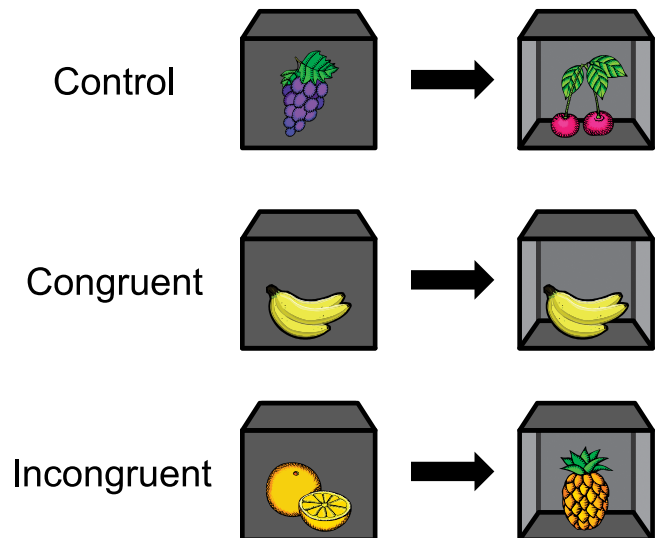


FIGURE 1. The three conditions of the decision task.

completed the MRI testing, which consisted of a high-resolution anatomical scan, followed by six fMRI runs (scanning parameters described below). The first three runs comprised the goal-directed learning phase (Figure 2a). During this phase, participants were presented with a series of cues and asked to respond correctly in order to receive rewarding outcomes (points). The cues or stimuli consisted of two sets of colored icons of 11 different commonly recognized fruits. Participants were instructed to respond to the cue by pressing the left or right response key associated with the fruit displayed on the screen. Correct responses led to the outcome associated fruit, and points were added to the participants' overall scores. Participants were not told which key was the correct response but had to learn as they went along. The quicker a correct response was made, the more points they received. Participants were instructed to earn as many points as possible during the task. Points served as an intrinsic reward to motivate participants to perform their best and did not impact participant payment for participation in the study.

The final three fMRI runs made up the goal-directed implementation phase (Figure 2b). During this phase, participants were presented with two of the previously learned cues. One of the cues was crossed out, and participants were instructed to respond to the cue that was not crossed out to receive the associated outcome by pressing the correct key. This phase of the task requires that participants have learned the associations and are able to engage the habitual learning used to solve the incongruent trials and the goal-directed learning used to solve the congruent and control trials.

A questionnaire was completed by participants at the end of the scanning session to test whether or not the correct cue–outcome associations were learned. Participants who did not learn the correct cue–outcome associations of more than 50% of the trials were excluded from the fMRI task analysis.

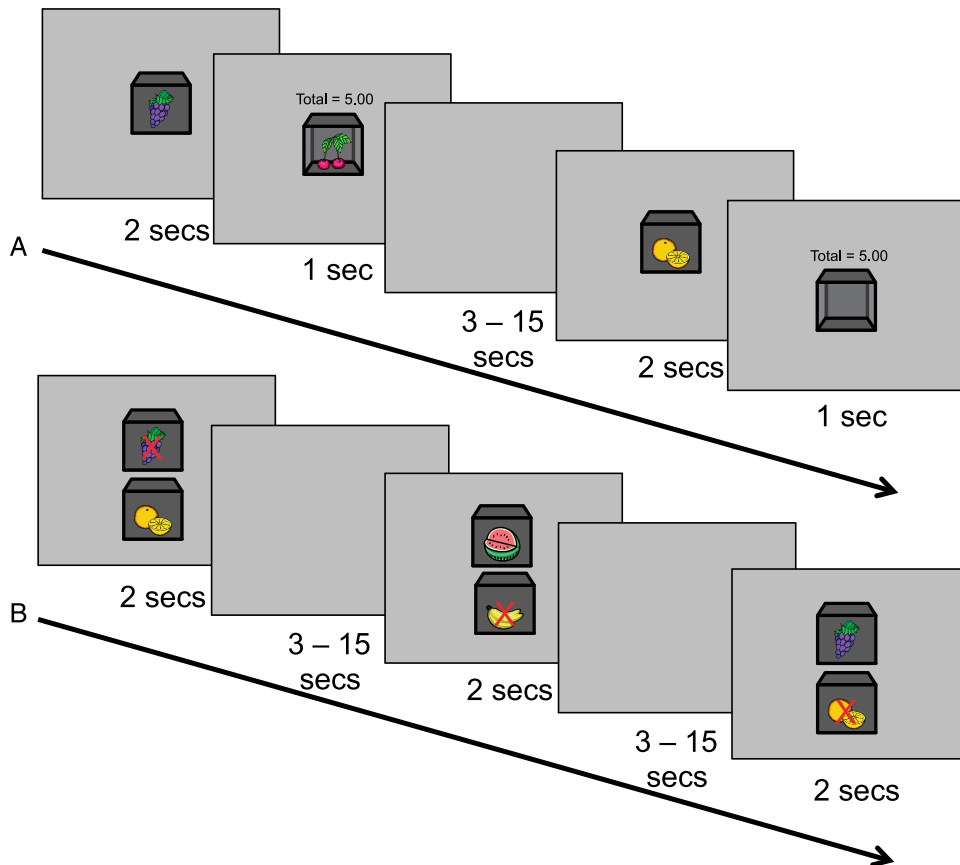


FIGURE 2. (A) Goal-directed learning phase. (B) Goal-directed implementation phase.

fMRI Data Acquisition

Scanning was performed at the University of Kansas Medical Center's Hoglund Brain Imaging Center on a 3-Tesla (indicating field strength) Siemens Skyra scanner using standard scanning parameters. First, a high-resolution anatomical scan (T1-weighted 3D MPRAGE, TR/TE = 23/2 ms, flip angle = 9°, FOV = 256 mm, matrix = 256 × 176, slice thickness = 1 mm) was acquired to align with the fMRI scans. Six functional scans, gradient echo blood oxygen level-dependent sequences of 50 contiguous slices at a 40° angle to the AC/PC line (TR/TE = 3,000/25 ms, flip angle = 90°, matrix = 80 × 80, slice thickness = 3 mm, in-plane resolution = 2.9 mm, for 80 data points) were acquired while participants completed the goal-directed learning and implementation of goal-directed behavior phases of the study. All participants were positioned so the anterior and posterior commissures were on the same horizontal line (the AC-PC plane 17–22°), which was verified by a localization scan to standardize head positioning between participants of varying weights and sizes.

Data Analysis

Data preprocessing and statistical analyses were performed using the Analysis of Functional Neuroimages software (AFNI; Medical College of Wisconsin; <http://afni.nimh.nih.gov/afni>). Preprocessing steps included motion correction, alignment, spatial smoothing,

and spatial normalization. The fMRI images were realigned to the third slice collected in each run to correct for motion for each run for every subject. Time points during which participants moved more than 0.3 mm within a temporal resolution (TR = 3,000 ms) were censored. In addition, participants would have been excluded from analysis if they had a maximum displacement of greater than 4 mm (one participant was excluded for excessive motion). The images were spatially smoothed with a 4-mm FWHM Gaussian blur. Anatomic images were aligned to functional images. Participants' anatomical scans were spatially normalized to Talairach stereotaxic space using AFNI's automated algorithm, and this transformation was applied to the participants' functional scans. Statistical contrasts were conducted using multiple regression analysis with motion parameters included as nuisance regressors.

Data analyses focused on voxelwise correlation analyses to determine the association between BMI and brain activation (i.e., percent signal change from baseline) during goal-directed learning and implementation of goal-directed behavior. The voxelwise correlation was restricted to brain regions of interest (ROIs) to estimate evoked signals and limit corrections for multiple tests to a subset of all voxels (Poldrack, 2007) in the prefrontal cortex, striatum, and insula regions. These regions have been associated with decision-making, goal-directed behaviors,

and evaluation of motivating stimuli as described above. A bilateral mask encompassing these regions was created using AFNI's Whereami program. The mask regions or a priori ROIs are shown in Figure 3. Activations were corrected for multiple comparisons within the mask based on Monte Carlo simulations using AFNI's 3dClustSim ($p_{\text{corrected}} < .05$; $p_{\text{voxelwise}} < .01$, cluster extent 36 voxels).

Goal-directed learning was assessed by comparing congruent and control conditions to the incongruent condition in the first three fMRI runs. Implementation of goal-directed learning was assessed by comparing congruent and control conditions to the incongruent condition during the final three fMRI runs. Activation in each condition compared to baseline (i.e., fixation periods) was also examined during the learning and implementation phases.

Four participants did not complete the fMRI scanning session because of claustrophobia and/or discomfort during scanning, resulting in disqualification from further participation. Six participants were excluded from the fMRI analysis because they learned 50% or fewer correct associations between cues and outcomes. Two participants did not complete the exit interview but performed at greater than 50% on the training phase and, therefore, were included in the analysis. In addition, one subject was excluded from fMRI analysis because of excessive motion throughout the fMRI study. The remaining 19 participants were included in the final analysis.

RESULTS

Demographic Characteristics

The demographic information for this sample is provided in Table 1. These women were, on average, middle aged (51.3 years; 47–55 years), overweight (BMI 25.7 kg/m²; 20–37.1 kg/m²), Caucasian (89.5%), and had a college degree (84.2%). There were no differences in demographic characteristics of those participants omitted from the final analysis.

Goal-Directed Training Phase

During the training phase of the decision task, BMI positively correlated with activation (e.g., percent signal during congruent-incongruent trials) in the dorsal medial prefrontal cortex (dmPFC; Figure 4a). Furthermore, BMI negatively correlated with activation

TABLE 1. Demographic Characteristics

Characteristic	<i>M</i>	Range
Age (years)	51.3	47–55
BMI (kg/m ²)	25.7	20.0–37.1
	<i>n</i>	%
Race		
Caucasian	17	89.5
African American	2	10.5
Highest educational level		
High school graduate	1	5.3
Some college	2	10.5
Associate degree	2	10.5
Bachelor's degree	8	42.1
Master's degree	5	26.3
Doctorate	1	5.3
Employment		
Business	10	52.6
Education/academia	4	21.0
Healthcare	3	15.7
Other	2	10.5

Note. *N* = 19. BMI = body mass index.

(e.g., percent signal change during control-incongruent trials) in the anterior insula (Figure 4b). In addition, we examined brain activation during control, congruent, and incongruent trials compared to baseline to examine brain activation associated specifically with goal-directed behavior, goal/habit-directed behavior, and habit-directed behavior, respectively. During goal-directed behavior (i.e., control-baseline), BMI was negatively correlated with activation in the lateral orbitofrontal cortex. There were no significant correlations for congruent or incongruent compared to baseline analyses. A complete list of activations during goal-directed learning is provided in Table 2.

Goal Implementation Phase

During the goal implementation phase of the decision task, there were no significant correlations found in the congruent-incongruent or control-incongruent contrasts. However, BMI negatively correlated with brain activation in the regions of the dlPFC (i.e., superior frontal gyrus) for the congruent-baseline and control-baseline analyses (Figure 5). In addition, BMI

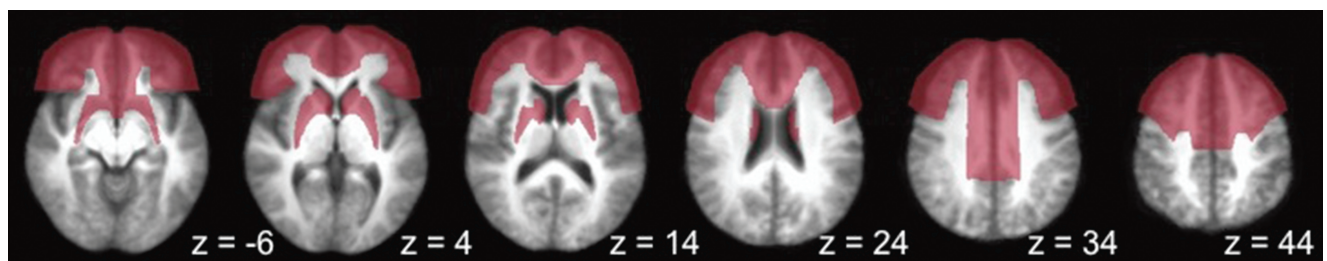


FIGURE 3. Mask of regions of interest (ROIs) applied to brain images to focus analysis of activations in these regions.

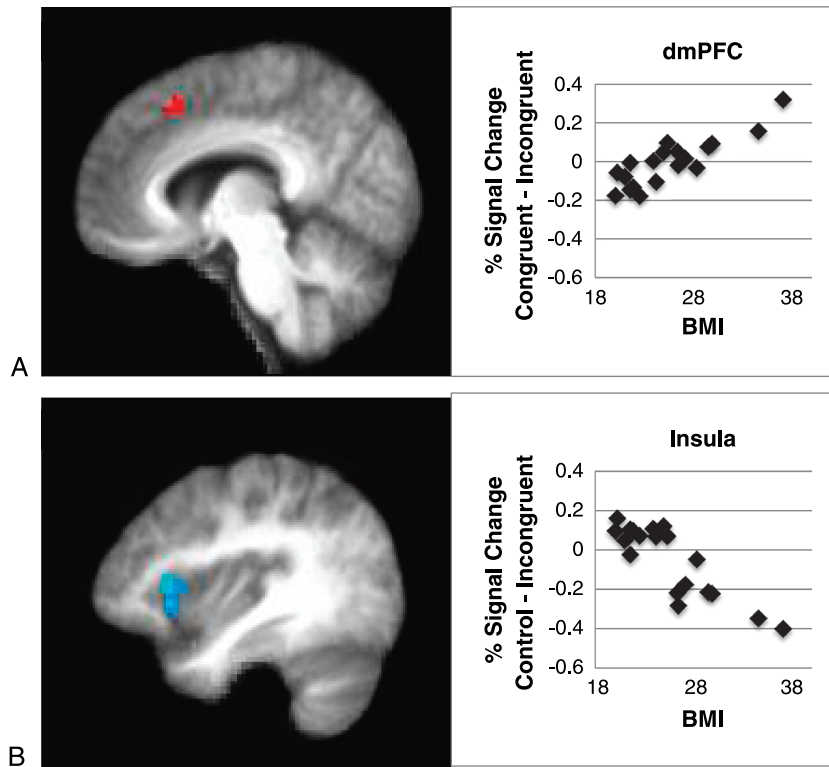


FIGURE 4. Correlations with BMI and brain activations in the dorsomedial prefrontal cortex (dmPFC) and insula (congruent–incongruent and control–incongruent analyses, respectively).

negatively correlated with activation in the middle frontal gyrus and the medial prefrontal cortex. A complete list of activations during goal-directed learning is provided in Table 3.

Behavioral Data

Overall, participants learned the task (mean accuracy 80%; *SD* = 9.6) and were able to accurately implement goal-directed learning (mean accuracy 61.1%; *SD* = 8.5). Accuracy was better during the training phase than the goal implementation phase ($t(18) = 10.2; p < .001$). Accuracy on the training task was correlated with BMI ($\rho = .483; p < .05$). However, BMI was not correlated with the ability to implement goal-directed behavior ($\rho = .073; p = .76$). During training, the behavioral and neuroimaging results were consistent in that BMI positively correlated with accuracy and with dmPFC activation. In addition, BMI and age were not correlated ($r = -.104; p = .69$). This

lack of association indicates that it is unlikely that the observed effects are related to age, rather than BMI.

DISCUSSION

This study characterized goal-directed brain responses in healthy weight to overweight women with no routine exercise program. During goal-directed learning, overweight women had greater activations in the dmPFC—a region involved in cognitive control—compared to healthy weight women. On the other hand, healthy weight women had greater activations in the anterior insula—a region involved in emotion processing—than overweight women. During the implementation of goal-directed behavior, healthy weight women had greater activations in the dlPFC—a region associated with self-regulation and planning. The findings of this study provide the basis for further investigation of functional and structural brain differences and the effects on modifiable lifestyle behaviors, such as PA, that may

TABLE 2. Learning Goal-Directed Behavior: Brain Regions Showing Correlations Between Brain Activation and BMI

Contrast	Region	Talairach coordinates			Cluster size	<i>r</i>
		<i>x</i>	<i>y</i>	<i>z</i>		
Congruent > incongruent	Dorsomedial prefrontal cortex	4	16	44	36	.73
Control > incongruent	Insula	-39	19	1	67	-.76
Control > baseline	Orbitofrontal cortex	24	46	-6	37	-.80

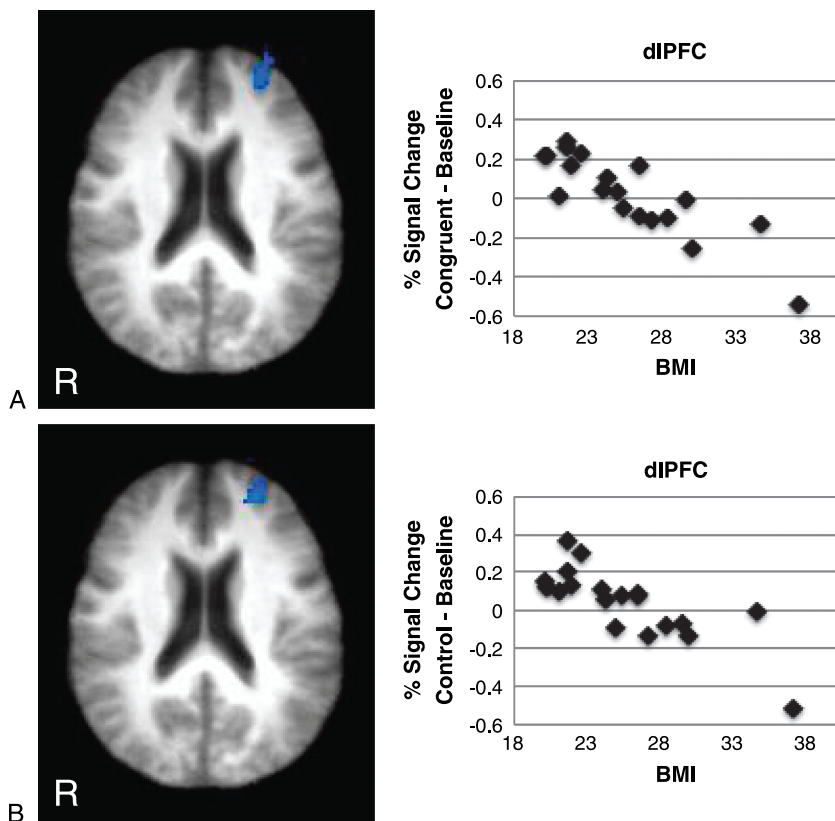


FIGURE 5. Negative correlations with BMI and brain activations in the dorsolateral prefrontal cortex (dIPFC) (congruent–baseline and control–baseline analyses).

be applied to other modifiable behaviors (e.g., diet, smoking, alcohol intake).

Previous studies found that participants more successful on the decision task had greater vmPFC activation during goal-directed decision making (de Wit et al., 2009). The current study did not show correlations between BMI and activation in the vmPFC. This could be because of differences in the analysis approach, such as the current study specifically examined the associations between BMI and brain responses during goal-directed learning and implementation of goal-directed behaviors in mid-life women. Furthermore, previous studies using this task typically included young adults as opposed to midlife women, which could account for some differences in behaviors. Additional studies are needed to understand the differences in vmPFC activation between the current study and previous research.

This study illustrated that the dIPFC was involved in the learning of goal-directed behavior to a greater degree in individuals with higher BMIs. The current study extends previous studies of goal-directed behavior, which showed increased activation in the dIPFC when dieters made choices about foods (Hare et al., 2009; Weygandt et al., 2013). There has been limited investigation of the transfer of cognitive skills for goal-directed behavior to outcomes in clinical populations. However, these findings have clinical importance for predicting future outcomes—such as fitness or weight loss—and identifying those individuals who will benefit most from intensive interventions.

In addition, as indicated by Bari and Robbins (2013), the insula and the orbitofrontal cortex are also involved in goal-directed behavior by integrating emotion processing information with the evaluation of rewarding and inhibiting responses

TABLE 3. Implementation of Goal-Directed Behavior: Brain Regions Showing Correlations Between Brain Activation and BMI

Contrast of Conditions	Region	Talairach coordinates			Cluster size	<i>r</i>
		<i>x</i>	<i>y</i>	<i>z</i>		
Congruent > baseline	Superior frontal gyrus	-24	64	16	140	-.83
	Middle frontal gyrus	49	16	34	40	-.79
Control > baseline	Superior frontal gyrus	-21	46	24	50	-.79
	Medial prefrontal cortex	4	-11	56	57	-.81

to rewarding stimuli. Processing of emotion has received minimal attention in the research literature relative to this goal-directed decision task. The ability to translate goals into action and, thus, to improve adherence and maintenance of health behaviors are associated with emotion processing. The development of interventions to support cognitive control and emotion self-regulation involved in achieving health goals holds promise for improving outcomes in overweight midlife women.

Limitations

The decision task was reproduced in the original form using common fruits; however, a task more directly related to energy balance needs to be tested in future study. The complexity of the decision task is acknowledged as a limitation in this study. Exit surveys tested participants' understanding of the decision task by asking participants to identify the correct answers to the fruit pairings. Scores of less than 50% correct indicated that selecting the correct responses on the decision task was no greater than chance. Only the participants identifying at least half of the correct answers on the exit survey were included in the final analysis. It is acknowledged that cognitive abilities gradually decline with age and consideration must be given to decision tasks that are appropriate for individuals in various age groups, such as middle age. In addition, recruitment was limited to healthy weight, overweight, and mildly obese individuals, limiting inference of the findings. It is acknowledged that the severely (morbidly) obese groups may differ from the healthy weight and overweight groups in some ways, and future study is needed to identify these differences.

Conclusions

This study used a translational approach combining nursing science, neurophysiology, and fMRI technology to characterize the cognitive control areas underlying goal-directed behavior. The science of health behavior change will benefit from integration of diverse sources of information to complement the widely accepted theoretical models in this field. The negative relationship between BMI and the training phase of goal-directed behavior identified in this study points to the need to focus intervention strategies on transforming goals into action with overweight and obese individuals. This may be achieved by strategies to enhance cognitive control and emotion self-regulation to improve adherence and long-term maintenance of health behaviors. These findings offer a new perspective on SCT and the construct of self-efficacy that has guided health behavior interventions over decades. The ultimate goal of this research is the translation of more effective health behavior interventions to clinical practice to address some of the greatest health challenges today.

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