Neuroimaging of Goal-directed Behavior in Midlife Women

Abstract

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 neurological basis of health behaviors, such as physical activity (PA). The goals of this approach are to develop 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 non-diabetic, midlife (age 47-55 years) women with BMIs ranging from 18.5 to 40 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.

Results: Brain responses while participants learned goal-directed behavior showed a positive correlation with BMI in the dorsal medial 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 (dLPC) negatively correlated with BMI. These brain regions (dmPFC, dLPC, insula) are associated with cognitive control and self-regulation.

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. On the other hand, healthy weight women activate regions associated with emotion processing, planning, and self-regulation 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 PA 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 test goal-directed behavior related to specific aspects of energy balance to improve health outcomes.
1 **Key Words:** health behavior; neurophysiology; neuroimaging; fMRI
Background

Midlife women are a critical focus for lifestyle interventions. A marked increase in the prevalence of biomarkers of cardiometabolic risk was found in 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 (CVD) 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 CVD are projected to triple, from $272.5 billion to $818.1 billion (Heidenreich et al., 2011). Further, the 2012 Economic Costs of Diabetes in a study in the United States (US) alone, showed cost estimates of diagnosed diabetes have risen to $245 billion, including $176 billion in direct medical costs and $69 billion indirect medical costs (Yang, 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, Hafdahl, & Mehr, 2011; Conn et al., 2007; Conn, Hafdahl, Moore, Nielsen, & Brown, 2009; Conn, Phillips, Ruppar, & Chase, 2012). The primary SCT constructs for health behavior change involve self-control that can be achieved by 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).

**Framework Guiding Analysis of this Study**

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. This approach involves the goal-directed and the habit-based systems in the brain. The semi-automated habit-based system is relatively more efficient than the goal-directed system, which also requires consideration of goals and outcomes (Adams, 1982; Dickinson, 1985). Based on the Dual System, participants more successful with goal-directed behavior are also more successful 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., tested the Dual System framework and demonstrated that engagement of the goal-directed system during learning was associated with increased activity in the vmPFC (de Wit et al., 2009). In a previous lifestyle intervention study, brain activations in the vmPFC and dlPFC while participants made decisions about food were shown to correlate with weight loss (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 demonstrated differential fMRI activations in healthy weight (HW), 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., physical activity, diet, smoking, alcohol intake) to improve health outcomes.

Objectives of Current Study

The current study used a goal-directed decision task to elicit goal-directed behavior, and characterize the associated brain activations in non-diabetic midlife women ranging from healthy
weight (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, and to alter the dominant cognitive behavioral approaches that are used to base interventions in this field.

**Method**

**Participants**

Thirty non-diabetic, healthy weight (BMI 18.5-25 kg/m²) to overweight/obese (BMI 25-40 kg/m²) females, age 47-55 years were recruited. This study was limited to females because coronary heart disease morbidity and mortality continue to increase in females, 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 magnetic resonance imaging scanner based on best clinical judgment, including any neurologic 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.

**Goal-directed Decision Task by fMRI**

Participants completed a two-hour testing session consisting of self-report measures and fMRI. The decision task based on the work of de Wit et al., (de Wit et al., 2009) tests goal-directed and habitual behavior. The task consists of three conditions. The first is cue-outcome congruent, the second is cue-outcome incongruent, and the third is cue-outcome unrelated control trials. According to de Wit et al. (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 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 score. 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.

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 subjects 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.

**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 23/2ms, flip angle 9°, FOV = 256mm, matrix = 256 x 176, slice thickness = 1 mm) was acquired to align with the fMRI scans. Anatomical and functional data were warped to standard stereotaxic space. Six functional scans, gradient echo blood oxygen level dependent (BOLD) 50 contiguous slices at a 40° angle to the AC/PC line, (TR/TE = 3000/25ms, flip angle = 90°, matrix = 80 x 80, slice thickness = 3 mms, in-plane resolution = 2.9 mms, 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 in Talairach space 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 subjects of varying weights and sizes.

**Data Analysis**

Data pre-processing and statistical analyses were performed using the Analysis of Functional Neuroimages software (AFNI; Medical College of Wisconsin). Pre-processing steps included motion correction, alignment and spatial normalization. Anatomical images were
aligned to functional images. Spatial normalization was performed using AFNI’s automated algorithm. A volume pixel or voxel is the smallest distinguishable box-shaped part of a three-dimensional brain image. 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 mask encompassing these regions was created using AFNI’s Whereami program. 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 due to claustrophobia and/or discomfort during scanning. Six participants were excluded from the fMRI analysis because they learned 50% or fewer correct associations between cues and outcomes. In addition, one subject was excluded from fMRI analysis due to excessive motion throughout the fMRI study. The remaining 19 subjects were included in the final analysis.

**Results**

**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 dmPFC (Figure 3a). Further, BMI negatively correlated with activation (e.g. percent signal change during Control – Incongruent trials) in the anterior insula (Figure 3b). 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 1.

**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 4). In addition, BMI negative correlated with activation in the middle frontal gyrus and the medial prefrontal cortex (MPFC). A complete list of activations during goal-directed learning is provided in Table 2.

**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 changes and the effects on modifiable lifestyle behaviors, such as PA, that may be applied to other modifiable lifestyle behaviors (e.g., diet, smoking, and alcohol intake).

Previous studies found that participants more successful on the decision task had greater ventromedial prefrontal cortex (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 due to 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 midlife women. Further, 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. The current study extends previous studies of goal-directed behavior which demonstrated increased activation in dlPFC when dieters made choices about foods (Hare, Camerer, & Rangel, 2009; Weygandt et al., 2013). This illustrated that the dlPFC was involved in the learning of goal-directed behavior to a greater degree in individuals with higher BMIs. In addition, the insula and the frontal cortex (OFC) are also involved in goal-directed behavior by integrating emotion processing information with the evaluation of rewarding and inhibiting responses to rewarding stimuli as indicated by Bari and Robbins (Bari & Robbins, 2013).

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.

Another consideration includes the potential intervening variables. While an exhaustive list of these variables is not practical to incorporate in a feasibility study, standardization was not instituted for the time of day the scans were conducted in this study. Menopausal status or phase of the menstrual cycle of the women in this study was not assessed, but involves neurohormonal mechanisms that may need to be accounted for in future fMRI studies. In addition, participants were included if they had no routine exercise program; however, their level of physical activity was not objectively assessed. Objective measurement of physical activity levels will be a consideration in future study. Additional research is needed to characterize not only goal-directed PA, but the association of the constructs of SCT and brain responses underlying learning and implementation of PA, as well as other health behaviors.

This study used a translational approach combining nursing science, neuropsychology and fMRI technology to characterize the neural processes underlying goal-directed behavior. The science of health behavior change will benefit from interprofessional collaboration to contribute to the existing empirical evidence for the commonly used theoretical models, such as SCT and related constructs. The negative relationship between BMI and the implementation phase of goal-directed behavior identified in this study points to the need to focus intervention strategies on transforming PA goals into action with overweight and obese individuals. These findings offer a new perspective on SCT and the construct of self-efficacy that has guided health
behavior interventions for decades. The ultimate goal of this research is the translation of an effective health behavior intervention to clinical practice.
Figure 1: The Three Conditions of the Decision Task

Control

Congruent

Incongruent
Figure 2: a) Goal-directed Learning Phase; b) Goal-directed Implementation Phase
Figure 3: Correlations with BMI and brain activations in the dmPFC and Insula (Congruent-Incongruent and Control-Incongruent analyses, respectively)
Figure 4: Negative correlations with BMI and brain activations in the dlPFC (Congruent-Baseline and Control-Baseline analyses)
Table 1: Learning of goal-directed behavior: Brain regions showing correlations between brain activation and BMI

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<th>Contrast</th>
<th>Region</th>
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<th>y</th>
<th>z</th>
<th>Cluster Size</th>
<th>r</th>
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<td>Congruent &gt; Incongruent</td>
<td>Dorsal medial prefrontal cortex (dmPFC)</td>
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<td>16</td>
<td>44</td>
<td>36</td>
<td>.73</td>
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<tr>
<td>Control &gt; Incongruent</td>
<td>Insula</td>
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<td>19</td>
<td>1</td>
<td>67</td>
<td>-.76</td>
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<td>Control &gt; Baseline</td>
<td>Orbitofrontal cortex</td>
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<td>46</td>
<td>-6</td>
<td>37</td>
<td>-.80</td>
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Table 2: Implementation of goal-directed behavior: Brain regions showing correlations between brain activation and BMI

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<td>Superior frontal gyrus</td>
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References


