*Look AHEAD Study Intervention.*

Detailed descriptions of the Look AHEAD study interventions have been published previously(18, 19). ILI participants were assigned a daily calorie goal (1,200–1,800 based on initial weight), with <30% of total calories from fat (<10% from saturated fat) and a minimum of 15% of total calories from protein, and were instructed to weigh themselves regularly. The physical activity goal was ≥175 min/week of moderate intensity activity (e.g., brisk walking). ILI participants were seen weekly for 6 months and three times/month for the next 6 months via group and/or individual meetings with trained interventionists. During years 2–4, participants were seen individually at least once a month, contacted each month by phone/e-mail, and were offered optional group classes. Following year 4, ILI participants were encouraged to continue individual monthly sessions, and annual campaigns were used to promote adherence to goals(19). During this time, all DSE participants were invited to attend three group sessions each year, which featured standardized protocols focused on diet, physical activity, and social support but did not include any behavioral strategies(18). Weight (kg) and height (cm) were measured using calibrated digital scales and wall-mounted stadiometers, respectively, and BMI was calculated at baseline and subsequent annual visits. “Current” weight and BMI were determined using each participant’s 10-year annual visit data if available, or the most recent annual visit (e.g., year 9 or 8). The intervention phase of Look AHEAD ended September 2012. Look AHEAD Brain MRI participants were followed in this intervention phase for an average of 9.8+0.7 years (ILI) and 9.9+0.7 years (DSE ) (p=0.13). The average time Look AHEAD Brain participants spent in the post-intervention phase prior to their MRI was 0.6+0.7 years for ILI and 0.5+0.8 years for DSE (p=0.19)(17).

*MRI Parameters:*

Details of the structural MRI parameters have been published previously(17). All MRI scans were conducted on Siemens 3-Tesla scanners utilizing the same software platform and 32- channel head coils. Scanning and assessment procedures were standardized across the three sites. Prior to scanning participants research staff, coordinators, and MRI technicians attended a centralized training meeting in Philadelphia to learn the protocol and practice the procedures and paradigms. Additionally, MRI physicists and technicians visited all three sites to provide on-site training and conduct test scans of MRI phantoms as well as a human volunteer. Quality assurance protocols of the Functional Biomedical Informatics Research Network (FBIRN) and Alzheimer’s Disease Neuroimaging Initiative (ADNI) using MRI phantoms to regularly assess scanner performance in mulit-site studies were employed before and throughout this study in order to assess and ensure scanner performance across the three sites. The imaging protocol consisted of sagittal 3D fluid-attenuated inversion recovery imaging, T2- and T1-weighted sequences, and 3 functional blood oxygen level dependent (BOLD) imaging runs. One of these functional runs was food cue-reactivity (described within the main document).

*Data Analytic Plan*

The Reading Center (Philadelphia) assessed all anatomical scans. Preprocessing and data analysis of functional scans were performed using Statistical Parametric Mapping Software (SPM8; Wellcome Trust Centre for Neuroimaging, University College London, UK; <http://www.fil.ion.ucl.ac.uk/spm/>) and a suite of processing scripts developed by researchers at Dartmouth College (available at <http://github.com/ddwagner/SPM8w>). This processing was centralized at the Providence site. Images were motion corrected (using b-spline interpolation), and regressors for motion artifacts larger than 1.5mm were created. Functional data were then normalized based on Montreal Neurologic Institute (MNI) stereotaxic space using a 12-parameter affine transformation and a nonlinear transformation using cosine basis functions. Images were spatially smoothed with a 6mm full-width-half-maximum (FWHM) isotropic Gaussian kernel.

The current work focuses on group differences in response to high calorie foods compared to non-foods. However, the food cue-reactivity paradigm allows for additional relevant contrasts. Responses to high calorie foods > low calorie foods and responses to all food relative to baseline were investigated. Statistical maps comparing ILI vs. DSE in response to high calorie > low calorie foods contained no regions demonstrating significant group differences at the FDR-corrected level of 0.05. In the contrast of all food > fixation baseline, a region of the right medial frontal gyrus (BA 8; 2, 55, 43) exhibited a significant group difference such that ILI had greater activity in this region than DSE (FDR-corrected cluster q value = 0.05).