Promise and Perils of Human Neuroimaging to Understand the Weight-Reduced State

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The purpose of this review is to provide an overview of neuroimaging tools that might prove useful to researchers studying the central nervous system (CNS) contribution to the weight-reduced state in humans. It focuses on three broad categories: functional, connectivity, and structural neuroimaging, providing on overview of each approach, including its broad purpose, what it measures, the study objectives that researchers might utilize the methodology for, and the common techniques. Examples from the literature in which the techniques were applied in studies of obesity and/or weight loss are used to illustrate both the promise and the perils of these approaches. Given the multitude of paradigms available, in functional magnetic resonance imaging (fMRI) in particular, the review cannot be comprehensive, but attempts to provide a condensed tutorial on commonly used and promising new applications in our field. Other methodologies, including those utilizing radioligand-binding and positron emission tomography (PET) to assess brain neurochemistry or magnetic resonance spectroscopy to measure brain metabolites are reviewed elsewhere (1, 2).

Functional Neuroimaging

Purpose and use. Functional neuroimaging strategies (Table 1) measure neural activity in response to the stimulus of interest (the "task"). The types of study objectives that might be met through this technique include mapping a particular brain function to the anatomic locations in the brain that mediate the function or behavior. Functional neuroimaging techniques are also used to 1) phenotype group differences in CNS response to a task or 2) measure the CNS response to a physiologic stimulus. Most techniques use indirect measures of neural activity; blood oxygen-level dependent (BOLD) imaging measures changes in blood oxygenation that follow a burst of neural activity, arterial spin labeling (ASL) measures cerebral perfusion, 18F-fluorodeoxyglucose (FDG) PET measures glucose metabolism, and ^{15}O-labelled water [^{15}O-H_2O] measures regional cerebral blood flow. Electroencephalography (EEG) and magnetoencephalography (MEG), on the other hand, directly measure electrical signals in the brain or detect the magnetic fields they produce, respectively.

Functional neuroimaging is predicated upon assessing brain response to a task. Food or taste cues are frequently utilized in the literature, but physiologic manipulation (i.e., consuming food,

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pharmacologic manipulation) alone or in combination with a task are other common methods. A number of standard behavioral tasks assessing general traits or cognitive abilities (e.g., impulsivity) have also been adapted to be food-specific. In actuality, all indirect measures of neural activity *compare* the brain response to two different tasks, because these measures are not quantitative. For example, early fMRI mapping studies compared BOLD response to images of food vs. object (tools) cues and found hunger-dependent activation by the food cues in amygdala, parahippocampal regions, and the anterior fusiform gyrus (n=17 subjects) (3). The same comparative principle is applied, albeit with a slower temporal resolution, by using PET or ASL. A subject's response is compared between a control vs. a test condition or a basal measure of neuronal activity vs. a post-intervention acquisition (for example, before and after ingesting a satiating meal in (4)). For all techniques, maps are derived which define the anatomic locations of areas within the brain that differed significantly in the indirect measure chosen, (i.e., BOLD response, regional cerebral blood flow, etc.). The term "activation" is used to distinguish differences in BOLD response as an indirect marker of underlying neural activity. "Clusters" of activation represent brain areas in which differences in the indirect measure of neural activity surpass a designated level of statistical significance (usually combined with an extent or cluster size criterion), corrected for the multiple comparisons conducted across all the voxels in which statistical testing was performed.

The extent of the brain over which inferential testing is applied is a critical issue in design and interpretation. Region of interest approaches restrict hypothesis-testing to selected brain areas which, to avoid bias, should be designated prior to study completion. While providing enhanced power to detect pre-hypothesized effects, region of interest approaches supply no insight into brain response outside the designated anatomic area. In contrast, whole-brain analyses are conducted across all brain voxels and ideally represent an unbiased approach to discover the neural substrates of a particular task. Due to the multiple comparisons involved in testing across all the voxels of the brain, whole brain analyses require larger sample sizes to have sufficient statistical power and are at risk of failing to detect physiologically-significant responses when power is insufficient.

Concerns related to small sample size and poor reproducibility for neuroimaging studies have been raised (5). Performing multiple comparisons across the whole brain or across many regions of the brain in a relatively small sample size increases the possibility of false-positive results. Moreover, flexibility and variability in the multi-step image processing and statistical analytic methods used in fMRI can influence study results (6). When combined with a lack of transparency in the image processing methods applied, such factors can significantly hamper the reproducibility of neuroimaging studies (5). Recently, authors and institutions have proposed steps to ameliorate these concerns (7, 8).

Recommendations include pre-registration and complete reporting of study methods and analytic strategies, open sharing of unthresholded data, validation and publication of all custom software code, replication studies, and larger sample sizes (5, 8).

Application of functional neuroimaging techniques. Initial studies in the field focused on identifying the neural correlates of response to food cues. It became apparent early on that fMRI readily distinguished regions with differential response between visual images of food vs. objects (3, 9) and that, amongst all foods, energy density also elicits divergent responses (9). To illustrate, using a region of interest approach among a restricted set of brain areas, we found that brain reward centers including the midbrain ventral tegmental area and areas of the striatum—such as the nucleus accumbens—had clusters of greater activation by energy dense foods than objects as did the hypothalamus, insular cortex (involved in taste processing), and visual cortex (10). In comparison, only the visual cortex region demonstrated activation by low-calorie food images as compared to objects and not regions involved in reward processing or appetite regulation. The central point for studies of the neurophysiology of weight loss is that the choice of task, including what images are presented, is a critical determinant of the brain areas that are engaged or activated in functional neuroimaging. Systematic reviews and meta-analyses are available for guidance on accumulated evidence as to the anatomic substrates responsive to particular tasks (11, 12, 13).

Functional neuroimaging studies were instrumental in documenting how brain response to food cues is altered by physiologic manipulations. To study appetitive responses, Goldstone, et al. imaged 20 subjects without obesity using a protocol measuring response to visual food cues in both the fasted and fed states (14). By focusing on particular regions of interest, they revealed that activation by high-calorie food images is enhanced by fasting within the amygdala, ventral striatum, insula, medial orbitofrontal cortex (OFC) and lateral OFC, whereas response to low-calorie food images may even be suppressed during fasting. Differences in activation between high- and low-calorie food cues were markedly reduced when subjects were in the fed condition, for which subjects consumed a filling breakfast of their own choice that, on average, consisted of 47% of their estimated daily caloric needs. The authors concluded that fasting biases attentional and reward processes toward highly energy dense food in our environment. Moreover, in a study of 23 normal weight adults (15), the degree of activation by high- vs. low-calorie foods in areas including the amygdala—which plays a role in cue-related eating (16)—and medial OFC positively correlated with subjective ratings of hunger. Regional activation by high-calorie food cues is enhanced by hunger (3) or ghrelin infusion (17) and suppressed by leptin (18, 19), glucagon-like peptide-1 plus peptide YY (20), liraglutide (21), intranasal insulin (22), and food intake (23, 24, 25). Such findings suggest that *activation by high-calorie food cues in key*

appetitive regulation regions is an objective marker of appetitive drive in the brain. In fact, the degree of activation within selected corticolimbic and insular areas positively predicts choice of higher fat foods (15) and caloric intake (24) at an *ad libitum* buffet meal immediately following fMRI acquisition.

Functional neuroimaging has also been applied to study weight loss (12). A recent study of 37 children with obesity undergoing a 6-month family-based behavioral weight loss program found worse treatment outcomes among children who, at baseline, failed to suppress activation by high-calorie food cues in key appetite-regulating brain regions after a meal.(26) As an example of a group phenotyping approach, individuals who formerly had obesity were compared to women with obesity and women of normal weight by using PET. Le et al., found an enhanced response in the dorsolateral prefrontal cortex to a meal among women (n=8) who formerly had obesity as compared to women with obesity (n=9) (27). Because of its role in cognitive control, the authors interpreted the findings as indicative of enhanced inhibitory control following a meal. Similar findings were found in studies of successful weight loss maintainers using PET (28) and BOLD fMRI (29).

Using a within-subjects approach, Holsen, et al., studied 18 patients before and 12 months after weight loss by sleeve gastrectomy (30). Regions regulating motivation and reward, such as the nucleus accumbens, amygdala, and striatum, were demonstrated by fMRI after surgery to have reduced activation during a task in which subjects focused on their desire for highly palatable foods, whereas the dorsolateral prefrontal cortex showed increased activation. Among 14 women imaged pre- and one-month post-Roux-en-Y gastric bypass (RYGB), reductions in desire to eat high-calorie foods were correlated with reductions in activation by high-calorie food cues in the dorsal striatum and dorsolateral prefrontal cortex (31). The latter finding was hypothesized to be related to a decline in need to evoke cognitive control as the physiologic urge for highly energetic foods dissipated (31). Other studies of bariatric surgery patients support that weight loss via bariatric surgery broadly alters food cue responsiveness in neural circuits governing attention, motivation, and reward processing (32, 33, 34, 35, 36); inhibitory control (36); and interoceptive awareness (32, 34) and gustatory processing (34). Studies have noted more robust changes in bariatric surgery patients than groups undergoing weight loss via gastric banding (32) or weight stable controls (33). Using fMRI with food cues, Rosenbaum et al., studied 6 participants with obesity before and after a 10% reduction in body weight accomplished by caloric restriction. At 10% weight reduction, they further evaluated participants with or without replacement of leptin. While the small sample size and low statistical threshold utilized limit conclusions about the neural substrates involved, their findings nonetheless provide initial support for the concept that neural responses to food cues are altered in the weight-reduced state consistent with a “long-range pattern” across distributed, functionally-related brain regions and that such changes might derive from a

relative leptin deficiency (37). Cumulatively, this literature suggests that effective bariatric surgery procedures fundamentally shift brain processing of appetite and satiety in a manner that reduces the appeal of high-calorie foods, combats the neurophysiology driving weight regain in the weight-reduced state when weight loss is evoked by energy deficit alone, and, ultimately, helps with successful weight maintenance.

The neural correlates of behavioral weight loss via calorie restriction were tested using a whole-brain approach by Neselier, et al. (38). Among 20 participants, there was a direct correlation between the amount of weight loss achieved and the degree of increase in activation by appetizing food cues (vs. scenery) from baseline to one month of weight loss in regions including the dorsolateral prefrontal cortex, inferior frontal gyrus, and dorsal anterior cingulate cortex, among others. Moreover, increasing activation to food cues (vs. scenery) within cognitive control regions predicted continued weight loss between one and three months. Among those with available data (n=14), the superior frontal gyrus, in particular, emerged as a region in which participants who did not sustain increased activation to food cues regained weight at 24 months of follow-up. These studies illustrate the importance of assessing inhibitory control and self-regulatory capacity in studies of the weight-reduced state. These cognitive processes influence the ability to sustain weight-reductions over time despite compensatory responses by adiposity and gut hormones (38) that promote weight regain.

Another important example of neural predictors of weight maintenance was a fMRI study by Murdaugh, et al. conducted in 25 adults with obesity imaged both before and after 12 weeks of weight loss (39). The degree of activation by high-calorie food images within regions of interest in the ventral tegmental area/substantia nigra (which houses key dopaminergic neurons driving motivated behavior) and putamen was predictive of the degree of weight regain over a 9-month period of weight maintenance, as was activation within the fusiform cortex as identified on whole-brain analyses. Other regions potentially influencing weight maintenance have been identified including the operculum, middle and inferior frontal gyrus (40), but additional data derived from larger sample sizes are required for definitive evaluation.

Promise and perils. Functional neuroimaging can be a potent tool with which to study CNS function *in vivo*. In terms of its promise for understanding the weight-reduced state, the response to high-calorie food cues specifically appears to offer investigators an objective measure of the appetitive state, which can be an important adjunct to our admittedly poorly reliable subjective appetite and self-reported food intake measures. Functional neuroimaging techniques simultaneously assess cognitive and appetitive contributors, both of which appear to be important to weight loss and maintenance. FMRI

is now more widely accessible, and can be implemented in multi-site studies (41). Finally, a body of literature has emerged from studies of both bariatric surgery and behavioral weight loss, albeit much of it in small samples, that supports the relevance of these measures to understanding weight loss and their potential for revealing CNS factors driving weight regain vs. maintenance.

Sample size, reproducibility, and transparency are critical issues which researchers need to consider in their study designs. As in all functional neuroimaging, the choice of task influences which areas of the brain are most responsive. Furthermore, all studies related to appetite should include careful management and assessment of the state of satiety of participants (11, 15), among other measures required to reduce confounding and variability in brain response to food cues (12, 42, 43). Standard techniques may lack the anatomic resolution to target small structures particularly in subcortical regions or the nuclei or subnuclei of critical regions such as the amygdala or hypothalamus. High resolution fMRI may be needed to achieve resolution on the order of 1 mm^3. Finally, functional neuroimaging results can be subject to genetic confounding (44) which can lead to faulty interpretations that, for example, obesity itself is characterized by a particular CNS response, whereas the signal instead represents genetic predispositions to both obesity and the identified CNS response (45).

Connectivity Studies

Purpose and use. Using fMRI, functional connectivity studies assess functional neural circuits within the brain (Table 2). It is now well-recognized that distributed brain regions work together in networks that can be defined by their function (46, 47). Functional connectivity studies have been used in our field to map a network to a particular element of appetite regulation, test group differences in functional network connectivity, or test the change in network function with a physiologic stimulus. The most common technique is BOLD fMRI obtained during a resting state scan, but functional connectivity can also be analyzed from task data and used in a psychophysiological interactions (PPI) analysis.

Resting state data acquisitions are used for intrinsic functional connectivity analyses. Participants lie still in the scanner and “let the mind wander.” This resting pattern of neural activity has natural, random-appearing low frequency oscillations. However, regions that are in communication with each other will tend to oscillate in parallel (48, 49). The degree of synchronicity between distributed brain regions is called the functional connectivity. Functional connectivity is reduced in neurodegenerative disorders (50).

Application of connectivity techniques. The role of intrinsic connectivity networks in appetite and body weight regulation is not yet fully understood. A recent study by Sewaybricker, et al. supported a

role for the salience network in feeding and appetite regulation (51). The salience network encompasses a group of nodes (e.g., anterior insula, hypothalamus, ventral tegmental area, prefrontal cortex) that take in interceptive information from the body and then marshal our attentional and cognitive resources to address the greatest immediate homeostatic need (52). Using a pre-defined set of nodes derived from a separate sample, the authors found that salience network connectivity was reduced after a meal (n=110), perhaps reflecting the fact that these nodes are no longer actively addressing nutritional needs and therefore direct cognitive resources toward other functions (53). Other studies have also shown reductions in connectivity by nutrient intake (54, 55, 56), further supporting that acute changes in regional connectivity reflect the appetitive state.

As opposed to defining an entire network, it is also possible to interrogate functional connectivity of a selected brain region by using it as a "seed." In an example of this approach, Neseliler et al. chose a seed region within the ventral medial prefrontal cortex, an area implicated in value coding during choice, and then tested whether connectivity with other regions of the brain was altered during voluntary weight loss. Individuals with the greatest weight loss success at one month showed reduced connectivity to visual association areas in the lingual gyrus and lateral occipital cortex and increased connectivity to the dorsolateral prefrontal cortex (38), potentially reflecting fundamental shifts in the neural organization of self-regulatory capacity during weight loss. As demonstrated by this study, a seed approach can be applied to a select brain region as a pre-defined analytic strategy for hypothesis testing to map the neurophysiologic changes or adaptions in connectivity of that region related to a task or intervention.

Promise and perils. Connectivity analyses are informative because they have a mechanistic aspect. In studying the weight-reduced state, they could reveal how network strength or regional patterns of communication might evolve during weight loss or persist in the weight-reduced state in a way that predicts weight maintenance. These network analyses are complementary to task fMRI, are accessible, and the sequences have been standardized to make them amenable to large, multi-site studies such as the Human Connectome Project (57).

Connectivity studies can also suffer from issues of reproducibility and sample size, because considerable variability in post-processing methods and analytic strategies persists, without proper transparency. A potential pitfall in interpretation is that, for dynamic connectivity studies, increasing or decreasing connectivity does not reliably equate to abnormal brain function, meaning that normal brain function can involve enhancing connectivity to one region while disengaging from another. Finally,

because their reliability is dependent on the duration of the acquisition (58), resting state acquisitions are not well suited to assessing shifts in connectivity due to rapid stimuli such as taste.

Structural Neuroimaging

Purpose and use. Structural neuroimaging techniques (Table 3) noninvasively assess tissue volume or composition. They are the mainstay of clinical neuroradiology for which they are used to detect disease states. In research, structural neuroimaging is used to assess tissue volume, composition, and microstructure. Common techniques include the basic sequences of T1-, T2-, and T2*-weighted images, but many other sequences are available that, when used in a complementary manner, provide insights into tissue composition and can be quantified for use in research studies. For studies of grey or white matter volume, voxel-based morphometry is the common analytic technique. From the technique of diffusion-weighted imaging, researchers can define the structural connectivity of white matter tracks or assess tissue microstructure. There are no tasks during structural neuroimaging.

Applications of structural neuroimaging. Volumetric studies assessing brain volume have yielded mixed findings in weight loss. Several have showed no change in overall gray matter volume with weight loss (59) or after six weeks of very low-calorie diet (60). Other findings include a greater 3-mo. reductions in grey matter volume in prefrontal cortex with greater weight loss (n=72) (61) as well as regional changes in white matter (60, 62).

Clinical neuroradiologists routinely evaluate tissue composition based on the degree of brightness or darkness on structural MRI studies to detect CNS disease in individual patients. Both normal tissue and disease processes infiltrating brain tissue have signature radiologic appearances characterized by how bright or dark the area looks. The appearance of brain structures on MRI reflects their biochemical and magnetic properties (e.g., water, lipid, iron content) and the measured energy they emit when subjected to a particular technique or "sequence." Sequences accentuate the brightness of certain tissues by varying the duration, orientation, and/or strength of the excitatory radiofrequency pulses applied within the magnetic field generated by the scanner. Unlike computed tomography (CT) methods, *the scale of brightness and darkness in an MR-generated structural image is not quantitative and hence is not comparable from one person to another or even from one scan acquisition to the next*. Therefore, a quantitative approach is required to measure tissue characteristics for research purposes. Structural images can be quantified through the use of a signal ratio; the parameter measured from the region of interest is compared to a control region, allowing a relative measure of the degree of brightness or darkness in the region of interest that is, in effect, normalized to

that of the control tissue. Alternatively, a multi-echo sequence can be implemented that allows researchers to fit a curve that quantifies the parameter, for example, the T2 relaxation time.

Recently, structural neuroimaging has been applied to document the translational relevance of preclinical studies establishing that a reactive gliosis occurs in the arcuate nucleus of the hypothalamus during high-fat diet feeding in rodent models of diet-induced obesity. Reactive gliosis consists of activation and expansion of microglial and astrocyte populations and occurs early after initiation of high-fat diet feeding, preceding weight gain (63). These microglial and astrocyte inflammatory responses are necessary and sufficient for the hyperphagia and weight gain that result in diet-induced obesity (64, 65), suggesting a role for hypothalamic gliosis in obesity pathogenesis (66). Advanced gliosis forms glial scars that inhibit normal neuronal functions such as dendrite outgrowth (67, 68). Tissue remodeling by glial cell infiltration might therefore significantly alter neuronal function within this critical region for energy homeostasis.

Using structural neuroimaging, robust reactive gliosis can be visually identified on T2-weighted images as bright-appearing lesions within healthy background tissue. Quantitatively, this high T2 signal (brightness) is measured via T2 signal ratios or T2 relaxation times. Histopathologic studies have determined that T2 signal correlates with increased number of glial cells as well as a reactive astrocytosis and decreased neuron populations (69, 70, 71). In the mediobasal hypothalamus (MBH), glial fibrillary acid protein staining intensity positively correlates with T2 relaxation time in high-fat diet fed rodents (72) and postmortem human brain slices (73). Using quantitative structural neuroimaging techniques, several studies found radiologic evidence of gliosis of the mediobasal hypothalamus in association with obesity in adults (63, 73, 74) and children (75). Moreover, longer MBH T2 relaxation times correlate with greater visceral adiposity (75, 76) and insulin resistance independent of obesity (73) and were observed in obese women with type 2 diabetes mellitus relative to women with obesity who were non-diabetic (62).

In mice, switching from high-fat to chow diet reverses gliosis (72). Two human studies have examined the effects of weight loss on gliosis by using structural neuroimaging. Van de Sande-Lee, et al. found that Roux-en-Y gastric bypass resulted in significant declines in MBH T2 relaxation time post-operatively in women with obesity (62). In contrast, Kreutzer, et al. found no significant decrease in MBH/amygdala signal ratio (n=7) from before to after bariatric surgery (74). Additional studies are required to establish whether hypothalamic gliosis persists or reverses after weight loss in humans.

Diffusion-weighted imaging can be acquired and processed to reveal tissue microstructure and/or to describe the structural connectivity of white matter tracts via diffusion tensor imaging and fiber

tractography. This technique detects the propensity for directional diffusion of water molecules through a tissue (i.e., isotropy). Variability in tissue microstructure due to cellularity, axonal alignment, or pathological processes such as ischemia, inflammation, tumor, or brain injury alters diffusivity, which can be interrogated by using analytic models to calculate parameters including mean diffusivity, apparent diffusion coefficients, fractional anisotropy, and newer metrics such as neurite density. Several of these measures were found to be altered in obesity (77, 78, 79, 80) including in the hypothalamus (78, 80). Whether tissue microstructure is altered by weight loss or in the weight-reduced state is currently undefined.

Promise and Perils. One caution with volumetric techniques is that they can be influenced by nutrition and hydration status; early studies in eating disorders suggested cerebral atrophy, but these were subsequently shown to principally resolve after re-feeding (81, 82, 83). Measures of tissue composition and microstructure are relatively nonspecific (84). Therefore, these tools provide only indirect evidence of the underlying neuropathological alterations occurring in obesity or in the weight-reduced state. Complementary studies of animal models or postmortem samples are needed to support causal inference. Nonetheless, structural neuroimaging offers the only feasible means of testing hypotheses *in vivo* in humans about whether structural reorganization, brain inflammation, or brain injury contribute to the physiology of the weight-reduced state.

Conclusion

Neuroimaging in humans provides a wealth of strategies for enhancing our understanding of the brain's role in defending elevated body adiposity in obesity. Existing studies support its promise for revealing CNS appetitive responses to weight loss via fMRI, both in terms of motivational and reward pathways as well as cognitive control and self-regulation. These fundamental brain processes rely on regional communication within neural networks – assessment of which is amenable to functional connectivity techniques. Moreover, structural neuroimaging suggests that cellular inflammatory responses occur in body-weight regulating areas of the brain in obesity, but the extent to which such chronic CNS inflammation inhibits weight loss or promotes weight regain remains unknown.

A broader understanding of the weight-reduced state could be attained by combining neuroimaging approaches. Structural neuroimaging is ideal for uncovering long-term changes in the CNS that might contribute to defense of elevated body adiposity whereas functional neuroimaging and connectivity approaches reveal the functional consequences of any structural changes for regulation of appetite and energy balance. For example, future studies could use T2- and diffusion-weighted imaging to assess whether hypothalamic tissue composition and structural connectivity contribute to individual

variability in changes in energy expenditure in the weight-reduced state. Complementary resting state and fMRI response to food cues approaches could provide mechanistic insights into the neural circuits regulating these physiologic responses to weight reduction. Future studies should also focus on how the physiology of the weight-reduced state affects structure or function within the executive control regions and networks that support self-regulatory capacity during weight maintenance. Regardless of approach, attention to sample size and transparency in analytic methods will be required to meet current standards for rigor in neuroscience. In sum, multimodal neuroimaging is a critical tool for uncovering the neurophysiology that characterizes the weight-reduced state and the extent to which this neurophysiology compels a return to elevated body adiposity. Treatment strategies that overcome or modify CNS-mediated biological drives will likely be required for patients to sustain substantial weight losses long-term.

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TABLES

Table 1. Functional Neuroimaging

Purpose
• Measure change in neural activity in response to a stimulus
Study objective
• Map function to anatomic location
• Test group differences in CNS response
• CNS response to physiologic stimulus
Techniques
• BOLD fMRI
• Arterial spin labeling (ASL)
• PET (FDG, ^{15}O water)
• EEG, MEG
Common Tasks
• Food cues
• Task + physiologic manipulation
• Food-specific modifications of behavioral tasks (e.g., Go No-Go)

CNS=central nervous system; BOLD=Blood oxygen-level dependent; PET=positron emission tomography; FDG=fluorodeoxyglucose; EEG=electroencephalography; MEG= magnetoencephalography

Table 2. Functional Connectivity Studies

Purpose
• Assess functional connections within the brain
Study objective
• Map distributed networks and define their function
• Test group differences in connectivity
• Test change with physiologic stimulus

Techniques
• BOLD functional magnetic resonance imaging
Common Tasks
• None during resting state scan • During task conduct (psychophysiological interactions [PPI] analysis)

BOLD=Blood oxygen-level dependent.

Table 3. Structural Neuroimaging

Purpose
• Assess tissue volume or composition • Assess structural connectivity
Study objective
• Detect disease states (clinical neuroradiology) • Test group differences in tissue volume or composition • Noninvasively assess tissue microstructure
Techniques
• T1-weighted, T2-weighted, FLAIR, etc. • Voxel-based morphometry (VBM) • Diffusion-weighted imaging • Diffusion tensor imaging (fiber tractography)
Tasks
• None

FLAIR=fluid attenuation inversion recovery

Figure 1

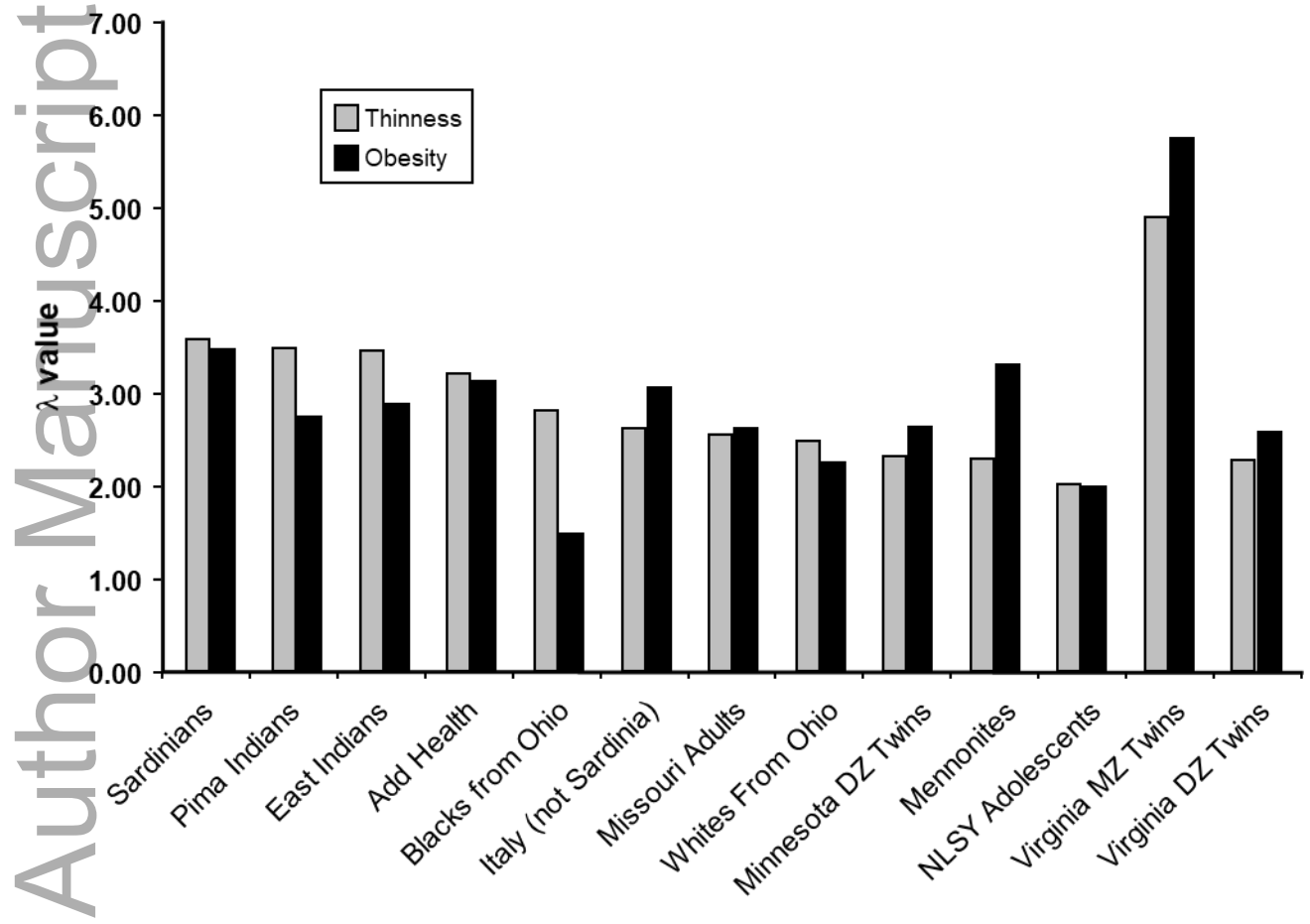

Figure 2