Neural Processing of Food Stimuli in Self-Regulation Brain Regions using Bayesian General Linear Modeling Approach

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Abstract

Background: One of the social concepts is self-regulation; the ability to regulate and control our thoughts, emotions and behaviors. With developments in neuroscience, the neural understanding of self-regulation has been increased. Weight management is a typical kind of self-regulation which leads to behavioral changes. Also in recent years, investigators have used functional Magnetic Resonance Imaging (fMRI) technique for assessing effects of different stimuli such as food on brain responses. The aim of the current study is to localize self-regulation areas in response to palatable food using a Bayesian Generalized Linear Model (GLM) approach.

Methods: A new proposed Bayesian approach was applied for assessing functional response to palatable food stimuli in a block design of fMRI data with 370 scans of one healthy woman. Regions of Interest (ROIs) including the dorsolateral and medial prefrontal cortex, the inferior frontal gyrus and the mid-ventrolateral frontal cortex were investigated. In this Bayesian approach, Stochastic Partial Differential Equation (SPDE) prior was considered for spatial dependency and AR(1) process was used for temporal correlation via pre-weighting residuals. Finally, inferences were conducted using fast Integrated Nested Laplace Approximation (INLA) approximation.

Results: The results of the present study revealed that palatable food as compared to non-food images elicit stronger activation in brain self-regulation areas including the dorsolateral and medial prefrontal cortex, the inferior frontal gyrus and the mid-ventrolateral frontal cortex.

Conclusion: Self-regulation areas of brain of people who are concerned about their weight, will be activated in confrontation with palatable foods.

Key words SPDE, INLA, fMRI,
Self-regulation regions, Food stimuli

Introduction

In the past two decades, functional Magnetic Resonance Imaging (fMRI) has become a valuable technology which has been widely used to study the human brain's mechanism in response to experimental stimuli for eliciting visual, auditory or advanced cognitive activities using detection of changes in the flow rate and blood oxygen saturation level(1).

One of the social cognitive concepts is self-regulation; the ability to regulate and control our thoughts, emotions and behaviors. Eating is typical kind of self-regulation and involves one's ability to change dietary behaviors to lose or gain weight and become healthier(2).

Recent developments in neuroscience have increased the neural understanding of self-regulation(3). Because of the availability of poor quality and calorie-dense fast food, the prevalence of overweight and obesity has raised research on food and dietary habits are becoming important issues. Many people are concerned about their weight so limit their food intake in order to avoid weight gain. The conflict between the appeal of palatable foods and weight management leads to self-regulation.

If an individual can self-regulate his or her eating behavior successfully, then change can take place, which can lead to obtaining the intended goal. The defensive self-regulation system of people who are conscious about their weight automatically becomes active in confrontation with palatable foods so leads to maintenance of weight management goals (4).

Also in recent years, investigators have used fMRI techniques for assessing effects of different stimuli such as food on brain responses(5). However, fMRI data have special characteristics: spatial correlation between thousands of variables named voxels and temporal correlations at hundreds of time points at each voxel leads to massive amounts of highly complex data so in addition to statistical modeling of fMRI data that considers both spatial and temporal structures, the computational cost dealing with analysis of such high dimensional data will be challenging. Because of disability of classical Generalized Linear Model (GLM) in considering fMRI data properties, some alternatives such as Bayesian approaches have been proposed(6, 7).

In a Bayesian GLM, specific prior distributions are assumed for the task activation and other unknown parameters in the model, considering them with the likelihood, compose a Bayesian hierarchical model.

Owing to a large amount of data, standard Markov Chain Monte Carlo (MCMC) methods are typically too time-consuming so a recently developed Bayesian inference tool based on integrated nested Laplace approximation (INLA) has been employed(8). INLA method can compute approximations to the posterior distributions and manage large data sets in a shorter time by using the sparsity of Gaussian Markov Random Fields (GMRFs). Also INLA is much faster than MCMC (9) and can be easily implemented using R-INLA package(10).

The present study uses fMRI data to identify self-regulation areas reactive to palatable food stimuli. A new proposed Bayesian GLM approach is applied for statistical analysis.

Predetermined self-regulation areas in recent studies include some regions in the prefrontal cortex (PFC) so response to food images will be assessed in these parts of the human brain (11-13).

Materials and Methods

1. Subjects

In a block experiment, thirty healthy, normal weight, right handed women with mean age of 22.1 years performed a passive viewing task with blocks of food and non-food images. For our aim in this research the first subject was selected. The fMRI data used in this study was downloaded from the OpenfMRI database. Its accession number is ds000157 (4).

2. Stimuli

During scanning, subjects alternatively viewed 16 blocks of food and non-food images (i.e., office utensils), with 8-16 seconds rest blocks. Halfway the task, there was 10 seconds break. 8 images were presented for 2.5 seconds each with 0.5 seconds inter-stimulus interval in the image blocks. All pictures were food objects on a white background.

3. Functional Magnetic Resonance Imaging

The functional scan was a T2 weighted gradient echo 2D-echo planar imaging sequence (64×64, repetition time=1600 ms, echo time=23 ms, flip angle=72.5, FOV=208×119×256 mm, SENSE factor AP=2.4, 30 axial 3.6 mm slices with 0.4 mm gap, reconstructed voxel size=4×4×4 mm).

In one functional run 370 scans were obtained which lasted 10 minutes. In addition to functional data, a high resolution T1-weighted anatomical MRI scan was made (3D gradient echo sequence, repetition time=8.4 ms, echo time=3.8 ms, flip angle=8, FOV=288×288×175, 175 sagittal slices, voxel size=1×1×1mm).

4. Data processing and statistical analysis

The data was pre-processed with regard to pipeline in Smeet et al and using SPM12 software package (http://www.fil.ion.ucl.ac.uk/spm/software/spm12/), which includes removal of spatial distortions, motion realignment, distortion correction, alignment to the structural image, bias field correction and intensity normalization(14); also Gaussian filter with 8 mm FWHM was used to smooth the images, high pass filtering was done with cutoff 128 s. These are standard steps in fMRI data preprocessing and are necessary to align the data into a common space and remove main sources of noise.

Design matrix was generated by fitting a boxcar function to each time series convolved with canonical hemodynamic response function.

5. Statistical analysis

New proposed method by Mejia in 2017 was applied to perform statistical inferences(10).

Consider the following GLM:

$$\mathbf{y}=\sum_{k=0}^{K}\mathbf{X}_k\boldsymbol{\beta}_k+\sum_{j=1}^{J}\mathbf{Z}_j\mathbf{b}_j+\boldsymbol{\varepsilon} \quad \varepsilon \sim N(0,V) \quad (1)$$

Here y is a TN ×1 vector containing the fMRI time series of all voxels, and the X_k and Z_j are TN ×N design matrices for the activation amplitudes β_k (including baseline β_0) and nuisance signals b_j, respectively. The matrix V is a T×T covariance matrix for an AR(p) process, where p is the degree of autoregressive.

To account for spatial correlation, spatial prior on each β_k for k = 0, … , K was considered, where K is number of tasks under investigation. One of the popular spatial structures is the class of Matérn Gaussian fields that have flexible covariance function between locations. We say $\beta(u)$ is a Matérn Gaussian process if the covariance between u and v $(u, v \in \mathbb{R}^d)$ is given by

$$Cov(u,v)=\frac{\sigma^2}{2^{\nu-1}\Gamma(\nu)}(\kappa\|u-v\|)^{\nu}K_{\nu}(\kappa\|u-v\|) \quad (2)$$

Where $K_\nu(.)$ is the modified Bessel function of the second kind with order $\nu > 0$, $\Gamma(.)$, is the gamma function, $K > 0$ is the spatial scale, and $\sigma^2 > 0$ is the variance.

However, covariance matrix of Matérn spatial process is dense so its inverse is difficult and is not computationally possible for big data sets. This problem has been addressed by solving the stochastic partial differential equation (SPDE) and obtaining an explicit GMRF representation for Matérn Gaussian fields (15).

Here, the steps of INLA-SPDE are briefly described as follows.

1) The non-convex hull meshes using coordinates of voxels was constructed. The spatial correlation structure for the SPDE part of the model was defined by the meshes. Herein, the Constrained Refined Delaunay Triangulation was made with the “inla. mesh.2d” function.

2) A projection matrix was calculated. Because the SPDE model was defined on the mesh, the process at the mesh vertices is required to be projected to the locations response. Details about the calculation of the projector matrix can be found in Lindgren et al. (16).

3) The SPDE model based on the constructed meshes in step 1 was defined. Here the Matérn correlation function was applied which was available in R-INLA.

4) A hierarchical model was specified using equation (1) according to Krainski et al (17). The hierarchical model implemented in INLA-SPDE includes three components (i.e. intercept, the fixed effect, and random effect). In this study, each stimulus was considered as random effects. Then the Normal family was considered for probability distribution of the response.

5) Finally, the posterior distribution of the parameters was estimated.

For more details about SPDE and INLA method refer to Blangiardo et al (18).

To consider temporal correlation of time series and to reduce the computational cost of fitting the Bayesian model, the fMRI time courses were first pre-whitened by assuming an AR (1) process on the residuals from a classical GLM with uncorrelated errors.

Pre-whitened steps are done as below.
(1) The p AR coefficients for each location in the brain were estimated.

(2) The pre-whitening matrix W for each location in the brain was computed resulting in N T×T matrices, where N is the number of voxels in the brain.

(3) Finally, the regression model Wy = WXβ + Wε was fit at each voxel to get estimates and standard errors for β for each subject and voxel.

To account for noise due to subject motion, six rigid body realignment parameters that were estimated in the motion realignment stage of preprocessing were included in the model as nuisance covariates. Furthermore, linear and quadratic time terms were included for considering scanner drift.

In this study, a Regions of Interest (ROIs) analysis was conducted focusing on the dorsolateral and medial prefrontal cortex, the inferior frontal gyrus and the mid-ventrolateral frontal cortex.

The mask of the selected regions was made using the WFU PickAtlas toolbox in MATLAB R2016b software(19). All brain images were mapped to Type 2 Eve Atlas of the SPM12 (20). Data are prepared by programming in MATLAB R2016b software and then model fitting is performed using R-INLA package (http://www.r-inla.org).

Results

In brain anatomy, PFC is the cerebral cortex which covers the front part of the frontal lobe. Subdivision parts of the prefrontal cortex based on Brodmann areas are mentioned in Table 1. From these regions, the dorsolateral and medial prefrontal cortex (BA9), the inferior frontal gyrus (BA45) and the mid-ventrolateral frontal cortex (BA47) were chosen for analysis. These regions are shown in Figure 1.

Prefrontal cortex	Brodmann areas
Lateral (Dorsolateral, Ventrolateral)	9, 46, 12, 44, 45, 47
Medial	9,10,24,25,32
Orbitofrontal	11,13,14
Caudal	8

Table 1: subdivision parts of the prefrontal cortex based on Brodmann areas

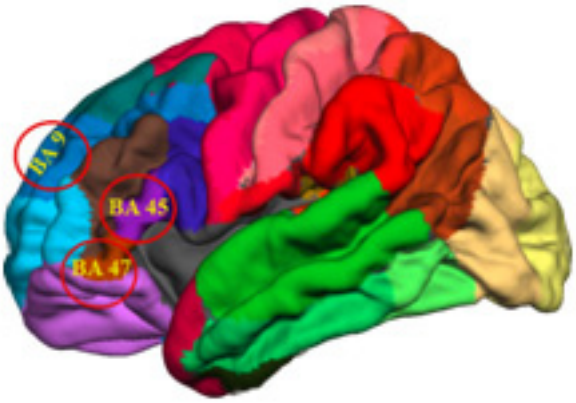

Figure 1: ROIs in present study based on Brodmann area atlas

Activation of mentioned areas in response to palatable food versus non-food stimuli was examined using Bayesian GLM model. The results of fitted model are illustrated as figures.

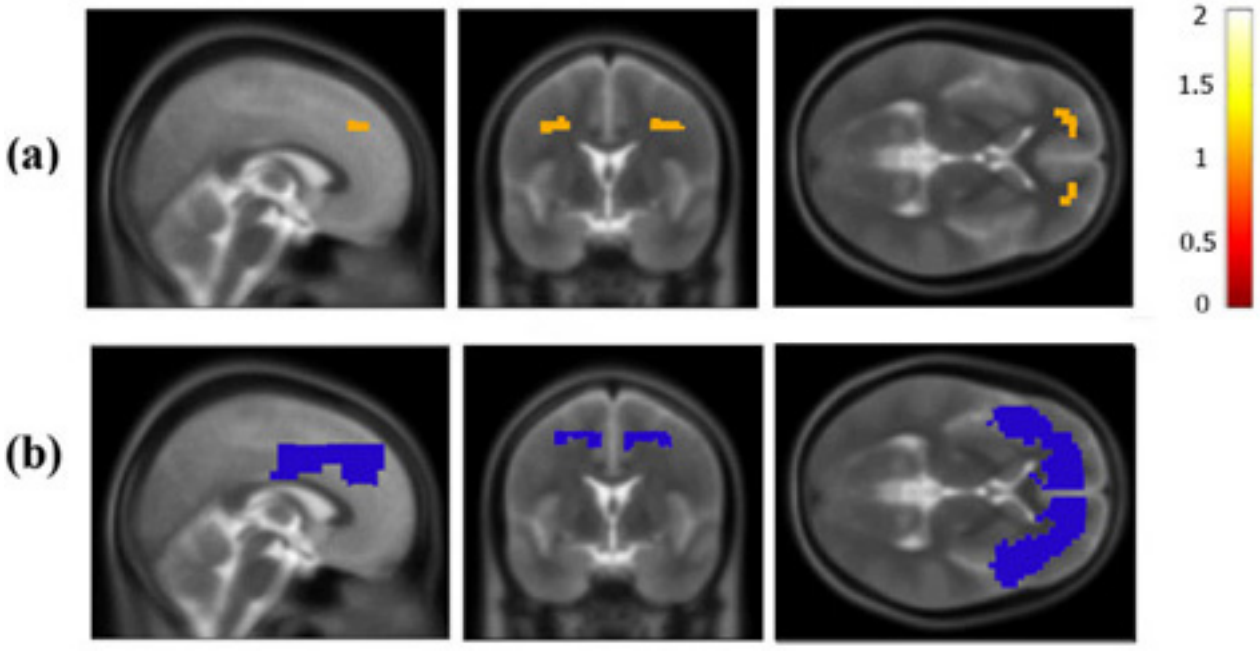

Figure 2: a) Brain regions with stronger activation in response to palatable food vs non-food images. b) The mask of dorsolateral and medial prefrontal cortex

Figure 2a displays the posterior mean of palatable food versus non-food images for the dorsolateral and medial prefrontal cortex in three different views: Sagittal, Coronal and Axial. The dorsolateral and medial prefrontal cortex were stronger activated during viewing of palatable food images.

The white and yellow colors indicate the stronger activation and the orange and red colors represent a weaker and zero activation, respectively. Figure 2b is the mask of the dorsolateral and medial prefrontal cortex and the voxels of this region are displayed in blue.

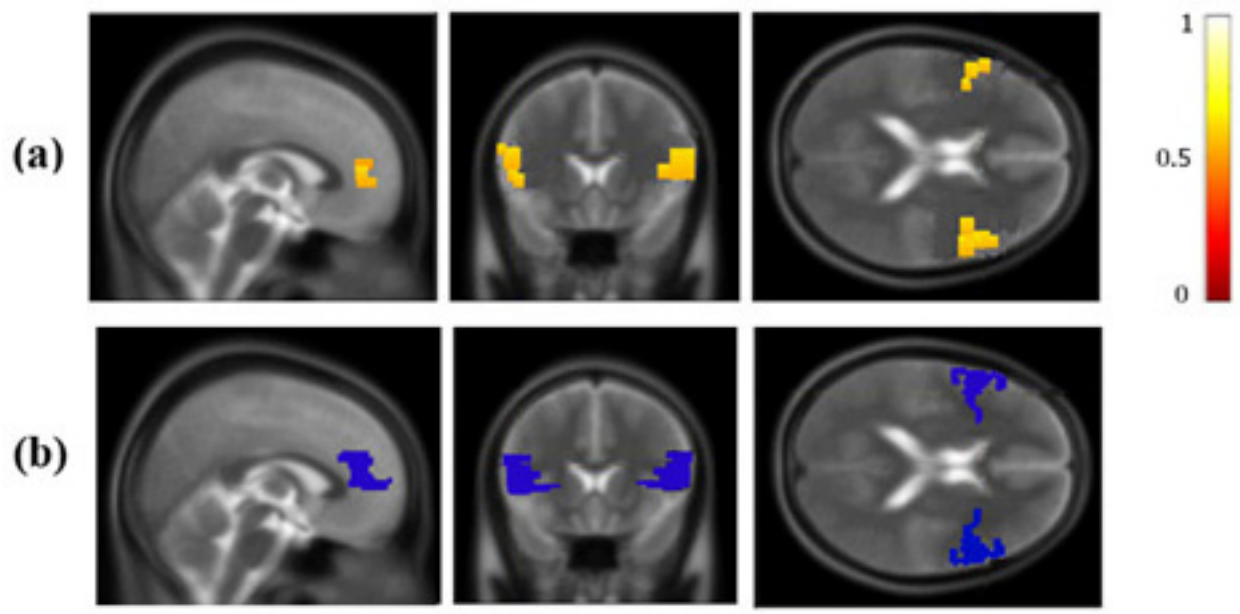

Figure 3: a) Brain regions with stronger activation in response to palatable food vs non-food images b) The mask of inferior frontal gyrus

Figure 3a displays the posterior mean of palatable food versus non-food images for the inferior frontal gyrus in three different views: Sagittal, Coronal and Axial. The inferior frontal gyrus was stronger activated during viewing of palatable food images.

The white and yellow colors indicate the stronger activation and the orange and red colors represent a weaker and zero activation, respectively. Figure 3b is the mask of the inferior frontal gyrus and the voxels of this region are displayed in blue.

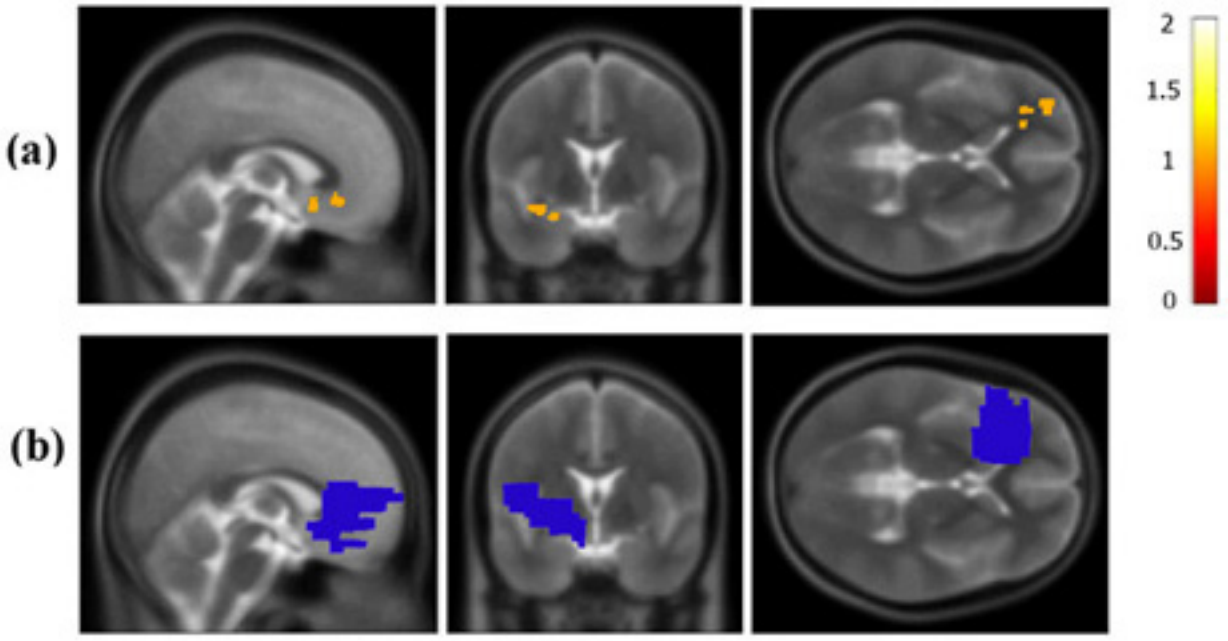

Figure 4: a) Brain regions with stronger activation in response to palatable food vs non-food images b) The mask of mid ventrolateral frontal cortex

Figure 4a displays the posterior mean of palatable food versus non-food images for the mid-ventrolateral frontal cortex in three different views: Sagittal, Coronal and Axial. The mid-ventrolateral frontal cortex elicited stronger activation during viewing of palatable food images.

The white and yellow colors indicate the stronger activation and the orange and red colors represent a weaker and zero activation, respectively. Figure 4b is the mask of the mid-ventrolateral frontal cortex and the voxels of this region are displayed in blue.

Discussion

One of the important aspects of human behavior is self-regulation which has been studied through the social aspect and personality psychology as well as cognitive psychology(21). Recent progressions in neuroscience have led to understanding the neural foundations of self-regulation. Weight management is a typical kind of self-regulation which leads to behavioral changes. Based on prior studies, prefrontal cortex is one of the most effective regions in the self-regulation cognitive function.

In the present research, INLA-SPDE approach was applied for assessing functional response to palatable food images in a block design fMRI data. The areas including the dorsolateral and medial prefrontal cortex, the inferior frontal gyrus and the mid-ventrolateral frontal cortex were considered. Using the described Bayesian approach, the mentioned regions in the frontal cortex elicited stronger activation during palatable food versus non-food images and our results were similar to previous studies. The results showed that self-regulation areas will be activated in people who are concerned about their weight. The results showed the self-regulation areas of people who are concerned about their weight will be activated in confrontation with palatable foods.

The results of previous studies showed that various cortical regions have been involved in self-regulation of which the prefrontal cortex is most notable for cognitive processes that are implicated in self-regulation(22-24). The three main areas of PFC particularly important to self-regulatory functioning are ventromedial PFC (vMPFC) including orbitofrontal cortex, lateral PFC, and the anterior cingulate cortex (ACC)(3, 25). Smeets et al addressed brain activation of self-regulation in response to food cues using fMRI technique. They concluded the activation of self-regulation areas in response to food cues will be adjusted by the importance of weight management goal. They used ROIs: the lateral prefrontal cortex, inferior frontal gyrus and the anterior cingulate cortex and observed activation in these areas(4). Charbonnier et al examined brain responses during food choices between equally liked high and low calorie foods. Food choice compared to non-food choice evoked stronger activation in the left insula, superior temporal sulcus, posterior cingulate gyrus and (pre) cuneus(26). Huerta et al conducted a meta-analysis of neural responses to visual food cues. They showed that regions that lay within the visual system proper (occipital lobe) have significant activations. The most robust activation convergence was in the right fusiform gyrus. Lateralized convergent activations were observed in the left insula, right postcentral gyrus, right precuneus, left inferior frontal gyrus, left middle occipital gyrus and left hippocampus. Bilateral convergent activations were seen in the fusiform gyrus, declive, parahippocampus and superior temporal gyrus(27).

A new Bayesian GLM approach was proposed and applied on cortical surface fMRI data from the Human Connectome Project (HCP). They mapped the volumetric fMRI data to the cortical surface manifold then used INLA for computational approximation(10).

In this study, INLA-SPDE approach was used for analysis of volumetric fMRI data. Most of the Bayesian methods for volumetric fMRI reduce computational trouble by using variational Bayes(VB); however, VB underestimates posterior variance so INLA approach was used as in the study of Mejia et al. INLA is a computationally efficient but highly accurate approximation Bayesian inference tool. Since INLA is less computationally demanding than MCMC, it gave the researchers capability of fitting a complex model based on flexible SPDE spatial processes in order to consider spatial correlation of voxels appropriately.

In this study, we considered only some areas in PFC, one can assess whole brain in response to food stimuli to find more related regions. Also, single subject analysis was conducted in the current research, for future works group analysis could be considered using multi subject Bayesian GLM approach proposed by Mejia et al. Based on literature, the genetic and environmental factors influence on self-regulation's development, so in addition to fMRI data, by collecting genetic information from this experiment, additional research could be done to assess the self-regulation cognitive process by considering and modifying genetic factors.

Conclusion

In conclusion, increased activations were observed in dorsolateral and medial prefrontal cortex, the inferior frontal gyrus and the mid-ventrolateral frontal cortex during viewing of palatable food versus non-food images. This suggests that self-regulation areas of people who are concerned about their weight, will be activated in confrontation with palatable foods. Although in the present study fMRI is used as a tool to study weight management, one of the goals will be to extend this research into the clinical area, such as developing pharmacological treatments for obesity, by means of assessing the fMRI response to administration of new drugs in obese populations.

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