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Diffusion-weighted imaging features of brain in obesity

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Abstract

Purpose: Obesity is characterized by an altered distribution of body fluid. However, distribution of fluid (extracellular/intracellular) in brain tissues has not been studied in obese subjects yet. The purpose of this study was to detect possible brain diffusion changes especially in satiety and hunger related centers in obese subjects by diffusion weighted imaging (DWI).
Methods: Conventional MRI and DWI of the brain was obtained from 81 obese patients (obese=68, morbid obese=13) and 29 age-matched, nonobese. The apparent diffusion coefficient (ADC) values were calculated in hypothalamus; amygdala; hippocampal gyrus; thalamus; insula; cingulate gyrus; orbitofrontal, dorsomedial and dorsolateral frontal, middle temporal and occipital cortex; cerebellum; midbrain and corpus striatum.
Results: The ADC values of hypothalamus, hippocampal gyrus, amygdala, insula, cerebellum and midbrain were significantly increased in patients (n:81) when compared to nonobese subjects. The ADC values of thalamus, hippocampal gyrus, amygdala, orbitofrontal, occipital, dorsolateral and middle temporal cortex, insula and midbrain were significantly increased in morbid obese when compared to nonobese subjects. The ADC values of orbitofrontal and occipital cortex were significantly higher in morbid obese than the values in the obese. The body mass index positively correlated with ADC values of amygdala, insula, orbitofrontal and middle temporal cortex.
Conclusion: We observed increased ADC values of distinct locations related to satiety and hunger that suggest altered fluid distribution and/or vasogenic edema in obese subjects. Awareness of this abnormalities in brain tissue composition/function in obesity may contribute to better understanding of the underlying mechanisms.

Keywords: Obesity; Brain; Diffusion weighted imaging; Vasogenic edema

1. Introduction

Obesity represents a major public health problem especially in developed countries and has a negative impact on the quality of life and longevity [1,2]. The obesity results from the chronic positive energy balance. The understanding of the relative contribution of energy intake and expenditure to the etiology of obesity is still a matter of discussion [1].

As obesity is a complicated issue, differences in brain function is likely to be important [2]. Neural system also plays an important role in regulating the hyperphagia in obese individuals [3]. To better understand the etiology of obesity, it is important to evaluate the role of the central nervous system in regulation of the eating behavior [4]. It has been shown that in subjects with normal weight, hunger was associated with increased neuronal activity in the hypothalamus, insular, orbitofrontal and anterior cingulate cortices; striatum; hippocampal and parahippocampal formations; precuneus; thalamus and cerebellum [1,5,6]. However, early satiety was associated with increased neuronal activity in the dorsolateral and ventromedial prefrontal cortices [5]. Obesity is characterized by an altered distribution of body fluid. Obese subjects have a greater volume of extracellular body fluid (ECF) than intracellular (ICF) compared to subjects with normal weight [7]. However, distribution of fluid (ECF/ICF) in brain tissues has not been studied in obese subjects yet.

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Advances in neuroimaging technology have given us the ability to evaluate the brain function in vivo and noninvasively [4]. Diffusion-weighted imaging (DWI) provides specific information about various pathological changes in the brain. DWI provides qualitative information, whereas apparent diffusion coefficient (ADC) maps allow quantitative measurement of the diffusion of water molecules, which is altered in pathologic conditions in the brain tissue [8].

The purpose of this study was to detect possible brain diffusion changes especially in the satiety and hunger related centers in obese subjects by DWI.

2. Material and methods

A total of 81 consecutive patients (42 females, 39 males; mean age: 42.2±12.1 years) who were referred to our endocrinology department and had the diagnosis of obesity based on standard clinical criteria were included in the study. Of these, 68 were obese (33 female and 35 males, 42.7± 12.2 years old) and 13 were morbid obese (9 females and 4 males, 40.2±14.8 years old). Twenty-nine nonobese healthy volunteers [body mass index (BMI) less than 30 kg/m^2] (14 female, 15 males, mean age: 39.2±7.7 years) were taken as the control group. None of the subjects had cerebrovascular disease including ischemic changes, leukoaraiosis cerebral and cerebellar atrophy. The procedures used were in accordance with the guidelines of the Helsinki Declaration on human experimentation. The study protocol was approved by the institutional ethical committee. All subjects were fully informed and gave their written informed consent.

BMI was calculated by dividing the weight in kilograms by the square of height in meters. BMI groups were defined using the World Health Organization classification system [9]. The obese group was categorized into two subgroups according to BMI values. Subgroup 1 consisted of 68 obese subjects (BMI ≥30, <40 kg/m^2), and Subgroup 2 consisted of 13 morbid obese subjects (BMI ≥40 kg/m^2). The control group consisted of 29 nonobese subjects with BMI less than 30 kg/m^2.

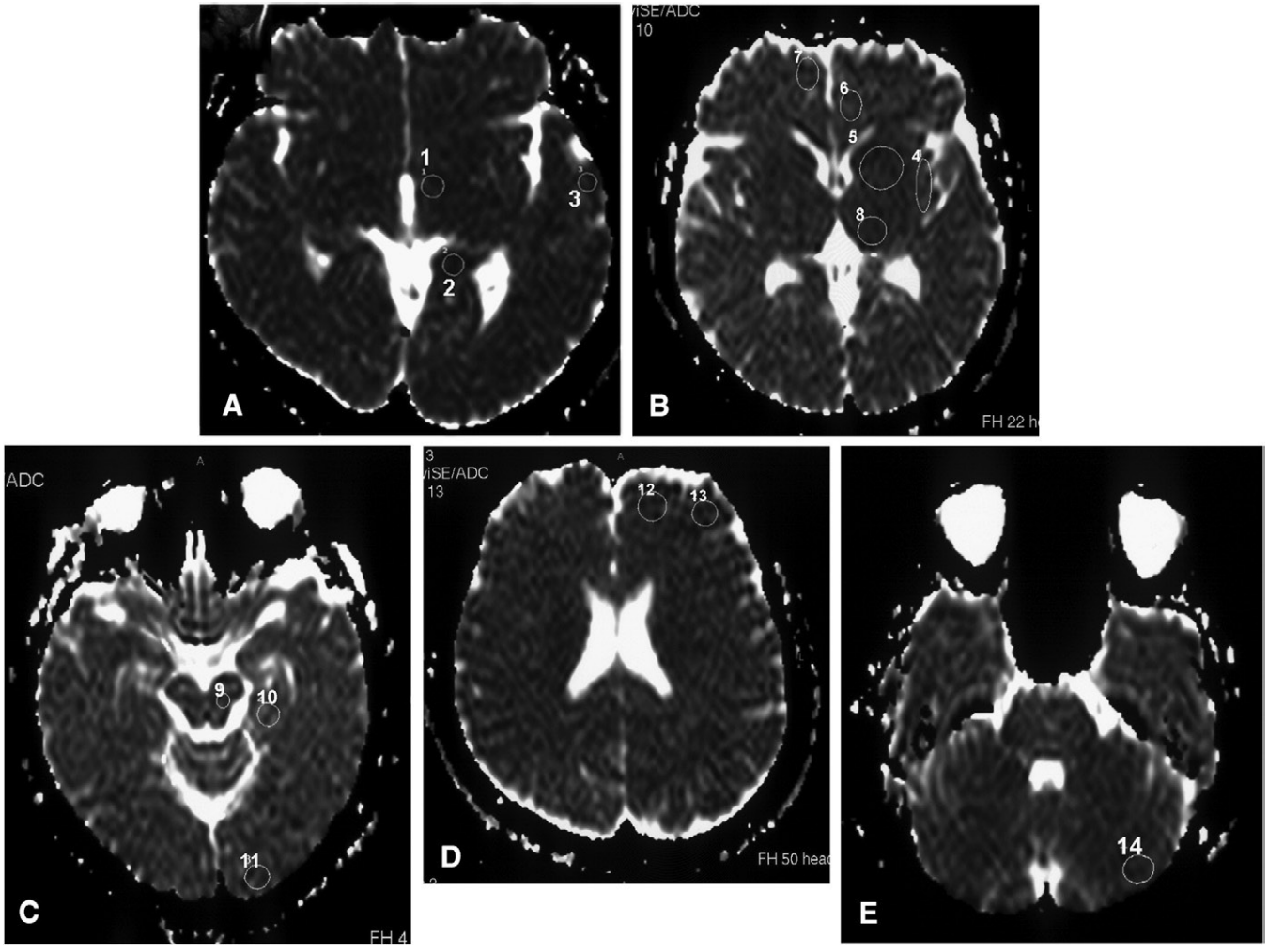

Fig. 1. ADC maps show ROIs of obese subject in: (A) hypothalamus (1), hippocampal gyrus (2) and middle temporal cortex (3); (B) insula (4), corpus striatum (5), cingulate gyrus (6), orbitofrontal cortex (7) and thalamus (8). (C) midbrain (9), amygdala (10) and occipital cortex (11). (D) dorsomedial frontal cortex (12), dorsolateral frontal cortex (13) and (E) cerebellum (14).

The magnetic resonance imaging (MRI) examination consisted of routine imaging and DWI. MRI was performed on 1.5-T system (Philips, Gyroscan Intera Master, Best, The Netherlands). T1-weighted images (TR=560 ms, TE=15 ms) were obtained in the axial and sagittal planes. Fast spin-echo T2-weighted images (TR=4530 ms, TE=100 ms) were obtained in the axial and coronal planes. Subjects with normal conventional MRI findings were included in study and were further evaluated with DWI. For DWI, a single-shot echoplanar pulse sequence (TR=4832 ms, TE=81 ms, field of view=230 mm, matrix size=128×128, number of acquisitions=2, slice thickness=5 mm, slice number=22, slice orientation=axial plane, scan time=28 s, interslice gap=1 mm) was used in all patients and the controls with two different *b* values (0 and 1000 s/mm^2). The ADC maps were reconstructed with the commercially available software. In the patients and the controls, 14 distinct neuroanatomic locations which were previously suggested to be related with satiety and hunger centers (hypothalamus; amygdala; hippocampal gyrus; thalamus; insula; cingulate gyrus; orbitofrontal, dorsomedial and dorsolateral frontal, middle temporal and occipital cortex; cerebellum; midbrain and corpus striatum) were selected for the analysis [1,5,10]. Regions of interest (ROIs) drawn by same experienced radiologist (A.A.) manually on the regions identified and ADC values were automatically calculated from the ADC map. We minimized partial volume effects by inspecting the slices above and below the region to avoid averaging with cerebrospinal fluid. The areas of ROIs were 80 mm^2 in insula; 50–60 mm^2 in corpus striatum and thalamus; 40–50 mm^2 in hypothalamus, hippocampal gyrus, midbrain and cerebellum and 30–40 mm^2 in amygdala, cingulate gyrus and orbitofrontal, dorsomedial and dorsolateral frontal, middle temporal and occipital cortex (Fig. 1). The similar ROI size used for an individual selected region in all patients, and the controls were carefully evaluated by the same experienced radiologist. ROI analysis were blinded on the condition of the subjects.

All statistical analyses were performed using a commercially available SPSS release 10.0 software package (SPSS, Chicago, IL, USA). The results are presented as the mean±S.D. The distribution of ADC values in the patient group, subgroups and the control group were evaluated with Kolmogorov–Smirnov test. Student *t* test and Mann–Whitney *U* test were used to assess whether there is a difference in the ADC values of 14 distinct locations between the patient group, subgroups, and the control group. Pearson test was used for correlation analysis. A *P* value below .05 was considered statistically significant.

3. Results

There was no significant difference in demographic variables between the patient and the control groups except body weight and BMI.

ADC values in hypothalamus; amygdala; hippocampal gyrus; thalamus; insula; cingulate gyrus; orbitofrontal, dorsomedial and dorsolateral frontal, middle temporal and occipital cortex; cerebellum; midbrain and corpus striatum were presented in Table 1.

The ADC values of hypothalamus (*P*=.02); hippocampal gyrus (*P*=.04); amygdala (*P*=.007); insula (*P*=.002); cerebellum (*P*=.01) and midbrain (*P*=.01) were significantly increased in patients (n:81) compared to nonobese subjects.

The ADC values of from insula (*P*=.004) were significantly higher in Subgroup 1 compared to nonobese subjects.

The ADC values of thalamus (*P*=.008); hippocampal gyrus (*P*=.037); amygdala (*P*=.001); orbitofrontal (*P*=.004), occipital (*P*=.018), dorsolateral (*P*=.004) and middle temporal cortex (*P*=.028); insula (*P*=.008) and midbrain (*P*=.004) were significantly higher in subgroup 2 (n: 13) compared to nonobese subjects.

The ADC values in orbitofrontal (*P*=.01) and occipital cortex (*P*=.02) were significantly higher in Subgroup 2 compared to Subgroup 1.

The body weight positively correlated with ADC values of hippocampus (*r*=.19, *P*=.04), insula (r=.23, *P*=.01), orbitofrontal (*r*=.20, *P*=.03) and middle temporal cortex (*r*=.26, *P*=0.05).

Table 1
Comparison of ADC values of different brain locations in the obese and the control subjects

Locations	ADC values (× 10^{-6}mm^2/s)			
	Nonobese (n=29)	Total (obese and morbid obese, n=81)	Obese (n=68)	Morbid obese (n=13)
Hippocampal gyrus	799,75±26	812,20±36 [a]	811,10±38	818,00±26 [b]
Amyglada	802,93± 41	829,55±10 [a]	824,00±10	858,61±59 [b]
Insula	746,63±16	804,43±37 [a]	802,66±36 [c]	813,69±42 [b]
OFC	756,56±42	776,06±61	768,64±54 [d]	814,84±83 [b]
Middle temporal	758,21±32	776,28±44	773,01±44	793,38±39 [b]
Cerebellum	705,10±31	726,27±51 [a]	724,48±48	735,61±66
Hypothalamus	726,41±34	757,55±10 [a]	756,25±10	764,38±94
Thalamus	716,20±17	718,40±76	715,39±82	734,15±18 [b]
Cingulate gyrus	770,51±28	771,80±47	775,22±47	753,92±41
DMFC	723,68±42	728,69±44	725,29±43	746,46±46
DLFC	732,31±36	750,93±91	745,61±95	778,76±60 [b]
Occipital cortex	739,94±29	747,27±42	742,0±39 [d]	774,84±49 [b]
Midbrain	733,15±35	761,19±72 [a]	756,32±71	786,69±75 [b]
Corpus striatum	690,62±22	691,97±28	691,60±28	693,92±24

OFC indicates orbitofrontal cortex; DMFC, dorsomedial frontal cortex; DLFC, dorsolateral frontal cortex.

[a] Differences between the patients with obese (total) and nonobese subjects.

[b] Differences between the patients with Subgroup 2 and nonobese subjects.

[c] Differences between the patients with Subgroup 1 and nonobese subjects.

[d] Differences between the patients with Subgroups 1 and 2.

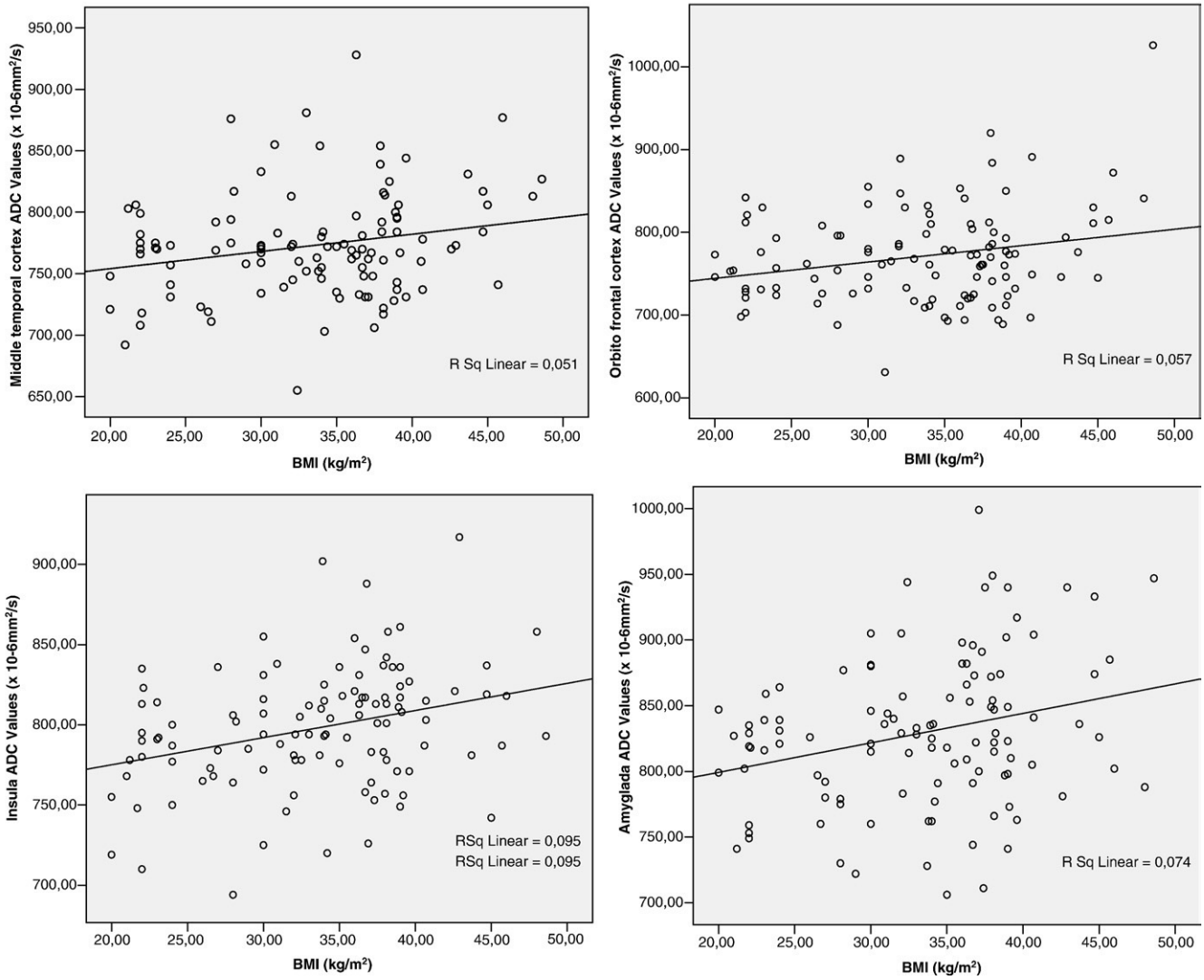

Fig. 2. The figure shows positive correlations between BMI (kg/m^2) and middle temporal cortex, orbitofrontal cortex, insula, and amygdala ADC values ($\times 10^{-6}$mm^2/s).

The BMI positively correlated with ADC values of amygdala (r=.19, P=.04), insula (r=0.27, P=.004), orbitofrontal (r=0.23, P=.01) and middle temporal cortex (r=0.22, P=.01) (Fig. 2).

4. Discussion

Obesity is a chronic disease proposed to be caused by neurochemical abnormalities [11,12]. The discovered complex hypothalamic neuropeptidergic pathways that control energy balance has irrefutably demonstrated that body fat content is, at least in part, under homeostatic control [11,13]. Altered fluid distribution has already been considered as a complication of abdominal obesity and source of error in body composition assessment. Greater understanding about this association might shed light on the etiology of obesity [7]. The excess extracellular volume might alternatively reflect cell dehydration and normal fluid shifts out of cells to the extracellular space in response to osmotic stress from plasma solute [14].

Diffusion-weighted imaging provides unique information about pathological changes in the brain in addition to the information obtained with conventional MRI [8]. DWI are designed to enhance the sensitivity of the MRI signal to the incoherent microscopic movement of water protons in tissue [15]. ADC values are rotationally invariant measurements of the diffusion of water molecules within a tissue. Diffusion of water molecules is primarily related to microscopic structural barriers that change the random movement of water on a molecular level. DWI is thought to be useful in differentiating cytotoxic edema from vasogenic edema [15,16]. Vasogenic edema is characterized by a relative increase in water in the extracellular space where water is relatively more mobile. Consequently, vasogenic edema results in increased ADC values. It has been shown that increased

ADC values might suggest ultrastructural changes and, therefore, would reflect microstructural damage [8,15,16].

In our study, we observed a significant increase in ADC values of various brain locations related with satiety (hypothalamus, hippocampal gyrus, amygdala, insula, cerebellum and midbrain) in obese subjects. These findings pointed out that obesity is associated with altered fluid distribution and increased ECF/ICF ratio in distinct brain locations, which might suggest vasogenic edema. The alterations in the brain locations which were related to satiety and hunger centers (thalamus, hippocampal gyrus, amygdala, insula, midbrain, orbitofrontal, occipital, dorsolateral and middle temporal cortex) were more prominent in morbid obese subjects. Since the mean age of nonobese, obese and morbid obese were comparable, these differences cannot be attributed the age of patients. On the other hand, the demonstration of positive correlation between body weight and BMI and ADC values in several satiety and hunger centers support the importance of this issue in obese subjects.

Previous studies demonstrated that the elevated BMI is associated with reduced brain volumes, suggesting greater global brain atrophy in middle-aged adults even after adjusting for age [17]. It is unclear through which mechanisms obesity affects brain volume. Likewise, it is presently unknown why obesity is associated with a greater ECF/ICF ratio and whether the phenomenon represents a cause or consequence of obesity. If attributed to hypertonicity, the altered fluid distribution in obesity could be more than a correlate of obesity or source of error in body composition assessment [7]. Several mechanisms have been hypothesized to explain the excess ECF/ICF volume observed in obesity. The phenomenon may reflect overhydration, excess total body water related to impaired fluid regulation, edema, hormones secreted by adipose tissue, a higher ECF/ICF ratio of adipose tissue and atrophied tissues or malnutrition [7]. In addition to the previous reports, we showed increased ADC values in satiety- and hunger-related centers, which may suggest altered fluid distribution due to vasogenic edema in brain tissue of obese patients as the first report in this subject. To elucidate the potential clinical implications of this alteration, further studies are needed.

5. Conclusion

We observed increase in ADC values of distinct locations related to satiety and hunger, which suggest altered fluid distribution and/or vasogenic edema in these locations in obese compared to nonobese subjects. Awareness of these abnormalities in the brain tissue composition/function in obesity may contribute to better understanding of the underlying mechanism and development of new prevention or treatment strategies.

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