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Microstructural effects of Ramadan fasting on the brain: a diffusion tensor imaging study

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PURPOSE
We aimed to examine whether the brain displays any microstructural changes after a three-week Ramadan fasting period using diffusion tenson imaging.

METHODS
This study included a study and a control group of 25 volunteers each. In the study group, we examined and compared apparent diffusion coefficient (ADC) and fractional anisotropy (FA) values of the participants during (phase 1) and after (phase 2) a period of fasting. The control group included individuals who did not fast. ADC and FA values obtained in phase 1 and phase 2 were compared between the study and control groups.

RESULTS
In the study group, ADC values of hypothalamus and, to a lesser extent, of insula were lower in phase 1 compared with phase 2 and the control group. The FA values of amygdala, middle temporal cortex, thalamus and, to a lesser extent, of medial prefrontal cortex were lower in phase 1 compared with phase 2 and the control group. Phase 2 ADC and FA values of the study group were not significantly different compared with the control group at any brain location.

CONCLUSION
A three-week Ramadan fasting period can cause microstructural changes in the brain, and diffusion tensor imaging enables the visualization of these changes. The identification of brain locations where changes occurred in ADC and FA values during fasting can be helpful in diagnostic imaging and understanding the pathophysiology of eating disorders.

Dietary changes such as hunger and thirst have metabolic, physiological, and neurological effects. Prior studies on the impact of hunger and thirst on brain functions were usually done with fasting individuals; and these studies investigated effects of fasting on psychomotor activities, sleep patterns, and motor cortex activity (1–3). A helpful way to understand effects of hunger and thirst on the brain is to examine neuroanatomical correlates of hunger and satiation with fasting individuals.

In Islam, fasting during Ramadan, which is the ninth month of a lunar year, is an obligatory practice. Fasting for Muslims entails abstaining from food and drink from dawn till dusk. Depending on the season that Ramadan coincides with and the location, the duration of fasting may vary between approximately 10 and 20 hours.

In the literature, different brain locations associated with hunger and satiety have been identified. In a study that used positron emission tomography, hunger was shown to be associated with an increase in neuronal activity in the hypothalamus, thalamus, basal ganglia, temporal cortex, cerebellum, insula, anterior cingulate, and orbitofrontal cortex; and satiety was found to be related to increased neuronal activity in prefrontal cortex (4–5).

Diffusion-weighted imaging (DWI) and diffusion tensor imaging (DTI) are magnetic resonance imaging (MRI) techniques that are used to measure the molecular motion of fluid and to quantify the direction and magnitude of diffusion (6–7). DWI produces apparent diffusion coefficient (ADC) as a measure of the diffusion, and DTI yields fractional anisotropy (FA) values to indicate the directionality of water diffusion. ADC and FA values can be used to deduce microstructural changes (8). Increased ADC values would indicate microstructural damage, and higher values of FA may suggest better structural integrity (8–9).

To date, there is not a single study that examined structural integrity in the brain during fasting using DTI. The purpose of our study was to examine whether microstructural changes occur in the neuroanatomical correlates of hunger and satiety centers after a three-week Ramadan fasting period.

Methods

Subjects

The study and control groups consisted of 25 volunteering adults each (15 females and 10 males in each group). Volunteers were employees of the university where the study took place. The mean ages of the study and control groups were 30.2±8.5 years (range, 19–51 years) and 32.2±7.4 years (range, 20–48 years), respectively. The mean age

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of the study and control groups were not significantly different (P = 0.371). The Institutional Ethics Committee approved the study, and participants provided written informed consent. All participants had the same working environment and had similar working conditions. Body mass indices (BMI) of all participants were calculated using the World Health Organization (2006) classification system. There was no significant difference in the mean BMI of fasting and control subjects. The majority of the study (n=20) and control groups (n=22) were within the normal weight range (BMI, 18.5–24.9 kg/m^2), and the rest were overweight (BMI, 25.0–29.9 kg/m^2).

Study design

In the study group, we examined ADC and FA values of the participants during and after a period of Ramadan fasting. In this study, to establish consistency among study group participants they were told to start fasting at 00:30 am, and they broke their fast around 8:30 pm every day in Ramadan. Apart from the fasting practice, the study group did not follow any other dietary restrictions. Weight of the study subjects were measured two times: at the beginning of Ramadan and at the end of the third week of Ramadan. The difference between these two measurements were less than 1 kg on average, which indicated stabilized body weights during this three-week period.

Measurements in the study group were carried out in two phases. The first phase (phase 1) was conducted during the last week of Ramadan fasting. In the first phase, all tests were performed 15 hours after the study group started their daily fasting. Glucose, hemoglobin A1c, insulin, and homeostasis model of assessment-insulin resistance (HOMA-IR) levels were also measured in the first phase to determine and exclude participants with insulin resistance. To identify participants with brain abnormalities, T1, T2, and fluid-attenuated inversion recovery (FLAIR) axial images were obtained. None of the participants had insulin resistance or any brain abnormalities including white matter T2 hyperintense foci; thus all of them were included in the study and were further evaluated with DTI. The second phase (phase 2) took place two months after the fasting period ended. In the second phase, study subjects were evaluated by DTI within one hour of having a meal and at roughly the same day time as in the first phase.

The control group included volunteers who did not follow the fasting practice during Ramadan. The reason for having a control group in this study was to compare ADC and FA values of the study group in the second phase (i.e., two months after Ramadan ended) and the ADC and FA values of the control group. Control group participants underwent the same tests as the study group to identify individuals with insulin resistance and brain pathology. None of the participants in the control group had insulin resistance or brain abnormalities, and all of them were kept in the study. Subsequently, control group participants were evaluated with DTI within one hour of having a meal and at roughly the same day time as the study group.

Magnetic resonance imaging

MRI was performed on a 1.5 T system (Avanto, Siemens Healthcare). T1-weighted three-dimensional magnetization prepared rapid acquisition gradient echo (3D-MPRAGE) (TR/TE/TI, 12.5/5/450 ms; matrix, 128×128; field of view, 200×230 mm), T2-weighted spin echo (SE) (TR/TE, 4530/100 ms; matrix, 128×128; field of view, 200×230 mm) and FLAIR images (TR/TE/TI, 8000/90/2500 ms; matrix, 128×128; field of view, 230×230 mm) were obtained in the axial plane. The DTI protocol consisted of a single-shot SE echo-planar sequence with fat suppression technique (TR/TE, 2700/89 ms; matrix, 128×128; field of view, 230×230 mm; slice thickness, 3 mm). Thirty diffusion encoding directions were used at b=0 s/mm^2 and b=1000 s/mm^2.

Image interpretation and analysis

The post-processing of DWI data sets was carried out on a workstation (Leonardo, software version 2.0, Siemens Healthcare), and the ADC and FA maps were reconstructed. ROIs were placed in hunger and satiety related centers, and ROI sizes were determined based on the size of the brain area measured (4, 5, 10). To standardize the measurements all ROIs were obtained from the left cerebral hemisphere. The areas of ROIs were 10 mm^2 in the left hypothalamus, hippocampus, insula, orbitofrontal cortex, thalamus, midbrain, amygdala, occipital cortex, and cerebellum; 8 mm^2 in the left middle temporal cortex, cingulate gyrus, medial prefrontal cortex, and lateral prefrontal cortex; and 30 mm^2 in the left corpus striatum (Fig). Two experienced radiologists (A.B., S.Y.), who were blinded to the satiety conditions of the participants, manually drew similar size ROIs on axial color-encoded ADC and FA maps of all participants. Imaging distortions were automatically corrected, and the data were co-registered in reference to T1-weighted 3D-MPRAGE images. ADC and FA values were obtained automatically with reference to corresponding ADC and FA maps.

Statistical analysis

All statistical analyses were performed using SPSS 17.0, a commercially available software package (SPSS, Inc.). Descriptive statistics for ADC and FA values were reported as mean± standard deviation. The ADC and FA comparisons were done using t tests and Cohen's d effect sizes. A P value below 0.05 was considered statistically significant in all analyses.

Results

Phase 1 and phase 2 ADC and FA values at 14 different brain locations in the study group are presented in Table 1. The mean ADC and FA values of the control group are presented in Table 2. Paired t test results showed that the mean ADC value of the hypothalamus was significantly lower in phase 1 compared with phase 2 with a Cohen's d effect size of 0.67 (P = 0.025). The mean ADC value of insula in phase 1 was also relatively lower compared with that in phase 2 with a Cohen's d effect size of 0.57 although the difference was not statistically significant (P = 0.052).

We also compared ADC values of the study group in phase 1 to the ADC values of the control group. The mean ADC values of the hypothalamus (P =

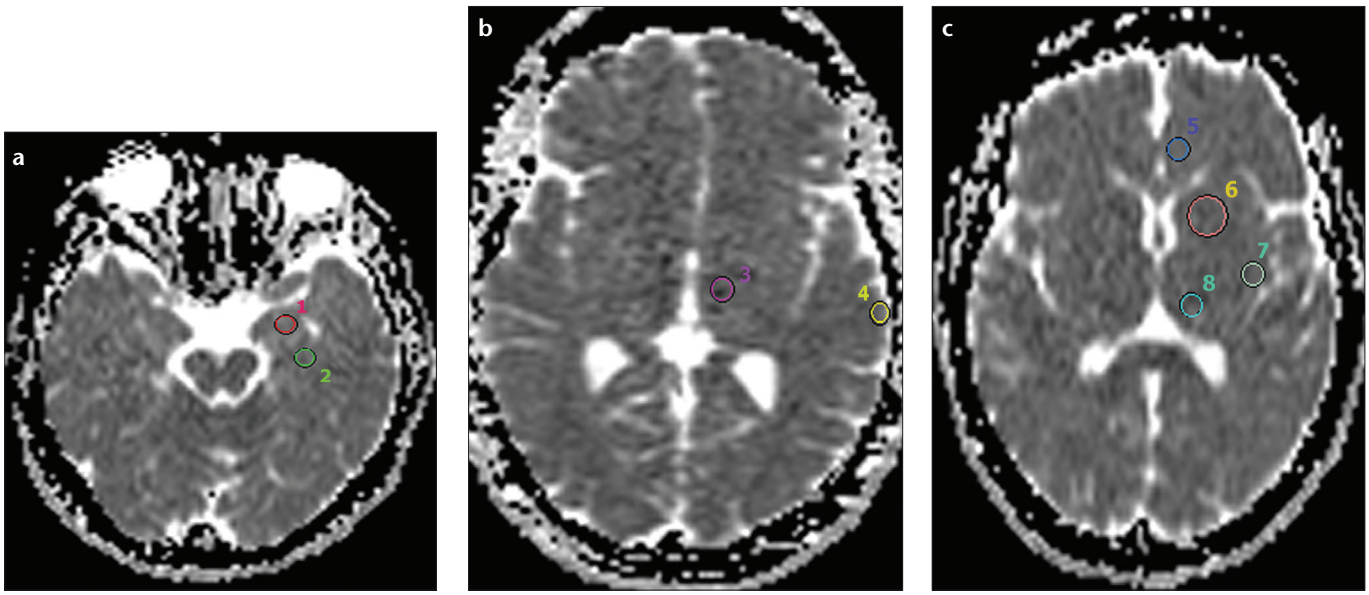

Figure. a–c. ADC maps show ROIs of participants in the study group: **(a)** amygdala (1), hippocampus (2); **(b)** hypothalamus (3), middle temporal cortex (4); **(c)** cingulate gyrus (5), corpus striatum (6), insula (7), and thalamus (8).

Table 1. Comparison of ADC and FA values between Phase 1[a] and Phase 2[b]

	FA (×10^{-3})		FA		ADC (×10^{-3} mm^2/s)		ADC	
Locations	Phase 1	Phase 2	*P*	Cohen's d	Phase 1	Phase 2	*P*	Cohen's d
Hypothalamus	456.6±85.6	470.2±91.2	0.573	0.15	683.0±150.0	763.1±77.5	0.025	0.67
Hippocampus	349.8±98.3	324.3±65.4	0.357	-0.31	759.9±99.4	760.0±59.3	0.997	0.00
Middle temporal cortex	161.3±34.0	213.6±55.8	<0.001	1.13	807.9±49.2	811.9±68.0	0.794	0.07
Insula	223.6±43.5	215.2±42.3	0.467	-0.20	826.0±43.7	851.4±44.8	0.052	0.57
Corpus striatum	236.0±51.2	235.7±48.2	0.987	-0.01	725.3±23.3	739.4±36.5	0.158	0.46
Cingulate gyrus	224.1±98.4	265.7±128.5	0.160	0.36	784.9±63.2	799.5±60.8	0.341	0.24
Orbitofrontal cortex	195.1±57.2	239.6±117.5	0.068	0.48	802.5±78.6	817.7±61.1	0.409	0.22
Thalamus	312.3±51.0	365.1±76.3	0.011	0.81	763.4±50.0	747.0±59.3	0.264	-0.30
Midbrain	469.6±91.5	478.9±91.9	0.674	0.10	766.4±64.3	773.2±54.3	0.735	0.11
Amygdala	196.5±44.8	276.4±62.8	<0.001	1.46	841.3±55.7	834.3±51.8	0.624	-0.13
Occipital cortex	204.2±71.9	231.8±46.1	0.115	0.46	791.5±38.7	790.2±45.5	0.921	-0.03
Medial prefrontal cortex	202.6±48.8	233.0±50.3	0.052	0.61	789.9±70.5	757.0±70.6	0.167	-0.47
Dorsolateral frontal cortex	182.4±46.2	203.0±61.9	0.266	0.38	834.0±80.9	820.6±73.4	0.591	-0.17
Cerebellum	209.0±132.5	196.4±30.2	0.633	-0.13	721.6±139.2	745.3±61.0	0.468	0.22

Data are presented as mean±standard deviation.
ADC, apparent diffusion coefficient; FA, fractional anisotropy.
[a]After a 3-week fasting period; [b]Two months after the end of Ramadan.

0.022; Cohen's *d*, 0.67) and the insula (*P* = 0.051; Cohen's *d*, 0.57) for the study group in phase 1 were statistically and practically lower than the mean ADC values of the same locations in the control group.

The mean FA values of the amygdala (*P* < 0.001) and middle temporal cortex (*P* < 0.001) were significantly lower in phase 1 compared with phase 2 with Cohen's *d* effect sizes of 1.46 and 1.13, respectively. The mean FA value of the thalamus (*P* = 0.011) was also significantly lower for phase 1 compared with phase 2 with a Cohen's *d* effect size of 0.81. The average FA value of the medial prefrontal cortex was relatively lower in phase 1 compared with phase 2 with a Cohen's *d* effect size of 0.61 although the difference was not statistically significant (*P* = 0.052).

The mean FA values of the amygdala (*P* < 0.001; Cohen's *d* = 1.50), middle temporal cortex (*P* < 0.001; Cohen's *d* = 1.15), thalamus (*P* = 0.007; Cohen's *d* = 0.79), and medial prefrontal cortex (*P* = 0.042; Cohen's *d* = 0.59) for the study group in phase 1 were lower than the mean FA values of the same locations in the control group.

Table 2. Descriptive statistics for ADC and FA measurements in the control group

Locations	FA ($\times 10^{-3}$)	ADC ($\times 10^{-3}$ mm^2/s)
Hypothalamus	470.3±91.8	762.4±75.8
Hippocampus	324.2±65.5	760.0±58.7
Middle temporal cortex	214.0±55.1	811.6±67.1
Insula	215.5±39.5	851.8±47.1
Corpus striatum	236.4±50.0	739.9±38.3
Cingulate gyrus	265.8±127.5	798.7±61.8
Orbitofrontal cortex	239.9±117.5	817.3±60.5
Thalamus	364.6±78.2	747.1±61.3
Midbrain	478.2±92.8	773.3±52.9
Amygdala	277.5±61.6	834.4±55.0
Occipital cortex	232.3±42.7	791.4±47.8
Medial prefrontal cortex	233.0±53.5	756.6±71.8
Dorsolateral frontal cortex	203.6±59.3	820.6±74.1
Cerebellum	197.0±29.2	742.7±59.0

Data are presented as mean±standard deviation.

Independent samples t test comparisons between the study group's ADC and FA values in phase 2 and the control group's ADC and FA values showed no statistically significant difference at any of the brain locations. Indeed, the largest Cohen's *d* value obtained for these comparisons was 0.04, indicating that the study group's phase 2 ADC and FA values and the control group's ADC and FA values were quite similar.

Discussion

In this study we show that there are microstructural changes in different brain locations during the fasting period.

Diet is essential for maintaining general health and is particularly important for the brain, as it requires a steady supply of energy (11–12). A number of studies on the lack of energy as a consequence of fasting consistently showed a decline in attention and cognitive functions and an increase in fatigue, headaches, and irritability (13–15).

DWI is a specific MRI technique that examines molecular motion of water at the cellular level (16). ADC is the most widely accepted DWI measure and provides information about the local cell breakdown (17). As a more recent MRI method, DTI allows for the measurement of the direction and magnitude of water diffusion. DTI produces FA as a measure of the orientational coherence of water diffusion. Low FA values may suggest loss of white matter integrity, decrease in axonal density, or disorganization of axonal structure (18–19).

Although neural mechanisms of hunger and satiation have been examined in studies that used neuroimaging techniques other than DWI, to our knowledge, no studies have been conducted with fasting individuals to investigate hunger- and satiety-related brain locations using DWI and DTI. One study that examined diffusion changes in hunger- and satiety-related centers using DWI was conducted with obese individuals (10). This study found increased ADC values for obese individuals at hypothalamus, amygdala, hippocampal gyrus, midbrain, insula, and cerebellum. The authors suggested that vasogenic edema could be the reason for the increase in ADC values (10).

We examined hunger- and satiety-related centers in the brain using DTI and determined that FA values of amygdala, middle temporal cortex, thalamus, and medial prefrontal cortex during fasting period were lower compared with FA values during satiety. These findings suggest microstructural changes, mainly due to loss of functional and structural integrity, at these locations. In addition ADC values of hypothalamus and insula during fasting were lower compared with the ADC values of these locations during satiety. The low ADC values of hypothalamus and insula could be secondary to a dysfunction similar to hypothalamic and insular inflammation. A recent study that was conducted with fasting mice and humans using advanced diffusion also suggested that changes in diffusion parameters could be associated with hypothalamic inflammation (20).

Hypothalamus and insula are parts of distinct neural networks associated with energy intake and regulation of appetite. Whereas the hypothalamus plays a major role in the homeostatic control, the insula is a key contributor to the hedonic, or reward-based, regulation of appetite (21). Long fasting hours in our study may model ungrounded diets that start with long hunger periods to restrict energy intake. Thus, our findings suggest that following such restricted diets may affect hypothalamus and insula, which may result in failure to accurately recognize hunger signals. The inaccurate perception of hunger signals can lead to refusing to eat or overeating, which are possible pathophysiologies of eating disorders such as anorexia and bulimia nervosa (22).

Neuroimaging studies about hypothalamus, insula, amygdala, middle temporal cortex, thalamus, and medial prefrontal cortex, which were the affected hunger and satiety centers in the current study, have highlighted the crucial role of these brain locations in the neurobiology of eating disorders and, particularly, in the related emotional regulation deficits (23–30). Hypothalamus, thalamus, and amygdala, which are parts of limbic system, have major roles in processing emotions and memory (25). Amygdala also plays a pivotal role in regulating anxiety and thus coping with self-injurious behavior (23). Dorsomedial prefrontal cortex has a central role in emotion regulation and the pathophysiology of major depression (26). The medial prefrontal cortex and temporal cortex are associated with socioemotional responses (24). In a previous study on patients

with anorexia nervosa, Frieling et al. (28) observed reduction in FA values of thalamic regions. These regions have been implicated in the etiopathogenesis of anorexia nervosa and contribute to impairments in cognitive domains, especially set-shifting ability. In another study, Kazlouski et al. (27) found reduced FA values mainly in the amygdala-related white matter tracts of anorexia patients, which play a major role in coping with self-injurious behavior.

Although all of the affected brain regions in this study have been implicated in the pathophysiology of eating disorders, most present data on brain abnormalities are still insufficient to answer some main questions about the eating disorders. Prior DTI studies on eating disorders included patients with anorexia nervosa, and, except for one, included either acutely ill patients (27) or patients after weight-restoration (30) making it impossible to answer whether microstructural abnormalities in the brain are a cause or result of these disorders, or whether these abnormalities are only related to malnourishment or underweight. The only study that included both ill and weight-recovered patients could also not answer these questions because microstructural abnormalities remained after weight-restoration (28). Indeed to solve this problem we need studies that use healthy participants that go through long periods of hunger (e.g., fasting individuals) or studies that include control groups consisting of acutely underweight and malnourished patients without an eating disorder. Thus, our study is informative for eating disorder studies, in that, microstructural changes in the brain regions, which have been implicated in the pathophysiology of eating disorders, were observed as a result of the three-week fasting period and were not related to malnutrition or underweight.

A limitation of the current study was the relatively small sample size, which may have been inadequate to detect the statistical significance of some effects (31). Also, the present study could have been improved by using a single group with measurements made on the same subjects before, during, and after the fasting period. However, we could initiate the study during Ramadan and thus used a control group. One other limitation of this study was that ROI-based analysis could affect the estimated diffusion parameters. Tract-based spatial statistics (http://www.fmrib.ox.ac.uk/fsl/) would have provided more accurate and detailed results and revealed more significant areas showing whole brain voxel-based changes (32). Furthermore, previous studies showed that ADC values may differ according to the ROI size (33). In the current study, ROI sizes were determined based on the size of the brain area measured. Thus, although the ROI sizes differed by the brain area, for the same brain area the ROI sizes were the same across the three measurements (i.e., study group phase 1, study group phase 2, and the control group). Finally, Ramadan fasting involves total abstaining from not only food but also fluids, which can impact serum osmolarity and, eventually, intracellular water content and quantitative values of DWI and DTI. In the current study we did not examine the effect of dehydration using a direct measure of body water content such as serum osmolarity. However, studies that investigated serum osmolarity changes in active Ramadan fasting groups found that Ramadan fasting did not affect serum osmolarity (34, 35).

In conclusion, we observed microstructural changes in the brain of healthy individuals after a three-week Ramadan fasting period, and DTI enabled the visualization of these microstructural changes. The identification of brain locations in which temporary changes occur in ADC and FA values during fasting may be helpful in diagnostic imaging and understanding the pathophysiology of eating disorders.

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Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Bahammam AS, Nashwan S, Hammad O, Sharif MM, Pandi-Perumal SR. Objective assessment of drowsiness and reaction time during intermittent Ramadan fasting in young men: a case-crossover study. Behav Brain Funct 2013; 9:32. [CrossRef]
2. Bahammam AS, Alaseem AM, Alzakri AA, Sharif MM. The effects of Ramadan fasting on sleep patterns and daytime sleepiness: An objective assessment. J Res Med Sci 2013; 18:127–131.
3. Boujraf S, Benejiba N, Belahsen F, Tizniti S, Garey LJ. The impact of restricted diet on brain function using BOLD-fMRI. Exp Brain Res 2006; 173:318–321. [CrossRef]
4. Tataranni PA, Gautier JF, Chen K, et al. Neuroanatomical correlates of hunger and satiation in humans using positron emission tomography. Proc Natl Acad Sci USA 1999; 96:4569–4574. [CrossRef]
5. Del Parigi A, Gautier JF, Chen K, et al. Neuroimaging and obesity: mapping the brain responses to hunger and satiation in humans using positron emission tomography. Ann N Y Acad Sci 2002; 967:389–397. [CrossRef]
6. Le Bihan D, Mangin JF, Poupon C, et al. Diffusion tensor imaging: concepts and applications. J Magn Reson Imaging 2001; 13:534–546. [CrossRef]
7. Hunsche S, Moseley ME, Stoeter P, Hedehus M. Diffusion-tensor MR imaging at 1.5 and 3.0 T: initial observations. Radiology 2001; 221:550–556. [CrossRef]
8. Huisman TA, Loenneker T, Barta G, et al. Quantitative diffusion tensor MR imaging of the brain: field strength related variance of apparent diffusion coefficient (ADC) and fractional anisotropy (FA) scalars. Eur Radiol 2006; 16:1651–1658. [CrossRef]
9. Planetta PJ, Schulze ET, Geary EK, et al. Thalamic projection fiber integrity in de novo Parkinson disease. AJNR Am J Neuroradiol 2013; 34:74–79. [CrossRef]
10. Alkan A, Sahin I, Keskin L, et al. Diffusion-weighted imaging features of brain in obesity. Magn Reson Imaging. 2008; 26:446–450. [CrossRef]
11. Attwell D, Laughlin SB. An energy budget for signaling in the gray matter of the brain. J Cereb Blood Flow Metab 2001; 21:1133–1145. [CrossRef]
12. McGrath-Hanna NK, Greene DM, Tavernier RJ, Bult-Ito A. Diet and mental health in the Arctic: is diet an important risk factor for mental health in circumpolar peoples?--a review. Int J Circumpolar Health 2003; 62:228–241. [CrossRef]
13. Afifi ZE. Daily practices, study performance and health during the Ramadan fast. J R Soc Health 1997; 117:231–235. [CrossRef]
14. Kadri N, Tilane A, El Batal M, Taltit Y, Tahiri SM, Moussaoui D. Irritability during the month of Ramadan. Psychosom Med 2000; 62:280–285. [CrossRef]
15. Roky R, Iraki L, HajKhlifa R, Lakhdar Ghazal N, Hakkou F. Daytime alertness, mood, psychomotor performances, and oral temperature during Ramadan intermittent fasting. Ann Nutr Metab 2000; 44:101–107. [CrossRef]
16. Attariwala R, Picker W. Whole body MRI: improved lesion detection and characterization with diffusion weighted techniques. J Magn Reson Imaging 2013; 38:253–268. [CrossRef]
17. Jiang H, van Zijl PC, Kim J, Pearlson GD, Mori S. DtiStudio: resource program for diffusion tensor computation and fiber bundle tracking. Comput Methods Programs Biomed 2006; 81:106–116. [CrossRef]

18. Cirillo M, Esposito F, Tedeschi G, et al. Widespread microstructural white matter involvement in amyotrophic lateral sclerosis: a whole-brain DTI study. AJNR Am J Neuroradiol 2012; 33:1102–1108. [CrossRef]
19. Barysheva M, Jahanshad N, Foland-Ross L, Altshuler LL, Thompson PM. White matter microstructural abnormalities in bipolar disorder: A whole brain diffusion tensor imaging study. Neuroimage Clin 2013; 2:558–568. [CrossRef]
20. Lizarbe B, Benitez A, Peláez Brioso GA, et al. Hypothalamic metabolic compartmentation during appetite regulation as revealed by magnetic resonance imaging and spectroscopy methods. Front Neuroenergetics 2013; 5:6. [CrossRef]
21. Berthoud HR. Metabolic and hedonic drives in the neural control of appetite: who is the boss? Curr Opin Neurobiol 2011; 21:888–896. [CrossRef]
22. Oberndorfer TA, Frank GK, Simmons AN, et al. Altered insula response to sweet taste processing after recovery from anorexia and bulimia nervosa. Am J Psychiatry 2013; 170:1143–1151. [CrossRef]
23. Wable GS, Barbarich-Marsteller NC, Chowdhury TG, Sabaliauskas NA, Farb CR, Aoki C. Excitatory synapses on dendritic shafts of the caudal basal amygdala exhibit elevated levels of GABAA receptor α4 subunits following the induction of activity-based anorexia. Synapse 2014; 68:1–15. [CrossRef]
24. Schulte-Rüther M, Mainz V, Fink GR, Herpertz-Dahlmann B, Konrad K. Theory of mind and the brain in anorexia nervosa: relation to treatment outcome. J Am Acad Child Adolesc Psychiatry 2012; 51:832–841. [CrossRef]
25. Takano A, Shiga T, Kitagawa N, et al. Abnormal neuronal network in anorexia nervosa studied with I-123-IMP SPECT. Psychiatry Res 2001; 107:45–50. [CrossRef]
26. Downar J, Sankar A, Giacobbe P, Woodside B, Colton P. Unanticipated rapid remission of refractory bulimia nervosa, during high-dose repetitive transcranial magnetic stimulation of the dorsomedial prefrontal cortex: a case report. Front Psychiatry 2012; 3:30. [CrossRef]
27. Kazlouski D, Rollin MD, Tregellas J, et al. Altered fimbria-fornix white matter integrity in anorexia nervosa predicts harm avoidance. Psychiatry Res 2011; 192:109–116. [CrossRef]
28. Frieling H, Fischer J, Wilhelm J, et al. Microstructural abnormalities of the posterior thalamic radiation and the mediodorsal thalamic nuclei in females with anorexia nervosa--a voxel based diffusion tensor imaging (DTI) study. J Psychiatr Res 2012; 46:1237–1242. [CrossRef]
29. Friederich HC, Walther S, Bendszus M, et al. Grey matter abnormalities within cortico-limbic-striatal circuits in acute and weight-restored anorexia nervosa patients. Neuroimage 2012; 59:1106–1113. [CrossRef]
30. Yau WY, Bischoff-Grethe A, Theilmann RJ, et al. Alterations in white matter microstructure in women recovered from anorexia nervosa. Int J Eat Disord 2013; 46:701–708. [CrossRef]
31. Sullivan GM, Feinn R. Using effect size-or why the P value is not enough. J Grad Med Educ 2012; 4:279–282. [CrossRef]
32. Smith SM, Jenkinson M, Johansen-Berg H, et al. Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. Neuroimage 2006; 31:1487–1505. [CrossRef]
33. Bilgili Y, Unal B. Effect of region of interest on interobserver variance in apparent diffusion coefficient measures. AJNR Am J Neuroradiol 2004; 25:108–111.
34. Attarzadeh Hosseini SR, Sardar MA, Hejazi K, Farahati S. The effect of Ramadan fasting and physical activity on body composition, serum osmolarity levels and some parameters of electrolytes in females. Int J Endocrinol Metab 2013; 11:88–94.[CrossRef]
35. Ramadan J, Telahoun G, Al-Zaid NS, Barac-Nieto M. Responses to exercise, fluid, and energy balance during Ramadan in sedentary and active males. Nutrition 1999; 15:735–739. [CrossRef]