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Research Article

Determining Correlation of Food Intake and Satiety Related Hormones with the Findings of Brain Computerized Tomography (CT) Scans and Psychological Disorders in Children with Mild to Moderate Traumatic Brain Injury

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ABSTRACT

Background: Traumatic Brain Injury (TBI) is an impairment with high prevalence amongst the pediatric population. Central Nervous System (CNS) regulates food intake and each region of the brain can be responsible for appetite control network. It seems that TBI might affect appetite control system which could result in overeating or reduced food intake. Hence, the aim of this cross sectional study was to determine, if there is a relationship between daily energy intake and satiety related hormones with Computerized Tomography scan (CT scan) findings in children with mild to moderate TBI.

Methods: Completing the demographic information (age, gender, medical disorders, etc.), dietary intake assessment, taking blood samples for biochemical evaluations, and evaluating psychological disorders using the "Rutter Children Behavior Questionnaire" were performed for each patient. The patient's CT scan was also used to determine the main area of brain injury. The timing of outcome measures was 3-6 months after injury.

Results: The results showed that in comparison with the Reference Dietary Allowance (RDA) values, calorie intake was inadequate in 32% of the patients, while 32% had excess calorie intake. It was shown that energy intake in patients with temporal lobe injury was significantly higher than in patients with frontal lobe injury or injuries to other sites of the brain. The results also showed that mean serum Ghrelin and Orexin levels in patients with temporal lobe injury were higher than patients with frontal lobe injury but no significant relationship was found regarding leptin and site of injury. Moreover, it was shown that children with frontal lobe injury had significantly more behavioral disorders.

Conclusion: To sum up, it seems that frontal lobe injury is associated with anorexia and hypophagia behaviors and temporal lobe injury might be associated with increased food intake.

Keywords: Brain concussion; Food intake; Appetite; Satiety; Pediatric; Depression; Behavior disorders

Abbreviations: TBI: Traumatic Brain Injury; CNS: Central Nervous System; CT scan: Computerized Tomography scan; RDA: Reference Dietary Allowance; GCS: Glasgow Coma Scale; CDC: Centers for Disease Control and Prevention.

INTRODUCTION

Traumatic Brain Injury (TBI) can be defined as the disruption in brain function, or other evidence of brain pathology, caused by an external physical force. TBI refers to one or a combination of brain injuries, such as skull fracture, extra-cranial and intra-parenchymal hemorrhage [1]. TBI is classified into three groups of mild, moderate and severe according to the Glasgow Coma Scale (GCS). Accordingly, GCS 13-15 is considered as mild, GCS 9-12 as moderate and GCS 3-8 as severe injuries [2].

The yearly incidence of TBI is estimated at 50 million cases worldwide, and the average rate of mortality for patients with severe TBI is 39%, and those who survive have significant disabilities, which itself is another socioeconomic concern [3,4]. In children and adolescents, TBI is the first cause of death and disability in the United States [5].

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Annually, about 500,000 children under the age of 14 suffer from head injuries [6]. As far as we know, there is no statistics on the brain trauma and its costs in Iran. But it seems that Iran is amongst the top countries in the world to have trauma accidents, most of which lead to brain injuries [7].

Patients with moderate to severe brain injury are often unable to meet their nutritional needs. Skull fracture might lead to damage in skull-based nerves, which are associated with chewing, swallowing, smelling and tasting. In addition, fractures of the face and teeth can delay the onset of oral nutrition [8]. For such patients, inadequate intake of nutrients is due to anorexia, early satiety, problems with taste and olfactory senses, inactivity, depression and dysphagia or complications such as aspiration [9].

The Central Nervous System (CNS) regulates food intake and the sense of hunger or satiety, and each region is a part of a complex network in appetite control; hence, it can be expected that in brain injury, a disruption will happen in appetite and food intake control. The ventromedial hypothalamus is the center of satiety while the lateral hypothalamus is the center for desire to eat; thus, the damage to the ventromedial hypothalamus can increase the desire to eat and vice versa the lateral hypothalamic injury can reduce the tendency to eat [10]. Findings also showed that the damage to the ventricular nuclei, thalamic vessels and hippocampus can lead to overeating [11]. On the other hand, brain stem injury might decrease appetite [12-14]. Numerous studies also suggested that the damage to the frontal lobe reduces the desire to eat [15]. Since the amygdala and hippocampus have role in food intake regulation and appetite control, temporal lobe damage might lead to increased food intake [16]. Findings suggest that following TBI, the changes in eating behavior might result in overeating or anorexia [17].

Therefore, the aim of this study for the first time was to determine whether there is a relationship between daily energy intake, satiety related hormones, and the degree and site of brain damage in children with mild to moderate TBI, using CT scan imaging.

MATERIALS AND METHODS

Study design

In this cross sectional study, pediatrics in the age range of 5-15 years old with mild to moderate TBI referred to the pediatric neurosurgery clinic affiliated with Shiraz University of Medical Sciences were enrolled. The patients were recruited prospectively and the sample size was calculated to be 50 patients based on the energy intake value in pelizzo study with the power of 80% and [18]. This study was approved by ethics committee of Shiraz University of Medical Sciences. (No. IR.SUMS. REC.1397.708) followed the principles of the Declaration of Helsinki.

Participants' characteristics

Children of 5-15 years old with mild to moderate TBI who were injured within the past 3-6 months without any other illnesses that could affect their food intake, such as cancer, liver and kidney failure, thyroid disorders, and diabetes were recruited.

Patients who were on parenteral nutrition, suffered multiple injuries or had a history of neurological or psychiatric problems, used any medications or supplements that could affect appetite and also were reluctant to participate in the study, were excluded.

After explaining the research objectives to the childrens' parents, they were asked to complete the consent form and the following steps were performed for each patient: Completing the demographic information (age, gender, medications, medical disorders), dietary intake assessment, taking blood samples for biochemical evaluations, assessing psychological disorders using the "Rutter Children Behavior Questionnaire" (the parent's form) and doing CT scan for determining the main area of brain injury (frontal, temporal, occipital, or other sites of brain).

Clinical manifestations assessment

Dietary intake assessment: to assess the children's dietary intake, data from three 24 h dietary recalls were taken. Two assessments were made on weekdays and a third one during the weekends. The data were assessed under the guidance of a skilled dietitian. The reported values were then entered into the Nutritionist 4 software. The average energy intake was then compared with the RDA values for each individual [8]. Adequate energy intake was defined as intake 75 to 110% of the RDA, while inadequate and excess intake were considered as intakes less than 75% and more than 110% of the RDA, respectively [19].

Evaluation of behavioral disorders: Children were assessed for behavioral disorders using the "Rutter Children Behavior Questionnaire" (the parent form), which was provided to the child's parents to answer the questions. It should be noted that the Rutter Behavioral Problems Questionnaire was developed by Michael Rutter in 1975, which is consisted of 31 items including 13 questions related to general health, habits and lifestyle (including complaints of headache, stomach pain with nausea, shortness of breath, urinary or fecal incontinency, refusal to go to school, speech problems, stealing behaviors, and eating and sleeping problems) and 18 questions related to child behavioral disorders (including behaviors such as restlessness, aggression, irritability, depression, disobedience, concentration problems, and lying) and is completed by parents. A score of 13 is the cut-off point, and children with a score of 13 or higher are considered as having behavioral disorders [20].

CT scan evaluation: Evaluation and interpretation of the patients' admission CT scan was done by the neurosurgeon to determine where the affected region of the brain was (frontal, temporal, parietal, occipital lobe, or other sites of brain) and if the cerebral hemorrhage existed. By referring to the patient's medical history, information on the day that the trauma had occurred, the length of hospitalization, the cause of trauma, the GCS at admission and also the therapeutic strategies were recorded. It is necessary to mention that the scan was performed in any case as part of clinical practice at Namazi hospital and it was not performed as part of the study protocol.

Biochemical assessment: Fasting blood samples were taken from each participant. The serums were prepared by centrifuging at 3000 rpm for 15 minutes and were stored at -70°C until further analysis. Serum leptin was measured by ELISA method, using German Mediagnost kit, serum Ghrelin was measured by ELISA method, using Chinese Crystallday kit, and serum Orexin A was measured by ELISA method, using Chinese Crystallday kit.

Statistical analysis

Data analysis was done, using SPSS software (version 24). Quantitative variables were reported as mean ± SD. The normality of quantitative variables was evaluated by Kolmogorov-Smirnov test. To compare the mean ± SD of normal quantitative variables by multivariate qualitative variables, one-way ANOVA was used and Kruskal-Wallis test, if the variables were not normal. Additional post-hoc tests were also used to compare the groups two by two. Comparison of variables in two groups

according to Rutter test score were done by independent sample t-test (for normal data) and Mann Whitney test for nonparametric ones. P<0.05 was considered to be statistically significant.

RESULTS

In this study of fifty patients (36 boys and 14 girls) with mild to moderate TBI were examined. The mean age (years), GCS at admission and length of hospitalization (day) of the patients was 8.82 ± 3.12, 10.12 ± 1.91 and 12.03 ± 17.26, respectively (Table 1).

Based on the GCS, most of the patients (88%) suffered from moderate TBI. The majority of them were taking anticonvulsant medications (levetiracetam or phenytoin). Sleep disorder and headache were reported among the most prevalent medical disorders in this population. Cerebral hemorrhage was observed in 28% of the children, most of which was related to the epidural hematoma. Most of the participants (64%) did not need surgery after TBI. About sixty-eight percent of the children had Rutter test score more than 13, which indicates the existence of psychological disorders. In this study, the most common cause of trauma was car accident and the most prevalent affected injury site was frontal and temporal lobe of the brain (Table 2).

The results showed that in comparison with the RDA values, calorie intake was inadequate in 32% of the patients, while 32% had excess energy intake (Table 3).

Based on the comparison of mean daily energy intake and serum levels of related satiety hormones in different categorical CT scan findings, there was a significant relationship between energy intake and the site of injury (p<0.001). Post-hoc analysis showed that energy intake in patients with temporal lobe injury was higher than patients with frontal lobe injury, skull base fracture or injuries to other sites of brain, meaning that overeating is more likely to happen in parietal lobe injuries. There was also a significant relationship between serum Ghrelin and Orexin A levels with the site of injury. According to post-hoc analysis mean serum Ghrelin (p=0.02) and Orexin A (p=0.04) levels in patients with temporal lobe injury were higher than patients with frontal lobe injury. No statistically significant relationship was found regarding leptin and site of injury. Furthermore, a significant relationship was found between Rutter test score and the area of brain injury (p=0.03). Children with frontal lobe injury had a higher Rutter test score, indicating that behavioral disorders are more common in those with frontal damage (Table 4).

Table 1: Demographic characteristics and biochemical variables in pediatrics with TBI.

Variable*	Total (50)	Boys (36)	Girls (14)	p-value
Age (years)	8.82 ± 3.12	8.91 ± 0.51	8.43 ± 0.88	0.65
GCS at admission	10.12 ± 1.91	9.97 ± 1.89	10.50 ± 1.99	0.4
length of hospitalization (days)	12.03 ± 17.26	11.55 ± 15.55	13.26 ± 21.67	0.42
Leptin (ng/ml)	4.82 ± 6.51	4.80 ± 6.78	4.87 ± 6.00	0.45
Ghrelin (ng/ml)	2.95 ± 3.71	2.89 ± 3.74	3.12 ± 3.74	0.97
Orexin A (pg/ml)	593.00 ± 552.64	576.00 ± 561.29	636.74 ± 547.82	0.76
Energy intake (kcal/day)	1514.56 ± 589.86	1622.4 ± 640.7	1237.3 ± 302.2	0.4
Energy intake adequacy (%) **	88.88 ± 29.02	90.4 ± 30.5	84.9 ± 25.2	0.6
Rutter test score	17.2 ± 8.3	17.2 ± 7.9	17.3 ± 9.6	0.5

Note: * The data are reported as mean ± SD;**p<0.05 was considered as significant.

Table 2: Medical records and CT scan findings of the patients.

Variable*	Total (50)	Boys (36)	Girls (14)
Severity of injury			
Mild	6 (12)	4 (11.1)	2 (14.3)
Moderate	44 (88)	32 (88.9)	12 (85.7)
Medical disorders			
No medical disorders	8 (16)	6 (16.7)	2 (14.3)
Seizure	6 (12)	4 (11.1)	2 (14.3)
Headache	18 (36)	13 (36.1)	5 (35.7)
Sleep disorders	18 (36)	13 (36.1)	5 (35.7)
Medications			
Levetiracetam	38 (76)	28 (77.8)	10 (71.4)
Phenytoin	12 (24)	8 (22.2)	4 (28.6)

Cerebral hemorrhage			
No hemorrhage	36 (72)	24 (66.7)	12 (85.7)
Epidural	12 (24)	10 (27.8)	2 (14.3)
Subdural	1 (2)	1 (2.8)	0 (0)
Intraventricular	1 (2)	1 (2.8)	0 (0)
Cause of trauma			
Car accident	32 (64)	22 (61.1)	10 (71.4)
Motor accident	8 (16)	6 (16.7)	2 (14.3)
Falling	7 (14)	5 (13.9)	2 (14.3)
Penetration of an objective	3 (6)	3 (8.3)	0 (0)
Surgery			
Yes	18 (36)	14 (38.9)	4 (28.6)
No	32 (64)	22 (61.1)	10 (71.4)
Rutters test score			
Less than 13	16 (32)	10 (27.8)	6 (42.9)
13 and more	34 (68)	26 (72.2)	8 (57.1)
Site of the injury			
Frontal lobe	18 (36)	13 (36.1)	5 (35.7)
Temporal lobe	17 (34)	13 (36.1)	4 (28.6)
Skull base fracture	7 (14)	4 (11.1)	3 (21.4)
other areas of the brain	8 (16)	6 (16.7)	2 (14.3)

*Data are reported as frequency (percent).

Table 3: Energy intake of the patients in comparison with the reference values.

Calorie intake	Total (50)	Boys (36)	Girls (14)
<75% of RDA	16 (32)	12 (33.3)	4 (28.6)
75-110% of RDA	18 (36)	11 (30.5)	7 (50)
>110% of RDA			

*Data are reported as frequency (percent).

Table 4: comparison of the mean energy intake, satiety hormones and Rutter test score with CT scan findings

Variable	Frontal injury	Temporal injury	Skull base fracture	Injuries of the other sites	p-value*
Energy intake (kcal/d)	1234.07± 605.93	1938.27 ±481.49	1312.54 ±280.74	1422.02 ±507.53	<0.001
Energy intake adequacy**	67.01 ±17.49	122.50 ±17.98	79.55 ±8.62	74.83 ±7.87	<0.001
Leptin (ng/ml)	6.21 ±7.80	3.35 ±5.62	2.83 ±1.36	6.5 ±7.60	0.19
Ghrelin (ng/ml)	1.84 ±2.96	5.43 ±4.67	1.88 ±1.37	1.13 ±0.49	0.006
Orexin A (pg/ml)	374.04 ±239.80	1000.87 ±751.11	472.81 ±280.68	324.11 ±129.68	0.01
Rutter test score	20.83 ± 7.47	13.47 ± 7.88	19.85 ± 9.8	14.62 ± 6.43	0.03

Note: *Data are reported as mean ± SD;**Ratio of individuals' energy intake compared to the RDA value.

Comparing energy intake and serum levels of satiety hormones in two groups of TBI children according to Rutter test score, showed that those with a higher Rutter score (which is indicative of more severe behavioral problems), had significantly lower levels of Orexin, Ghrelin and energy intake than those with lower scores (Table 5). For considering confounding factors affecting energy intake such as age, gender and surgery admission, regression modelling and univariate general linear model was performed. The results showed that energy intake sufficiency was not significantly different between girls and boys and between children who underwent surgery. Therefore sex and admission to surgery had no effect on the relationship between energy intake sufficiency and CT scan findings (Table 6). Although energy intake sufficiency was significantly different between various ages, using the regression model showed that age had no effect on the relationship between CT scan findings and energy intake sufficiency (Table 7). Also the levels of the hunger hormones ghrelin and orexin were not significantly different between girls and boys, between different ages, and between children who underwent surgery. Therefore, age, sex, and admission to surgery had no effect on the relationship between ghrelin and orexin levels with CT scan findings. Serum leptin level was not significantly different between girls and boys and between children who underwent surgery or not. Therefore sex and admission to surgery had no effect on the relationship between serum leptin level and CT scan findings. But serum leptin level was significantly different between various ages (Table 6). However, using the regression model, it was shown that age had no effect on the relationship between CT scan findings and serum leptin level (Table 7).

Table 5: Comparison of energy intake and serum levels of satiety hormones with Rutter test score.

Variable	Rutter score<13 (n=16)	Rutter score>13 (n=34)	p-value*
Energy intake (kcal/day)	1709.63 ± 691.6	1422.75 ± 521.63	0.1
Energy intake adequacy (%) **	107.71 ± 29.28	80.02 ± 24.66	0.002
Leptin (ng/ml)	2.46 ± 3.15	5.92 ± 7.38	0.15
Ghrelin (ng/ml)	4.9 ± 4.43	2.04 ± 2.96	0.03
Orexin A (pg/ml)	985 ± 666.69	408.53 ± 376.69	0.001

Note: *Data are reported as mean ± SD;**Ratio of individuals' energy intake compared to the RDA value.

Table 6: Energy intake and satiety related hormones by sex, age and admission to surgery.

	Boy	Girl	p value
	(n=36)	(n=14)	
Energy intake (kcal/d)	1622.37 ± 640.7	1237.31 ± 302.2	0.29
Leptin (ng/ml)	4.8 ± 6.78	4.87 ± 6	0.45
Ghrelin (ng/ml)	2.89 ± 3.74	3.12 ± 3.74	0.97
Orexin A (pg/ml)	576 ± 561.29	636.74 ± 547.82	0.76
	Surgery	No surgery	p value
	(n=18)	(n=32)	
Energy intake (kcal/d)	1360.23 ± 488.6	1601.36 ± 630.43	0.07
Leptin (ng/ml)	5.44 ± 7.43	4.46 ± 6.03	0.8
Ghrelin (ng/ml)	2.67 ± 3.88	3.11 ± 3.65	0.9
Orexin A (pg/ml)	498.31 ± 485.39	646.26 ± 587.71	0.6
	5-8 years	9-13 years	14-15 years	p value
	(n=23)	(n=22)	(n=5)	
Energy intake (kcal/d)	1423.48 ± 512.86	1486.83 ± 543.42	2055.44 ± 920.65	0.01
Leptin (ng/ml)	2.15 ± 4.25	7.43 ± 7.8	5.56 ± 4.7	0.005
Ghrelin (ng/ml)	4.23 ± 4.45	2 ± 2.8	1.24 ± 0.46	0.09
Orexin A (pg/ml)	873.66 ± 677.31	362.53 ± 265.48	316 ± 84.69	0.05

Note: * The data are reported as mean ± SD. **p <0.05 was considered as significant.

Table 7: Tests of Between-Subjects Effects.

	Dependent Variable	df	F	p value
CT scan* age	Energy intake sufficiency	3	0.64	0.6
CT scan* age	Leptin	3	0.44	0.72

Note: *UNIANOVA Energy intake sufficiency by CT scan with age and UNIANOVA leptin by CT scan with age;**p<0.05 was considered as significant.

DISCUSSION

Correlation of food intake and satiety related hormones with CT scan findings

The current study showed that in comparison with RDA values, calorie intake was inadequate in 32% of the patients while 32% had excess energy intake. In addition, there was a significant relationship between energy intake and the site of injury. There was also a significant relationship between serum Ghrelin and Orexin levels with the site of injury. To the best of our knowledge, this is the first study to examine the relationship between satiety/hunger hormone levels with the site of injury in children with traumatic brain injury. In a study by Pelizzo on pediatrics with neurological disorders, the results showed that daily energy intake was lower than the expected needed level in 23.8% and higher than normal in 50% of the patients [21].

Our findings also indicated that there was a significant relationship between energy intake and the affected area of brain based on CT scan findings. Energy intake in patients with temporal lobe injury, was significantly higher than in patients with injuries to other sites of brain and it was also shown that energy intake in patients with frontal lobe injury was significantly lower than in patients with injuries to other sites of brain.

In line with the results of this study, Goddard in a case report of a 25 year-old man, showed the association between glioma injury of the right frontal lobe and hypophagia or anorexia nervosa [15]. While in a case study on a 42-year-old man, Das showed a correlation between frontal lobe injury caused by a road accident with severe overeating behavior, and reported that the patient's weight increased from 78 kg to 108 kg within a year [22]. A case report by Levine on two patients also showed over eating behaviors in a patient with occipital and right temporal injury and hypophagia behaviors in a patient with encephalomalacia in temporal and right frontal [23]. Furthermore, a case report by Castano reviewed eating disorders in four patients with severe TBI, indicated hypophagia behaviors in patients with frontal lobe, thalamus and diffused axonal injuries, and overeating behaviors in patients with temporal and hypothalamus injuries [24].

The CNS regulates food intake and each region of the brain is responsible for eating behavior and appetite control. Therefore, it can be expected that brain injury can disrupt the regulation of food intake. It seems that frontal lobe injury might be associated with anorexia and hypophagia behaviors, and temporal lobe injury with over eating. The temporal lobe of the brain consists of two important parts of amygdala and hippocampus that play important roles in food intake and body weight regulation. Therefore, regulation of satiety could be impaired following temporal lobe injury, which may be an explanation for excessive food intake [16]. On the other hand, the frontal lobe is consisted of different parts, one of which is the Broca area, which controls the behavior, decision making and emotional outbursts [25]. As it was also shown in the current study, children with frontal lobe injury had a higher Rutter test score, indicating more behavioral problems in patients with damage to this site of brain. Therefore, one of the causes of anorexia in patients with frontal lobe injury might be associated with cognitive problems and depression that may lead to decreased food intake secondary to psychological impairment, especially post-traumatic depression [26].

Moreover, in the current study, the mean serum levels of Ghrelin and Orexin were significantly higher in children with temporal lobe injury than in children with frontal lobe injury, which might be another reason for higher calorie intake and better appetite in patients with temporal lobe injury. As we know Ghrelin is called a hunger hormone increasing food intake released mainly from gastrointestinal tract. It also plays a role in improving learning and memory by regulating synaptic terminals and producing synapses in the hypothalamus and hippocampus [27]. Interestingly, the ghrelin receptor is found in the basolateral complex of the amygdala, a brain region that is located in temporal lobe and play important role in regulating food intake [28]. Orexin (hypocretin) is also a neuropeptide that regulates appetite and feeding behavior. It stimulates food intake and increase the craving for food. Orexin also activates orexin neurons, monoaminergic and cholinergic neurons in the hypothalamus/brainstem regions. The activities of monoaminergic neurons are known to be associated with sleep and awakeness. Decreased levels of orexin have been shown to be related to behavioral problems as well as sleep disorders [29]. Orexin is also produced by the lateral hypothalamus and the Orexin Receptor (OX1R) is expressed in many regions of the brain, including the prefrontal cortex, which may be an explanation for loss of orexin production from neurons [30].

The results according to regression and univariate general linear modelling showed that sex and admission to surgery had no effect on the relationship between energy intake sufficiency and CT scan findings. Regarding age, after adjustment we found that age had no effect on the relationship between CT scan findings and energy intake sufficiency. Also age, sex, and admission to surgery had no effect on the relationship between ghrelin and orexin levels with CT scan findings. Regarding serum leptin level, sex and admission to surgery had no effect on the relationship between serum leptin level and CT scan findings. After adjusting for age, it was shown that it had no effect on the relationship between CT scan findings and serum leptin level. It was the first research that assessed the relationship of energy intake and satiety related hormones with CT scan findings considering confounding factors.

Correlation of food intake and satiety related hormones with psychological disorders

Our findings also demonstrated that children with frontal lobe injury had more behavioral problems and these children had significantly lower levels of Orexin and Ghrelin too. Thus children with more severe behavioral problems had significantly lower food intake. As mentioned earlier, the frontal lobe is consisted of motor and pre-motor areas and

the Broca area, which controls behavior that may be an explanation for psychological disorders following frontal lobe injury [25]. Therefore, one of the causes of decreased food intake in patients with frontal lobe injury might be due to cognitive problems and depression [26].

In a study by Fedoroff JP a significant relationship between lesions in prefrontal cortex and depression was found in the acute phase of TBI [31]. In another study in patients with TBI, the results indicated that plasma ghrelin levels were significantly lower in patients with cognitive disorders than in patients without cognitive disorders and plasma ghrelin level was an independent predictor of cognitive disorders 3 months after TBI [31].

This study had some limitations including low sample size, food recall bias, and no cooperative patients due to complicated nature of brain injury. Prospective studies with large population and follow up periods are needed to discover the gaps regarding nutritional status and its association with brain injury in different areas.

CONCLUSION

Traumatic brain injury might disrupt food intake. It seems that frontal lobe injury is associated with anorexia and hypophagia behaviors and temporal lobe injury might be associated with increased food intake. More studies are needed to investigate this relationships in detail. There is a relationship between satiety related hormones and the exact area of brain injury in these patients.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Ethics Committee of Shiraz University of Medical Sciences (No. IR.SUMS.REC.1397.708). All methods in the present study were performed in accordance with the principles of the relevant guidelines and regulations of Declaration of Helsinki, which is a statement of ethical principles that directs physicians and other participants in medical research involving human subjects. Informed consent was obtained from parents/Legal guardians of the patients involved in the study' after explaining the aim, method and goal of the study.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author upon request.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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AUTHORS' CONTRIBUTIONS

SB: design, data gathering, data analysis, preparing the manuscript. MSM: data gathering, preparing the manuscript .ME: concept, design, data analysis preparing the manuscript, and the correspondence, SE: design, data analysis preparing the manuscript. All authors have read and approved the manuscript.

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