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Evaluation of Brain Metabolites in Children With Anorexia Nervosa Using 7T Ultra-High-Field Magnetic Resonance Spectroscopy

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Daiki Kondo [1], Yasunori Wada [1], Yu Matsuo [1], Jun Ito [1], Sachiko Tanifuji [1], Maya Asami [1], Tsuyoshi Matsuda [2, 3], Manami Akasaka [1]

1. Pediatrics, Iwate Medical University, Yahaba, JPN 2. Life Sciences and Technology, Institute of Global Well-Being Science, Hirosaki University, Aomori, JPN 3. Division of Fundamental Research, Institute for Biomedical Sciences, Iwate Medical University, Yahaba, JPN

Corresponding author: Daiki Kondo, knddik0531imu@gmail.com

Abstract

Anorexia nervosa (AN) is a disorder characterized by extreme food restriction that leads to significant weight loss and malnutrition. AN has effects on the central nervous system and may be associated with reduced brain volume. Magnetic resonance spectroscopy (MRS) is a noninvasive assessment technique that measures metabolic substances in the brain and provides additional value to standard magnetic resonance imaging. MRS studies of pediatric patients with AN have been limited to 1.5T and 3T systems, and the findings have been inconsistent. Ultra-high-field 7T MRS has detected decreased levels of myoinositol (Ins) and glutamate (Glu) in adults. Our study used 7T MRS to accurately measure brain metabolites in pediatric patients with AN and compared the results with those of a normal control (NC) group. Although the children with AN were obviously malnourished, as evidenced by blood tests, chest radiography, and bone density test results, occipital creatine levels were significantly lower in the AN group; however, this difference may have been influenced by age differences between the groups. No significant differences were observed in other brain metabolites in the early stages of disease. Therefore, no clear disease-specific alterations in brain metabolites could be identified. Because brain metabolic changes may become apparent as chronic malnutrition persists, as seen in adults, prolonged malnutrition associated with AN must be prevented.

Categories: Psychiatry, Nutrition, Pediatrics
Keywords: 7 tesla, anorexia nervosa, eating disorder, magnetic resonance spectroscopy, malnutrition

Introduction

Anorexia nervosa (AN) is a disorder characterized by severe weight loss resulting from food restriction caused by an intense desire to be thin and a lack of insight regarding this condition. AN leads to malnutrition that can be severe or even fatal if left untreated. Individuals with AN exhibit various physical signs and abnormal test results. Effects on the central nervous system include brain volume reduction; however, studies of adults have shown that this can be reversed with nutritional status improvement [1,2]. The pathophysiological mechanism underlying brain volume reduction has not been fully elucidated. Although animal models suggest a link to decreased astrocyte numbers and density, no pathological reports of humans are available. Decreased cell division associated with malnutrition is considered a contributing factor; additionally, astrocyte dysfunction occurs as the condition prolongs [2,3]. Although these changes are associated with short-term cognitive impairments such as learning and memory deficits, longitudinal studies of their long-term effects are lacking; therefore, many aspects are unclear.

Magnetic resonance spectroscopy (MRS) is a noninvasive assessment technique capable of measuring metabolic substances in the brain, such as myoinositol (Ins) and glutamate (Glu). Ins and Glu are present in astrocytes and serve as indicators of their function.

Few MRS studies involving pediatric patients with AN and 1.5T or 3T scanners have been conducted, and their conclusions have been inconsistent. Ultra-high-field 7T MRS enables high-precision measurement of brain metabolites, including trace amounts that are difficult to resolve with conventional scanners. Only one study of AN that used 7T MRS and reported decreases in Glu and Ins, which are primarily found in astrocytes, is available; however, it only included adults with long illness durations, and the effects of comorbid psychiatric disorders and polypharmacy with antipsychotic medications could not be ruled out [4]. Therefore, this exploratory study aimed to evaluate brain metabolites, including N-acetylaspartate (NAA), N-acetylaspartylglutamate, Glu, glutamine (Gln), γ-aminobutyric acid (GABA), creatine (Cr), choline (Cho), Ins, and lactic acid (Lac), in the right basal ganglia, right frontal cortex, and right occipital cortex of pediatric patients with AN using 7T MRS and compare the results with those of the recruited normal control (NC) group.

Materials And Methods

Participant recruitment

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Iwate Medical University (approval no. MH2024-068). Written informed consent was obtained from all participants or their parents. The study has been reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Patients with nonspecific symptoms such as headaches or dizziness who presented to Iwate Medical University Hospital or affiliated hospitals between April 2023 and November 2025 comprised the NC group. Because recruiting healthy children solely for research MRI examinations was difficult, children with nonspecific symptoms who required MRI examinations and were considered unlikely to have apparent organic diseases were recruited as controls. At enrollment, none of the participants had a known history of neurological or psychiatric disorders or were taking medications. Participants with organic diseases identified during the initial clinical evaluation were to be excluded; however, no participants met this exclusion criterion. All eight participants who underwent 7T MRS as controls were included in the NC group. These participants were six years of age or older but younger than 18 years of age and had no history of extreme weight loss (body mass index (BMI) <14; percentage of standard body weight <65%) or AN. Informed consent for participation in this study was obtained from both the participant and parent or guardian.

Patients with AN who required treatment at our hospital between November 2024 and November 2025 comprised the study group (AN group). Informed consent to participate in this study was obtained from both the patient and parent or guardian.

AN was comprehensively diagnosed using the following criteria outlined in the guidelines for the treatment of eating disorders: body weight ⩽85% of standard body weight and a shift of ⩾1 standard deviation (SD) below the growth curve or weight loss ⩾3 kg and bradycardia or amenorrhea (excluding premenarche); a history of persistent weight loss (food avoidance, self-induced vomiting, excessive exercise, or laxative abuse); distorted perceptions of body weight and shape; and pathological preoccupation with body weight, body shape, food, or eating. A diagnosis of AN was confirmed only after blood test results and imaging findings ruled out other organic diseases.

Survey items

Physical measurements (height, weight, BMI, and percentage of standard weight) of the NC group were collected. In addition to physical measurements (height, weight, BMI, percentage of standard weight, and growth records), blood test results (complete blood count, biochemistry, endocrine markers, vitamins, and trace elements), cardiothoracic ratios, and bone density measurements of the AN group were collected. Standard weight was calculated using sex-specific first-order standard weight formulas derived from data available in the 2000 Ministry of Education, Culture, Sports, Science, and Technology School Health Statistics Survey Report in Japan (age, 5-17 years).

7T MRS protocol

MRS examinations were performed using a 7T MRI scanner (Discovery MR950; GE Healthcare, Waukesha, WI, USA) equipped with a two-channel transmit and 32-channel receive head coil (NM008-32-7GE-MR950; Nova Medical, Wilmington, MA, USA). Using the stimulated echo acquisition mode (repetition time = 6.0 seconds; echo time = 8.6 ms), regions of interest with a voxel size of 15 × 15 × 15 mm^3 in the right basal ganglia (Figure *1A*), right frontal cortex (Figure *1B*), and right occipital cortex (Figure *1C*) were defined [5]. Lac, NAA, NAAG, Glu, Gln, GABA, Cr, Cho, and Ins were quantified using LCModel (Stephen Provencher Inc., Oakville, Ontario, Canada). The Cramér-Rao lower bound (CRLB; %SD) was used to assess data reliability. Spectral analysis was performed using LCModel version 6.3-1R, with spectra fitted over the range of 0.2-4.0 ppm. The standard macromolecule spectra provided by LCModel were used, and the spline baseline constraint parameter (DKNTMN) was set to 5 [5]. Only data with a CRLB ⩽15% for each metabolite were included in the analysis. Data with a CRLB >15% were treated as missing values and excluded from the statistical analysis. This reliability threshold was established before data analysis. Regions of interest were defined by referencing those used in a previous 7T MRS study [6]. No tissue-composition correction was applied to the metabolite concentrations.

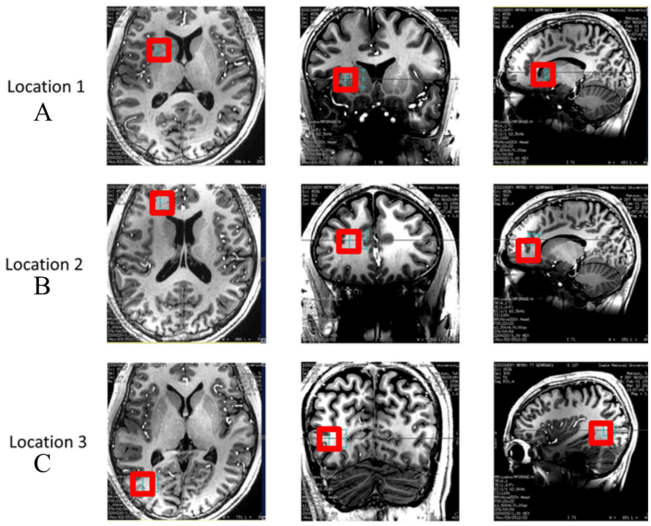


FIGURE 1: Regions of interest were defined as follows: location 1, right basal ganglia; location 2, right frontal cortex; and location 3, right occipital cortex.

Regions of interest for 7T magnetic resonance spectroscopy. (A) Right basal ganglia, (B) right frontal cortex, and (C) right occipital cortex. Axial, coronal, and sagittal images are shown for each region. Red squares indicate the regions of interest.

Statistical analysis

Data are presented as the median and interquartile range (IQR). Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 24 (Released 2016; IBM Corp., Armonk, NY, USA). Comparisons between groups were conducted using the Mann-Whitney U test, and $p < 0.05$ (two-sided) was considered significant. Because this was an exploratory study, no correction for multiple comparisons of brain metabolites across brain regions was applied. For brain metabolites that exhibited significant differences on MRS, the relationship with age was evaluated using Spearman's rank correlation coefficient to assess the bivariate association. Associations with sex were evaluated using the Mann-Whitney U test. In all cases, the significance level was set at $p < 0.05$ (two-sided).

Results

Number of case participants and physical characteristics

The number of study participants and their physical characteristics are provided in Table *1*. The AN group comprised nine participants (eight females (88.9%) and one male (11.1%)), whereas the NC group comprised eight participants (four females (50.0%) and four males (50.0%)). The AN group comprised a higher proportion of female participants. The median ages in the AN and NC groups were 12 years (IQR, 11-13.5 years) and 14 years (IQR, 13-14.8), respectively ($p = 0.036$). The median heights in the AN and NC groups were 148.4 cm (IQR, 137.9-151.8 cm) and 158.4 cm (IQR, 154.2-164.1 cm), respectively ($p = 0.006$). The median weights in the AN and NC groups were 26.1 kg (IQR, 24.4-32.3 kg) and 53.2 kg (IQR, 43.1-56.7 kg), respectively ($p = 0.001$). The median BMIs in the AN and NC groups were 13.1 (IQR, 11.7-14.8) and 19.6 (IQR, 18.1-22.2), respectively ($p < 0.001$). The median percentages of standard body weight in the AN and NC groups were 71.1% (IQR, 60.2%-80.0%) and 99.3% (IQR, 91.8%-107.2%), respectively ($p = 0.002$). These findings indicate that age in the AN group was significantly younger than that in the NC group. Additionally, they indicate that height, weight, BMI, and percentage of standard body weight in the AN group were significantly lower than those in the NC group.

Variable	AN group (n=9)	NC group (n=8)	p-value
Male, n(%)	1 (11.1%)	4 (50%)	-
Female, n(%)	8 (88.9%)	4 (50%)	-
Age, years	12 (11.0-13.5)	14 (13.0-14.8)	0.036
Height, cm	148.4 (137.9-151.8)	158.4 (154.2-164.1)	0.006
Weight, kg	26.1 (24.4-32.3)	53.2 (43.1-56.7)	0.001
BMI, kg/m^2	13.1 (11.7-14.8)	19.6 (18.1-22.2)	<0.001
Percentage of standard body weight, □	71.1 (60.2-80.0)	99.3 (91.8-107.2)	0.002
Duration of weight loss, months	10.5 (3.5-20.8)	-	-
Weight loss, %	17.8(7.9-26.7)	-	-

TABLE 1: Comparison of the AN and NC groups.

Data are presented as the median (interquartile range) unless otherwise indicated. Sex is presented as the number of participants (n) and percentage (%). Between-group comparisons were performed using the two-sided Mann-Whitney U test. A p-value < 0.05 was considered statistically significant.

AN, anorexia nervosa; BMI, body mass index; NC, normal control

In the AN group, the weight loss duration from peak weight was 10.5 months (IQR, 3.5-20.8 months), and the weight loss rate was 17.8% (IQR, 7.9%-26.7%). In the NC group, two participants were asymptomatic volunteers, two had chronic headaches, two had orthostatic dysregulation, and two had involuntary movements (one with essential tremor and one with conversion disorder). The diagnoses of essential tremor and conversion disorder were established after enrollment.

Characteristics of the AN group

Table *2* presents the test results of the AN group. We compared each median test value in the AN group with the normal reference range for children. Only the abnormal values are provided.

Variable	AN group (n=9), Median (interquartile range)	Reference range
Total cholesterol, mg/dL	214 (180.5-275.5)	<190
LDL-cholesterol, mg/dL	117 (105-210)	<110
Free T3, pg/mL	2.32 (1.39-3.26)	2.33-4.84
IGF-1 (somatomedin C), ng/mL	86.5 (44.25-132.25)	113-654
LH, mIU/mL	<0.3	0.5-6.6
FSH, mIU/mL	2.4 (0.35-3.45)	2.4-7.1
Total ketone bodies, mmol/L	0.29 (0.07-2.16)	<0.13
Acetoacetic acid, mmol/L	0.058 (0.019-0.456)	<0.055
3-hydroxybutyric acid, mmol/L	0.241 (0.035-1.700)	<0.085
Cardiothoracic ratio, %	39.2 (36.85-43.7)	50
Bone mineral density, g/cm^2	0.636 (0.521-0.828)	-
Bone mineral density (Z-score)	-3.15 (-4.06 to -1.25)	-

TABLE 2: Clinical characteristics of the AN group.

Data are presented as the median (interquartile range) unless otherwise indicated. Data were available for all nine participants in the AN group for each variable.

AN, anorexia nervosa; FSH, follicle-stimulating hormone; IGF-1, insulin-like growth factor 1; LDL, low-density lipoprotein; LH, luteinizing hormone; T3, triiodothyronine

In the AN group, total cholesterol and low-density lipoprotein cholesterol were elevated (214 mg/dL and 117 mg/dL, respectively). Free triiodothyronine (2.32 pg/mL) and somatomedin C (86.5 ng/mL) were low. Both luteinizing hormone (0.3 mIU/mL) and follicle-stimulating hormone (2.4 mIU/mL) were low and within the prepubertal range. Total ketone (0.29 mmol/L), acetoacetate (0.06 mmol/L), and 3-hydroxybutyrate (0.241 mmol/L) levels were elevated. The cardiothoracic ratio indicated by radiography was reduced (39.2%). Bone mineral density was 0.636 g/cm^2, with a median Z-score of -3.15, which indicated a marked decrease compared with that of peers of the same age. These findings were consistent with laboratory test abnormalities and imaging findings of previously reported patients with AN and malnutrition.

7T MRS results

Table *3* shows the 7T MRS results of the AN and NC groups. The number of valid measurements for each metabolite in each brain region is presented in Table *3*. In one patient in the AN group, the examination was discontinued after imaging of the basal ganglia; therefore, data from the frontal and occipital cortices were not obtained. Measurements with %SD values exceeding 15% were excluded from the analysis. Among the acquired measurements, the numbers of excluded metabolite measurements in the basal ganglia, frontal cortex, and occipital cortex were 14/81 (17.3%), 17/72 (23.6%), and 20/72 (27.8%) in the AN group and 12/72 (16.7%), 23/72 (31.9%), and 22/72 (30.6%) in the NC group, respectively. No significant differences in any of the striatum parameters were observed between groups. Because of the high number of missing Lac values, a precise statistical test could not be performed. No significant differences in any of the frontal lobe parameters were observed between groups. Because of the high number of missing Gln, Lac, and Cr measurements, reliable statistical interpretation was limited. Occipital lobe Cr in the AN group was significantly lower than that in the NC group (3.069 mmol/kg wet weight (IQR, 2.881-3.801) vs. 5.186 mmol/kg wet weight (IQR, 4.115-5.623)); p = 0.006 (Figure *2*).

Location	Metabolites	AN group	NC group	U statistic	p-value
Basal ganglia (Location 1; Figure 1A)	GABA	2.424 (2.161-2.662), n=8	2.585 (2.183-2.884), n=8	22	0.758
	NAA	5.951 (4.244-6.319), n=9	6.245 (4.979-6.827), n=8	27	0.423
	NAAG	2.848 (1.849-3.17), n=6	2.494 (1.946-2.611), n=5	8	0.243
	Glu	7.63 (7.287-7.842), n=9	7.747 (6.757-8.068), n=8	34	0.888
	Gln	2.434 (1.923-2.791), n=9	2.45 (2.114-2.889), n=7	28	0.758
	Lac	n=0	1.531(1.531-1.531), n=1	-	-
	Ins	3.4845 (2.942-4.04), n=8	3.735 (3.474-4.416), n=8	23	0.382
	Cho	1.639 (1.47-1.734), n=9	1.521 (1.358-1.592), n=8	23	0.236
	Cr	6.171 (5.461-6.581), n=9	5.934 (5.827-6.308), n=7	30	0.918
Frontal cortex (Location 2; Figure 1B)	GABA	1.577 (1.276-1.78), n=6	1.63 (1.261-2.278), n=7	16	0.534
	NAA	6.52 (6.272-6.830), n=8	7.232 (6.316-8.337), n=8	27	0.382
	NAAG	1.095 (0.979-2.225), n=5	2.074 (1.269-3.566), n=4	8	0.413
	Glu	6.251 (5.771-6.554), n=8	6.16 (5.881-6.904), n=8	29	0.798
	Gln	1.791 (1.48-2.001), n=5	1.636 (1.636-1.636), n=1	2	1
	Lac	n=0	2.369 (2.369-2.369), n=1	-	-
	Ins	4.62 (4.127-5.931), n=8	5.202 (4.288-5.854), n=8	27	0.645
	Cho	1.853 (1.557-2.107), n=8	1.769 (1.396-1.863), n=8	22	0.328
	Cr	4.588 (3.745-5.268), n=7	4.705 (4.306-4.898), n=4	14	1
Occipital cortex (Location 3; Figure 1C)	GABA	1.401 (1.321-1.638), n=7	1.464 (1.441-2.092), n=5	10	0.268
	NAA	7.536 (7.190-8.342), n=8	6.89 (5.922-7.894), n=8	19	0.195
	NAAG	3.233 (2.274-3.793), n=5	1.655 (1.436-2.087), n=5	3	0.056
	Glu	5.501 (5.084-6.359), n=8	6.162 (4.914-7.181), n=8	27	0.645
	Gln	1.742 (1.742-1.742), n=1	n=0	-	-
	Lac	n=0	n=0	-	-
	Ins	4.803 (4.324-5.074), n=8	5.074 (4.461-5.747), n=8	19	0.195
	Cho	1.734 (1.400-1.946), n=8	1.602 (1.361-1.870), n=8	26	0.574
	Cr	3.069 (2.881-3.801), n=7	5.186 (4.115-5.623), n=8	5	0.006

TABLE 3: Comparison of brain metabolite concentrations in each region in the AN and NC groups.

Data are presented as the median (interquartile range), with the number of valid measurements (n) shown for each metabolite.

Measurements with %SD values exceeding 15% were excluded from the analysis. In one patient in the AN group, data from the frontal and occipital cortices were not obtained because the examination was discontinued.

AN, anorexia nervosa; Cho, choline; Cr, creatine; GABA, γ-aminobutyric acid; Glu, glutamate; Gln, glutamine; Ins, myoinositol; Lac, lactic acid; NAA, N-acetylaspartate; NAAG, N-acetylaspartylglutamate; NC, normal control

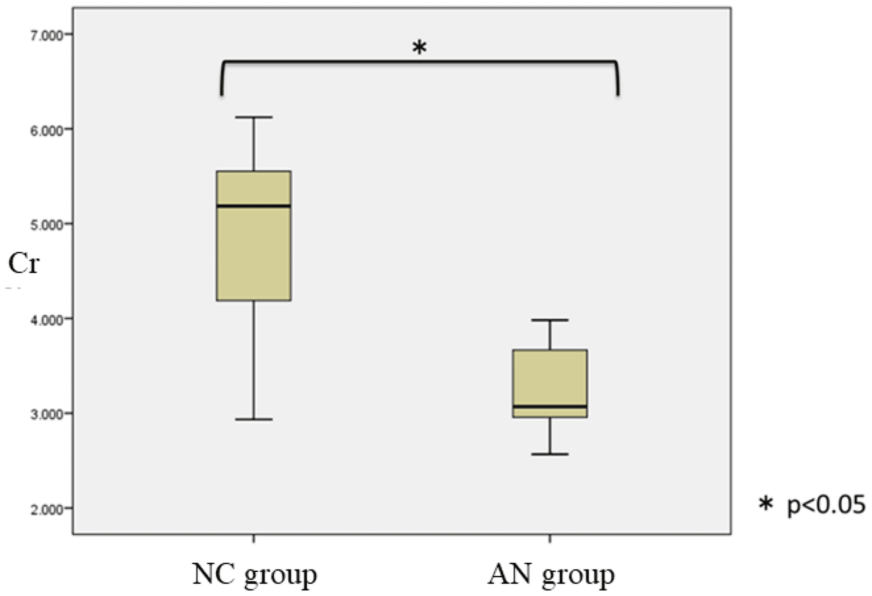


FIGURE 2: A significant difference in occipital lobe creatine (Cr) was observed in the normal control (NC) and anorexia nervosa (AN) groups.

Comparison of occipital creatine (Cr) concentrations between the anorexia nervosa (AN) and normal control (NC) groups. Boxes represent the interquartile range, horizontal lines indicate the median, and whiskers represent the most extreme values within 1.5 times the interquartile range from the first and third quartiles. The groups were compared using the two-sided Mann-Whitney U test (U = 5, p = 0.006). A p-value < 0.05 was considered statistically significant. AN group, n = 7; NC group, n = 8.

However, the values of two female participants in the AN group were missing. No significant differences in any other parameters were observed between groups. Because of the high number of missing Gln and Lac measurements, reliable statistical comparisons could not be performed for these metabolites.

Regarding Cr in the occipital lobe, where a significant difference was observed, significant differences in sex and age were found between groups; therefore, we analyzed the bivariate relationships between occipital lobe Cr and sex and age. Subsequently, a significant correlation between occipital lobe Cr and age was observed ($\rho = 0.625$; $p = 0.01$) (Figure *3*); however, no significant correlation between occipital lobe Cr and sex was observed (Figure *4*).

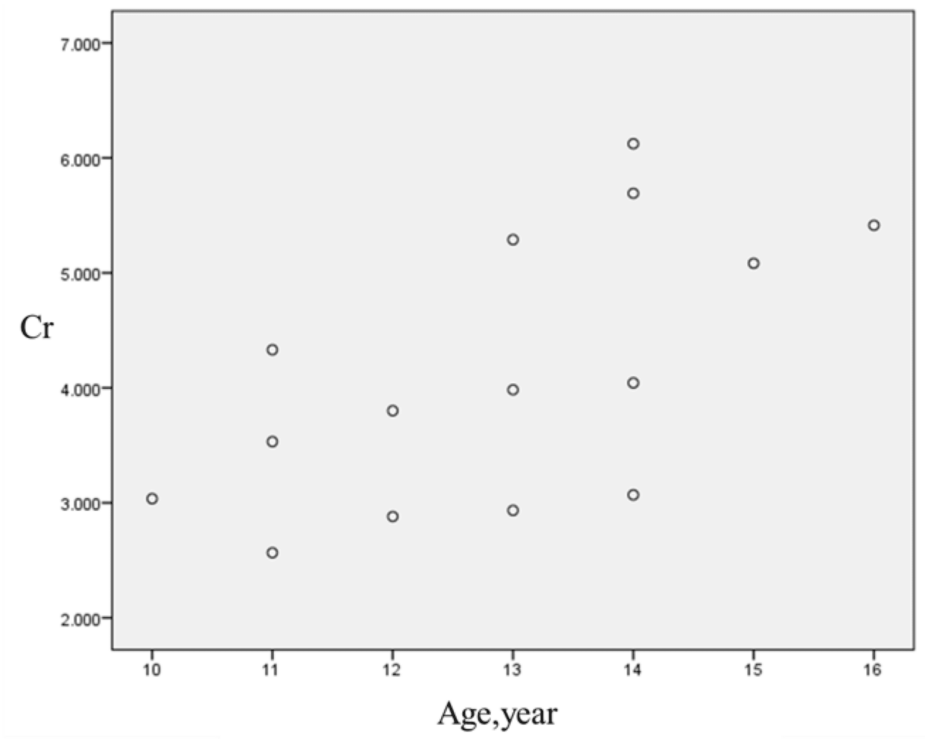


FIGURE 3: A significant correlation between occipital lobe creatine (Cr) and age was observed.

The association between age and occipital creatine (Cr) concentration was evaluated using Spearman's rank correlation coefficient (ρ = 0.625, p = 0.010). A p-value < 0.05 was considered statistically significant (n = 15).

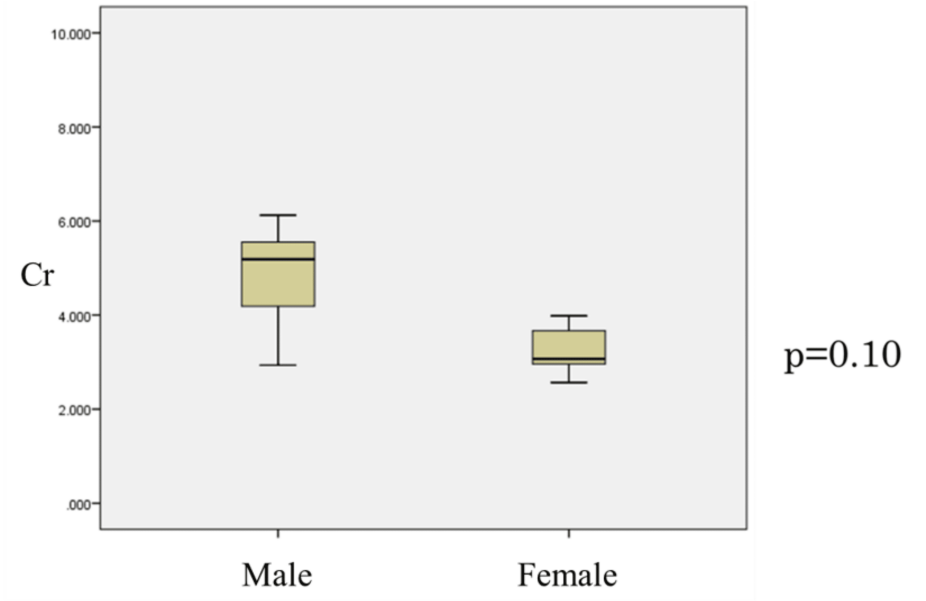


FIGURE 4: No statistically significant difference between sex and occipital lobe creatine (Cr) was observed.

Box plots show the distribution of occipital creatine (Cr) concentrations by sex. The horizontal lines within the boxes indicate the median, and the boxes represent the interquartile range (IQR). Whiskers represent the most extreme values within 1.5 times the interquartile range from the first and third quartiles. Differences between sexes were assessed using the two-sided Mann-Whitney U test (U = 11, p = 0.10). A p-value < 0.05 was considered statistically significant. Male, n = 5; female, n = 10.

Discussion

To the best of our knowledge, this study is the first to use 7T MRS to evaluate brain metabolites in pediatric patients with AN. Given the small sample size, this study should be regarded as an exploratory investigation, and the findings should be interpreted with caution. The study population comprised participants who were not using any oral antipsychotic medications and had a short illness duration (10.5 months; IQR, 3.5-20.8 months). Therefore, the potential effects of chronic malnutrition and pharmacological treatment were minimized.

Group comparisons indicated that only occipital lobe Cr was significantly lower in the AN group without correction for multiple comparisons. Because significant differences in age and sex were observed between groups, we evaluated the relationship between occipital lobe Cr and age and sex and found that Cr tended to increase with age, whereas no statistically significant association with sex was detected. Therefore, determining whether lower occipital Cr observed in the AN group reflected disease-specific changes or residual confounding attributable to age differences between groups was not possible. These results suggest that low occipital Cr in the AN group may have been influenced by age differences between groups. Several previous studies of the relationship between Cr observed on MRS and age have been reported. A study conducted at our hospital found that Cr increased rapidly during infancy [6]. Other literature indicated that Cr continues to increase from approximately 5 to 10 years of age [7,8] and remains relatively stable after puberty [8]. Studies that included various age groups also reported age-related increases in Cr. One study reported that the rate of increase in Cr during childhood and adolescence is faster than that during adulthood [9]. These changes reflect developmental changes in energy metabolism and neural activity within the brain. Because of the limited sample size, multivariable analyses simultaneously adjusted for age and sex were attempted but yielded unstable results; therefore, they were not considered statistically reliable. Consequently, residual confounding cannot be completely excluded.

Regarding the relationship between Cr and sex, a study of children 6 to 15 years of age that compared metabolites in seven brain regions reported no significant differences in Cr between sexes [10]. However, because of the small sample size and differences in sex distribution between the AN and NC groups, the potential influence of sex on occipital Cr levels cannot be completely excluded.

Based on the aforementioned findings, Cr in MRS studies may be influenced by age during not only infancy but also childhood through adolescence. This study supports this inference. Although many studies reported data based on Cr as an internal marker during adulthood, when Cr levels stabilize, age should be considered when evaluating the ratios of brain metabolites using Cr as an internal standard from infancy through adolescence.

In the present study, no significant differences in brain metabolites (other than occipital lobe Cr) were observed between groups. These results suggest that malnutrition caused by AN may not cause significant changes in metabolites, including NAA (a marker of neuronal activity), Ins (associated with astrocyte numbers), and Gln (an indicator of astrocyte function), during the early stages of disease. In the AN group, a significant decrease in BMI was observed and blood tests revealed results reflective of malnutrition, such as elevated total cholesterol, low free triiodothyronine, low somatomedin C, and elevated ketone bodies. Additionally, reduced bone density and a decreased cardiothoracic ratio were confirmed. Nevertheless, no clear differences in brain metabolites were observed; therefore, significant changes in brain metabolites may not be present during the early stages of AN. Although brain volume was not directly measured in this study, animal studies have suggested that reduced astrocytes may contribute to brain volume loss. However, whether a similar mechanism exists in humans is unclear.

Furthermore, decreased Glu and Ins have been observed in studies of adults with AN (mean age, 29.1 years (range, 18-41 years); mean illness duration, 12.7 years (range, 3-26 years)) [4]. These findings raise the possibility that prolonged malnutrition may be associated with changes in brain metabolism; however, this hypothesis requires further investigation in longitudinal studies.

In this study, the median duration of weight loss was 10.5 months (IQR, 3.5-20.8 months). However, the specific time when changes in brain metabolites become apparent is unclear. Nevertheless, early improvement of nutritional status may be important, although the effects of nutritional recovery on brain metabolites could not be evaluated in this study.

This study had some limitations. This was an exploratory study with a small sample size. Significant differences in age and sex between the AN and NC groups existed. Therefore, the observed difference in occipital Cr should be considered a preliminary finding that requires confirmation in larger studies. In addition, the significant difference in height between the groups may reflect differences in growth and developmental stage, as well as the effects of malnutrition. These differences in baseline characteristics may have influenced cerebral metabolite concentrations. Because tissue-composition correction was not performed, differences in gray matter, white matter, and cerebrospinal fluid fractions within the voxels may have influenced the measured metabolite concentrations. Furthermore, some measurements were excluded because their %SD values exceeded 15%, and data from the frontal and occipital cortices were not obtained in one patient in the AN group. Because the number of valid measurements differed depending on the brain

region and metabolite, the possibility that missing data influenced the results cannot be completely excluded. The control group included children with nonspecific symptoms; therefore, it may not represent a strictly healthy population. Furthermore, the possibility that underlying conditions in the control group may have influenced brain metabolite concentrations cannot be excluded. Because exploratory comparisons of a large number of brain metabolites across multiple brain regions were conducted without correction for multiple comparisons, the possibility of statistically significant differences attributable to chance cannot be completely ruled out. Furthermore, because this was a cross-sectional study, changes in brain metabolites over time associated with prolonged disease duration or improvements in the nutritional status could not be evaluated. Future research should include large-scale validation studies and longitudinal studies before and after nutritional recovery to clarify the temporal progression of changes in brain metabolites. Longitudinal studies that include evaluations of patients before and after nutritional recovery are necessary to determine whether metabolic alterations emerge as malnutrition becomes chronic, as well as whether such changes are reversible following treatment.

Conclusions

This study used 7T MRS to evaluate brain metabolites in pediatric patients with AN and found that occipital lobe Cr levels were significantly lower in the AN group than in the recruited NC group. However, no statistically significant differences were detected in most measured metabolites. Because of the small sample size, limited statistical power, missing measurements, and differences in age and other baseline characteristics between groups, definitive conclusions regarding disease-specific changes could not be drawn. The observed association between age and occipital Cr should also be considered preliminary. Metabolic changes may emerge with prolonged illness, but this hypothesis requires investigation in longitudinal studies. Further studies with larger sample sizes and appropriately matched healthy controls are necessary to clarify the effects of AN on brain metabolites in children and adolescents.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Daiki Kondo, Jun Ito, Manami Akasaka, Yasunori Wada

Acquisition, analysis, or interpretation of data: Daiki Kondo, Manami Akasaka, Yu Matsuo, Sachiko Tanifuji, Tsuyoshi Matsuda, Maya Asami

Drafting of the manuscript: Daiki Kondo, Tsuyoshi Matsuda

Critical review of the manuscript for important intellectual content: Jun Ito, Manami Akasaka, Yasunori Wada, Yu Matsuo, Sachiko Tanifuji, Tsuyoshi Matsuda, Maya Asami

Supervision: Jun Ito, Manami Akasaka, Yasunori Wada, Sachiko Tanifuji, Maya Asami

Disclosures

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