Original article

Effect of skipping breakfast on cerebral blood flow and cardiovascular function under a mental load in healthy female students

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Summary. This study aimed to investigate the influence of skipping breakfast on the performance of a mental arithmetic load from the physiological viewpoint. In 16 healthy female university students who habitually eat breakfast, cerebral blood flow measured (CBF) by near-infrared spectroscopy, blood glucose, ketone bodies, autonomic nerve activity measured by electrocardiography, and energy expenditure measured by indirect calorimetry were monitored during a mental arithmetic load after eating and not eating breakfast, and cross-over evaluations were performed. The number of correct answers given to the arithmetic test; the levels of blood glucose, energy expenditure, and respiratory quotient; and the changes in deoxyhemoglobin in the CBF were significantly lower on the day breakfast was eaten than not eaten ($p<0.05$). In contrast, significant increases in ketone bodies, parasympathetic nervous system activity, and changes in the tissue oxygenation index in CBF were observed during the arithmetic test on the day breakfast was not eaten than eaten ($p<0.05$). Poorer performance, low levels of deoxyhemoglobin, and high levels of tissue oxygenation index in CBF were observed during mental loads in the students who skipped breakfast. This study suggested that physiologically, skipping breakfast may cause problems in academic performance.

Keywords: skip breakfast, mental loads, cerebral blood flow, sympathetic activity, energy expenditure, NIRS.

Introduction

Several studies have indicated that skipping breakfast causes problems such as poor academic performance among students (1,2), and randomized controlled trials have shown positive effects on the attendance rates of schoolchildren who eat breakfast (3,4). Beneficial effects of breakfast on aspects of memory have also been observed in experimental studies (5-7). Several studies have attempted to identify the mechanisms by which nutritional factors influence study function or performance (8-11). Both academic performance and questionnaires are usually assessed when investigating the relationship between breakfast and schoolwork. To our knowledge, few reports (11) have investigated this relationship with physiological experiments, and thus, the mechanism remains insufficiently identified. Some reports investigated cerebral blood flow in response to hunger and satiety at rest as measured with positron emission tomography (PET) or magnetic resonance imaging (12,13). Fasting increased cerebral blood flow at rest in both reports (12,13). To our knowledge, however, no reports have investigated cerebral blood flow in response to hunger and satiety in physiological experiments.

The aim of this study was to investigate the influence of skipping breakfast on study performance by measurement of cerebral blood flow with near-infrared spectroscopy (NIRS) and cardiovascular function with the electrocardiogram (ECG).

Materials and Methods

Subjects

The subjects recruited for this experimental study were university students who ate breakfast every day. The eligibility criteria for entry to the study were 1) age between 18 and 24 years old, 2) body mass index between 18.5 and 25 kg/m^2, 3) physically and psychiatrically healthy (no cardiovascular diseases, no diabetes, no metabolic diseases, and no orthopedic limitations), 4) did not smoke, and 5) routinely ate breakfast every day. A questionnaire survey was performed beforehand, and women who responded that they routinely ate breakfast every day were included as study subjects. We defined always eating breakfast as 1) breakfast was the first meal of the day and was eaten from 5:30 am to 9:30 am; 2) the breakfast had an energy content of at least 20% of daily energy needs; 3) the breakfast included not only drink but also chewable food; and 4) breakfast was eaten every day including holidays.

Sixteen female university student volunteers (mean age, 20.9 years, standard deviation [SD] 0.79) from a university in Aichi, Japan participated in this study. About 30% of young Japanese men do not eat breakfast. Also, even though people say that they eat breakfast, many men only drink liquids such as milk, the energy content providing their daily energy needs is low, or breakfast is not eaten seven times per week (14). Therefore, we enrolled only female subjects who clearly ate breakfast according to the above four conditions.

The Ethics Committee of the Aichi Gakusen University School of Home Economics approved this study (approval no. 200701). This study was performed from January 10, 2009 to February 25, 2012. All subjects were provided detailed information on the experiment, and they gave us written informed consent. This study was conducted in accordance with the Declaration of Helsinki.

The subjects' heights were measured by a stadiometer, and weights were measured by a body weight scale. Menstrual cycles in the females were investigated via basal temperature and diary before the study. To avoid any influence of the menstrual cycle on the measurements, we ensured that none of the subjects were menstruating and as much as possible were in the luteal phase. All subjects performed the test with an interval of about 28 days between the eat-/skip-breakfast day to the skip-/eat-breakfast day. The order of eating or skipping breakfast was determined by random assignment. All subjects refrained from drinking alcohol on the night prior to the experiment. They were also asked not to bathe or exercise before the experimental day. Then, all subjects ate the same dinner and performed a trial of the mental load examination from 8:00 pm to 8:30 pm at home on the day before the experimental day regardless of whether it was an eat-breakfast day or skip-breakfast day. The dinner was composed of rice, boiled fish, braised potatoes, carrots, onion, meat, seaweed soup, and an orange. The total calorie count was 650 kcal for the females, and the calorie ratio of protein (P), fat (F), and carbohydrate (C) (P:F:C calorie ratio [%]) was P:F:C = 18:23:59. An identical breakfast of 500 kcal was prepared that consisted of cornflakes, milk, meatballs, salad, and seaweed soup, with a P:F:C ratio = 14:23:63. These energy values and P:F:C calorie ratios were based on *The Dietary Reference Intakes for Japanese (2010, 2015* (15,16), which reported the daily energy value to be 1750 kcal in 20-year-old women. The total calorie count of meals on one day for breakfast (B):lunch (L):dinner (D) was B:L:D = 500:600:650 kcal in this study.

The subjects slept at home and woke up 120 min before the examination. They were also asked whether their sleep times lasted for 8 h. The breakfast was eaten at home 90 min before the mental load examination on the eat-breakfast day. The subjects recorded their sleep duration and wakeup time and provided this information in a questionnaire answered before the examination. The subjects also submitted a picture of the examination breakfast they ate that was checked by the researchers. Then the subjects were taken to the experimental room in the university and were allowed to rest for 30 min before the test.

Mental Load Examination

A mental arithmetic test was used in our study because, to our knowledge, it has often been used in reports assessing cardiovascular function (17). The mental arithmetic included the repeated subtraction of the same number within a given time. The 15-min test involved the serial subtraction of 17 from 8500, i.e., 8500 minus 17, 8483 minus 17, 8466 minus 17, and so on (13). The subjects were encouraged to hurry by the supervisor before the test period began. The examination was given on a PC monitor. The mental arithmetic test used to provoke changes in blood pressure or pulse is often performed as a paper test (18,19). However, the arithmetic in this study was performed without the aid of paper because inaccurate cerebral blood flow is measured when a paper test is performed; when the subject looks down, the cerebral blood flow value can become unstable (20). When the subjects answered the question, the correct or incorrect answer was shown on the monitor, as were the total number of answers, correct answers, incorrect answers, and rate of correct answers (%).

This examination was conducted 2 h after the subjects had woken up (start time: from 8:00 am to 9:30 am). After the initial 30-min rest period, the subjects were fitted with devices to measure ECG, NIRS, and energy expenditure (EE) and then instructed to rest for 15 min before starting the test. The rate of correct answers to the arithmetic test was compared between the eat-breakfast day and skip-breakfast day.

Indicators of Physical Activity

Cerebral blood flow, cardiovascular function (heart rate [HR] and autonomic nerve activity), and EE of the subjects were monitored during the mental load examination. Blood glucose and ketone body levels were also measured just before the arithmetic test.

The hemoglobin level monitored from each subjects' forehead was used as the indicator of cerebral blood flow. A two-channel NIRS system (NIRO-200; Hamamatsu Photonics KK, Hamamatsu City, Japan) was used to measure the hemoglobin level (21). The device shows the monitored oxyhemoglobin level (HbO_2), deoxyhemoglobin level (Hb), total hemoglobin level (tHb, sum of HbO_2 and Hb), and tissue oxygenation index (TOI [%]), which can be expressed as HbO_2 / (HbO_2 + Hb) * 100 (22-24). The device's sensors were attached to the right and left sides the subjects' forehead (25). Measurement of the hemoglobin level was conducted automatically every 4 seconds. Changes in the HbO_2level (ΔHbO_2), which is an indicator of changes in cerebral blood flow associated with the arithmetic test, were calculated as the value of the hemoglobin level measured during the 10-min arithmetic test subtracted by the value of the hemoglobin level measured during the 15-min rest time prior to the test.

Each subject's ECG was recorded during the examination to assess HRs. Sympathetic nerve activity as assessed by the ECG was used an indicator of cardiovascular function: the ratio of the low-frequency (0.04-0.15 Hz) component (LF) to the high-frequency (0.15-0.40 Hz) component (HF) of the RR interval (LF/HF) indicates sympathetic nerve activity (26). A TM 2425-ECG multi-biomedical recorder (A&D Co. Ltd., Tokyo, Japan) was used for this measurement (27). This recorder automatically analyzed LF, HF, and LF/HF for determination of HR variability between the rest and the examination conditions. Changes in LF/HF (ΔLF/HF), which is an indicator of the change in sympathetic nerve activity caused by performance of the arithmetic test, were calculated as the value of LF/HF measured during the 10-min arithmetic test subtracted by the value of LF/HF measured during the 15-min rest time prior to the test. ΔHF was calculated as the value of the HF component of the RR interval, which indicates parasympathetic nerve activity (25-28).

EE during the examination was measured each minute and was expressed as the adjusted oxygen uptake per minute volume according to body weight (29). The oxygen and carbon dioxide uptake per minute volume, which was determined from exhaled air captured from the mouth and nose of each subject, was measured using an AE310SRC calorimeter (MINATO Medical Science, Ltd., Osaka, Japan) (30). The respiratory quotient (RQ) was also calculated with an AE310SRC calorimeter. Finger blood glucose concentrations were measured with a Glutest Pro R glucose test meter (Arkray Inc., Japan) (31). Ketone body concentrations in finger blood were measured with a ketone body test meter, the Precision EQ seed (Abbot Global Inc., Japan) (32). The change in EE (ΔEE) per minute per kilogram during the arithmetic test was calculated as the value of EE measured during the 10-min arithmetic test subtracted by the value of EE measured during the 15-min rest time prior to the test.

Table 1. Characteristics of the Study Subjects

	All subjects	
Number	16	
Age (years)	20.9(0.78)	
Height (cm)	158.8(4.55)	
Weight (kg)	51.6(7.26)	
Body mass index (kg/m^2)	20.4(2.47)	
	Skip-breakfast day	**Eat-breakfast day**
Body temperature	35.8(0.7)	36.3(0.1)
Blood glucose value (mg/dL)	77.0(7.7)	97.1(18.5)
Blood ketone body value (mg/dL)	0.15(0.1)	0.08(0.0)

Before this study, all subjects habitually ate breakfast everyday. Values are shoen as mean and standard deviation. Differences between the two groups were tested by Student t-test. *; A p value of less than 0.05 was accepted as statistically significant. The test was run from 8:00 am to 9:30 am.

Statistical analysis

The target sample size was 16 for a single group. This would provide at least 80% power with a two-day (eat-breakfast day and skip-breakfast day) significance level of α= 0.05. Data are presented as the mean ± SD for HR, LF/HF, HF, LF, RQ, EE, and answers and as the mean ± SE for cerebral blood flow. Differences between the two groups (eat-breakfast day and skip-breakfast day) were tested by paired Student *t*-test. A *p* value <0.05 was accepted as statistically significant. IBM SPSS statistics 22 for Windows (IBM Japan Inc., Tokyo, Japan) was used for the statistical analyses.

Results

The characteristics of the subjects are presented in Table 1, which shows the mean height and body weight and the body mass index (kg/m^2) calculated. The number of answers given during the arithmetic tests and the rate of correct answers are shown in Figure 1. The mean number of answers to the test was 66.5 (SD 30.7) on the skip-breakfast day and 83.1 (SD 31.1) on the eat-breakfast day, and the difference between them was statistically significant (p=0.04). However, the rates of correct answers were not significantly different: 98.7% (SD 2.49) for the skip-breakfast test and 99.4% (SD 0.80) for the eat-breakfast test.

Table 1 also shows the levels of blood glucose, blood ketone bodies, and body temperature. The blood glucose level measured just before the test on the skip-breakfast day was significantly lower than that on the eat-breakfast day (p=0.001). The blood ketone body level on the skip-breakfast day was significantly higher than that on the eat-breakfast day (p=0.02).

The hemoglobin levels are summarized in Figure 2. The mean ΔHbO_2 measured at the forehead was not significantly different between the skip-breakfast day and the eat-breakfast day. The mean ΔHb values measured at the left-side forehead and right-side forehead in the test on the skip-breakfast day were both significantly lower than those on the eat-breakfast day (both, p=0.01). The mean ΔtHb values were not significantly different between the skip-breakfast day and the eat-breakfast day.

Changes in the TOI (ΔTOI) at the left-side forehead in the test on the skip-breakfast day was sig-

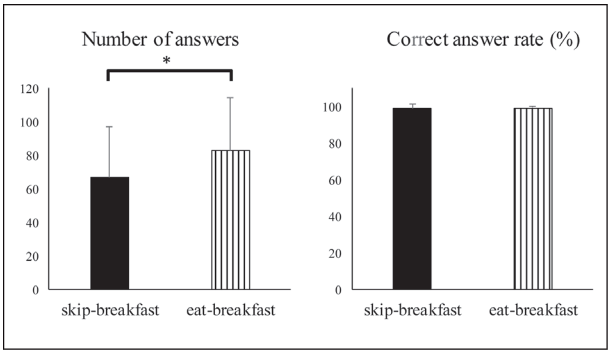

Figure 1. Comparison of the number of answers to an arithmetic test between the skip-breakfast day and eat-breakfast day. Boxes and bars indicate the mean and standard deviation, respectively. Differences between the two groups were tested by Student *t*-test. A *p* value <0.05 was accepted as statistically significant.

nificantly higher than that on the eat-breakfast day (p=0.001). The mean ΔTOI measured at the right-side forehead on the skip-breakfast day was higher than that on the eat-breakfast day, but the difference was not statistically significant (p=0.39).

Figure 3 shows cardiovascular function as assessed by the ECG. The HRs at rest and during mental arithmetic on the skip-breakfast day were significantly lower than those on the eat-breakfast day (p=0.04).

The LF and HF during mental arithmetic on the skip-breakfast day were significantly higher than those on the eat-breakfast day (p=0.02, p=0.03, respectively). The LF reflected influences of both the sympathetic and parasympathetic nervous systems (33). The ΔLF value measured during the test on the skip-breakfast day was significantly higher than that on the eat-breakfast day (p=0.04). ΔHF reflected the parasympathetic nervous system activity in this study. The ΔHF value measured during the test on the skip-breakfast day was significantly higher than that on the eat-breakfast day (p=0.03). The ΔLF/HF indicated sympathetic nervous system activity, but no statistically significant difference was observed in this value between the two days.

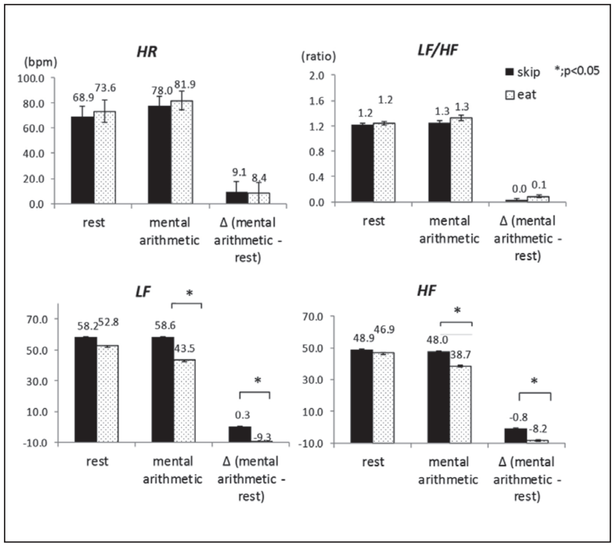

Figure 3. Comparison of the changes in heart rates (HR), sympathetic nerve activity (ΔLF/HF), and parasympathetic nerve activity (ΔHF) during performance of an arithmetic test between the skip-breakfast day and eat-breakfast day. Boxes and bars indicate the mean and standard error, respectively. Differences between the two groups were tested by Student t-test. A p value <0.05 was accepted as statistically significant.

The mean EE at rest and during the arithmetic test on the skip-breakfast day were significantly lower than that on the eat-breakfast day (both, p=0.01) (Figure 4). However, the mean ΔEE was not significantly different between the skip-breakfast day and

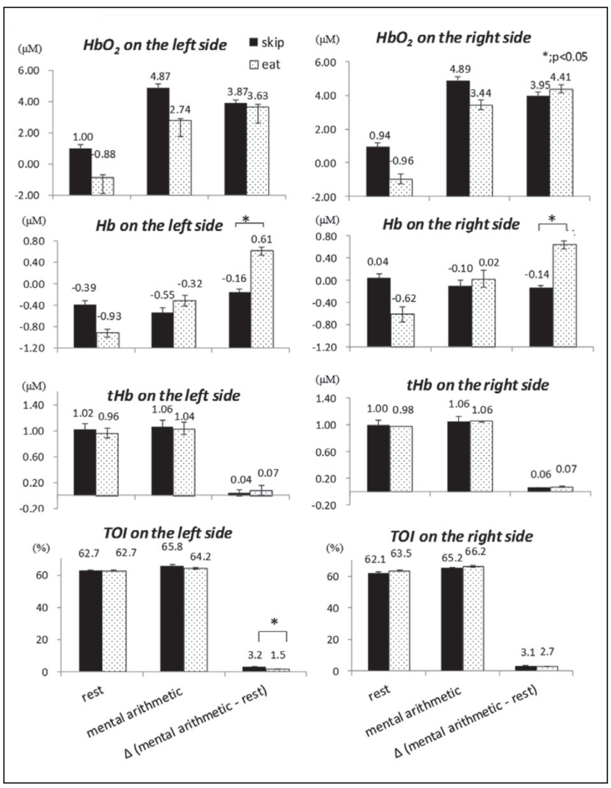

Figure 2. Hemoglobin concentration in the portal area measured by 2-channel NIRS. Boxes and bars indicate the mean and standard error, respectively. Differences in the two groups were tested by Student t-test. A p value <0.05 was accepted as statistically significant.

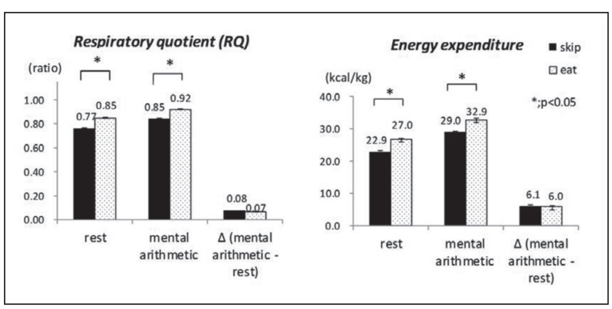

Figure 4. Comparison of the changes in energy expenditure (EE) and respiratory quotient (RQ) between the skip-breakfast day and eat-breakfast day. Boxes and bars indicate the mean and standard error, respectively. Differences between the two groups were tested by Student t-test. A p value <0.05 was accepted as statistically significant.

eat-breakfast day. The RQ levels at rest and during the arithmetic test were significantly lower than those on the eat-breakfast day (both, p=0.0001), but the ΔRQ was not significantly different between the examined groups (Figure 4).

Discussion

The aim of this study was to investigate the influence of skipping breakfast on study performance (mental arithmetic test) from ECG and cerebral blood flow data in crossover evaluations of female university students who eat habitually breakfast between the day they ate breakfast and the day they skipped breakfast. The number of correct answers given to the arithmetic test; the levels of blood glucose, EE, and RQ; and the changes in deoxyhemoglobin in the cerebral blood flow were significantly lower on the day breakfast was eaten than not eaten. In contrast, significant increases in ketone bodies, parasympathetic nervous system activity, and changes in the TOI in cerebral blood flow were observed during the arithmetic test on the day breakfast was not eaten rather than eaten.

Several studies have described the negative influence of omitting breakfast on academic performance or cognitive function (1-11). Politt et al. reported that diminished speed and accuracy on memorization tests for visual and auditory short memory, recognition memory, and spatial memory were observed among children who omitted breakfast (33). In the present study, the rate of correct answers to the arithmetic test among the students who skipped breakfast was lower than that of the students who habitually ate breakfast. This result was consistent with that of prior studies.

When cerebral blood flow at rest was investigated, Tataranni et al. found that hunger was associated with significantly increased cerebral blood flow in the vicinity of the hypothalamus and insular cortex and also in the paralimbic and limbic areas, thalamus, caudate, precuneus, putamen, and cerebellum as measured with PET (12). They noted in their report that their PET scanner could not measure cerebral blood flow during the performance of a systematic mental activity (12). The PET scanner could not discern any difference during the test. A change in the hemoglobin level indicates a change in blood flow (34). We monitored the change in hemoglobin level by NIRS at the subjects' forehead during the performance of a systematic mental activity. The forehead is nearest to Brodmann area 10 in the prefrontal area of the brain, which is activated by the performance of arithmetic tasks (35). There are three indicators of the change in hemoglobin level. It has been shown that HbO_2 is increased by arithmetic or cognitive tasks, and Hb is decreased by such tasks (36-39). We compared the changes in HbO_2 and Hb levels between the students who skipped and those who ate breakfast in a crossover test. Although statistical significance was not achieved, our study showed that the change in HbO_2 level was higher on the skip-breakfast day than on the eat-breakfast day. The change in Hb level was, however, significantly lower on the skip-breakfast day than on the eat-breakfast day. Also, the mean tHb changed only negligibly regardless of whether breakfast was eaten or skipped. The TOI was significantly higher on the skip-breakfast day than on the eat-breakfast day. These findings suggested that eating or skipping breakfast does not influence cerebral blood flow in terms of a change in oxygen expenditure during an arithmetic task and that the oxygen in the HbO_2 was not adequately used on the skip-breakfast day compared to the eat-breakfast day.

These results reflect the possibility that breakfast consumption may be related to cerebral activity. NIRS has been shown to be a feasible method with which to measure hemodynamic response and cerebral blood flow in the superficial cortex (40). Also, NIRS could sensitively measure changes in cerebral oxygenation following the administration of pharmacological agents (40).

To date, however, only a small number of studies have assessed the cerebral hemodynamic effects of dietary components, and the majority of these have only collected data from the prefrontal cortex (41,42). Thus, further studies are needed to clarify this relation.

Sympathetic nerve activity can be assessed by LF/HF, whereas parasympathetic nerve activity can be assessed by HF. The LF component is not only exclusively determined by sympathetic processes but is subject to parasympathetic influences as well (43). Although the change in LF/HF by the arithmetic test on the skip-breakfast day was not significantly different between the two test days, HF on the skip-breakfast day was significantly higher than that on the eat-breakfast day. This result suggested that the sympathetic nervous system was no more activated by the arithmetic task performed in the early morning on the skip-breakfast day than it was on the eat-breakfast day. The phenomenon of a larger change in LF/HF caused by performing the arithmetic task on the skip-breakfast day was likely induced by the parasympathetic nervous system, which is activated in people who skip breakfast (38). HF measured at rest was higher on the skip-breakfast day than on the eat-breakfast day, and the LF/HF was not different. However, both HF and LF/HF were higher on the skip-breakfast day than on the eat-breakfast day after the mental arithmetic test, and the change in HF was significantly different between the two days.

The arithmetic test used in the present study required the subjects to expend energy. Both the mean EE and RQ measured on the skip-breakfast day were significantly lower than those on the eat-breakfast day. The oxygen consumed during fat burning in the body is smaller than that consumed during carbohydrate burning, and the RQ of fat EE is lower than that of carbohydrate EE (43). Also, blood glucose levels on the skip-breakfast day were significantly lower than those on the eat-breakfast day. However, the levels of ketone bodies were significantly higher than those on the eat-breakfast day.

These results suggested a shortage of blood glucose on the skip-breakfast day during the arithmetic test, so that fat (i.e., ketone bodies) expenditure on the skip-breakfast day was larger than that on the eat-breakfast day. It may be that the higher TOI during cerebral blood flow on the skip-breakfast day was the result of lower oxygen consumption. Further, the limitations introduced by skipping breakfast may also be related to the shortage of some vitamins in the tricarboxylic acid cycle (TCA circuit) on the skip-breakfast day (11,44). However, we did not investigate the effect of vitamins, so we cannot prove this assumption. The change in HF was large on the skip-breakfast day. An activated sympathetic nervous system likely induced the decrease in EE.

Pivik et al. reported that to determine the influence of a morning meal, they analyzed the electroencephalographic (EEG) activity recorded while children solved mental loads (11). Relative to the children who ate breakfast, those who continued to skip breakfast showed greater power increases in upper theta and two alpha bands across the measurement sites. Taken together the findings suggested that neural network activity involved in processing numerical information is functionally enhanced and performance is improved in children who have eaten breakfast, whereas greater mental effort is required for such mathematical thinking in children who skip breakfast (45).

Under an activated parasympathetic nervous system, cerebral blood flow on the skip-breakfast day was not increased in comparison with that on the eat-breakfast day in our study. The rate of correct answers to the arithmetic test on the skip-breakfast day was also not better than that on the eat-breakfast day. These results suggested that an inefficiency of EE affected study performance in the students who skipped breakfast.

This study has some limitations. First, because the sample size was small, the difference between the mean numbers of answers to the test was statistically significant, however, the rates of correct answers were not significantly different for the skip-breakfast test and for the eat-breakfast test. Second, because we recruited students based on their breakfast habits, only women were included. A future study needs to consider both sexes to determine any differences between the sexes.

In conclusion, low concentrations of blood glucose and Hb, also high concentrations of ketone bodies and TOI of cerebral blood flow were observed during mental loads in the students who skipped breakfast. When those who skipped breakfast performed the arithmetic task, their blood glucose was low, ketone bodies were expended to gain energy, and their cerebral blood flow as indicated by the Hb level was not increased. Further, their sympathetic nervous system was not adequately activated, nor was their EE adequately increased in comparison to the students who ate breakfast every day. Poorer performance and inefficient Hb use were observed during the mental arithmetic loads in the students who skipped breakfast. This study suggests that physiologically, skipping breakfast may cause problems with academic performance.

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