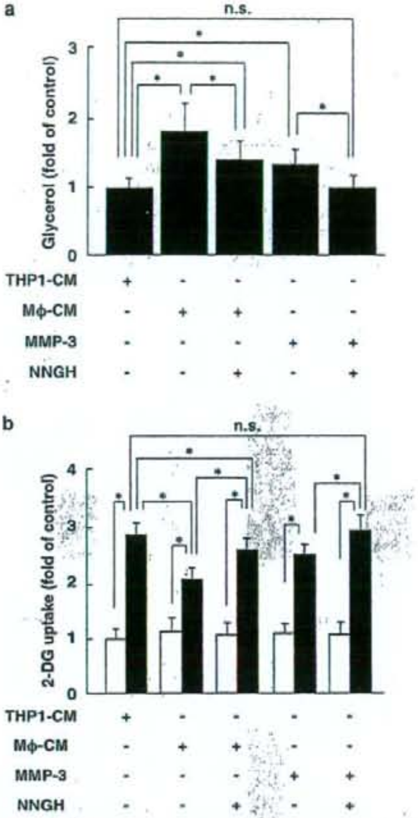

Figure 5 Effect of matrix metalloproteinase (MMP)-3 on lipolysis and insulin-induced glucose incorporation in 3T3-L1 adipocytes. (a) Glycerol release was measured in the media of 3T3-L1 adipocytes after treatment with 50%THP1-CM, 50% Mϕ-CM or 100 μg ml^{-1} human MMP-3, in the absence or presence of 60 μM NNGH for 6 h. The relative ratios of glycerol content with those treated with THP1-CM (control) were presented. Data are expressed as mean ± s.d. ($n = 8$). *$P < 0.05$. n.s., not significant. (b) 2-DG uptake was measured in 3T3-L1 adipocytes in the absence (open column) or presence (closed column) of 100 nM insulin for 15 min after treatment with either 50% THP1-CM, 50% Mϕ-CM or 100 μg ml^{-1} human MMP-3, in the absence or presence of 60 μM NNGH, for 6 h. Relative ratios of 2-DG contents with those treated with THP1-CM in the absence of insulin are indicated. Data are expressed as mean ± s.d. ($n = 6$). *$P < 0.05$. n.s., not significant.

3T3-L1 adipocytes incubated with Mϕ-CM, in comparison to those incubated with THP1-CM. The increase in glycerol release observed in the cells incubated with Mϕ-CM was inhibited by 38% in the presence of NNGH. The glycerol release in the media of 3T3-L1 adipocytes incubated with MMP-3 was also significantly increased, in comparison to those incubated with THP1-CM. The increased release was almost abolished by the NNGH treatment. Next, the effect of MMP-3 on the insulin-induced glucose incorporation into 3T3-L1 adipocytes was analyzed (Figure 5b). The glucose uptake was significantly decreased in the media of 3T3-L1 adipocytes incubated with Mϕ-CM, in comparison to those incubated with THP1-CM. The decrease in glycerol release by the incubation 3T3-L1 cells with Mϕ-CM was recovered by 69% in the presence of NNGH. The glycerol release in the media of 3T3-L1 adipocytes incubated with MMP-3 was significantly decreased, in comparison to those incubated with THP1-CM, and that reduction thereafter almost completely recovered due to the NNGH treatment. Therefore, Mϕ-CM induces lipolysis, and reduces insulin-induced glucose uptake in 3T3-L1 adipocytes, possibly in part through the secretion of MMP-3.

High-fat intake induced the expression of MMP-3 in mesenteric fat tissues as well as the induction of F4/80 gene

To assess the expression of MMP-3 gene in adipose tissue Mϕ, the levels of MMP-3 mRNA were examined in mesenteric fat tissue from mice fed with high-fat diet in relation to the expression of the F4/80 gene, an Mϕ-specific antigen[15,20] (Figure 6). High-fat intake for 2 weeks significantly induced the expression level of F4/80 mRNA in mesenteric fat tissue by 2.2-fold in comparison to the level in the control mice. The levels of MMP-3 and TNF-α genes in mesenteric fat tissue were also significantly induced by 2.8- and 2.5-fold in the mice fed the high-fat diet compared in the control mice, respectively. The expression of F4/80, MMP-3 or TNF-α gene in subcutaneous fat tissues was not significantly different between the mice fed with regular chow and high-fat diet. The MMP-3 protein expression was analyzed in either visceral or subcutaneous fat tissue specimens (Figure 7a). The MMP-3 protein levels in visceral fat tissues, but not in subcutaneous fat, were significantly higher in the mice fed with a high-fat diet than those fed with regular chow. The insulin-induced glucose uptake activity in the adipocytes prepared from visceral fat tissues was significantly decreased in the mice fed with high-fat diet in comparison to those consuming regular chow (Figure 7b). These results indicate

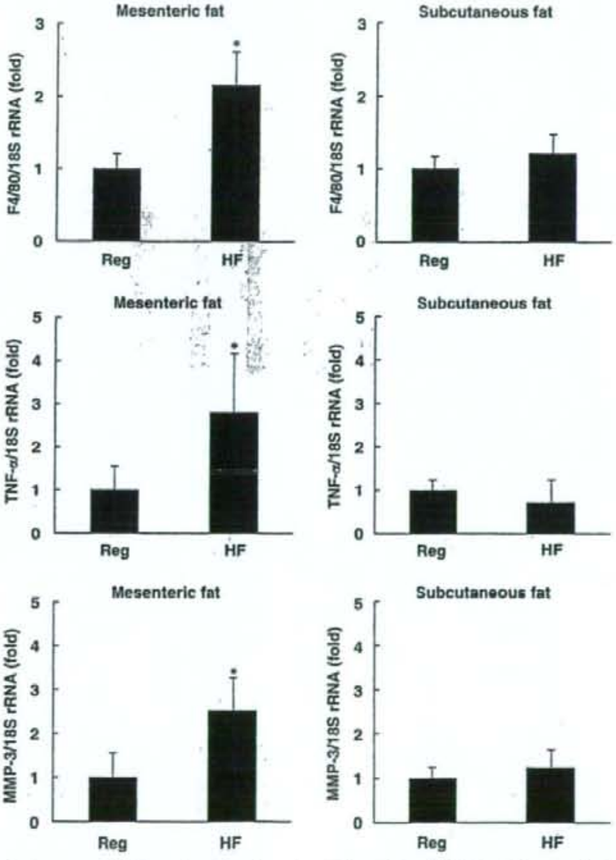

Figure 6 High fat induces F4/80, tumor necrosis factor-α (TNF-α) and matrix metalloproteinase (MMP)-3 mRNA expression in mesenteric fat. Mesenteric or subcutaneous fat tissues were prepared from C57BL/6 mice fed regular chow (Reg) or high-fat (HF) diet. F4/80, TNF-α and MMP-3 mRNA levels were analyzed using quantitative real-time RT–PCR. Relative ratios of mRNA levels in mice fed high-fat to those fed regular chow were presented. Data are expressed as mean ± s.d. ($n = 6$). $^*P < 0.05$ in comparison to the value of the control.

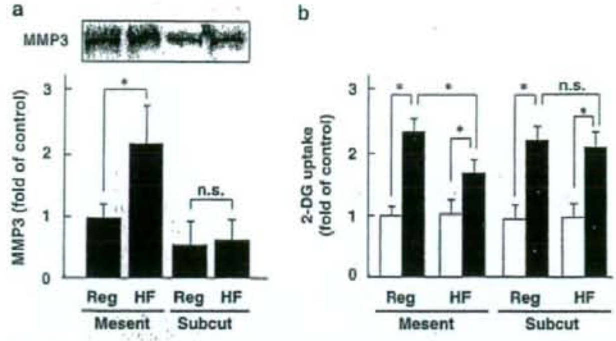

Figure 7 High fat induces matrix metalloproteinase (MMP)-3 protein expression, and reduces insulin-induced glucose incorporation of adipocytes in mesenteric fat. Mesenteric (Mesent) or subcutaneous (Subcut) fat tissues were prepared from C57BL/6 mice fed regular chow (Reg) or high-fat (HF) diet. (**a**) The MMP-3 protein expression of tissue extracts were analyzed by western blot analysis using an antibody against MMP-3. Relative ratios of MMP-3 protein levels with those of mesenteric fat tissues of mice fed regular chow (control) are indicated. Data representative of three experiments are shown. Bars are expressed as mean ± s.d. ($n=6$). $^*P<0.05$. n.s., not significant. (**b**) The 2-DG uptake was measured in single adipocytes prepared from fat tissues in the absence (open column) or presence (closed column) of 100 nM insulin for 15 min. The relative ratios of 2-DG contents with basal of cells prepared from mesenteric fat of mice fed regular chow are indicated. Data are expressed as mean ± s.d. ($n=6$). $^*P<0.05$. n.s., not significant.

that high-fat intake causes Mϕ recruitment into visceral fat, and possibly leads to the induction of the MMP-3 and TNF-α expression, as well as the inhibition of glucose incorporation of adipocytes.

Discussion

The current study demonstrated that Mϕ-CM influences the expression of TNF-α from 3T3-L1 adipocytes. This induction of TNF-α is attenuated by an MMP-3 inhibitor, NNGH. The active form of MMP-3 showed the capability for the induction of lipolysis and the inhibition of the insulin-induced glucose uptake, as well as for the enhanced secretion of TNF-α. These findings suggest that MMP-3 thus plays a role in the modulation of the adipocyte function from Mϕ in adipose tissues.

Recent observations suggested that inflammatory conditions evoked in fat tissues recruit activated Mϕ, possibly enhancing and/or continuing the chronic process in fat tissues.[8,9] TNF-α is suspected to be one of the key players among many cytokines in the interactive modification of function in Mϕ and adipocytes.[4,7] Based on the results obtained herein using a culture system, infiltrating Mϕ may therefore modify the maturation process and secretion level of TNF-α in adipocytes in fat tissues. The expression of TNF-α is observed in 3T3-L1 preadipocytes, and declines gradually after the beginning of maturation in the presence of inducers.[21] The mice with transplanted cultured 3T3-L1 cells showed that the transplanted adipocytes in visceral space, and not subcutaneous space, secret TNF-α and the secreted molecules actually disturb the systemic insulin sensitivity, based on the decreased insulin action in tissues.[5] The induced expression of TNF-α is also observed in the adipocytes in visceral spaces of subcutaneously lipectomized mice.[22] Therefore, the adipocytes that accumulate in visceral space are potentially sensitive to induce the TNF-α gene expression in mice.

Recent studies have indicated that extracellular matrix (ECM) degradation is important for adipogenesis. MMPs are essential for proper matrix remodeling, a process that takes place during adipose tissue formation. Human mature adipocytes secret MMP-2 and -9 and their proteolytic activities are induced during differentiation of murine-cultured adipocytes.[23] mRNA levels for MMP-2, MMP-3, MMP-12, MMP-14, MMP-19 and TIMP-1 are strongly induced in obese adipose tissues in a genetic or a diet-induced model of obesity.[24] The treatment of cultured preadipocytes with either synthetic MMP inhibitors or neutralizing antibodies decreases differentiation.[22] These previous studies using cultured adipocytes suggest that MMP activity is required for adipocyte conversion. The body weight of MMP-3-deficient mice is increased in comparison to that of wild-type mice, as is the weight of the isolated subcutaneous and gonadal fat deposits.[25] MMP-11-deficient mice develop adipocyte hypertrophy in comparison to wild-type mice.[26] Furthermore, the membrane-anchored metalloproteinase, MT1-MMP, acts as a 3D-specific adipogenic factor that directs the dynamic adipocyte-ECM interactions critical to WAT development.[27] These studies using knockout models revealed critical roles of MMPs in fat tissue development and adipogenesis, and possibly also in fat accumulation accompanied with insulin resistance. A recent study reported that the MMP-3 expression levels are negatively correlated with percent body fat, and the MMP-3 gene variants are associated with both BMI and type 2 diabetes in Pima Indians.[28]

The mice with transplanted cultured 3T3-L1 cells showed that the transplanted adipocytes in the visceral space, and not subcutaneous space, increased TNF-α gene expression.[5] A microarray analysis revealed that the MMP-3 gene expression is drastically induced in addition to TNF-α.[6] Therefore, the MMP-3 gene expression in visceral fat seems to be directly linked to cytokine expression in adipocytes. The current study showed that the active form of MMP-3 enhanced glycerol release, as well as TNF-α protein secretion, from 3T3-L1 adipocytes. The incubation of adipocytes with MMP-3 inhibited insulin-induced glucose uptake in adipocytes. Therefore, the induction of MMP-3 gene expression may modulate lipid and glucose metabolism in visceral adipocytes, leading to the induction of TNF-α secretion. The treatment of 3T3-L1 preadipocytes with the MMP inhibitor Ilomastat has been shown to prevent their differentiation into adipocytes.[29] The subcutaneous administration of MMP inhibitor KB-R7785 reduced the plasma glucose and insulin levels with a concomitant decrease in the TNF-α production in KK-A^y mice.[30] These observations indicate that Mϕ-MMP may thus play a functional role in the induction of TNF-α gene expression impairing insulin sensitivity in adipocytes.

Recently, MMP-3 has been shown to be a signaling molecule via the ERK pathway, followed by proinflammatory cytokine induction, and induce superoxide generation in microglia.[31] Moreover, activated MMP-3 is present in the nuclear compartment of malignant and nontransformed hepatocytes, and is associated with the onset of apoptosis.[32] These studies suggested a novel function of MMP-3 as a signaling molecule active for intracellular functions. The current results showed that high-fat intake induced a decrease in insulin-induced glucose incorporation in adipocytes, as well as an increase in Mϕ-infiltration and TNF-α expression in visceral fat tissue. Therefore, MMP-3 may affect the lipid metabolism of adipocytes through the ECM degradation and the activation of other extracellular and intracellular molecules leading to the lipolysis and glucose incorporation. Therefore, Mϕ-derived MMP-3 may modulate the secretion of TNF-α in adipocytes by modulating the lipid metabolism, which is tightly linked to visceral fat accumulation and systemic insulin resistance.

In conclusion, this study suggests that MMP-3 is important for the function of pathological link between Mϕ and adipocytes, which leads to insulin resistance in metabolic syndrome through the regulation of cytokine expression such as TNF-α. The further elucidation of the role of MMP-3 and its secretion from activated Mϕ and adipocytes is therefore expected to contribute to the elucidation of the unexpected relationship between chronic inflammation and disturbed insulin sensitivity in humans.

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分担研究報告書

職域におけるメタボリックシンドローム 富山職域コホート研究

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研究要旨

富山職域コホートは、富山県にある企業の従業員を追跡する職域コホートである。就労中の男女，特に地域ではコホート設定が困難な働き盛りの中高年男性における循環器疾患のリスクの評価や、リスクと就業状態の関連等の検討を行っている。

今回，ウエスト周囲径と代謝異常の関連とその性差につき検討を行った。男性と比較し，女性では代謝異常とウエスト周囲径との関連は弱かった。また，ROC 曲線から求めた代謝異常合併を反映するウエスト周囲径は男性 80cm，女性 72cm であった。この基準値における女性の陽性的中率は 7%と低値であった。以上より，女性では，ウエスト周囲径と代謝異常の関連は弱く，従来から行われてきているウエスト周囲径と代謝異常との関連から日本人の適切なウエスト周囲径のカットオフ値を決定する方法には限界があるものと思われた。

A. 研究目的

富山県にある企業の従業員を追跡する職域コホートである。就労中の男女，特に地域ではコホート設定が困難な働き盛りの中高年男性における循環器疾患のリスクの評価や、リスクと就業状態の関連等の検討を行っている。

B. 研究方法

コホートの概要

富山県にあるアルミ製品製造業企業の黒部事業所及び滑川事業所従業員を対象としたコホートである。1980 年以降、研究者が産業医として従業員の健康管理を 25 年にわたり行っている。コホート規模は約 8,000 人で、男女比は約 2 対 1 である。

本コホートは職域コホートであるため、従業員全体が毎年 95%以上の受診率で健診を受診しており、各種検査値の高い率での経年追跡が可能である。また現業系従業員では転勤が少なく、また、途中退職も比較的少ないため長期の追跡が可能である。

本コホート研究グループは本事業所での産業医活動を通して、詳細なエンドポイント発生の把握を実施している。すなわち、在職中の脳卒中、虚血性心疾患、悪性新生

物、精神疾患等の発症および死亡の把握、健診データ追跡による在職中の高血圧、糖尿病、高脂血症等の発症の把握である。また、一般に職域コホートでは定年退職後の疾患発症の追跡が困難であるが、本コホートでは退職後も近隣に在住するものがほとんどのため、1990年以降退職者については郵送による退職後健康調査を毎年実施し、生活習慣病の治療状況、脳血管疾患・心疾患の発症および死亡を追跡している。在職中および退職後の脳心事故発症者については同意を得た上で、医療機関での医療記録調査を実施している。

以上より、本コホートの特色としては、（１）地域ではコホート設定が困難な青壮年期の男性を多く含むコホートであること、（２）青壮年期男性のライフスタイルや危険因子に影響が大きいと考えられる職業面での要因について詳細な情報が収集されていること、（３）各種危険因子の経年推移が高い追跡率で把握されていること、が挙げられる。

C. 研究結果

研究の成果

代謝異常と腹部肥満の関連における性差

（Sakurai M, Takamura T, MiuraK, Kaneko S, Nakagawa H. Middle-aged Japanese women are resistant to obesity-related metabolic abnormalities. Metabolism, in press.）

【目的】大規模な職域集団の横断研究から、肥満と代謝異常との関連，およびその性差を明らかにすることを目的とする。

【方法】対象は日本のアルミ製品製造事業所に勤務する35-59歳の男性2,935人，女性1,622人。定期健康診断にウエスト周囲径（中点レベル）の測定を行い，ウエスト周囲径と代謝異常の関連を検討した。また，ROC曲線から，代謝異常の合併を反映するウエスト周囲径を求め，陽性的中率からスクリーニングとしての有用性を検討した。

【結果】男性では，ウエスト周囲径の増加に伴い平均代謝異常合併数は増加し，日本人のウエスト周囲径の基準である85cmを超えると，平均代謝異常合併数は1を超えた。一方女性では，ウエスト周囲径が増大しても平均代謝異常合併数は1を超えることはなく，ウエスト周囲径と代謝異常合併数の関連は弱かった（図１）。

ROC曲線より，代謝異常の合併を最も良く反映するウエスト周囲径は，男性で80cm，女性で73cmであり，これまでの報告と同様であった(図2)。しかしながら，女性では陽性反応的中率は7%と低く，すなわち女性でウエスト周囲径が73cmを超えているもののうち7%にしか実際の代謝異常は認めない，という結果であった。

【結論】女性では，ウエスト周囲径と代謝異常の関連は弱く，従来行われてきたウエスト周囲径と代謝異常との関連から日本人の適切なウエスト周囲径のカットオフ値を決定する方法には限界があるものと思われた。

D.まとめ

富山職域コホートでは、職域の特徴を生かしたコホート研究を、引き続き継続して展開していく予定である。現在、働き盛りの中年労働者の生活習慣，職業的要因と循環器疾患危険因子との関連を検討中であり，今後横断研究，縦断研究としてメタボリックシンドロームの疫学に関する研究の成果を発表していく。

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３）森河裕子，三浦克之，櫻井勝，石崎昌夫，中川秀昭，城戸照彦，成瀬優知，東山正子，青木千夏．夜勤交代勤務への対処行動としての寝酒習慣と循環器疾患リスクファクターとの関連．第81回日本産業衛生学会（2008年6月，札幌）

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６）由田克士，三浦克之，櫻井勝，中川秀昭，石田裕美．職場において実施したやさしく負荷の小さな減量プログラムの効果について．第67回日本公衆衛生学会総会（2008年11月，福岡）

F. 知的財産権の出願・登録状況（予定を含む）

なし

図 1

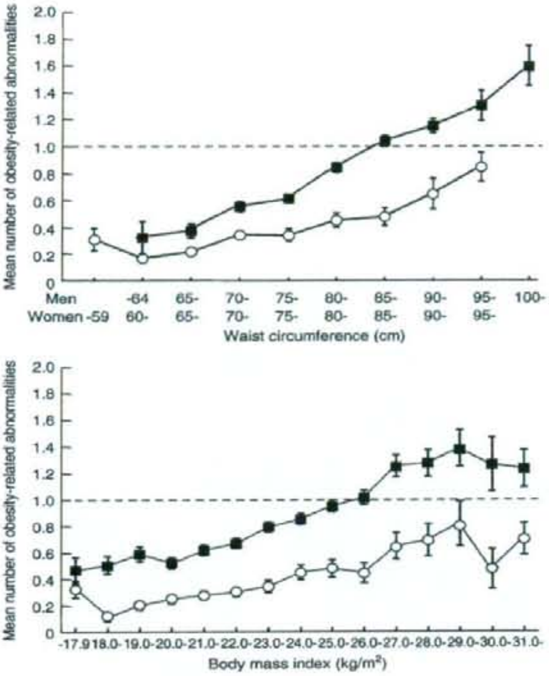
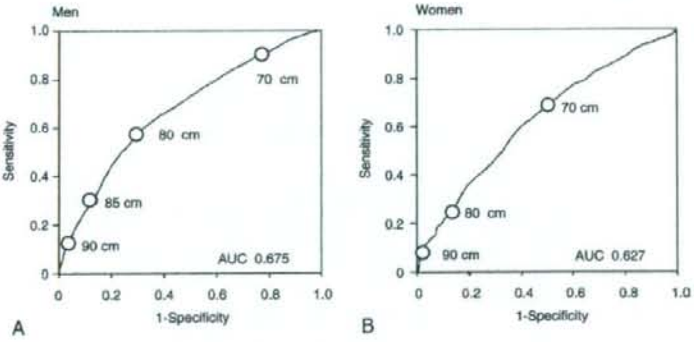


図 2



Cutoff point for waist circumference

	Sensitivity	Specificity
Men		
70 cm	0.94	0.16
80 cm	0.59	0.69
85 cm	0.32	0.86
90 cm	0.13	0.96
Women		
70 cm	0.67	0.52
73 cm	0.55	0.64
80 cm	0.27	0.85
90 cm	0.09	0.98

C

研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表雑誌	巻号	ページ	出版年
Y. Morikawa, K. Miura, S. Sasaki, K. Yoshita, S. Yoneyama, M. Sakurai, M. Ishizaki, T. Kido, Y. Naruse, Y. Suwazono, M. Higashiyama, H. Nakagawa.	Evaluation of the effects of shift work on nutrient intake: a cross-sectional study	J Occup Health	50	270-278	2008
Ishizaki M, Nakagawa H, Morikawa Y, Honda R, Yamada Y, Kawakami N; The Japan Work Stress and Health Cohort Study Group.	Influence of job strain on changes in body mass index and waist circumference - 6-year longitudinal study	Scand J Work Environ Health	34	288-296	2008
M. Sakurai, T. Takamura, K. Miura, S. Kaneko, H. Nakagawa.	BMI may be better than waist circumference for defining metabolic syndrome in Japanese women.	Diabetes Care	31	e12	2008
櫻井勝，三浦克之，中村幸志，石崎昌夫，森河裕子，城戸照彦，成瀬優知，中川秀昭	中年期日本人男性における腹部肥満の有無別に見た代謝異常集積と脳心血管疾患発症との関連	日循予防誌	44	1−9	2009

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Evaluation of the Effects of Shift Work on Nutrient Intake: A Cross-sectional Study

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Abstract: Evaluation of the Effects of Shift Work on Nutrient Intake: A Cross-sectional Study: Yuko MORIKAWA, *et al.* Department of Epidemiology and Public Health, Kanazawa Medical University—The aim of this study was to investigate the effects of shift work on nutrient intakes, including macronutrient intake and micronutrient intake, in a large sample size. The study population included 2,254 male manual workers, 20–59 yr of age, employed in a factory. A self-administered diet history questionnaire was used. The subjects were classified into 3 groups according to their work schedule: (i) fixed day workers; (ii) shift workers without midnight shifts; and (iii) shift workers with midnight shifts. The nutrient intakes of the groups were compared by age group. There was a significant difference in nutrient intakes between subjects aged 20–29 yr and those aged 30 yr and over. Among subjects aged 20–29 yr, the energy density value for saturated fat and the energy adjusted intakes of calcium, potassium, vitamin A, and vitamin B1 were the lowest among shift workers with midnight shifts. Among subjects aged 30 yr and over, the total energy intake was the highest among shift workers with midnight shifts; the difference was significant compared to fixed day workers. Shift workers with midnight shifts had the highest intake of cereals among subjects 30 yr of age and older. In conclusion, there were no significant differences in nutrient intakes between fixed day workers and shift workers without midnight shift. Shift work, particularly midnight shift work, affected nutrient intake. The impact of shift work on nutrient intakes differed by age and the type of shift work.
(J Occup Health 2008; 50: 270–278)

Key words: Shift work, Nutrition, Food intake, Macronutrients, Micronutrients, Cross-sectional study

Shift work has been associated with an increased risk of cardiovascular disease[1–3]. Changes in biomarkers and lifestyle are considered to be related to the increased risk of cardiovascular disease. Previously, the results of studies dealing with the effects of shift work on biomarkers were inconsistent. However, recently, the majority of cross-sectional studies have shown that shift workers have a higher prevalence of cardiovascular disease and higher levels of cardiovascular disease biomarkers[4–9]. Intervention studies indicate that the introduction of a better shift schedule improves biomarkers[10], while introducing a worse shift schedule causes the workers to gain weight[11]. Increased risks of obesity and weight gain among shift workers have been reported by a few studies[12–14]. We previously reported an increased risk of hypertension, diabetes mellitus, and weight gain among shift workers[15–17].

Studies of the effects of shift work on eating habits and nutrient intake have previously been conducted. Most studies did not find a difference between shift workers and daytime workers with respect to their total calorie intake and their dominant macronutrient intake[21, 23–25].

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Instead, many reports found that there were changes in eating habits and food selection among shift workers[18–22]. However, most previous studies dealing with this issue had small sample sizes. Furthermore, compared to the number of studies that evaluated intra-individual differences in nutrient intakes by shift, there have been few studies that have examined the differences in nutrient intakes between shift workers and daytime workers. Furthermore, most studies have not considered the lifestyle effects of shift work by age and shift work history.

This study investigated the effects of shift work on nutrient intakes, including both macronutrient intake and micronutrient intake, in a large sample size. We also examined the effects of workers' age and the number of years that the workers had worked shifts on the relationship between shift work and nutrient intakes. A self-administered diet history questionnaire that was developed for use in epidemiological studies was used to assess nutrient intake.

Subjects and Methods

Study population

The study population consisted of male manual workers, aged 20–59 yr, working in a factory producing light metal products. A self-administered questionnaire survey was done in 2003 that included questions on nutritional intake and work conditions. There were a total of 4,736 male employees aged 20–59 yr; of these, 3,715 provided valid responses, for a valid response rate of 78.4%. The 2,254 employees who indicated that they were engaged in manual work were chosen as the subjects for this analysis. The number of years that the employees had worked shifts and behavioral factors were obtained from the self-administered questionnaire; the subjects' height and body weight were obtained from annual health examination data.

In the target company, the shift schedule included a rotating 3-shift schedule and a 2-shift schedule. The 3-shift workers rotated counterclockwise: two thirds of them had a non-continuous shift system (5 day shifts, 5 night shifts, and 5 evening shifts with weekend holidays), and one third of them had a continuous shift system (3 or 4 day shifts, 3 or 4 night shifts, and 3 or 4 evening shifts, with 1 rest day between successive shifts). Both rotating shift schedules changed shifts at 08h00, 16h30, and 00h15, or 06h30, 13h00, and 21h30. Whether worker are allocated to shift work or not depends on the job in the section. Certain jobs, such as those involving the operation of machines that melt, heat, mix, or cast, are routinely done by 3-shift workers, while jobs involving the processing or construction of aluminum products are done by fixed day workers or 2-shift workers.

The subjects were classified into 3 groups according to their work schedule: (i) fixed day workers; (ii) shift workers without midnight shifts; and (iii) shift workers with midnight shifts. The number of subjects, the length of time that they had done shift work, and anthropometric data are shown by age group in Table 1. In the 30–39-years-olds, there was a significant difference in BMI among the three groups by work schedule. Other characteristics were not significantly different among the three groups.

Data collection

Dietary habits during the preceding month were assessed using a self-administered diet history questionnaire (DHQ)[26]. The DHQ was developed to estimate the dietary intakes of macronutrients and micronutrients in epidemiological studies in Japan. The detailed description of the methods used for calculating dietary intakes and the validity of the DHQ have been previously published[26]. Briefly, the DHQ consists of the following seven sections: general dietary behaviors; major cooking methods; consumption frequency and semi-quantitative portion size of 122 selected food and non-alcoholic beverage items; dietary supplements; consumption frequency and semi-quantitative portion sizes of cereals usually consumed as staple foods (rice, bread and noodles) and miso (fermented soybean paste) soup; and open-ended items for foods consumed regularly but not appearing in the DHQ. Items and portion sizes were derived primarily from data in the National Nutritional Survey of Japan and several recipe books for Japanese dishes.

Estimates of dietary intake for 148 food and beverage items, energy and nutrients were calculated using an ad hoc computer algorithm developed for the DHQ that was based on the Standard Tables of Food Composition in Japan. In this study, the energy adjusted values of dietary intakes were calculated using the percentage of energy for energy providing nutrients and the amount per 1,000 kcal for non energy-providing nutrients and foods. The food groups examined for comparison were as follows: "rice, bread and noodles," potatoes, confectionaries, "fat and oil," pulses, fruits, vegetables, "fish and shellfish," meat and dairy products.

The body mass index (BMI) was calculated as the weight (kg) divided by the height squared (m^2). Health-related behaviors were also obtained by questionnaire.

Statistics

The nutrient intakes and individual characteristics were compared among the groups with 3 different work schedules using one-way ANOVA. The prevalence of smoking was compared among the groups using the χ^2-test. Each analysis was carried out on age-stratified data. The software package used for the analysis was SPSS 11.0 (SPSS Inc, Chicago, IL, USA).

Table 1. Characteristics of the groups of work schedule

Age class	Work schedule	n	Age (yr)	p^a	History of shift work (yr)	p^a	Body mass index (kg/m^2)	p^a	Height (cm)	p^a	Current smokers (%)	p^b
20–29												
	Daytime	167	25.2 (2.9)	ns	0.8 (1.7)	ns	22.3 (2.9)	ns	171.9 (5.7)	ns	88 (52.7)	ns
	Shift workers (midnight shift(–))	80	24.4 (2.9)		2.1 (2.2)		22.7 (4.7)		171.1 (5.5)		40 (50.0)	
	Shift workers (midnight shift(+))	161	25.1 (2.8)		4.8 (3.0)		22.4 (3.3)		171.5 (5.4)		95 (59.0)	
	Total	408	25.0 (2.8)		2.6 (3.0)		22.4 (3.5)		171.6 (5.5)		223 (54.7)	
30–39												
	Daytime	235	34.6 (2.9)	ns	3.8 (4.7)	ns	22.7 (2.7)	0.003	171.9 (5.7)	ns	134 (57.0)	ns
	Shift workers (midnight shift(–))	53	34.3 (2.8)		7.4 (5.8)		24.3 (3.4)		172.1 (4.6)		30 (56.6)	
	Shift workers (midnight shift(+))	155	34.1 (2.9)		11.8 (4.7)		23.2 (3.5)		171.8 (5.6)		97 (62.6)	
	Total	443	34.4 (2.9)		7.0 (6.1)		23.1 (3.1)		171.9 (5.6)		261 (58.9)	
40–49												
	Daytime	384	44.7 (2.6)	ns	6.1 (7.1)	ns	23.4 (3.0)	ns	169.7 (5.2)	ns	223 (58.1)	ns
	Shift workers (midnight shift(–))	92	44.5 (2.8)		8.0 (8.0)		23.8 (3.2)		169.5 (6.6)		45 (48.9)	
	Shift workers (midnight shift(+))	175	44.5 (2.7)		17.4 (8.0)		23.7 (3.0)		169.7 (6.0)		106 (60.6)	
	Total	651	44.6 (2.7)		9.4 (8.9)		23.5 (3.1)		169.6 (5.6)		374 (57.5)	
50–59												
	Daytime	519	54.3 (2.7)	ns	7.7 (9.6)	ns	23.0 (2.6)	ns	167.0 (6.1)	ns	257 (49.5)	ns
	Shift workers (midnight shift(–))	101	54.2 (2.5)		13.2 (11.0)		23.4 (2.9)		167.1 (5.9)		52 (51.5)	
	Shift workers (midnight shift(+))	132	54.1 (2.7)		21.4 (11.2)		23.0 (2.9)		166.7 (5.8)		69 (52.3)	
	Total	752	54.3 (2.7)		10.8 (11.3)		23.0 (2.7)		167.0 (6.0)		378 (50.3)	

Mean (standard deviation), ^{a} *p*-value tested by one way ANOVA, ^{b} *p*-value tested by χ-square test.

Results

Comparison of nutrient intakes

Table 2 shows the comparisons of total energy and the energy density value for nutrient intakes (% of energy for energy-providing nutrients and weight per 1,000 kcal for non energy-providing nutrients) among the three groups of 20–29-yr-old workers. The total energy intake was the highest in shift workers without midnight shifts, but there were no significant differences among the groups in total energy intake. The energy density values for macronutrient were not significantly different among the three groups. However, shift workers with midnight shifts had the lowest percent of energy from saturated fat with statistical significance. The energy density values for calcium, potassium, vitamin A, and vitamin B1 were the lowest in shift workers with midnight shifts; the energy density value of potassium, vitamin A and vitamin B1 in shift workers with midnight shifts were significantly lower than those in fixed day workers, and those of calcium and vitamin A were significantly lower than those in shift workers without midnight shifts. On the other hand, the daily alcohol intake was the highest in shift workers with midnight shifts, though there were no significant differences among the groups. There were no significant differences in micronutrient intakes between fixed day workers and shift workers without midnight shifts.

Table 3 shows the results for 30–39-yr-old workers. The total energy intake was the highest in shift workers with midnight shifts, followed by shift workers without midnight shifts and fixed day workers; there was a significant difference between shift workers with midnight shifts and fixed day workers. There were no significant differences among the three groups in energy density values for micronutrients except for vitamin B1.

Table 4 shows the results of the 40–49-yr-old workers. The total energy intake was the highest in shift workers with midnight shifts, followed by shift workers without midnight shifts and fixed day workers; the differences among the groups were not statistically significant. There were no significant differences among the three groups in the energy density values for nutrients, except for polyunsaturated fatty acids; the percent of energy for polyunsaturated fatty acids was the lowest in shift workers with midnight shifts, and the difference between shift workers with midnight shifts and fixed day workers was statistically significant.

Table 5 shows the results for 50–59-yr-old workers. The total energy intake was the highest in shift workers with midnight shifts, followed by shift workers without midnight shifts and fixed day workers; there was a significant difference between shift workers with midnight shifts and fixed day workers. The energy density value for dietary fiber was significantly lower in shift workers with/without midnight shifts than in fixed day workers.

Comparison of food intake

The energy adjusted food intakes were compared among the three groups of workers. The food groups with p-values less than 0.10 tested by one-way ANOVA are listed in Table 6. Among the 20–29-yr-olds, energy adjusted intakes of dairy products were significantly lower in shift workers with midnight shifts than in fixed day workers and shift workers without midnight shifts. Intakes of meat and vegetables were the lowest in shift workers with midnight shifts. Among the 30–39-yr-olds, intakes of all food groups were not different among groups of work schedule. Among the 40–49-yr-olds, energy adjusted intakes of meat and "fat and oil" were the lowest in shift workers with midnight shifts with statistical significance. Among the 50–59-yr-olds, shift workers with midnight shifts tended to show lower intake of vegetables.

Discussion

To evaluate the effects of shift work on nutrient intake, manual workers employed in a Japanese factory were surveyed. The shift system in the target company consisted primarily of a rotational shift system that was either continuous or non-continuous. While changing shifts weekly with weekend holidays is a common schedule, other shift change systems involving shorter time spans are also in use. Two thirds of the shift workers had midnight shifts, while the remaining shift workers did not have midnight shifts. For the purposes of the analysis, the workers were classified into three groups: shift workers with midnight shifts; shift workers without midnight shifts; and fixed day workers. Given the hypothesis that the quantity and quality of the effects of irregular work on nutrient intake would differ by the workers' age and the number of years they had worked shifts, the workers were stratified by age group for the analyses. In the target company, the particular shift schedule varied depending on the needs of the process performed in each section. Changing sections was not common for the manual workers. Therefore, among the shift workers, their age was well correlated with the number of years that they had worked shifts. Also, marital status would have some effects on nutritional intake, but we don't have such data. Analysis by age strata might diminish the influence of marital status.

The survey of nutrient intake was carried out using the self-administered dietary questionnaire (DHQ) developed by Sasaki[26]. The validity of the DHQ for epidemiological use has been verified. Since this questionnaire asks frequencies and quantities of items during the previous one month, it would be more useful for a survey targeting shift workers who eat irregularly according to their shift

Table 2. Energy intake and energy adjusted values of nutrients of the groups of work schedule, 20–29 yr old

Nutrients		Fixed day workers[a]		Shift workers without midnight shift[b]		Shift workers with midnight shift[c]		p-value	Multiple comparison		
									a/b	a/c	b/c
Energy	kcal/day	2,068	(608)	2,230	(783)	2,097	(712)	ns			
Total protein	% energy	11.0	(2.0)	11.4	(2.0)	10.8	(2.0)	ns			
Total carbohydrate	% energy	60.6	(7.8)	60.2	(8.7)	61.1	(8.7)	ns			
Total fat	% energy	23.6	(6.6)	24.0	(7.2)	22.5	(7.2)	ns			
Saturated fatty acid	% energy	5.9	(1.7)	6.1	(2.2)	5.4	(2.1)	0.041			
Monounsaturated fatty acid	% energy	8.4	(2.9)	8.3	(2.7)	8.0	(2.9)	ns			
Polyunsaturated fatty acid	% energy	5.9	(1.8)	5.9	(1.6)	5.8	(1.8)	ns			
Calcium	mg/1,000 kcal	180.8	(85.7)	188.6	(70.1)	161.6	(67.9)	0.015			0.03
Iron	mg/1,000 kcal	2.80	(0.70)	2.90	(0.69)	2.69	(0.68)	ns			
Sodium	mg/1,000 kcal	1,748	(446)	1,702	(450)	1,749	(510)	ns			
Potassium	mg/1,000 kcal	904	(251)	895	(254)	830	(237)	0.017		0.02	
Vitamin A	μg/1,000 kcal	314	(166)	336	(182)	259	(142)	<0.001		0.006	0.002
Vitamin B_1	mg/1,000 kcal	0.345	(0.108)	0.350	(0.096)	0.317	(0.096)	0.016		0.04	
Vitamin C	mg/1,000 kcal	38.1	(24.6)	38.1	(23.9)	34.5	(19.4)	ns			
Total dietary fiber	g/1,000 kcal	4.86	(1.39)	4.98	(1.48)	4.67	(1.31)	ns			
Alcohol	g/day	9.1	(12.4)	8.5	(14.3)	12.2	(24.4)	ns			

Mean (standard deviation), p-value tested by one way ANOVA, *post hoc* multiple comparison was tested by the Scheffe test. a/b: p-value between day workers and shift workers without midnight shift, a/c: p-value between day workers and shift workers with midnight shift, b/c: p-value between shift workers without/with midnight shift.

Table 3. Energy intake and energy adjusted values of nutrients of the groups of work schedule, 30–39 yr old

Nutrients		Fixed day workers[a]		Shift workers without midnight shift[b]		Shift workers with midnight shift[c]		p-value	Multiple comparison		
									a/b	a/c	b/c
Energy	kcal/day	2,129	(610)	2,182	(627)	2,356	(781)	0.005		0.004	
Total protein	% energy	11.1	(1.9)	11.0	(2.1)	11.0	(1.9)	ns			
Total carbohydrate	% energy	59.2	(8.0)	58.1	(9.6)	58.4	(8.1)	ns			
Total fat	% energy	22.4	(5.8)	24.1	(7.9)	22.9	(7.0)	ns			
Saturated fatty acid	% energy	5.6	(1.6)	5.9	(2.2)	5.5	(1.8)	ns			
Monounsaturated fatty acid	% energy	7.8	(2.4)	8.7	(3.4)	8.2	(3.0)	ns			
Polyunsaturated fatty acid	% energy	5.7	(1.6)	6.1	(2.2)	5.8	(1.8)	ns			
Calcium	mg/1,000 kcal	178.4	(66.9)	174.1	(66.6)	168.3	(56.9)	ns			
Iron	mg/1,000 kcal	2.82	(0.67)	2.92	(0.96)	2.75	(0.67)	ns			
Sodium	mg/1,000 kcal	1,765	(514)	1,744	(659)	1,755	(535)	ns			
Potassium	mg/1,000 kcal	919	(240)	957	(336)	900	(226)	ns			
Vitamin A	μg/1,000 kcal	300	(169)	293	(150)	282	(148)	ns			
Vitamin B_1	mg/1,000 kcal	0.328	(0.091)	0.653	(0.131)	0.312	(0.082)	0.021			0.02
Vitamin C	mg/1,000 kcal	34.4	(20.8)	40.9	(28.3)	32.8	(19.1)	ns			
Total dietary fiber	g/1,000 kcal	4.92	(1.37)	4.79	(1.78)	4.70	(1.43)	ns			
Alcohol	g/day	18.0	(25.7)	16.9	(21.1)	18.9	(23.5)	ns			

Mean (standard deviation), p tested by one way ANOVA, *post hoc* multiple comparison was tested by the Scheffe test. a/b: p-value between day workers and shift workers without midnight shift, a/c: p-value between day workers and shift workers with midnight shift, b/c: p-value between shift workers without/with midnight shift.

Table 4. Energy intake and energy adjusted values of nutrients of the groups of work schedule, 40–49 yr old

Nutrients		Fixed day workers [a]		Shift workers without midnight shift [b]		Shift workers with midnight shift [c]		p-value	Multiple comparison		
									a/b	a/c	b/c
Energy	kcal/day	2,183	(665)	2,193	(538)	2,315	(831)	ns			
Total protein	% energy	10.7	(2.1)	11.1	(1.7)	10.6	(2.1)	ns			
Total carbohydrate	% energy	59.0	(8.9)	60.1	(8.0)	60.7	(8.7)	ns			
Total fat	% energy	20.6	(6.8)	20.3	(5.7)	19.4	(6.2)	ns			
Saturated fatty acid	% energy	5.0	(1.9)	5.0	(1.6)	4.7	(1.7)	ns			
Monounsaturated fatty acid	% energy	7.2	(2.7)	7.0	(2.1)	6.6	(2.4)	ns			
Polyunsaturated fatty acid	% energy	5.4	(1.7)	5.2	(1.5)	5.0	(1.6)	0.045		0.038	
Calcium	mg/1,000 kcal	174.0	(70.9)	174.4	(65.9)	167.6	(66.5)	ns			
Iron	mg/1,000 kcal	2.74	(0.71)	2.82	(0.67)	2.72	(0.76)	ns			
Sodium	mg/1,000 kcal	1,766	(562)	1,756	(476)	1,763	(539)	ns			
Potassium	mg/1,000 kcal	895	(562)	912	(262)	870	(244)	ns			
Vitamin A	μg/1,000 kcal	271	(152)	280	(151)	261	(160)	ns			
Vitamin B_1	mg/1,000 kcal	0.305	(0.093)	0.335	(0.109)	0.307	(0.109)	ns			
Vitamin C	mg/1,000 kcal	33.0	(21.0)	35.7	(23.1)	35.4	(25.9)	ns			
Total dietary fiber	g/1,000 kcal	4.88	(1.47)	4.98	(1.43)	4.90	(1.44)	ns			
Alcohol	g/day	25.4	(30.3)	21.1	(25.3)	26.4	(37.8)	ns			

Mean (standard deviation), *p* tested by one way ANOVA, *post hoc* multiple comparison was tested by the Scheffe test. a/b: *p*-value between day workers and shift workers without midnight shift, a/c: *p*-value between day workers and shift workers with midnight shift, b/c: *p*-value between shift workers without/with midnight shift.

Table 5. Energy intake and energy adjusted values of nutrients of the groups of work schedule, 50–59 yr old

Nutrients		Fixed day workers [a]		Shift workers without midnight shift [b]		Shift workers with midnight shift [c]		p-value	Multiple comparison		
									a/b	a/c	b/c
Energy	kcal/day	2,109	(604)	2,181	(720)	2,276	(725)	0.025		0.024	
Total protein	% energy	11.3	(2.2)	11.5	(2.4)	11.2	(2.2)	ns			
Total carbohydrate	% energy	60.4	(8.6)	60.1	(9.1)	60.9	(8.9)	ns			
Total fat	% energy	19.1	(6.1)	18.7	(6.6)	18.3	(6.3)	ns			
Saturated fatty acid	% energy	4.6	(1.7)	4.5	(1.9)	4.4	(1.7)	ns			
Monounsaturated fatty acid	% energy	6.5	(2.3)	6.3	(2.5)	6.2	(2.3)	ns			
Polyunsaturated fatty acid	% energy	5.1	(1.5)	5.0	(1.6)	4.9	(1.6)	ns			
Calcium	mg/1,000 kcal	186.4	(67.8)	186.9	(78.2)	174.4	(60.4)	ns			
Iron	mg/1,000 kcal	2.92	(0.75)	2.89	(0.73)	2.78	(0.74)	ns			
Sodium	mg/1,000 kcal	1,800	(542)	1,811	(584)	1,664	(505)	ns			
Potassium	mg/1,000 kcal	954	(261)	943	(263)	903	(253)	ns			
Vitamin A	μg/1,000 kcal	311	(171)	288	(151)	291	(169)	ns			
Vitamin B_1	mg/1,000 kcal	0.318	(0.102)	0.317	(0.116)	0.318	(0.113)	ns			
Vitamin C	mg/1,000 kcal	38.3	(23.5)	36.5	(27.6)	36.3	(26.8)	ns			
Total dietary fiber	g/1,000 kcal	5.37	(1.62)	5.06	(1.38)	5.04	(1.60)	0.037			
Alcohol	g/day	24.1	(34.7)	25.5	(25.6)	25.0	(27.8)	ns			

Mean (standard deviation), *p* tested by one way ANOVA, *post hoc* multiple comparison was tested by the Scheffe test. a/b: *p*-value between day workers and shift workers without midnight shift, a/c: *p*-value between day workers and shift workers with midnight shift, b/c: *p*-value between shift workers without/with midnight shift.

Table 6. Food intakes of the groups of work schedule by age groups (listed items found to be statistically different among the three groups)

Age Food		Fixed day workers ^{a}		Shift workers without midnight shift ^{b}		Shift workers with midnight shift ^{c}		p-value	Multiple comparison a/b	a/c	b/c
20–29											
Meat	g/1,000 kcal	25.7	(1.8)	25.8	(2.1)	21.6	(2.1)	0.054			
Diary products	g/1,000 kcal	27.2	(3.2)	31.0	(3.2)	18.5	(3.6)	0.003		0.025	0.012
Vegetables	g/1,000 kcal	31.9	(2.2)	27.7	(2.7)	25.0	(2.5)	0.056			
40–49											
Meat	g/1,000 kcal	15.8	(2.1)	18.9	(1.8)	13.7	(2.2)	0.007			0.008
Fat and oil	g/1,000 kcal	8.1	(1.7)	7.7	(1.6)	7.0	(1.7)	0.021		0.021	
50–59											
Vegetables	g/1,000 kcal	35.2	(2.1)	31.8	(1.9)	30.0	(1.9)	0.056			

Food items compared among groups were "rice, bread and noodles," potatoes, confectionaries, "fat and oil," pulses, fruits, vegetables, "fish and shellfish," meat and dairy products.

Geometrical mean (geometrical standard deviation), p tested by one way ANOVA, *post hoc* multiple comparison was tested by the Scheffe test. a/b: p-value between day workers and shift workers without midnight shift, a/c: p-value between day workers and shift workers with midnight shift, b/c: p-value between shift workers without/with midnight shift

schedule. To determine our subjects' characteristics, the nutrient intakes of our study population were compared with the data collected by the National Nutrition Survey conducted in Japan in 2004[27]. For the National Nutrition Survey, the samples were selected by stratified random sampling, and the nutritional intakes were evaluated based on dietary records. Despite the difference in the method used to evaluate nutrient intake, our subjects' energy intakes were similar to the national mean for each age group. However, our subjects tended to eat more carbohydrate, less protein, and less fat.

The results of the nutrient intake comparisons among the 3 groups differed between the 20–29-yr-olds and those 30 yr of age or older. The total energy intake was not different among the three groups in the 20–29-yr-old age group, but in the older age groups, the total energy intake of shift workers with midnight shifts was higher than that of fixed day workers. Among 20–29-yr-olds, intakes of some micronutrients, such as calcium, potassium, vitamin A, and vitamin B1, were the lowest in shift workers with midnight shifts; these findings were not seen in the older age groups. In 20–29-yr-old age groups, intakes of meat, dairy products and vegetables were the lowest in shift workers with midnight shift, results which were coincident with the results of comparison of nutrients intakes. We did not find significant effects of shift work without midnight shift on nutritional intakes in the comparison with fixed daytime workers. An irregular work schedule, particularly one that includes midnight shifts, tended to affect nutrient intakes differently, depending on age and shift work history. Younger shift workers, who were not accustomed to midnight shifts, tended to eat less than older shift workers, who were accustomed to midnight shifts, and tended to eat more.

Most previous studies dealing with this issue had a small sample size and usually did not consider the differences in the effects of shift work on lifestyle by age and shift work history. Most studies agree that shift work affects the distribution of food intake over 24 h and the selection of food items[18–22]. In summary, shift workers preferred to eat cold food and fast food; fewer of them eat hot food: they tend to nibble rather than have a meal[21], and have fewer meals[18, 25]. These eating habit changes may increase or decrease intakes of nutrients. However, most studies did not find any differences in total energy and macronutrient intakes[21, 23, 24], though one Japanese study reported that shift workers had a decreased energy intake[25]. The fact that most studies found no differences in total energy and macronutrient intakes may be the result of failing to take into account age and number of years of shift work. It has also been reported that workers who work irregular hours develop a loss of appetite and become reluctant to prepare meals due to difficulties in adjusting to social life and internal circadian rhythm[28]. It has also been reported that the total energy and nutrient intakes increase when individuals eat with others[29]; however, shift workers have fewer opportunities to take meals with their families and friends. These effects appeared to be most prominent among younger workers with midnight shifts, who decreased their micronutrient intakes. On the other hand, the higher total energy intake of older (≥30 yr) shift workers with midnight shifts may be due to the fact that these individuals had become used to shift work: as they got older, they adjusted their social/family life, though they continued to snack.

Previously, we reported an increased risk of hypertension, diabetes mellitus, and weight gain among shift workers based on cohort studies of the same target population[15–17]. The increased risk of hypertension was only found in younger workers[15]. Workers who transferred from fixed day work to shift work and workers who had continued shift work had a greater weight gain during the follow-up period than other workers[17]. The present study showed that younger shift workers with midnight shifts had lower intakes of some micronutrients, while older shift workers had higher total intakes; these findings may be related to those of our previous cohort studies[15–17], but our conclusions are limited by the cross-sectional design of the present study.

To generalize the results from the present study, one needs to consider the characteristics of the subjects of this study, since the effects of shift work on nutrient intake and eating habits are modified by local circumstances, socioeconomic factors, and the shift schedule. The subjects of this study were manual workers who had permanent contracts in the main factory of a large company. Therefore, their socioeconomic status was considered to be relatively good. The shift schedule used in this factory is the usual system that is used in Japanese factories. The factory is located in a rural area where it is not convenient to eat out, but proper meals are served at lunch in the factory's cafeteria. Therefore, our results suggest that shift work, particularly when it includes midnight shifts, affects nutrient intake, even with better socioeconomic conditions.

To conclude, shift work, particularly when it includes midnight shift work, affects nutrient intakes. The type and extent of the effect of shift work on nutrient intakes depends on age and shift work history.

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Original article

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Influence of job strain on changes in body mass index and waist circumference—6-year longitudinal study

by Masao Ishizaki, PhD,[1] Hideaki Nakagawa, PhD,[2] Yuko Morikawa, PhD,[2] Ryumon Honda, PhD,[1] Yuichi Yamada, PhD,[1] Norito Kawakami, PhD,[3] The Japan Work Stress and Health Cohort Study Group[4]

Ishizaki M, Nakagawa H, Morikawa Y, Honda R, Yamada Y, Kawakami N, The Japan Work Stress and Health Cohort Study Group. Influence of job strain on changes in body mass index and waist circumference—6-year longitudinal study. *Scand J Work Environ Health* 2008;34(4):288–296.

Objectives This study examined the effect of changes in psychosocial workplace characteristics on weight gain and abdominal obesity.

Methods Twice, at an interval of 6 years, the authors conducted examinations of job demand–control–support and measurements of body mass index and waist circumference among 2200 men and 1371 women aged 30–53 years and working in a factory. The scores of the psychosocial work characteristics in each examination were dichotomized at the median values for the men and women separately and then categorized into three groups as follows: group I: low score in both the first and second examinations, group II: low score in the first examination and high score in the second (or high at the first and low at the second), and group III: high in both the first and second examinations.

Results Although there was no statistically significant association between psychosocial work characteristics and the change in body mass index, for both genders, the change in waist circumference increased more in group III than in group I. Similarly, the odds ratios for the change in waist circumference above the 75th percentile for groups II and III increased more than in group I, being 1.13 [95% confidence interval (95% CI) 0.87–1.46 and 1.39 (95% CI 1.07–1.79) for the men in groups II and III, respectively, and 1.27 (95% CI 0.90–1.78) and 1.78 (95% CI 1.26–2.52) for the women in groups II and III, respectively.

Conclusions The results suggest that high job strain is a risk factor for increased abdominal obesity.

Key terms job control; job demand; waist circumference change.

Several studies have shown that psychosocial work stress, such as low job control and job strain combined with high job demand and low job control, which are considered to be work stressors in the job demand–control model proposed by Karasek, are related to the development of coronary heart disease (CHD) (1, 2). The pathophysiological mechanism underlying the relationship between work stress and CHD has been suggested to be increased ambulatory blood pressure (3, 4) and abnormalities of blood coagulation and fibrinolytic function (5).

On the other hand, although obesity is an important CHD risk factor, it is still unclear whether work stress is connected to weight gain. The metabolic syndrome, which is a pathophysiological state in which a cluster of factors such as abdominal obesity, atherogenic dyslipidemia, raised blood pressure, and glucose intolerance are believed to promote CHD, is attracting increasing attention (6). A cross-sectional analysis in the Whitehall II study suggested a biological explanation that socioeconomic inequality in CHD was partly attributable to the metabolic syndrome, because people with a lower

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