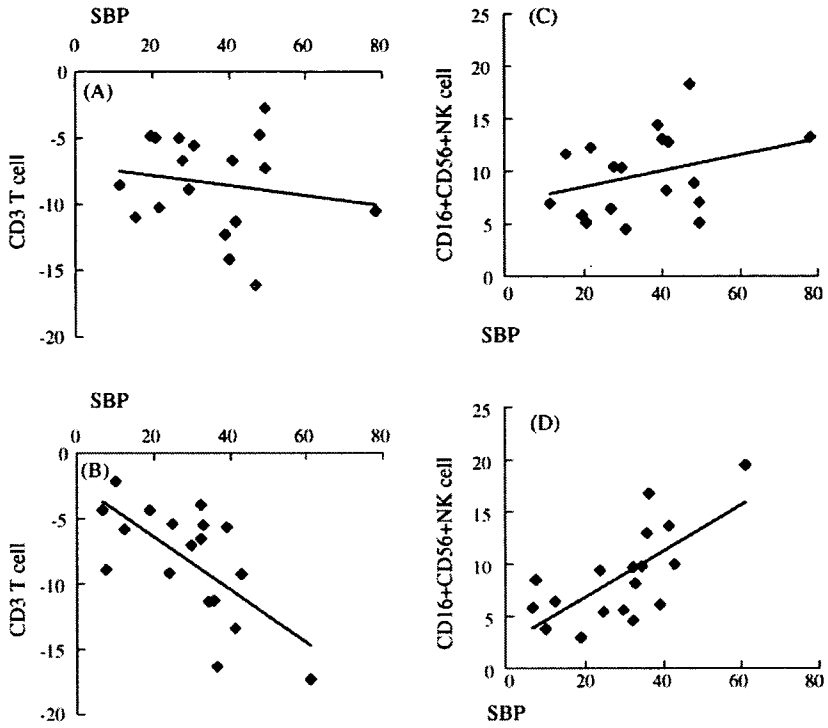

Fig. 3. Scatterplotting of SBP and immune parameters in controllable and uncontrollable groups. A and C: controllable group; B and D: uncontrollable group.

acute stress has been suggested to be adaptive for survival (Engler et al., 2004; Segerstrom and Miller, 2004). An increase of antigen-nonspecific peripheral innate immune cells, here represented by NK cells, might be interpreted as preparation for the potential invasion of bacteria or other antigens by injuring accompanying fight/flight behaviors. A decrease of T cells and B cells might represent trafficking of such cells into the lymph nodes, where helper T cells are sensitized to antigens and cascades of antigen-specific immune responses are initiated. Additionally, the increased NKCA and S-IgA secretion rate by the acute stress task might represent enhancement of functional aspects of innate and mucosal immunity, which might also be adaptive for survival under acute stress. These responses in cardiovascular and immune parameters are consistent with previous studies (Delahanty et al., 2000, 1996; Willemsen et al., 2002; Isowa et al., 2004; Kimura et al., 2005).

It has been suggested that increase of NK cells during acute stress should be mediated by increased blood flow and blood pressure, and effects by E and NE through surface receptors (mainly, β2- and α-adrenoreceptors) (Benschop et al., 1993; Mills et al., 2000; Farag et al., 2002). Although we did not measure catecholamines directly, HRV parameters were evaluated as indirect indices of autonomic activity. As our results indicated, changes in the proportion of NK cells robustly correlated with cardiovascular indices whereas they showed only a limited correlation with HRV. These results suggest that the redistribution of NK cells observed in this study is considered to be mainly caused by an increase of blood pressure rather than an enhancement of autonomic activity. Because blood pressure levels are regulated not only by autonomic activity but also many other endocrine factors (e.g., vasopressin, atrial natriuretic peptide, opioids, oxytocin, angiotensin and so on), the observed increase of peripheral NK cells likely took place as the result of the integrated effects of such cardiovascular and neuroendocrine activities. On the other hand, because the physical effects of increased blood pressure cannot explain the decrease of T cells and B cells in peripheral circulation and the increase of NKCA, such immune changes under acute stress might be mediated mainly by neuroendocrine factors. This speculation is supported by reports that T cells and B cells have receptors for various neuroendocrine substances (Landmann et al., 1984; Van Tits et al., 1990; Kohm and Sanders, 2001).

4.2. *Effects of controllability*

Contrary to our prediction, no effects of controllability of the acute stress task were observed in any immune parameters. These results are consistent with the previous study by Peters et al. (1998), who reported that there were no effects of stress controllability on immune parameters except IL-6 concentration. On the other hand, although Peters et al. (1998, 1999) suggested that an effect of controllability appeared in cortisol level as an index of the HPA axis, we did not observe any effects of stress controllability in cortisol. Considering the null effect in the present study and the inconsistent and mixed results in previous studies (Weisse et al., 1990; Sieber et al., 1992; Gomez et al., 1994; Peters et al., 1998, 1999, 2003), immune and endocrine reactivity to acute stress might not be as sensitive to the controllability of stressors as previously thought.

However before reaching any definitive conclusions, some caveats regarding the present study must be recognized. First, in this study, the difference of perceived controllability between the C and UC conditions was only marginally significant, and thus we must suspend the conclusion that the experimental manipulation of controllability was substantially valid. Second, effects of controllability on the immune system and the HPA axis might have been concealed by the relatively wide inter-individual differences and the small sample size. Third, as regards to the HPA axis, circadian variation might have affected the results of cortisol in this study. The observed trend that the concentration of cortisol decreased according to the progress of the experimental session in all groups suggests such effects of circadian variation. During the time period in the present experiment (i.e., 9:00 a.m.–2:00 p.m.), cortisol levels usually drop; this circadian variation might be contaminated in the reported results. Further studies to control such factors more rigorously are awaited.

4.3. Associations among immune, cardiovascular, and endocrine reactivity in uncontrollable acute stress

As unpredicted results, correlations between the cardiovascular parameters, specifically SBP and DBP, and the immune parameters, especially T cells, helper T cells, and NK cells, were prominent in the UC condition, whereas few and slight correlations among those parameters were found under the C condition (see Table 3). In addition, beginning at 5 min after the start of the task and continuing until the end of the task, uncontrollability served to consistently strengthen the association between cardiovascular and immune parameters. Further, the scatterplotting of indices of blood pressure and immune parameters (see Fig. 3) appeared to suggest that those effects were not just artifacts. Taken together, the findings in the present study for the first time suggest that uncontrollability of acute stress, at least in some situations, might have the effect of strengthening the correspondence between the autonomic nervous and immune systems rather than increasing the reactivity in each system.

Recent neuroanatomical and functional neuroimaging findings can offer suggestions in considering the mechanisms underlying such effects. Much evidence has indicated that the contingency between a stimulus and reward or punishment in a situation should be represented in the orbitofrontal cortex (OFC) in the frontal lobe (O'Doherty et al., 2001a,b). The OFC receives inputs from sensory associative cortices of all modalities and from limbic structures such as the amygdala and the hippocampus (Carmichael et al., 1994; Carmichael and Price, 1995), and has rich connections to the hypothalamus and the periaqueductal gray matter (PAG), that have been implicated in the modulation of autonomic and endocrine functions (Price, 1999; Kringelbach and Rolls, 2004). Based on this neuroanatomical architecture, the OFC might evaluate how one can control the current situation and regulate autonomic and endocrine systems to optimize levels of their activity to meet the current demand. In an uncontrollable situation, when the situation is evaluated as still somewhat controllable and worthy of allocating more resources, sympathetic nervous and endocrine systems might be more activated, and thus enhancement of innate immunity and suppression of specific immunity might be emphasized through increased secretion of catecholamines and glucocorticoid (Peters et al., 1998; Swenson and Vogel, 1983). On the other hand, when the situation is evaluated as totally uncontrollable, the OFC might tune the activity of autonomic and endocrine systems to minimum levels to avoid allocation of resources in vain, in order to increase the chances of survival. In such a case, influences on innate and specific immunity should also decrease. Such processes will lead to relatively wide individual differences in levels of activity in the autonomic, endocrine, and immune systems. Consequently, the correspondence between autonomic activity and immune activity might be strengthened in an uncontrollable stress situation. While, this is speculation because measurement of brain activity was not conducted in this study, our previous research has documented significant activation in lateral and medial OFC under uncontrollable compared with controllable stress using position emission tomography (PET) (Ohira et al., 2004).

4.4. Limitations of the study

First, the relatively small sample size ($N = 43$) and large standard deviation in each parameter suggest that the observed effects in this study might not be robust, although they were statistically significant. Second, the levels of S-IgA secretion at baseline and after stress treatment in the current study were lower than those observed in previous studies (Willemsen et al., 1998; Ring et al., 1999). This inconsistency may be attributable to differences in the methodologies. The S-IgA assay employing ELISA in the studies of Willemsen et al. (1998) and Ring et al. (1999) measured the volume both of IgA monomer of fragment of IgA and S-IgA. However, we measured only the volume of S-IgA secreted in saliva. In addition, values of S-IgA reported in our previous experiments (Isowa et al., 2004; Kimura et al., 2005) are similar to values of S-IgA in the present study. Third, it is still unclear whether the reported results are limited for the mental arithmetic task or can be generalized for other acute stress tasks. The present findings must be replicated using other acute stress tasks and manipulations of controllability over the tasks.

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Visceral sensitivity

Can modulating corticotropin releasing hormone receptors alter visceral sensitivity?

S Fukudo, K Saito, Y Sagami, M Kanazawa

Activation of corticotropin releasing hormone (CRH) receptor 2 (CRH-R2) reduces visceral sensitivity induced by colorectal distension in conscious rats. This finding is relevant to the increased interest in the potential use of therapeutic agents that act on CRH receptors in the treatment of irritable bowel syndrome

Clarifying the adverse effects of stress on bodily function is a crucial paradigm for medical research. Evidence that psychosocial stress aggravates digestive diseases has been accumulating and stress induced exacerbation of symptoms in patients with functional gastrointestinal disorders is well recognised.[1] Corticotropin releasing hormone (CRH), a 41 amino acids peptide produced mainly in the paraventricular nucleus of the hypothalamus, is considered to be a major mediator of the stress response.[2] Indeed, stress is known to induce release of hypothalamic CRH, resulting in pituitary secretion of adrenocorticotropic hormone (ACTH). In addition, stress related activation of CRH receptors has been reported to alter gastrointestinal functions.[3] Moreover, physical or psychological stress is known to delay gastric emptying,[4] accelerate colonic transit,[5] and evoke colonic motility[6] in rats.

Two major G protein coupled receptors for the CRH have been identified, CRH receptor 1 (CRH-R1) and receptor 2 (CRH-R2).[7–9] CRH-R1, which is highly expressed in the anterior pituitary, neocortex, hypothalamus, hippocampus, amygdala, locus coeruleus, and cerebellum, has been reported to mediate stress induced physiological changes, including stimulation of the hypothalamo-pituitary-adrenal axis, elevation of plasma levels of catecholamines, increased colonic motility,[10] and exaggerated stress related behaviour, especially anxiety.[11 12] In addition, stimulation of this receptor is believed to activate adenylate cyclase, an enzyme that catalyses the formation of cyclic AMP (cAMP).[7–9]

We have previously reported increased colonic motility and visceral perception in response to administration of CRH in patients with irritable bowel syndrome (IBS).[13] In addition, earlier studies have indicated that gastrointestinal dysmotility[14] and visceral hypersensitivity[15] are major events in the pathophysiology of IBS. Moreover, patients with IBS have been reported to suffer from a variety of chronic or acute psychiatric conditions, including depression, generalised anxiety, panic, social phobia, and somatisation.[16] Various studies have suggested a relationship between stress induced changes in colonic motility and CRH action in the paraventricular nucleus of the hypothalamus.[17] Accordingly, it has been shown that intracerebroventricular injection of CRH stimulates gastrointestinal motility in a way similar to that induced by stress[18] and that intraperitoneal injection of CRH induces defecation and clustered spike bursts longer than basal spike bursts in rats.[10]

CRH-R1 antagonists have been shown to prevent stress-like gastrointestinal motor responses following central or peripheral injection of CRH.[10] In addition, it has been reported that CRH-R1 deficient mice show impaired response to stress, as indicated by absence of increased ACTH and corticosterone levels following exposure to stress, as well as less pronounced anxiety related behaviour.[11 12] From these findings, it is reasonable to assume that CRH mediates gastrointestinal and behavioural responses to stress via CRH-R1. Actually, in a recent study,[19] we have shown that administration of an α-helical CRH or CRH-R1 antagonist attenuates hippocampal noradrenaline release and reduces the frequency of abdominal contractions induced by acute colorectal distension in rats. We have also shown that the CRH-R1 antagonist used in that study[19] reduced plasma ACTH and anxiety after acute colorectal distension but not after chronic colorectal distension, probably due to habituation. Another important finding of our previous study[19] is that pretreatment with the CRH-R1 antagonist blocked chronic colorectal distension induced increase in rats faecal pellet output. Because the CRH-R1 antagonist used in our previous study[19] is an agent that crosses the blood-brain barrier, both central CRH-R1 and

peripheral CRH-R1 are thought to be responsible for colorectal distension induced sensitisation. Nevertheless, CRH and CRH-R1 in the brain may play a major role in colorectal distension induced anxiety, ACTH release, visceral hypersensitivity, and changes in colonic motility.

Evidence supporting the concept that peripheral CRH and CRH-R1 play important roles in brain-gut sensitisation is increasing. Several studies have identified immunoreactive CRH[20] and urocortin [21] as well as CRH-R1 and CRH-R2 mRNAs in human colonic mucosa.[21] In addition, reverse transcription-polymerase chain reaction (RT-PCR) has revealed expression of CRH-R1 mRNA in both the myenteric and submucosal plexus in the guinea pig.[22] Application of CRH has been shown to evoke depolarising responses associated with elevated excitability in both myenteric and submucosal neurones.[22] On the other hand, peripheral injection of CRH has been reported to induce discrete effects on colonic secretory and motor function, and permeability.[23] We have previously reported that intravenous administration of a non-selective CRH antagonist (α-helical CRH) blunts the exaggerated motility response in the sigmoid colon to electrical stimulation in IBS patients compared with normal subjects.[24] In the same study, we have shown that administration of α-helical CRH induces a significant increase in barostat bag volume in normal subjects but not in IBS patients, and a significant reduction in the ordinate scale of abdominal pain and anxiety evoked by rectal electrical stimulation in IBS patients. However, plasma ACTH and serum cortisol levels were generally not suppressed following administration of α-helical CRH at 10 μg/kg. Although the precise sites of action of α-helical CRH are unknown, we suggested in our previous study that blunting the colonic motor response is mainly due to blockage of peripheral CRH-R1 and that drug anxiolytic or antinociceptive effects are probably based on inhibition of central CRH-R1 via circumventricular organs, which are relatively unprotected by the blood-brain barrier.[24] These findings and concepts, which put in the context of existing preclinical and clinical data, support the testing of new CRH antagonists, particularly potent CRH-R1 antagonists, in IBS and the view that the CRH-R1 receptor is a promising target for the treatment of IBS.[25]

In this issue of *Gut*, however, Million and colleagues[26] provide a new theory for modifying gut sensitivity via CRH-R2 *(see page 172)*. Using RT-PCR, they proved the existence of CRH-R2 in the dorsal root ganglia and spinal cord and hypothesised that CRH-R2 activation may influence visceral pain induced by colorectal distension in conscious rats. By assessing the possible sites and mechanisms of action for CRH-R2 activation, they showed that two repeated colorectal distensions produced visceral sensitisation and phosphorylation of extracellular signal related kinase 1/2 (ERK 1/2) and that intravenous administration of human urocortin 2, a selective CRH-R2 agonist, prevented visceral sensitisation and reduced the second response compared with the first one. Million *et al* also demonstrated that administration of human urocortin 2 dampened distension induced phosphorylation of ERK 1/2 and robust inferior splanchnic afferent spike activity and that treatment with astressin$_2$-B, a CRH-R2 receptor antagonist, reversed the inhibitory effects of human urocortin 2 both in vivo and in vitro.[26]

CRH-R2 is highly expressed in the anterior pituitary, hypothalamus, hippocampus, amygdala, lateral septum, and other peripheral tissues, including the spleen, stomach, and gut.[7–9] Compared with CRH-R1, the functional role of CRH-R2 is relatively obscure. However, recent reports put forward the concept that activation of CRH-R2 signalling pathways may be important to reduce anxiety and stress response.[27 28] There are other functional differences between CRH-R1 and CRH-R2. For example, activation of CRH-R1 causes a proinflammatory response whereas stimulation of CRH-R2 provokes anti-inflammatory changes.[29] In addition, the study by Million and colleagues[26] offers evidence of the contrasting roles of CRH-R1 and CRH-R2 in visceral nociception. While CRH-R1 is involved in the pronociceptive effects of visceral pain, CRH-R2 mediates antinociceptive responses. These findings are supported by a recent report from another group.[30]

Several questions arise from these animal experiments. Do endogenous CRH-R2 ligands such as CRH, urocortin 1, urocortin 2, urocortin 3 (stresscopin), and stresscopin related peptides play an inhibitory role in visceral hypersensitivity in IBS patients? If so, are selective CRH-R1 antagonists more effective for visceral hypersensitivity than non-selective CRH antagonists? Moreover, do agents that block CRH-R2 have any adverse effects on the pathophysiology of IBS? Do CRH-R2 agonists have therapeutic value for IBS and/or allied functional gastrointestinal disorders, even though stress induced inhibition of gastric emptying is mainly mediated via CRH-R2? What are the major steps from the synthesis of cAMP by activated CRH-R2 in the dorsal root ganglia and spinal cord to reduced phosphorylation of ERK 1/2 in the laminae I and II? Thus the disclosed nature of CRH-R2 reported in the present issue of *Gut* brings us an exciting paradigm on research and drug development of the CRH neuropeptide family.

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Incretin

To be or not to be—an incretin or enterogastrone?

M Horowitz, M A Nauck

Glucagon-like peptide 1 does not comfortably fulfil the criterion of a gut derived factor responsible for an enhanced meal related insulin response; it appears logical to add the definition of a "physiological incretin hormone"

Incretin hormones are gut derived peptides that augment the insulin releasing action of hyperglycaemia. In his seminal review, based on the 1978 Claude Bernard lecture, delivered at the European Association for the Study of Diabetes Meeting, Werner Creutzfeldt defined the term incretin as "an endocrine transmitter produced by the gastrointestinal tract which is: (a) released by nutrients, especially carbohydrates and (b) stimulates insulin secretion in the presence of glucose if exogenously infused in amounts not exceeding blood levels achieved after food ingestion".[1] At that time, the best characterised incretin candidate was glucose dependent insulinotropic polypeptide (GIP), although there was evidence that GIP was not the only incretin.[1 3] An incretin role for GIP was established, along the lines of Creutzfeldt's definition,[1] by intravenous infusion in healthy subjects, both alone and in combination with glucose, and demonstrating that the insulinotropic property of GIP was dependent on a permissive rise in blood glucose.[2] Subsequent experiments, performed under more physiological conditions, with plasma GIP and glucose concentrations mimicking the postprandial state, confirmed these observations.[4] That relatively uncomplicated infusion experiments had the capacity to predict the physiological role of GIP with regard to its effects on insulin secretion is testimony to the fact that, metabolically speaking, GIP is apparently devoid of additional actions which have the potential to confound such experiments.[5]

The situation with glucagon-like peptide 1 (GLP-1) is far less straightforward. The GLP-1/glucose infusion experiment results in effects similar to those observed with GIP,[6] and GLP-1, accordingly, fulfils the definition of an incretin hormone, as put forward by Creutzfeldt.[1] However, studies which have evaluated the effects of GLP-1 on the metabolic response to a meal, by infusing physiological or pharmacological amounts of GLP-1,[7] or interfering with endogenous GLP-1 action with the well characterised GLP-1 antagonist exendin(9–39),[8–10] have revealed a complex pattern of GLP-1 actions. In particular, as a result of its effect on slowing gastric emptying substantially, exogenous GLP-1 attenuates the postprandial rise in glycaemia, leading to lesser substrate (glucose) mediated insulin secretion and an overall reduction, rather than an increase, in the insulin secretory response to a meal.[7 11 12] In other words, inhibition of gastric emptying by exogenous GLP-1 outweighs its direct insulinotropic effects. This was highlighted in a recent study demonstrating that intravenous erythromycin, as a result of its prokinetic properties, abolishes the deceleration of gastric emptying induced by exogenous GLP-1 in healthy subjects and that this is associated with a marked reduction in its glucose lowering effect.[12] Furthermore, the GLP-1 antagonist exendin(9–39) increases, rather than lowers, the insulin response to a meal.[13] Based on these observations it is clear that GLP-1 does not comfortably fulfil the criterion of a gut derived factor responsible for an enhanced meal related insulin response; furthermore, it appears logical to add the definition of a "physiological incretin hormone" to that provided by Creutzfeldt,[1] and assigning such a role to GLP-1 appears inappropriate based on current data.[11]

In their important study in the current issue of *Gut*, Schirra and colleagues[14] have introduced a new approach to evaluation of the incretin role of GLP-1 in healthy subjects ***(see page 243)***. They used intraduodenal administration

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ORIGINAL ARTICLE

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Job strain and sick leave among Japanese employees: a longitudinal study

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Abstract *Objectives:* The present study is an investigation of the association between job stress, determined on the basis of a demand–control model or worksite social support at the baseline, and absence due to illness among employed Japanese males and females. *Methods:* We analyzed 448 male and 81 female subjects who had taken no sick leave in the year preceding the baseline (1997) and observed them all until 1999. A self-administered questionnaire was the source information collected. It consisted of questions on socio-demographic variables, occupations, health-related behavior, a Japanese version of the Job Content Questionnaire, and the number of absences in the year preceding both the baseline and follow-up. Logistic regression analyses were used to determine how the characteristics of a job at the baseline affected sickness absence of 5 days or longer per year; controls were established for the gender, age, level of education completed, occupation, number of cigarettes smoked daily, and the amount of alcohol consumed weekly. *Results:* Compared to the lowest tertile of the ratio of demand to control (job strain), the highest tertile was significantly associated with an increased risk of sickness absence of 5 days or longer per year (odds ratio 3.02; 95%CI 1.00–9.16) at follow-up. The dose–response relationship was supported (p for trend < 0.05). However, individual variables of job demand, job control, and worksite social support were not significantly associated with the risk of absence from illness. *Conclusions:* The study provided prospective evidence that job strain leads to an increased risk of sick leave among Japanese employees.

Keywords Job strain · Sick leave · Demand-control model · Japanese employee · Prospective study

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Introduction

The effects of job strain, as defined by the job demand–control model [6] or the job demand–control–support model [5], on sickness absence among employees have been investigated in previous research. Cross-sectional studies indicated that job strain is associated with the number of days attributed to sick leave taken 12 months prior to the study [3, 11]. Longitudinal studies have shown that lower job control is associated with an increased risk of short (0–7 days) [18, 26], long (7 days or longer) [18], and very long term (1 month or more) of sick leave [1], as well as the frequency and length of the sick leave [16, 19]. Greater social support at work has also been linked with a reduced risk of short-term spells of sick leave [2, 18, 26] or long-term sick leave [1].

The findings with respect to associations between job demand and sick leave have been inconsistent. For example, some studies have shown an association between *lower* job demand and an *increased* risk of sickness absence [18, 19]. The effects of the demand of a job on sick leave are generally observed in favorable labor market conditions in which employees have the choice of taking sick leave or changing jobs [19]. When an employee is highly committed to the job, the job demand may preclude taking sick leave [18]. In such cases, some employees may find it difficult to take sick leave because of self-imposed and external pressures to perform their jobs completely. In addition, among these previous longitudinal studies, only two showed a significant association among job strain, a combination of greater job demand and less job control, and an increased risk

of short-term sick leave [2, 18]. Furthermore, reports from these studies indicated that the association was observed only among limited groups of employees, i.e., male employees with low levels of employment [18] and female employees [2].

Moreover, from a methodological viewpoint, most previous longitudinal studies [1, 2, 18, 26, 16] did not consider sick leave at the baseline, which might have resulted in a limited interpretation of the findings: if subjects with greater sick leave days reported high job stress at the baseline, an apparent association would be expected between baseline job strain and sick leave at the follow-up. The relationship between job strain and sick leave has been examined in only one study in which controls were established for sick leave at the baseline [19]. However, this study did not reveal any significant association between job strain and sick leave because the job demand was negatively associated with sick-leave absences. Thus, there is still limited evidence in longitudinal studies for an association between the job demand–control (–support) model and sick leave.

It is generally accepted that Japanese employees take fewer sick leave days than their western counterparts. For instance, Japanese companies have reported that 2.8% [14] of male employees took 7 days or longer sick leave per year, while 14.5% of the male workers in the UK Whitehall II study took an equivalent amount [25]. In a previous study the employees ($n = 1,183$) at the baseline who took 7 days or longer sick leave in a year was 6.2% for males and 8.6% for females. Japanese employees appear to have greater commitment to their jobs and companies [12]. Moreover, it is suggested that Japanese ethics may discourage employees from taking sick leave even when they are ill [15]. The characteristics of the Japanese labor market may account for the differences between job strain and sick leave that are reported in western countries.

Several studies in Japan have explored the effects of mental health-promotion programs [22, 23] and related improvements in the working environment [9]. These studies indicate that such psychosocial interventions may have a positive effect on sick leave patterns related to job stress and lack of social support received at the worksite. However, to date, no epidemiological evidence is available on the association between job strain and sick leave in Japan. Most previous studies on the association between job stressors and sick leave, except the one from Singapore [27], were conducted in western countries, such as the EU, the UK, and the US. It is important to investigate whether or not the association between the job demand–control (–support) model and sick leave can be generalized to non-western working populations.

The purpose of this study was to determine whether job strain and social worksite support for Japanese employees at the baseline can predict how sick leave will be used. At the baseline, only subjects without a history of taking sick leave were used in the study; this restriction was used to obtain a clearer effect of job strain on taking sick leave. In previous studies [1, 2, 16], a worksite social-support scale was established by combining the support from supervisor and co-worker. In this study, to determine differences in the outcome, the effects of support from supervisors and co-workers were examined separately.

Methods

Study subjects

In 1997, a baseline questionnaire was given to 2,625 employees of an electronics firm in Gifu Prefecture, Japan, whose age ranged from 18 to 60. A total of 2,364 (90%) employees (1,902 males and 462 females) returned the questionnaire. Of these, 2,035 employees (1,688 males and 347 females) completed all of the relevant questions in the baseline questionnaire, and these subjects were followed-up. In 1999, follow-up studies were conducted and complete responses obtained from 1,183 subjects (997 males and 186 females) (follow-up rate 58%).

Among the follow-up individuals, 448 males and 81 females reported that they had not used sick leave in the year preceding the baseline (45 and 44%, respectively). The analyses were restricted to those subjects who had not reported the use of sick leave at the baseline in order to test strictly the relationship between job strain and the use of sick leave.

The characteristics of the male/female subjects were as follows: the average age (standard deviation) was 33.5/31.7 (9.8/7.6) years, and 41.7/16.0% of the subjects had completed more than 12 years of education. The male/female employee were categorized into three occupations: managers (13.2/0.0%), white-collar workers (professionals, technicians, clerks, and service workers) (43.8/59.3%), and blue-collar workers (mechanics, laborers and unspecified) (43.1/40.7%).

Measures

Self-administered questionnaires were used for data collection in 1997 and 1999. The questionnaire asked for information on socio-demographic variables, occupations, health-related behavior, and sick leave and included a Japanese version of the Job Content Questionnaire (JCQ).

The JCQ was designed to measure work environment characteristics based on the demand–control–support model [5–7]. The Japanese version of the JCQ has been validated and tested for reliability [8]. The questionnaire consists of scales of job demand (five items), job control (nine items), supervisory support (four items), and co-worker support (four items); Likert-scale response options from 1 (completely disagree) to 4 (completely agree) were used. Cronbach's alpha coefficients among the study subjects were 0.66 for job demand, 0.84 for job

control, 0.85 for supervisor support, and 0.73 for co-worker support. Job demand, job control, and worksite social support at the baseline were calculated by summing the scores according to the JCQ guideline [7] and dividing the results into tertile. As an indicator of job strain, the ratio of job demand to job control was also calculated and divided into tertile.

Sick leave absences were measured by self-reporting as the total for the year preceding the baseline and the follow-up. The average number (standard deviation) of days used for sick leave was 2.3 (9.0) at the baseline ($n=1,688$) and 2.7 (16.5) at the follow-up ($n=997$) for males and 3.8 (20.0) at the baseline ($n=347$) and 2.5 (3.9) at the follow-up ($n=186$) for females. Considering the small number of sick leave days, this study sample was divided into two groups based on the sick leave days for the past year at follow-up: 5 days or longer ($n=33$) and 0–4 days ($n=496$).

Health-related behavior included the number of cigarettes smoked daily and the amount of alcohol consumed weekly. The number of cups was estimated from the amount and type of alcohol consumed: one cup was equal to 350 ml of beer, 120 ml of wine, or 40 ml of whisky.

Table 1 The association between studied variables at baseline (1997) and sickness absence (5 days or longer per year) at follow-up (1999) among employed Japanese males ($n=448$) and females ($n=81$) who had no sickness absence at baseline

Variable	Sickness absence of 5 days or longer					
	N	*n*	%	Crude OR	95%CI	
					Lower	Upper
Job demand						
Low	168	7	4.17	1.00		
Medium	191	10	5.24	1.27	0.47	3.42
High	170	16	9.41	2.39	0.96	5.97
Job control						
Low	172	13	7.56	1.00		
Medium	192	10	5.21	0.67	0.29	1.57
High	165	10	6.06	0.79	0.34	1.85
Job strain (job demand/control ratio)						
Low	176	6	3.41	1.00		
Medium	176	13	7.39	2.26	0.84	6.09
High	177	14	7.91	2.43	0.91	6.49
Supervisor support						
Low	162	10	6.17	1.00		
Medium	79	5	6.33	1.03	0.34	3.11
High	288	18	6.25	1.01	0.46	2.25
Co-worker support						
Low	118	9	7.63	1.00		
Medium	165	6	3.64	0.46	0.16	1.32
High	246	18	7.32	0.96	0.42	2.20
Gender						
Male	448	31	6.92	1.00		
Female	81	2	2.47	0.34	0.08	1.45
Age						
29 years or less	215	13	6.05	1.00		
30–39 years	189	14	7.41	1.24	0.57	2.72
More than 40 years	125	6	4.80	0.78	0.29	2.12
Education						
12 years or less	329	16	4.86	1.00		
More than 12 years	200	17	8.50	1.82	0.90	3.68
Occupation						
Managers	59	6	10.17	1.00		
White collar	244	13	5.33	0.50	0.18	1.37
Blue collar	226	14	6.19	0.58	0.21	1.59
Smoking						
Non-smoker	303	16	5.28	1.00		
1–14 per day	57	1	1.75	0.32	0.04	2.47
15 or more per day	169	16	9.47	1.88	0.91	3.85
Drinking						
None	102	7	6.86	1.00		
one cup	233	11	4.72	0.67	0.25	1.79
two cups or more	194	15	7.73	1.14	0.45	2.89

The variables were classified into tertiles except for gender, education, and occupation

Statistical analysis

The odds ratios (ORs) and 95% confidence intervals (95% CIs) of using 5 days or longer sick leave for the year preceding the follow-up were calculated with a simple logistic regression analysis and showed crude odds ratio for all variables (Table 1). Confounding factors included gender, age (categorized = < 29 years, 30–39 years, = > 40 years), education completed (categorized = < 12 years and > 12 years), occupation, daily tobacco consumption (categorized non-smoker, 1–14 per day, = > 15 per day), and weekly alcohol consumption (categorized non-drinker, one cup per week, = > two cups per week). These variables affect health outcomes and were treated as confounding factors in previous studies on sick leave related to job strain [18, 26, 2, 21]. Job strain, supervisory support, and co-worker support were entered by force in a multiple logistic regression model using sick leave as a dependent variable, and any trend in the pattern was determined (Table 2). Analyses were conducted by using SPSS 11.0J [24].

Results

The crude ORs and 95% CIs for sick leave in the follow-up study are shown in Table 1 according to the studied variables at the baseline. A medium or high level of job strain, in comparison with a low level of job strain, at the baseline was marginally and significantly associated with increased risk of being absent for 5 days or longer during the previous year, as determined by the follow-up study. A high level of job demand was also marginally and significantly associated with increased risk. Subjects with high job control or high worksite support at the baseline were less likely to have taken sick leave as reported in the follow-up study, but the associations were

Table 2 The association between pyschosocial job characteristics at baseline (1997) and sickness absence (5 days or longer per year) at follow-up (1999) among employed Japanese males ($n = 448$) and females ($n = 81$) by logistic regression analysis, including the results for the confouding factors

Variable	Sickness absence of 5 days or longer ($n = 33$)			
	Adjusted OR	95%CI		p value for trend
		Lower	Upper	
Job strain (job demand/control ratio)				
Low	1.00			
Medium	2.11	0.74	5.98	
High	3.02	1.00	9.16	< 0.05
Supervisor support				
Low	1.00			
Medium	1.02	0.32	3.28	
High	1.00	0.41	2.47	n.s.
Co-worker support				
Low	1.00			
Medium	0.42	0.14	1.30	
High	0.84	0.33	2.16	n.s.
Gender				
Male	1.00			
Female	0.45	0.09	2.20	
Age				
29 years or less	1.00			
30–39 years	1.07	0.42	2.70	
More than 40 years	0.35	0.07	1.71	
Education				
12 years or less	1.00			
More than 12 years	1.88	0.68	5.18	
Occupation				
Managers	1.00			
White collar	0.22	0.05	1.00	
Blue collar	0.29	0.05	1.67	
Smoking				
Non-smoker	1.00			
1–14 per day	0.35	0.04	2.84	
15 or more per day	1.94	0.85	4.45	
Drinking				
None	1.00			
one cup	0.41	0.14	1.23	
Two cups or more	0.68	0.23	1.95	

not statistically significant. There were no significant differences in gender, age, occupation, and weekly alcohol consumption between the two groups, one that took 0–4 sick days and the other that took 5 days or longer. However, in the group that look 5 days or longer sick leave, the daily tobacco consumption and higher level of education completed were marginally and significantly higher.

The multiple logistic regression analysis indicated that individuals exposed to high strain at the baseline were three times more likely to have taken 5 days or longer sick leave after adjusting for gender, age, education completed, occupation, daily tobacco consumption, and weekly alcohol consumption (Table2), and, in addition, the risk increased significantly along with increasing levels of job strain ($p < 0.05$). Worksite social support was not associated with a reduction in the risk of sick leave. The logistic regression model with job demand and job control, in place of job strain (demand/control ratio), as independent variables provided no significant associations (OR 1.22; 95%CI 0.43–3.48 and OR 2.00; 95%CI 0.75–5.36 for medium and high demands, respectively; OR 0.62; 95%CI 0.24–1.59 and OR 0.44; 95%CI 0.14–1.39 for medium and high controls, respectively). The trend in the risk of 5 days or longer sick leave was not significant when considering job demand or job control.

The different figures may appear with a different dichotomization of the number of sick leave days. Analyses were repeated with different dichotomizations (Table 3). Similar association was shown with the dichotomization of 4 days or longer, and the dose–response relationship was supported. Higher strain was associated with sick leave of six or more days and seven or more days, but the associations were not statistically significant.

Discussion

After adjusting for gender, age, education, occupation, and health-related behavior, a high level of job strain was found to be associated with an increased risk of sick leave in the follow-up study of Japanese employees who had not taken sick leave at the baseline. The present study demonstrated a prospective association between job strain and sick leave.

In the present study, the total number of sick leave days taken in the previous year was counted and the data divided into two groups, one of 5 days or longer and the other of less than 5 days. The findings here are compatible with earlier studies that focused on short-term spells of sick leave. Bourbonnais and Mondor [2] found that female employees with high demand and low control over their jobs were quite likely to take more short-term sick leave (incidence ratio 1.20). North et al. [18] found that men who reported high job demand and low job control took 10–20% more sick leave for short-term periods. Kristensen [11] indicated that absences due to sickness were not a simple indication of the adverse health effects of job stressors but, rather, could be determined individually by integrating several relevant factors, such as work environment characteristics, an employee's personal perception of his health status, and his coping possibilities. Kivimaki et al. [10] suggested that short-term sick leave indicates employees have coped with job stress. If Kivimaki's results could be applied to our sample, it might be concluded that subjects who were exposed to high job strain developed coping behavior.

Although the trends were as expected, the individual variables of job demand and job control were not significantly associated with increased risk of taking sick leave. In agreement with Karasek's theory, the combination of high job demand and low job control may be the best predictor of health outcome. With regard to job demand, low-scale reliability of the variable may result in an underestimation of the associations.

Co-worker support resulted in a reduction in the risk of sick leave, and, in this study, supervisory support was not associated with sick leave. As reported elsewhere, Japanese employees' behaviors for sick leave in relation to their colleagues may be unique [15]. Japanese employees may not use sick leave, even when they are sick, because they do not want to inconvenience their co-workers or supervisors. On the other hand, a conscientious

Table 3 The association between pyschosocial job characteristics at baseline (199 7) and sickness absence (4, 6, and 7 days or longer per year) at follow-up (1999) among employed Japanese males ($n = 488$) and females ($n = 81$) by logistic regression analysis, adjusted by gender, age, education, occupation, smoking, and drinking

Variable	Sickness absence of 4 days or longer a year ($n = 41$)			Sickness absence of 6 days or longer a year ($n = 25$)			Sickness absence of 7 days or longer a year ($n = 20$)		
	Adjusted OR*	95%CI		Adjusted OR*	95%CI		Adjusted OR*	95%CI	
		Lower	Upper		Lower	Upper		Lower	Upper
Job strain (job demand/control ratio)									
Low	1.00			1.00			1.00		
Medium	1.86	0.70	4.97	1.96	0.62	6.19	2.27	0.63	8.17
High	3.27	1.20	8.96	2.64	0.76	9.16	2.51	0.60	10.51
p for trend	$p < 0.05$			n.s.			n.s.		

* Odds ratio was adjusted for gender, age, education, occupation, smoking, and drinking

supervisor would advise an employee to take sick leave when ill. Associations between worksite support and the use of sick leave, because of its complexity, may require further study. A comparative study examining supervisory and co-worker supports separately might produce valuable insights.

Job strain was significantly associated with the number of sick days taken: 4 days or longer and 5 days or longer, and the dose–response relationship was supported. Similar associations were found when we used different outcomes of more frequent sick leave (6 days or longer); however, the associations were insignificant and the dose–response relationship became unclear. The reason considered was that the power was insufficient to detect the association, because the number of subjects who had much more frequent sick leave was small.

The present study had several limitations. The retrospective power analyses suggested that the number of the participants to contrast the differences between the risk and non-risk groups by 80% power was more than 400 in one group. Probably, observed negative findings reflected lack of study power. The follow-up rate of the study sample was relatively low (58%). Compared to the non-respondents at the follow-up study, the respondents had some significant differences on the variables at the baseline: the rate of males was higher, the education level, and job control were lower. This finding could not explain whether the relationship between job strain and the use of sick leave might either be overestimated or underestimated because the information on non-respondents, including the reasons for their leaving the company, was insufficient. In addition, the measures of work environment characteristics and the data on sick leave were based on self-report. Self-reporting of sick leave may be valid [4], but the present study should be replicated using more objective information. Furthermore, no effort was made to distinguish between the frequency of sick leave and its duration. Finally, no adjustments were made for baseline health status and personality, which could potentially confound the association [27, 17, 20, 13].

In spite of these limitations, the present study indicates that a high level of job strain may be associated with an increased risk of sick leave among Japanese employees who take sick leave less frequently than their counterparts in western countries, although further study may be required.

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ORIGINAL ARTICLE

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Psychosocial work characteristics and sickness absence in Japanese employees

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Abstract *Objectives*: This study was undertaken to examine the association between sickness absence in Japanese employees and job demand/control and occupational class as psychosocial work characteristics. *Methods*: The study was cross-sectional in design with data collected from 20,464 male and 3,617 female employees, whose mean age was 40.9 years (SD ± 9.1 years) and 36.9 years (SD ± 10.8 years), respectively. The participants were asked to write the total number of sick leaves they had taken during the past year, and a comparison was made between the group with more than 6 days of sickness absence and the group with 0–6 days as a reference group. Job demands, job control, and worksite support from supervisors and colleagues were analyzed by the Job Content Questionnaire, and likewise by the Generic Job Stress Questionnaire of the National Institute for Occupational Safety and Health. *Results*: Both low job control and low support at the worksite were associated with a high frequency of sickness absence. But there was no clear relationship between job demands and sickness absence. The lowest sickness absence rate was found in male managers and the highest in male and female laborers. *Conclusion*: This is the first report of a large-scale survey of Japanese employees to show a high frequency of sickness absence associated with increased work stress and a socioeconomically low occupational class.

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Keywords Sickness absence · Work stress · Occupational class

Introduction

Sickness absence at the workplaces is importantly related to low productivity and increased costs, and is related to the general health of employees. According to the Whitehall II, a cohort study of British civil servants, ill health was strongly associated especially with a longer spell of sickness absence (Marmot et al. 1995). The study of civil servants demonstrated that there was a clear association between medically certified sickness absence and mortality (Kivimäki et al. 2003), and a Finnish study also demonstrated a similar association (Vahtera et al. 2004a). They proposed that sickness absence could be used as a measure of health differentials in the working population even though sickness absence was influenced by multiple factors, including geographical, organizational, and personal ones (Searle 2003).

In Japan not many studies have been conducted on absence from work from the viewpoint of employee health. One of the reasons for this is that obtaining the complete data of employees' sick leaves is difficult, because they often take paid holidays within their rights instead of sick leaves even when they are really sick (Ogura et al. 1998). Another reason may be that the rate of absence from work in Japan is relatively low among OECD countries (Organisation for Economic Co-operation and Development 1991). A Japanese study of eight companies of over 1,000 employees each showed that the mean of the frequency of sickness absence of more than 6 consecutive days was 3/100 person years (Muto et al. 1999). This figure was low compared with the mean frequency of sickness absence of more than 7 consecutive days in the Whitehall II study (North et al. 1993); 12/100 person years for males and 30/100 person years for females. Moreover, a comparison study between the Japanese employed at a manufacturing factory and the Whitehall II demonstrated that the incident rate of

the first occurrence of more than 7 consecutive day sickness absence in Japan was lower than that in the United Kingdom (Morikawa et al. 2004).

In the meantime, it has been reported that sickness absence was influenced by various personal factors, such as gender, smoking, alcohol consumption, marital status, educational background, physical load, and social class (North et al. 1993; Niedhammer et al. 1998; Smulders and Nijhuis 1999; Voss et al. 2001). Besides, high work stress elucidated by Karasek's job demand/control model as a psychosocial work characteristic had advanced effects not only on various disorders such as coronary heart disease and psychiatric and musculoskeletal problems but also on sickness absence. Previous studies on the relationship between job demand/control and sickness absence pointed out that low control and low support were the main risk factors of increased sickness absence even after adjustment for age, smoking, alcohol consumption, marital status, education and occupation (Niedhammer et al. 1998) or adjustment for smoking, alcohol consumption, and sedentary status (Vahtera et al. 2000).

On the other hand, although several studies in Japan reported that sickness absence was associated with various factors such as sense of coherence, health promotion programs, and overtime working (Nasermoaddeli et al. 2003; Shimizu et al. 2003, 2004), few Japanese studies can be found on the influence of job demand/control on sickness absence. In addition to this, some indexes related to the health of Japanese employees were different from those in the UK study showing a socioeconomic gradient. While the rates of obesity, smoking, and lack of exercise were the highest in the low employment grade workers in the British study, Japanese data showed that higher grade employees had higher body mass index, and that leisure time physical activity was less even in managers, professionals, and manual workers than in clerks and service workers (Martikainen et al. 2001; Takao et al. 2003).

This situation prompted us to examine the association between job demand/control model and sickness absence and also the association between occupational class and sickness absence by using the baseline data from a multi-site prospective study for the Japanese in order to elucidate the relationship between psychosocial work factors and health.

Methods

Nine companies or factories participated in the baseline study. They were a light metal factory, three electrical manufacturing factories, two steel products factories owned by the same company, a heavy-metal products factory, an automobile plant, and a car products factory. The methods of collecting data were slightly different from firm to firm. All the employees were invited to participate at four sites. All the workers undergoing an annual medical checkup were invited at three sites. At another site the participants were restricted to the males aged 35 and over who underwent the checkup. And at the remaining site participating subjects were limited to supervisors and managers. All the information about the baseline study was obtained from the self-administered questionnaires conducted from April 1996 to May 1998; 21,248 males, 3,745 females, and 111 of unknown gender aged from 18 to 72 years replied. The average response rate was 85.2%, ranging from 73 to 100%, with the exception of 47% at a steel products factory. Details are available in previous reports (Takao et al. 2003; Kawakami et al. 2004).

Sickness absence

The participants were requested to write the total number of sick leaves they had taken during the past year, and with 6 days being close to the 90th percentile of the total sick leave of the participants, a comparison was made between the group taking more than 6 days of sickness absence and the group taking 0–6 days as a reference group.

Psychosocial work characteristic

Job demands, job control, and worksite support from supervisors and colleagues analyzed by the Job Content Questionnaire (JCQ) (Kawakami et al. 1995) and likewise by the Generic Job Stress Questionnaire of the National Institute for Occupational Safety and Health (GJSQ) (Haratani et al. 1993, 1996) were classified as equally as possible into tertiles. In addition, job strain was defined as the ratio of job demands divided by job control.

The GJSQ has been used as frequently as JCQ to evaluate psychosocial work characteristics in Japan (Kawakami and Haratani 1999; Nakata et al. 2004). Out of the 13 scales of job stressors of GJSQ, we selected four scales, i.e. quantitative workload as job demands, job control, support from supervisors, and support from colleagues, which are composed of 11 items, 16 items, 4 items, and 4 items, respectively. Questions were scored on a Likert scale of 1–5 and the possible ranges of the scores were 11–55 in job demands, 16–80 in job control, 4–20 in support from supervisors, and 4–20 in support from colleagues.

Occupational class

We classified occupations into nine categories: eight categories assessed by ILO (International Labour Office Staff 1991), i.e. managers, professionals, technicians, clerks, service workers, skilled workers, machine operators and laborers, and an additional category for the other occupations. As the number of female managers was only five, we included the female managers in the professional group.

Other personal characteristics as confounding factors

The personal factors we adopted as possible covariates were categorized as follows. Smoking habit was divided into non-smoking or current smoking. Alcohol consumption was calculated in terms of ethanol volume consumed per week: none, 175 g and less, 176–350, 351–525, and 526 g and more. Marital status was divided into married, single, divorced, and widowed. Educational level was classified as 'less than 12 years of education', '12–15 years', and 'more than 15 years'. Cohabitation with children was asked about to determine the family status. Health status referred to current diseases and any history of hypertension, hyperlipidemia, diabetes, or other diseases including cardiovascular, digestive, hepatic, renal, musculoskeletal, malignant neoplasms, and psychiatric problems. Anyone having any one of these diseases was classified into the "disease" group.

Statistical methods

Statistical analyses were undertaken using the SAS program package, and males and females were analyzed separately. The differences of sickness absence in terms of age and occupational classes were determined by χ^2 test. Logistic regression analyses were conducted to estimate the odds ratios of sickness absence according to both psychosocial work characteristics and occupational classes after adjustment for age, smoking, alcohol consumption, marital status, educational level, cohabitation with children, history of disease as confounding factors, and companies as well because of the different constituents of the participants among companies. The subjects in this study were limited to the full-time employees up to 60 years of age. No statistical change in the result was observed even when we filled in the blanks of JCQ and GJSQ with the mean values.

Results

Valid data of sickness absence were obtained from 20,464 males and 3,617 females, whose mean age was 40.9 years (SD ± 9.1 years) and 36.9 years (SD ± 10.8 years), respectively. Frequencies of sickness absence for four age groups are shown in Table 1. The frequency of sickness absence was the highest for the 31–40 year-old male group and for the 51–60 year-old female group. No significant trend toward increased frequency with advanced age was recognized. The frequencies were higher for females than for males with the exception of the 31–40 year-old group.

The correlation coefficients between the scores of JCQ and GJSQ in terms of psychosocial work characteristics were 0.53 for job control, 0.65 for job demands, 0.56 for support from supervisors, and 0.40 for support from colleagues in males, and 0.40, 0.66, 0.56, and 0.40, respectively, in females. Table 2 shows the odds ratios of sickness absence according to the potential confounding factors. Current smokers, divorced or diseased people showed higher rates of sickness absence, while people who drink less or live with children showed lower rates. Males with a lower level of education showed a higher rate of sickness absence, while in females the highest level of education was related to a higher rate but not statistically significantly so.

Table 3 shows the odds ratios of sickness absence according to psychosocial work characteristics. In males, increased job control and support from supervisors and colleagues were significantly associated with lower sickness absence in both JCQ and GJSQ, with the exception that the association between support from colleagues and sickness absence in GJSQ was not significantly correlated. With increased job strain, sickness absence escalated. Regarding job demands, only the high job demand in GJSQ was significantly associated with decreased sickness absence. No significant change in the trend was noted other than slight attenuation of the associations after adjustment for possible confounders.

Table 1 The frequency of sickness absence (> 6 days/year) by age

	Males	Females
18–30 years of age	285/3,181 (9.0%)	151/1,309 (11.5%)
31–40 years of age	595/6,276 (9.5%)	71/861 (8.2%)
41–50 years of age	667/7.753 (8.6%)	87/957 (9.1%)
51–60 years of age	302/3,254 (9.3%)	63/490 (12.9%)
P^a	0.32	0.01

[a] χ^2 test

Table 2 Odds ratios (95% confidence intervals) of sickness absence (> 6 days/year) according to potential confounding factors

	Males	Females
Current smoking		
No	1	1
Yes	1.31 (1.18–1.46)	1.43 (1.00–2.04)
Alcohol consumption (g/week)		
No	1	1
1–175	0.68 (0.60–0.77)	0.82 (0.66–1.03)
176–350	0.63 (0.53–0.75)	1.11 (0.32–3.73)
351–525	1.01 (0.75–1.37)	
526–	1.34 (0.78–2.30)	
Marital status		
Married	1	1
Single	1.22 (1.09–1.37)	1.16 (0.91–1.47)
Divorced	2.22 (1.62–3.04)	1.64 (0.88–3.08)
Widowed	1.21 (0.63–2.33)	1.44 (0.75–2.76)
Education (years)		
≤ 11	1.84 (1.57–2.15)	0.88 (0.50–1.56)
12–15	1.37 (1.22–1.54)	0.64 (0.37–1.10)
≥16	1	1
Cohabitation of children		
No	1	1
Yes	0.90 (0.81–0.99)	0.76 (0.61–0.94)
Disease		
No	1	1
Yes	2.49 (2.23–2.78)	2.37 (1.91–2.95)

Table 3 Odds ratios (95% CI) of sickness absence (> 6 days/year) in relation to psychosocial work characteristics

	JCQ				GJSQ			
			After adjustment				After adjustment	
	Medium	High	Medium	High	Medium	High	Medium	High
Job control								
Male	0.83 (0.73–0.94)	0.68 (0.59–0.78)	0.85 (0.73–0.98)	0.77 (0.66–0.90)	0.81 (0.72–0.90)	0.56 (0.50–0.64)	0.83 (0.73–0.94)	0.67 (0.58–0.77)
Female	0.86 (0.65–1.14)	0.80 (0.61–1.05)	0.89 (0.66–1.22)	0.82 (0.60–1.12)	0.97 (0.75–1.26)	0.95 (0.72–1.25)	0.94 (0.71–1.24)	0.84 (0.62–1.14)
Job demands								
Male	0.95 (0.84–1.07)	0.94 (0.83–1.06)	1.01 (0.89–1.14)	1.00 (0.88–1.14)	0.93 (0.82–1.04)	0.86 (0.76–0.97)	0.95 (0.84–1.07)	0.91 (0.80–1.04)
Female	1.08 (0.82–1.41)	0.98 (0.75–1.28)	1.13 (0.85–1.52)	1.00 (0.75–1.34)	1.15 (0.88–1.51)	1.06 (0.81–1.39)	1.24 (0.92–1.67)	1.13 (0.85–1.51)
Support from supervisors								
Male	0.88 (0.76–1.03)	0.80 (0.72–0.89)	0.94 (0.80–1.10)	0.90 (0.80–1.00)	0.83 (0.74–0.93)	0.86 (0.76–0.97)	0.89 (0.78–1.00)	0.93 (0.82–1.06)
Female	0.96 (0.73–1.27)	0.64 (0.50–0.83)	0.95 (0.70–1.29)	0.65 (0.49–0.86)	0.79 (0.60–1.04)	0.95 (0.73–1.23)	0.72 (0.53–0.96)	0.89 (0.67–1.18)
Support from colleagues								
Male	0.80 (0.70–0.91)	0.76 (0.67–0.85)	0.88 (0.76–1.01)	0.86 (0.76–0.97)	0.91 (0.81–1.02)	0.93 (0.83–1.05)	0.94 (0.83–1.06)	0.98 (0.87–1.12)
Female	0.72 (0.54–0.95)	0.78 (0.61–1.01)	0.78 (0.58–1.05)	0.81 (0.61–1.08)	0.91 (0.69–1.19)	0.94 (0.73–1.22)	0.93 (0.70–1.25)	0.88 (0.66–1.16)
Job strain (demands/control)								
Male	1.23 (1.08–1.39)	1.49 (1.34–1.68)	1.13 (0.99–1.30)	1.28 (1.11–1.46)	1.09 (0.95–1.25)	1.28 (1.12–1.46)	1.04 (0.90–1.20)	1.15 (1.00–1.33)
Female	1.14 (0.87–1.50)	1.06 (0.81–1.41)	1.24 (0.92–1.68)	1.21 (0.89–1.63)	1.23 (0.92–1.64)	1.37 (1.03–1.82)	1.23 (0.89–1.70)	1.38 (1.00–1.90)

Reference is the low level in each factor

JCQ Job Content Questionnaire; *GJSQ* Generic Job Stress Questionnaire of the National Institute for Occupational Safety and Health; *after adjustment* odds ratios are controlled for age, smoking habit, alcohol consumption, marital status, education, cohabitation of children, disease, occupational classes and company

The associations were similar in females although they lacked statistical power. But the association between support from supervisors and sickness absence in GJSQ was not as clear as that in JCQ, while in contrast the association between job strain and sickness absence in GJSQ was clearer.

There were no significant interactions between job strain and the supervisors' support or the colleagues' support in either sex.

In Table 4, the frequency of sickness absence in terms of occupational classes was the highest for laborers of both sexes, and was the lowest for male managers and for female service workers.

Table 5 shows the odds ratios of sickness absence according to the occupational classes with professionals as the reference group. In males, the odds ratio in managers was lower than that in professionals, whereas the odds ratio in laborers was higher than that in professionals. No significant difference was noted in the associations among the occupational classes even after psychosocial work characteristics by JCQ were taken into account. Furthermore, there was no significant change when GJSQ was used instead of JCQ (results not shown). In females, laborers also showed the highest odds ratio, though the difference was not statistically significant.

Discussion

We revealed that even after adjustment for several potential confounding factors, both high level of job strain induced by low job control and low level of support at the worksite were associated with an increased number of employees taking more than 6 days of sick leave in 1 year.

Incidentally, the relationship between short spells of sickness absence and health is controversial. A short spell of sickness absence for which no medical certificate was required did not strongly reflect predictive employees' health (Vahtera et al. 2005). One-day absences were more frequent at the start and the end of a working week (Vahtera et al. 2001). Furthermore, the possibility of taking fake sick leaves without health problems could not be excluded. Therefore, we compared the group taking more than 6 days of sickness absence, which accounted for about the 90th percentile of the total sick leaves of the participants, with the group taking 0–6 days. In spite of its different categorization of the groups, the result of the present study is consistent with that of previous researches. Decreases in job demands, job control, and worksite support were related to a high rate of more than 7 consecutive days of sickness absence in the Whitehall II study (North et al. 1996). A 1-year follow-up of the Gazal study with 12,555 participants from the national electricity and gas company in France reported that low level of job control for both sexes and low level of worksite support for males were associated with an increased number of cases with more than 7 consecutive days of sickness absence. But,

Table 4 The frequency of sickness absence (>6 days/year) according to occupational classes

	Males	Females
Managers	173/3,125 (5.5%)	
Professionals	234/2,846 (8.2%)	11/92 (12.0%)
Technicians	256/2,954 (8.7%)	11/108 (10.2%)
Clerks	117/1.319 (8.9%)	119/1.204 (9.9%)
Service workers	14/219 (6.4%)	4/78 (5.1%)
Skilled workers	275/2,683 (10.2%)	9/110 (8.2%)
Machine operators	432/4,530 (9.5%)	71/865 (8.2%)
Laborers	205/1,455 (14.1%)	107/841 (12.7%)
Others	102/974 (10.5%)	25/214 (11.7%)
P^a	<0.01	<0.01

[a] χ^2 test

Table 5 Odds ratios (95% CI) of sickness absence (>6 days/year) with occupational class

	Model I[a]	Model II[b]
Males		
Managers	0.64 (0.52–0.79)	0.67 (0.54–0.84)
Professionals	1	1
Technicians	1.04 (0.85–1.26)	0.99 (0.81–1.21)
Clerks	1.03 (0.81–1.32)	1.01 (0.78–1.29)
Service workers	0.65 (0.36–1.17)	0.66 (0.37–1.20)
Skilled workers	1.14 (0.92–1.41)	1.07 (0.86–1.33)
Machine operators	1.04 (0.85–1.28)	0.97 (0.78–1.20)
Laborers	1.49 (1.18–1.89)	1.40 (1.09–1.80)
Others	1.20 (0.92–1.58)	1.20 (0.91–1.58)
Females		
Professionals	1	1
Technicians	1.19 (0.45–3.10)	1.03 (0.39–2.74)
Clerks	1.08 (0.51–2.26)	0.86 (0.40–1.83)
Service workers	0.63 (0.18–2.20)	0.55 (0.15–1.95)
Skilled workers	0.96 (0.34–2.68)	0.83 (0.29–2.36)
Machine operators	1.09 (0.50–2.37)	0.80 (0.36–1.78)
Laborers	1.53 (0.71–3.30)	1.19 (0.54–2.62)
Others	1.22 (0.52–2.86)	0.98 (0.41–2.36)

Reference is the professional group
[a]Adjusted for age, smoking habit, alcohol consumption, marital status, education, cohabitation of children, disease and company
[b]Adjusted for the variables in model I, and job strain and support from supervisors and colleagues

job demands showed no statistically significant relationship with sickness absence (Niedhammer et al. 1998). Additionally, the 6-year cohort study of the same population also demonstrated that low job control for both sexes and low worksite support for males predicted a higher incidence of 8–21 days of sickness absence (Melchior et al. 2003).

In addition, neither JCQ nor GJSQ questionnaire altered the result much. The correlations of psychosocial work factors between JCQ and GJSQ ranged from moderate to slightly high. However, we have found no study on sickness absence by GJSQ so far, and so we think GJSQ can also be used to elucidate the relationship between work characteristics and sickness absence.

Regarding sickness absence among different occupational classes, we found the lowest rate of sickness absence in male managers and the highest in both male and female laborers. The result shows some similarity with some European studies in that sickness absence increased with lower occupational classes (North et al. 1993; Niedhammer et al. 1998; Westerlund et al. 2004), but the occupational gradient of sickness absence of this study was small compared with that of European studies. This trend in this study did not change much after adjusting for confounding factors including health status, though we admit that for the cross-sectional study we cannot exclude the healthy worker effect, namely that people in the higher occupational classes are healthier to begin with. Besides, the difference in sickness absence rates among various occupational classes diminished after adjustment for job demands/control and support at the worksite, but with a statistically significant difference remaining in males. Therefore, we think that the socioeconomic gradient with regard to sickness absence also exists in Japan though it may not be as marked as in European countries.

In two Gazal cohort studies for the French (Niedhammer et al. 1998; Melchior et al. 2003) and a cohort study for the Belgians (Moreau et al. 2004) the relationship between psychosocial work characteristics and sickness absence did not change after adjustment for personal characteristics including occupational classes. Similarly, our study recognized no meaningful change in the relationship between psychosocial work characteristics and sickness absence even when occupational classes were taken into account.

This relationship, however, diminished after adjusting for employment grade instead of occupational classes in the Whitehall II study (North et al. 1996). This may be because the target subjects in the Whitehall II study were all civil servants—namely typical white-collar workers—whose employment grades markedly reflected the socioeconomic status linked up with hierarchy, income and educational background and other factors. On the other hand, the subjects of our study and the Gazal study were composed of blue and white-collar employees. Therefore, it might be possible that occupational classes did not sufficiently reflect confounding factors, e.g. physical load at work.

The present study demonstrated that the association between psychosocial work characteristics and sickness absence in females was weaker than that in males. Other psychosocial factors such as work–family interaction seemed to have a great influence on health and sickness absence in females. In fact, it was reported that in young dual-income Japanese 83% of working females did more than half of the household chores while 71% of working males entrusted other family members with housework (Ministry of Health Labour and Welfare 2004).

There are some limitations in this study that should be noted. First, since all information was obtained by self-administered questionnaires, several factors may have contributed to misclassification, e.g. difficulty with remembering the exact total days of sickness absence. Second, we failed to assess the characteristics of nonresponders, thereby not completely avoiding selection