Coemergence of insomnia and a shift in Th1/Th2 balance toward Th2 dominance.

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Abstract

Objectives: Insomnia is associated with physical and mental disorders. We examined the effect of insomnia on immune functions, focusing on T helper1/T helper2 (Th1/Th2) balance by a cross sectional design.

Methods: We provided a self-administered questionnaire for evaluating sleep habits, smoking, and medical disorders to 578 men without any toxic exposure (20-64 years old) and measured natural killer (NK) cell activity in 324 men and production of interferon-gamma (IFN-γ) and interleukin-4 (IL-4) after stimulation with phytohemagglutinin (PHA) in 254 men. According to the criteria of DSM-IV, in which insomnia is classified into primary and secondary insomnia, we assessed the effect of insomnia on immune functions controlling for age and smoking in groups with and without medical disorders respectively.

Results: The prevalence of insomnia in the present study was 9.2%. In the absence of medical disorders, insomniac men had a significantly lower IFN-γ and IFN-γ/IL-4 than non-insomniac men. Men with insufficient sleep or difficulty initiating sleep (DIS) had a significantly lower IFN-γ/IL-4 than those without insufficient sleep or DIS. In the presence of medical disorders, insomniac men had a significantly higher IL-4 than non-insomniac men. Men with difficulty maintaining sleep (DMS) had a significantly lower IFN-γ/IL-4 than men without DMS. NK cell activity was independent of insomnia.

Conclusions: The present results showed a link between insomnia unrelated to medical disorders and a shift in Th1/Th2 balance toward Th2 dominance, indicating that sleep quality should be reconsidered in terms of etiology of immune-related diseases.

Key Words: sleep, insomnia, life style, immune functions, Th1 and Th2, NK cell activity

Introduction

Sleep plays a role in host defense, exerting an influence on immune system. Disrupted sleep and circadian rhythm alter immune functions [1-3]. Peripheral blood mononuclear cell (PBMC) counts and in vitro PHA-stimulated IL-2 production are significantly higher during sleep deprivation than nocturnal sleep [1]. After partial sleep deprivation, reduction of NK cell activity was observed [2]. A recent study showed that total sleep deprivation elevated serum TNF-α recepter1 and plasma IL-6 levels [4]. Almost all the findings from the studies on depression, asthma, HIV, and bacterial infections supported the existence of the association between sleep and immune functions [5-9].

Most investigations on the relationship between sleep and immunity have been conducted in sleep-deprived humans and animals. However, there have been scarce findings on immune functions associated with sleep quality in real life. Insomnia is a highly prevalent complaint [10,11] and the subjects with insomnia have an increased risk of heart diseases, diabetes, stroke, anxiety, and depression [12]. Insomnia also results in impaired performance leading to absenteeism from work, reduced productivity, and a higher rate of accidents [12,13]. Thus it is worth while elucidating the relationship between insomnia and immunity in order to bring relief into those problems mentioned above and to enrich our knowledge about the effects of insomnia on human health.

Th1 and Th2 imbalance has an adverse effect on health and diseases. Th1 cells play an important role in eradicating intracellular pathogens and are also implicated in many autoimmune diseases. Th2 cells enhance IgE productions from B cells and mediate allergic processes. IFN-γ and IL-4 are representative cytokines secreted from Th1 and Th2 cells, respectively, and IFN-γ/IL-4 ratio, which reflects Th1/Th2 balance, is of critical importance in the pathogenesis of immune-related diseases. In addition, NK cell functions is partly regulated by Th1/Th2 balance, since NK cells and their cytotoxicity are promoted by IFN-γ and inhibited by IL-4. Recently a longitudinal study showed that those subjects with a lower level of NK cell activity have an increased risk of cancer [14]. A rapid progress has been made in understanding the immune mechanisms involved in depression, asthma, HIV, and bacterial infections, and showed the contribution of Th1 and Th2 cells are significantly important to these mechanisms. An elevated proinflammatory cytokine level in sleep loss suggests that Th1/Th2 balance may be altered in insomnia [4].

The objective of the present study is to examine a possible link between insomnia and Th1/Th2 balance by a cross sectional design. We provided a self-administered questionnaire to male subjects for evaluating the subjective sleep quality and problems and medical disorders according to DSM-IV criteria [15], in which insomnia is subdivided

into primary insomnia and insomnia related to specific etiologies, and measured PHA-stimulated IFN- γ and IL-4 productions and NK cell activity. In addition to medical disorders, age [16,17] and smoking behaviors [17-19] have been proposed as factors regulating immune functions. Therefore, these factors were also included in the questionnaire and were analyzed as confounding factors.

Methods

Subjects

At first, 578 adult men without exposure to any toxic substances (20-64 years old) were recruited from an electric equipment manufacturing company in Japan. They were administered a self-check questionnaire for evaluating sleep habits, smoking behaviors, and medical disorders. Based on their self-reported illness, the subjects were divided into 263 men who did not have any medical disorders (20-64 years old) and 315 men who had any medical disorders (20-64 years old) (Table 1). We obtained heparinized blood samples from the subjects and measured NK cell activity in 324 men (21-64 years old) and cytokine productions in 254 men (20-64 years old) with written informed consent.

Sleep questionnaire

Insomniac individuals were identified using a sleep questionnaire that was developed for the present study. The most central feature of insomnia is the subjective perception of inadequate sleep duration or quality [20]. Based on criteria in the previous studies [21], insomnia was categorized as the perception of insufficient sleep along with having experienced one or more of the following symptoms during the past year: difficulty initiating sleep (DIS); difficulty maintaining sleep (DMS); early morning awaking (EMA).

Four questionnaire items provided information about sleep-associated problems during the past year:

Q1. Do you sleep well? Possible ratings: 1=very well, 2=well, 3=normal, 4=poor, 5=fairly poor.

Q2. How long does it take you to fall asleep? Opened-question.

Q3. Do you tend to wake up frequently during the night? Possible ratings: 1=no, 2=yes.

Q4. Do you tend to wake up too early in the morning? Possible ratings: 1=very often, 2=often, 3=occasional, 4=never.

For a definition of insufficient sleep, DIS, DMS, and EMA, the following criteria were required following the previous study [22]: poor sleep; sleep latency exceeding 30 minutes; troubled by nocturnal awakening; often wake up too early. The prevalence of insomnia in the current study was 9.2 % (Table 2). The prevalence of insomnia with and without any medical disorders was 5.9 % and 3.3 %, respectively.

Cigarette smoking questionnaire

The number of cigarettes smoked per day was assessed by a questionnaire.

Table 1. Frequensies of Medical Disorders in 578 Male Workers

Disease categories	n
Psychiatric disorders	7
Hypertension	38
Ischemic heart diseases	5
Other heart diseases	22
Cerebral infarction and hemorrhage	4
Diabetes mellitus	18
Malignancies	2
Gastrointestinal diseases	88
Liver diseases	16
Renal diseases	15
Musculoskeletal diseases	176
Other disorders	46

Table 2. The Prevalence of Insomnia and the Characteristics of Sleep Problems

		+ [1]	- [2]	Total
Insomnia[3]	n	53	524	577
	%	9.2	90.8	100
Insufficient sleep	n	58	519	577
	%	10.1	89.9	100
DIS[4]	n	145	430	575
	%	25.2	74.8	100
DMS[5]	n	277	299	576
	%	48.1	51.9	100
EMA[6]	n	162	415	577
	%	28.1	71.9	100

[1] The subjects with insomnia and relevant sleep problems.

[2] The subjects without insomnia and relevant sleep problems.

[3] Insomnia = the perception of insufficient sleep along with having experienced one or more of DIS, DMS, and EMA during the past year.

[4] DIS = difficulty initiating sleep.

[5] DMS = difficulty maintaining sleep.

[6] EMA = early morning awaking.

Immunological assessments

Preparation of Peripheral blood mononuclear cell (PBMC)

Heparinized blood samples were collected at 10 am from consenting male subjects. The cells were stored at room temperature and processed within 4 h. PBMC were isolated by density-gradient centrifugation on a Lymphoprep (Nycomed, Oslo), according to the manufacturer's instructions. After isolation, the PBMC were washed twice and resuspended at 2×10^6/ml in RPMI 1640 medium containing 10% FCS, 2 mM glutamine, 100 U/ml penicillin and 100 U/ml streptomycin (Dainippon, Tokyo).

Cytotoxicity assay

NK cell activity was measured against K562 using a standard 4h -^{51}Cr release assay. Target cells were labeled with [^{51}Cr] sodium chromate (New England Nuclear, Boston, MA) at 37°C for 1h, washed, and resuspended at 2×10^5/ml in RPMI 1640 medium containing 10% FCS, 2 mM glutamine, 100 U/ml penicillin and 100 U/ml streptomycin. Labeled target cells were incubated with effector cells at E: T=20: 1 in U-bottom 96-well plates at 37°C for 4h. Radioactivity in the supernatant was determined by a gamma counter. The assay was performed in quadruplicate. The percentage of specific lysis as cytotoxicity was determined according to the formula: % specific lysis = [(mean experimental cpm release - mean spontaneous cpm release)/(mean maximal cpm release - mean spontaneous cpm release)].

Cytokine assay

For determination of IFN-γ and IL-4, a whole blood assay was applied [1]. Blood was drawn into syringes pretreated with heparin (Beckton-Dickson, NJ, USA) at 10 am and stored at room temperature for no longer than 4h before the assays. Aliquots of 50 μ l of blood were resuspended under laminar airflow in 400 μl of RPMI 1640 medium containing 2 mM glutamine, 100 U/ml penicillin and 100 U/ml streptomycin. For stimulation of IFN-γ and IL-4, 2.5 μ g of PHA (Sigma-Aldrich Japan, Tokyo) was added, dissolved in 50 μ l of a medium containing 50% RPMI and 50% sterile water (final concentration, 5 μ g/ml). At the end and in the beginning of each measurement, an unstimulated control was included to exclude contaminations of blood and reagents. The samples were incubated for 48 h at 37°C with 5% carbon dioxide in humidified air. The supernatants were harvested and stored at -80°C until assay. The samples were thawed only once and all cytokine levels were measured in duplicate by ELISA kits (Human Immunoassay ELISA kit, BioSource International, Camarillo, CA), according to the manufacturer's instructions.

Statistical Analysis

For statistical analysis, data on IFN-γ, IL-4, IFN-γ /IL-4 were logarithmically

transformed because of their skewed distributions (Table 3). Pearson's correlation analysis was performed to evaluate the associations among age, smoking behaviors, and immune functions. ANCOVA (analysis of covariance) was applied to assess the effect of insomnia and medical disorders on immune functions controlling for age and smoking. A p value < 0.05 was considered to indicate statistical significance. All tests were two-tailed.

Results

Age, smoking, and immune functions

Age was inversely correlated with NK cell activity, IFN-γ, and IFN-γ/IL-4 ratio (NK cell activity: r = -0.171, p = 0.002; IFN-γ : r = -0.181, p = 0.004; IFN-γ/IL-4 ratio: r = -0.181, p = 0.004). The number of cigarettes smoked per day was inversely correlated with NK cell activity and positively correlated with IFN-γ and IL-4 production (NK cell activity: r = -0.113, p = 0.042; IFN-γ : 0.249, p < 0.001; IL-4: r = 0.229, p < 0.001). The results suggest that both age and smoking should be adjusted in evaluating the relationship between insomnia and immune functions.

Correlations among immunological variables

As shown in Table 4, there is a strong positive association between IFN-γ and IL-4 levels. IFN-γ/IL-4 ratio was more correlated with IL-4 than with IFN-γ.

Insomnia and immune functions

The subjects were divided into 4 groups according to the presence or absence of insomnia and medical disorders. One-way ANCOVA with LSD post hoc was conducted to assess the effect of insomnia on immune functions controlling for age and smoking. As shown in Figure 1, NK cell activity was independent of insomnia. In the absence of medical disorders, IFN-γ was significantly lower in insomniac men than non-insomniac men. In the presence of medical disorders, IL-4 was significantly higher in insomniac men than non-insomniac men. In the absence of medical disorders, IFN-γ/IL-4 ratio was significantly lower in insomniac men than non-insomniac men.

Insomniac symptoms and IFN-γ/IL-4 ratio

The subjects were divided into 4 groups according to the presence or absence of insomniac symptoms and medical disorders. ANCOVA with LSD post hoc was applied to assess the effect of insomniac symptoms on IFN-γ/IL-4 ratio. Figure 2 shows that in the absence of medical disorders, those men who complained of insufficient sleep had a lower IFN-γ/IL-4 ratio compared with those who did not complained of insufficient sleep and men with DIS had a lower IFN-γ/IL-4 ratio than those without DIS. In the presence of medical disorders, IFN-γ/IL-4 ratio in men with DMS was lower than those without DMS. IFN-γ/IL-4 ratio was not associated with EMA.

Table 3. Descriptive Analysis of Immunological and Lifestyle Variables

Variable	n	Mean	(	SD	)	Median	(	Range	)
NK cell activity (%)	324	50.96	(	12.92	)	52	(	7 - 73	)
IFN-γ (pg/ml)	251	95.18	(	105.53	)	50	(	1 - 522	)
IL-4 (pg/ml)	254	12.10	(	13.86	)	7.6	(	0 - 83	)
IFN-γ / IL-4	251	13.35	(	14.25	)	8.28	(	0.27 - 87.50	)
Age (y)	578	37.93	(	9.13	)	37	(	20 - 64	)
Insufficient sleep[1]	577	2.23	(	0.92	)	2	(	1 - 5	)
DIS (min)	575	16.21	(	13.84	)	10	(	0 - 100	)
DMS[2]	576	1.48	(	0.50	)	1	(	1 - 2	)
EMA[3]	577	2.98	(	0.88	)	3	(	1 - 4	)
Smoking (cigarettes/d)	571	12.39	(	12.19	)	15	(	0 - 60	)

[1] sufficient sleep: 1 = very well, 2 = well, 3 = normal, 4 = poor, 5 = fairly poor.

[2] wake up frequently: 1 = no, 2 = yes.

[3] wake up too early in the morning: 1 = very often, 2 = often, 3 = occasionally, 4 = never.

Table 4. Correlation Matrix between Immune Functions (n = 251)

	IFN-γ		IL-4		IFN-γ / IL-4	
Variable	r[1]	p	r	p	r	p
IFN-γ (pg/ml)						
IL-4 (pg/ml)	0.68	< 0.001***				
IFN-γ / IL-4	0.29	< 0.001***	-0.48	< 0.001***		

[1] Pearson's correlation coefficients. * p < 0.05; ** p < 0.01; *** p < 0.001.

Fig. 1

Legend:
- ☐ Non-Disease and Non-Insomnia
- ▤ Non-Disease and Insomnia
- ■ Disease and Non-Insomnia
- ▨ Disease and Insomnia

***
*

% specific lysis

100—

50—

2.0—

1.0—

* * * *

N = 134 10 158 19   106 8 119 14   108 8 120 14   106 8 119 14

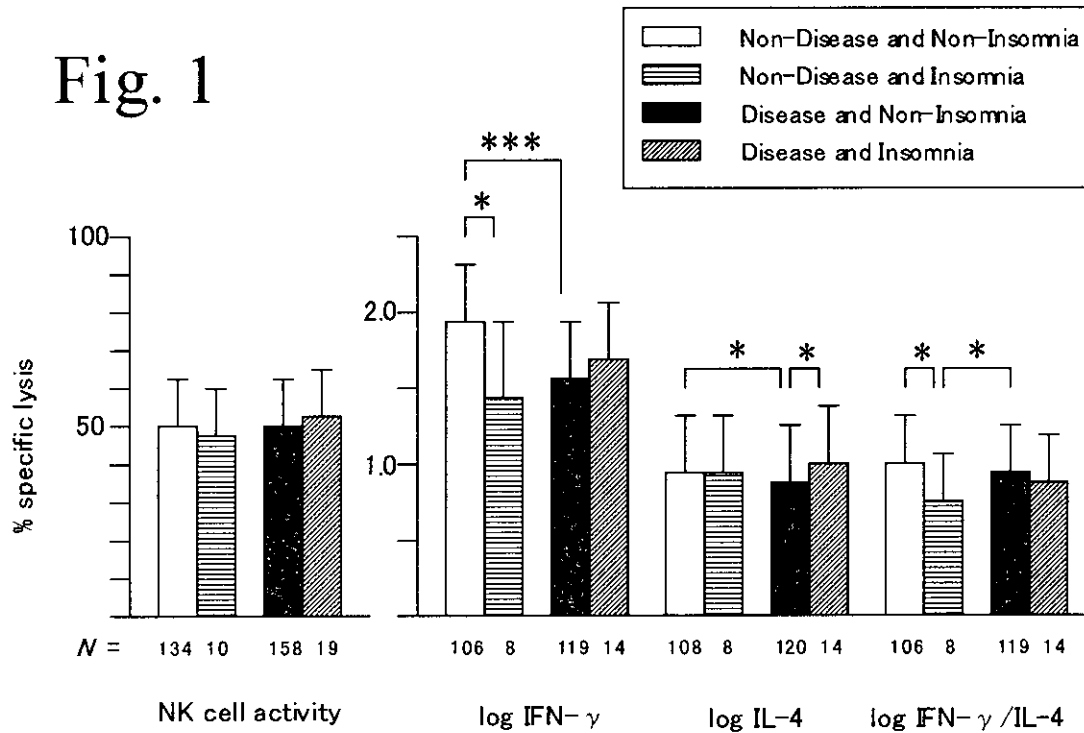NK cell activity   log IFN-γ   log IL-4   log IFN-γ/IL-4

Fig. 1. Means (SD) of immunological variables in the presence or absence of insomnia and medical disorders. The means of immune functions among 4 categories were compared by ANCOVA (analysis of covariance) with LSD post hoc controlling for age and smoking.

(NK cell activity) ANCOVA: $F_{(3, 315)} = 1.954$, $p = 0.121$. Multiple comparisons (non-insomnia vs. insomnia): without any medical disorders: $p = 0.481$; with medical disorders: $p = 0.335$.

(IFN-γ) ANCOVA: $F_{(3, 241)} = 4.829$, $p = 0.003$. Multiple comparisons (non-insomnia vs. insomnia): without any medical disorders: $p = 0.034$; with medical disorders: $p < 0.001$.

(IL-4) ANCOVA: $F_{(3, 244)} = 3.165$, $p = 0.025$. Multiple comparisons (non-insomnia vs. insomnia): without any medical disorders: $p = 0.949$; with medical disorders: $p = 0.025$.

(IFN-γ/IL-4) ANCOVA: $F_{(3, 241)} = 3.051$, $p = 0.029$. Multiple comparisons (non-insomnia vs. insomnia): without any medical disorders: $p = 0.013$; with medical disorders: $p = 0.205$.

$p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Fig. 2

Legend:
- □ Non-Disease and Non-Insomniac symptoms
- ☰ Non-Disease and Insomniac symptoms
- ■ Disease and Non-Insomniac symptoms
- ▨ Disease and Insomniac symptoms

y-axis: log IFN-γ/IL-4

N = 104 10   118 15   87 27   104 28   67 47   70 63   87 27   96 37
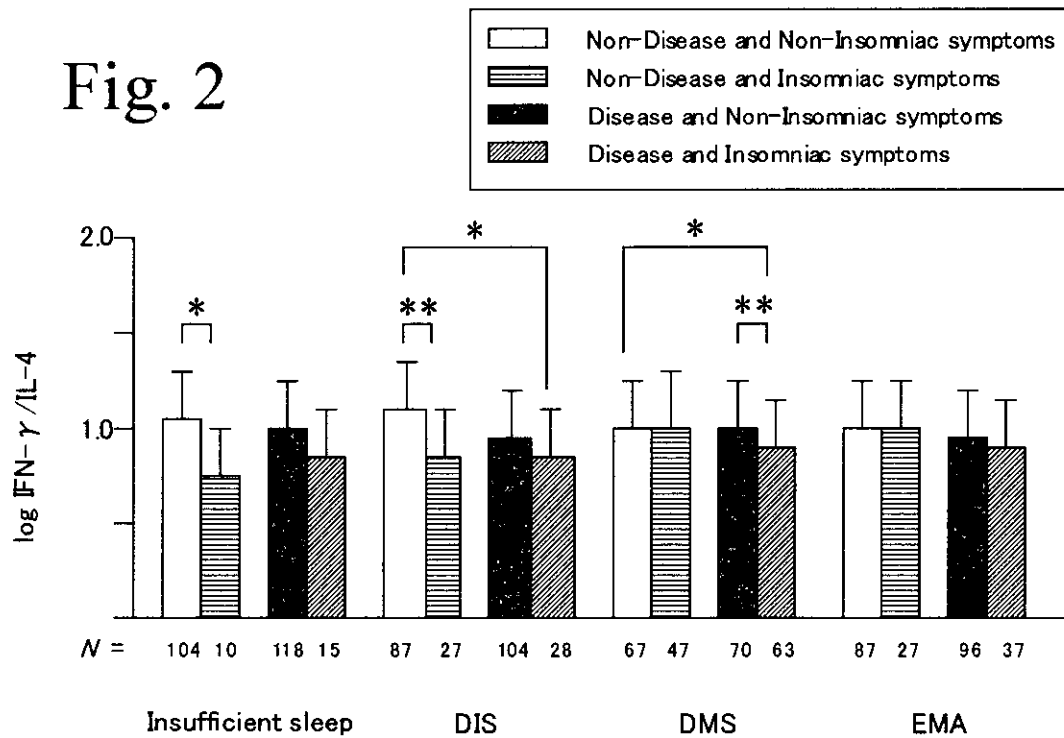
Insufficient sleep   DIS   DMS   EMA

Fig. 2. Means (SD) of IFN- γ /IL-4 ratio in the presence or absence of insomniac symptoms and medical disorders. The means of IFN- γ /IL-4 among 4 categories were compared by ANCOVA (analysis of covariance) with LSD post hoc controlling for age and smoking.

(Insufficient sleep) ANCOVA: F (3, 241) = 2.696, p = 0.047. Multiple comparisons (non-insomnia vs. insomnia): without any medical disorders: p = 0.014; with medical disorders: p = 0.415.

(DIS) ANCOVA: F (3, 240) = 3.155, p = 0.026. Multiple comparisons (non-insomnia vs. insomnia): without any medical disorders: p = 0.009; with medical disorders: p = 0.324.

(DMS) ANCOVA: F (3, 241) = 3.062, p = 0.029. Multiple comparisons (non-insomnia vs. insomnia): without any medical disorders: p = 0.606; with medical disorders: p = 0.006.

(EMA) ANCOVA: F (3, 241) = 0.637, p = 0.592. Multiple comparisons (non-insomnia vs. insomnia): without any medical disorders: p = 0.796; with medical disorders: p = 0.436.

* p < 0.05; ** p < 0.01; *** p < 0.001.

Discussion

In the present study, the subjects were divided into men with and without medical disorders according to the criteria of DSM-IV, in which insomnia is classified into primary insomnia and insomnia related to specific etiologies, and then, the effects of insomnia on immune functions was differentially evaluated. Primary insomnia lacks in any medical disorders and substance exposures, and men with this relevant type of insomnia had a lower IFN-γ level and IFN-γ/IL-4 ratio than non-insomniac men. Secondary insomnia is the case in which underlying medical conditions should be involved as a cause. Men with relevant insomnia had a higher IL-4 level than non-insomniac men, whereas there is no significant difference in IFN-γ and IFN-γ/IL-4 ratio between them. In the case with secondary insomnia, however, it is likely that the results are not absolutely reliable considering the effects of medication and the variety of pathophysiology of respective disorders. Because of a small number of concurrent insomnia in men with respective medical disorders, the underlying mechanisms cannot be reasonably inferred. In this article, consideration is to be focused on the results relevant to primary insomnia.

With respect to insomniac symptoms, DIS and insufficient sleep in the absence of medical disorders were associated with a shift in Th1/Th2 balance in favor of type 2. It is well known that DIS and DMS are sleep problems typical in anxiety and underlying conditions such as depression, respectively. Because psychiatric disorders were excluded from the case without medical disorders, it is possible to say the results may suggest that subclinical anxiety was associated with a Th2-shift. Only a handful of studies examined immune alterations in anxiety [23]. This implication remains to be explored.

IFN-γ was lower in insomniac men without medical disorders than non-insomniac men. IFN-γ/IL-4 ratio was contributed by IL-4 rather than by IFN-γ. The correlations of IFN-γ and IL-4 with IFN-γ/IL-4 ratio was considerably smaller compared with that between IFN-γ and IL-4, which indicates that IFN-γ/IL-4 ratio is relatively independent of IFN-γ and IL-4 levels. It may be inappropriate to discuss Th1/Th2 balance using the data on IFN-γ or IL-4 as alternatives.

However, our present results clearly indicate a link between insomnia and Th1/Th2 balance and can be interpreted as insomnia causing a shift in Th1/Th2 balance toward Th2 dominance. Among the possible mechanisms that mediate the effect of sleep on cytokine productions, the autonomic nervous system (ANS) and the hypothalamic-pituitary-adrenal axis may be involved in the causality.

ANS is considered to help organize immune responses sequentially and spatially [24]. Sympathetic nerve stimulations by hyperarousal suppress immunocompetent cells in the blood stream [24]. Norepinephrine

and epinephrine inhibit the production of IL-12, tumor necrosis factor-alpha (TNF-α), and IFN-γ by antigen-presenting cells and Th1 cells, whereas they stimulate the production of IL-10 and transforming growth factor-beta (TGF-β) [25]. Other neurotransmitters (eg, neuropeptide Y, vasoactive intestinal peptide) produced within the lymphoid microenvironment modulate several immunological functions including cytokine productions [26,27]. Together these studies suggest that sympathetic activation may contribute to a Th2-shift in Th1/Th2 balance observed in insomniacs.

Glucocorticoids favor Th2 development [28,29]. Many studies have reported that sleep loss and disordered sleep increase plasma cortisol concentration [1,30]. Because, however, the effect of sleep loss on cortisol release is generally small, it is unlikely that cortisol mediates the effect of disturbed sleep on immune functions. Anyway, as we did not assess either ANS function or glucocorticoid level, further investigation should be undertaken.

On the other hand, insomnia may be the result of a Th2-shift in Th1/Th2 balance. Clinical and experimental evidences can endorse this hypothesis. Some anti-allergic drugs evoke sleepiness. Human histocompatibility leukocyte antigens (HLA) association observed in narcolepsy suggests that autoimmunity plays an important role in the disorder [31]. Sleep quality in infants with milk allergy suffering from chronic insomnia became normalized after cow's milk was excluded from the diet [32]. In the present study, DIS unrelated to medical disorders was significantly associated with a Th2-shift in Th1/Th2 balance. This agrees with the previous report showing that spontaneous sleep is inhibited by IL-4 injection in rabbits [33].

Furthermore, empirical studies have revealed a very high prevalence of concurrent atopic disorder in people with depression, who almost always complain about insomniac symptoms [34]. Individuals with allergy substantially have cholinergic hyperresponsiveness and β-adrenergic hyporesponsiveness in ANS. Similar autonomic imbalances play a causal role in depressive behaviors as well [35]. It is hypothesized that imbalance in ANS underlies the insomnia-related Th2-shift in Th1/Th2 balance.

The present results suggest that, when the effect of a lifestyle factor on human immunity is to be elucidated, other factors also should be considered. Most studies to date have compared the effect of sleep and sleep deprivation on immune functions. Because we assessed sleep quality non-intrusively, other factors were controlled. Age-related decline in NK cell activity and IFN-γ/IL-4 ratio observed in the present study coincide with the findings from the previous studies [16,17]. Although smoking-induced alteration in Th1/Th2 balance was not found in the present study, smoking was entered into a

general linear model since many studies showed Th2 dominance in smokers [18,19]. In addition, psychological stress does not simply act as a sleep-disturbing factor [36], but suppresses cellular immunity and induces a shift in Th1/Th2 balance toward a predominant type 2 cytokine response [37]. Further studies controlling for socio-psychological factors are needed.

Despite the difficulty in interpretation of the data that is due to the nature of the cross-sectional design, the present results indicate that a shift in Th1/Th2 balance toward Th2 dominance in insomnia is worth considering not only from the perspectives of neuro-immune interactions but also from therapeutic and preventive applications for allergy, autoimmunity and other detrimental diseases such as cancer. Further studies including DSM- IV diagnosis of specific insomnia should be undertaken.

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Relationship between Traumatic Life Events and Alteration in the Stress Response

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研究要旨　何らかの、トラウマティックなイベントに遭遇することにより、抑うつ傾向、不安傾向が高まり、また、仕事の要求度即ち、ストレッサーに対する感受性も亢進しうることが示唆されたので報告する。

緒言

日本では、昨今のグローバル化、成果主義の導入、そして長引く不況とリストラの中、自殺者数が 1998 年以降 3 年連続で年間 3 万人を超え、これら急激な労働環境の変化と自殺増加の関連が指摘されており、労働者のメンタルヘルスは注目を集めている。労働者のメンタルヘルスについての研究には様々なものがあり、Karasek の Job Demands-Control Model やそれを拡張した Johnson の Job Demands-Control-Social Support Model に照らして職業性ストレスについて検討した研究は多い。一方で、過去のトラウマティックライフイベントへの曝露が後の身体的・精神的健康に影響を与え、うつや自殺と関連することが示されている一方で、一般労働者における過去のトラウマティックライフイベントによる影響をみた研究は少ない。産業現場におけるトラウマティックストレスについては、2001 年の米国中枢同時多発テロ以降、多くの企業において新たに対応が迫られているが、労働者とトラウマティックライフイベントについてのこれまでの研究は、消防士など日常トラウマティックな状況に曝露しやすい対象についてのもののみであった。一般労働者については、一部日常的なライフイベントと職業性ストレスの関連について検討した研究はあるものの、トラウマティックライフイベントについてみたものは少ない。しかし、PTSD の生涯有病率は 2 - 1 0 ％であり、これに PTSD の診断は満たさないがトラウマティックライフイベントに曝された人も含めると、一般就労者においてもそれらの体験をもつ者の割合はかなりものになると考えられる。このことからも、過去のトラウマティックライフイベントの体験の有無が労働者にどのような影響を与えるのかは、今後の産業保健を考えていく上で重要な所見である。よって、過去のトラウマティックイベントを体験した者としていない者では Job Demands-Control-Social Support Model においてどのような違いが見られるのか、トラウマティックイベントがストレス反応に対して Job Demands - Control - Social Support Model のいずれかの要素と何らかの交互作用をもつ（Indirect 仮説）のかどうかを知り、どのような条件をもつ者がメンタルヘルス上の問題を持

ちやすいのか、またどのような条件をもつ者がどのような対応を必要としているのかを検討することは産業領域の健康管理上重要である。また、これはトラウマティックライフイベントがストレス耐性に与える影響を考える上でも重要となる。

そこで本研究では、大規模な一般勤労者集団を対象として、トラウマティックライフイベントが勤労者のストレスとメンタルヘルスに対してどのような影響を与えるのかを、ストレスの3つの重要な要素、ストレッサー、ソーシャルサポート、ストレス反応としてのうつ、不安を、包括的に、レトロスペクティブな横断研究で検討することを目的とする。

方法

日本の地方都市にあるメーカーT社において、健康診断時に質問票を配布、回収した。対象者は、男性2959人（平均年齢 39.30 ± 11.08）、女性279人（平均年齢 37.14 ± 9.33、）、計3238人で、男女間には年齢において有意差がみられた（$p < 0.05$）。

尺度として、SDS、シーハン不安尺度、カラセックの Job Content Questionnaire(JCQ)を用いた。また、出来事の同定には日本語版出来事チェックリストを用い、併せて出来事からの年数を聞いた。加えて、出来事を体験した者には、IES-R も用いた。その上で、まず①各 traumatic event を体験した者の頻度を性別に概観し、②14個の traumatic event を因子分析した上で因子に分け、次に③過去に出来事に曝露した群と曝露してない群を年齢を調整した上で上記尺度について男女別に共分散分析で比較し、④各因子間のいずれにおいてそれぞれの尺度得点が高くなるのかを年齢を共変量とした上で共分散分析によって検討し、⑤出来事からの年数と各尺度との関係をピアソンの積率相関係数によって示し、最後に⑥各尺度得点を従属変数、性別、トラウマティックイベントの有無、ストレインの高低、上司サポートの有無、同僚サポートの有無を固定変数とし、年齢を共変量とした GLM によって、それぞれの主効果と交互作用を検討し、インダイレクト仮説について検討した。統計には、SPSS ver. 11 を用いた。

結果および考察

結果は Table 1 - 6 に示した。

統計解析の観点を変更すれば、さらにいろいろな側面が見えてくるものと思われる。

今回の解析結果によれば、何らかの、トラウマティックなイベントに遭遇することにより、抑うつ傾向、不安傾向が高まり、また、仕事の要求度即ち、ストレッサーに対する感受性も亢進しうることが示唆されたと言えよう。

また、トラウマからの年数が経つにつれ、そういった傾向は一般に小さくなってくるが、
女性の場合、ストレッサーへの感受性にマイナスに働くことも示唆された。

これらはレトロスペクティブなデータであり、今後、前向きの研究が重要である。

ストレッサーへの感受性にかんしては、トラウマの有無との交互作用もみられ、強いストレスに対して、トラウマ体験が対してのみ、逆に、感受性が時間を追うごとに強まる可能性も示唆された。

Table 1. 性別にみた各出来事の体験者数

	女性	男性
自然災害	9	167
火事・爆発	4	57
交通事故	25	355
有毒暴露	0	7
その他	7	71
暴行	3	30
身体的虐待	3	16
凶器暴行	0	22
監禁	0	7
目撃体験	6	112
言葉暴行	23	141
性的暴行	10	16
知人の事故	4	65
ショック	4	29

Table 2. 出来事の因子分析

	因子得点係数			
	Factor I	Factor II	Factor III	Factor IV
監禁	0.55			
有毒曝露	0.33			
火事・爆発		0.33		
自然災害		0.31		
交通事故		0.26		
目撃経験		0.18		
その他			0.29	
知人の事故			0.23	
言葉の暴力			0.18	
ショック			0.14	
身体虐待				0.32
性的暴力				0.29
暴行				0.18
凶器暴行				0.15
回転後の負荷量平方和　合計	1.58	1.14	0.81	0.75
累積%	11.27	19.40	25.21	30.54

バリマックス回転による因子分析

Table 3. 出来事の有無による各尺度の比較

		event なし (n=2256)		event 有り (n=703)		F	
		Mean	SE	Mean	SE		
Male	SDS	41.20	0.15	42.53	0.27	18.36	*
	シーハン不安尺度	33.11	0.40	44.90	0.71	7.23	*
	カラセック 要求度	32.55	0.11	33.52	0.19	10.53	*
	カラセック 裁量権	65.20	0.23	65.50	0.41	1.56	
	カラセック 上司サポート	10.97	0.05	10.83	0.09	0.00	
	カラセック 同僚サポート	11.48	0.03	11.42	0.06	0.10	
Female	SDS	41.50	0.48	42.72	0.82	2.07	
	シーハン不安尺度	31.51	1.29	44.13	2.20	24.67	*
	カラセック 要求度	29.37	0.36	31.20	0.61	7.24	*
	カラセック 裁量権	59.93	0.68	59.70	1.17	0.89	
	カラセック 上司サポート	10.85	0.18	10.89	0.31	0.46	
	カラセック 同僚サポート	11.32	0.13	11.11	0.22	0.47	

年齢を共変量とした ANCOVA * p<0.05

Table 4.

因子間の各尺度得点の比較

		イベントなし		因子1		因子2		因子3		因子4		F	
		平均値	SE	平均値	SE	平均値	SE	平均値	SE	平均値	SE		
Male	SDS	41.19	0.15 ab	43.38	4.98	41.67	0.34 cd	43.62	0.45 ac	44.20	1.19 bd	7.94	*
	シーハン不安尺度	33.12	0.40 abc	36.58	13.30	43.61	0.92 ad	46.97	1.21 bd	47.28	3.18 c	54.21	*
	カラセック要求度	32.55	0.11 ab	31.32	3.54	33.24	0.24 ac	34.06	0.32 bc	32.68	0.85	6.07	*
	カラセック裁量権	65.20	0.23	63.01	7.69	65.78	0.53	65.59	0.70	62.42	1.84	0.93	
	カラセック上司サポート	10.97	0.05	11.44	1.59	10.96	0.11	10.61	0.14	10.78	0.38	1.52	
	カラセック同僚サポート	11.48	0.03	10.96	1.14	11.55	0.08	11.22	0.10	11.24	0.27	1.90	
Female	SDS	41.51	0.48			43.27	1.54	43.73	1.09	39.39	1.99	1.95	
	シーハン不安尺度	31.51	1.29 abc			42.37	4.15 a	44.21	2.93 b	46.55	5.35 c	8.30	*
	カラセック要求度	29.37	0.36 a			29.34	1.14 b	32.52	0.81 ab	30.32	1.47	4.34	*
	カラセック裁量権	59.92	0.68			57.87	2.18	58.71	1.54	65.26	2.81	1.69	
	カラセック上司サポート	10.85	0.18			10.73	0.59	10.56	0.42	12.42	0.76	1.60	
	カラセック同僚サポート	11.33	0.13			10.81	0.41	11.07	0.29	11.87	0.53	1.07	

年齢を共変量とした ANCOVA　＊ $p < 0.05$　同行内の同アルファベット間に有意差がある