implementing theory-based stress-reduction approaches by dealing with real-life complex phenomena in the workplace.[21, 22] Successful intervention will further strengthen the validities of the measurements and models as well as provide strong causal evidence between psychosocial factors and health.

ACKNOWLEDGMENTS

I owe my colleagues and teachers thanks for their encouragements and valuable help: Drs Hiroshi Yanagawa, Masahiro Igarashi, Kazunori Kayaba, Yosikazu Nakamura, Eiji Kajii, Shizukiyo Ishikawa, Tadao Gotoh, Naoki Nago, Kazuomi Kario, Seishi Yamada, Masafumi Mizooka, Machi Sawada, Shinya Hayasaka, Hitoshi Matsuo, Manabu Yoshimura, Kenichiro Sakai, Hideki Origuchi, Youichi Takaki, Shuzou Takuma, Kaname Tsutsumi, Norito Kawakami, Soshi Takao, Kyoko Kondo, Kaho Tsuda, Tsunetaka Matoba, Tatsuya Ishitake, Teruichi Shimomitsu, Fumio Kobayashi, Kanehisa Morimoto, Makiko Nagami, Yuko Odagiri, Yumiko Oya, Masahiro Irie, Akiko Miki, Yuri Kawano, Tetsunojo Uehata, Töres Theorell, Johannes Siegrist, Richard Peter, Johan Hallqvist, Christina Reuterwall, Christer Hogstedt, Peter Fredlund, Nils Emlund, Jeffery V Johnson, Ulf de Faire, and Kristina Orth-Gomér. I also acknowledge the Japan Epidemiological Association and the Editorial Board of the Journal of Epidemiology for giving an opportunity to write this article.

REFERENCES

1. Hemingway H, Kuper H, Marmot M. Psychosocial factors in the primary and secondary prevention of coronary heart disease: an updated systematic review of prospective cohort studies. In: Yusuf S, Cairns JA, Camm AJ, Fallen EL and Gersh BJ, eds. Evidence-based cardiology. 2nd ed. BMJ Publishing Group. London, 2003: 181-218.
2. Ishikawa S, Gotoh T, Nago N, Kayaba K, Jichi Medical School Cohort study group. The Jichi Medical School (JMS) Cohort Study: design, baseline data and standardized mortality ratios. J Epidemiol 2002; 12: 408-17.
3. House JS, Kahn RL. Measures and concepts of social support. In: Cohen S and Syme SL, eds. Social Support and Health. Academic Press. Orlando, Florida, 1985: 83-108.
4. Tsutsumi A, Tsutsumi K, Origuchi H, Takaki Y, Takuma S, Kayaba K, Igarashi M. Development of a perceived social support scale: for a Japanese population. Jpn J Public Health 1994; 41: 965-74.
5. Tsutsumi A, Kayaba K, Ishikawa S, Kario K, Matuso H, Takuma S. Jichi Medical School Social Support Scale (JMS-SSS): Revision and tests for validity and reliability. Jpn J Public Health 2000; 47: 866-78.
6. Tsutsumi A, Tsutsumi K, Kayaba K, Igarashi M. Health-related behaviors, social support, and community morale. Int J Behav Med 1998; 5: 166-82.
7. Schnall PL, Belkić K, Landsbergis P, Baker D, eds. Occupational Medicine: State of the Art Reviews-The Workplace and Cardiovascular Disease. Hanley & Belfus. Philadelphia, PA, 2000.
8. Karasek R, Theorell T. Healthy work: stress, productivity, and the reconstruction of working life. Basic Books. New York, 1990.
9. Uehata T. Stress, life style and health. Bull Inst Public Health 1993; 42: 385-401.
10. Tsutsumi A, Kayaba K, Yoshimura M, Sawada M, Ishikawa S, Sakai K, Gotoh T, Nago N and the Jichi Medical School Cohort study group. Association between job characteristics and health behaviors in Japanese rural workers. Int J Behav Med 2003; 10: 125-42.
11. Tsutsumi A, Kayaba K, Tsutsumi K, Igarashi M, Jichi Medical School Cohort Study Group. Association between job strain and prevalence of hypertension: a cross sectional analysis in a Japanese working population with a wide range of occupations: the Jichi Medical School Cohort Study. Occup Environ Med 2001; 58: 367-73.
12. Theorell T, Tsutsumi A, Hallquist J, Reuterwall C, Hogstedt C, Fredlund P, Emlund N, Johnson JV. Decision latitude, job strain, and myocardial infarction: a study of working men in Stockholm. Am J Public Health 1998; 88: 382-8.
13. Tsutsumi A, Kayaba K, Ishikawa S, Gotoh T, Nago N, Yamada S, Mizooka M, Sakai K, Hayasaka S, and the Jichi Medical School Cohort study group. Job characteristics and serum lipid profile in Japanese rural workers: The Jichi Medical School Cohort study. J Epidemiol 2003; 13: 63-71.
14. Kivimäki M, Leino-Arjas P, Luukkonen R, Riihimaki H, Vahtera J, Kirjonen J. Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees. BMJ 2002; 325: 857-60.
15. Siegrist J. Adverse -60 health effects of high-effort/low-reward conditions. J Occup Health Psychol 1996; 1: 27-41.
16. Tsutsumi A, Ishitake T, Peter R, Siegrist J, Matoba T. The Japanese version of the Effort-Reward Imbalance Questionnaire: a study in dental technicians. Work Stress 2001; 15: 86-96.
17. Tsutsumi A, Nagami M, Morimoto K, Matoba T. Responsiveness of measures in the effort-reward imbalance questionnaire to organizational changes: a validation study. J Psychosom Res 2002; 52: 249-56.
18. Tsutsumi A, Kayaba K, Theorell T, Siegrist J. Association between job stress and depression among Japanese employees threatened by job loss in a comparison between two complementary job-stress models. Scand J Work Environ Health 2001; 27: 146-53.
19. Tsutsumi A, Kayaba K, Nagami M, Miki A, Kawano Y, Ohya Y, Odagiri Y, Shimomitsu T. The effort-reward imbalance model: experience in Japanese working population. J Occup Health 2002; 44: 398-407.
20. Tsutsumi A, Takao S, Mineyama S, Nishiuchi K, Komatsu H,

Kawakami N. Effects of a supervisory education for positive mental health in the workplace: A quasi-experimental study. J Occup Health. (in press)
21. Theorell T, Karasek RA. Current issues relating to psychosocial job strain and cardiovascular disease research. J Occup Health Psychol 1996;1:9-26.
22. Tsutsumi A, Kawakami N. A review of empirical studies on the model of effort-reward imbalance at work: reducing occupational stress by implementing a new theory. Soc Sci Med 2004;59:2335-59.

Original Article

Five-year Stability of Job Characteristics Scale Scores among a Japanese Working Population

Kazunori Kayaba,[1] Akizumi Tsutsumi,[2] Tadao Gotoh,[3] Shizukiyo Ishikawa,[3] and Yoshihiko Miura.[1]

BACKGROUND: The job characteristics scale of job strain, which combines high job demands and low decision latitude based on Karasek's model, has been applied to studies on health care and cardiovascular disease. However, little is known about the long-term stability of this scale with exposure of workers to job. We investigated the 5-year intraindividual variation in job characteristics scores among healthy community workers.
METHODS: Subjects of the study were 458 community dwelling persons forming part of the Jichi Medical School Cohort Study at Yamato (currently, Minami-Uonuma city), Niigata prefecture. The Japanese version of the World Health Organization Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (WHO-MONICA) Psychosocial Study Questionnaire was implemented twice (from 1992 through 1995, and in 1999) to measure job demands and decision latitude levels. Intraclass correlation coefficients were computed to evaluate stability of scores of the questionnaire.
RESULTS: Intraclass correlation coefficient of the decision latitude scores was 0.629 (95% confidence interval: 0.564 - 0.686) and that of the job demands scores was 0.551 (0.476 - 0.617). Subgroup analyses by age, sex, education level, years since first employment, number of co-workers, and job category and status at baseline revealed similar results. In contrast, subjects who experienced position changes within the same enterprise or changed jobs showed lower correlation coefficients of both decision latitude and job demands scores compared to those who experienced no change in job contents.
CONCLUSION: The Japanese version of the WHO-MONICA Psychosocial Study Questionnaire showed statistically significant long-term stability and could be to some extent responsive to change in job strain levels.
J Epidemiol 2005; 15:228-234.

Key words: job strain, Karasek's model, WHO-MONICA Psychosocial Study Questionnaire, long-term stability, population study.

The job characteristics scale of job strain, which combines high job demands and low decision latitude based on Karasek's model,[1] has been applied to studies on health care and cardiovascular disease in North America, Europe and East Asian countries.[2,3,4] Moreover, a number of studies[5,6,7,8,9] have reported acceptable levels of reliability based on internal consistency using data at only one time point. The Japanese version[10] of the World Health Organization Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (WHO-MONICA) Psychosocial Study Questionnaire[11] is one of the representative scales used for the Karasek's model in Japan. An acceptable level of internal consistency has also been reported for this.[12]

In prospective studies, job strain levels at baseline have been regarded as representative of chronic levels and consequently used as long-term risk indicators. Although it is plausible that job characteristics change even within a job title and that employees develop coping skills against stressful situations deriving from such changes, few studies have reported the long-term stability of

Received May 11, 2005, and accepted July 21, 2005.
This study was supported by a grant-in aid from the Foundation for the Development of the Community, Tochigi, Japan.
[1] Saitama Prefectural University, School of Health and Social Sciences.
[2] Okayama University Graduate School of Medicine and Dentistry.
[3] Jichi Medical School, Division of Community and Family Medicine, Center for Community Medicine.
Address for correspondence: Kazunori Kayaba, Professor of Public Health, School of Health and Social Services, Saitama Prefectural University, 820 Sannomiya Koshigaya Saitama 343-8540, Japan (e-mail: kayaba-kazunori@spu.ac.jp)

the job characteristics scale with exposure to job strain. We therefore investigated the 5-year intraindividual variation in job characteristics scores among healthy community workers in Japan.

METHODS

This study formed part of the Jichi Medical School Cohort Study, a large-scale population-based prospective study designed to explore the risk factors for cerebro-cardiovascular disease in 12 Japanese communities. Local governments in all areas approved the study and informed consent was obtained from all participants. Details of the study design were published previously.[13]

The cohort study population in the present analyses comprised residents from a community in Yamato (currently, part of Minami-Uonuma city), Niigata prefecture. Baseline data were collected from 1993 through 1995 with mass screening for cerebro-cardiovascular diseases conducted in accordance with the health and medical service law for the aged. Invitations to participate were sent to eligible individuals by the local government office of Yamato in accordance with the law; all residents aged 19 to 69 years were included. Those undergoing treatment or care for cardiovascular diseases was excluded from the cohort. A total of 2404 participants agreed to participate in the cohort study. For the present analyses, retired persons (154), full-time housewives (846), and subjects without job category data (27) were excluded from the participants. Full-time farmers (372) were also excluded from the analyses because little is known about validity and reliability of the job characteristics scale for Japanese farmers. Thus, 987 full- and part-time workers were eligible for potential subjects for the analyses; 95% worked for small-size enterprises employing ≤50 members of staff. All were followed-up annually, after collection of baseline data, by home visits, phone calls, mail, and interviews during annual health examinations. Of the 987 participants at baseline examination, 17 died and 47 dropped out because of moving. Four hundred and fifty eight (46.4 percent), 199 men and 259 women, attended the follow-up examination in 1999. The mean follow-up period was 5 years. The subject selection process for the present analyses is shown in Figure 1.

Sociodemographic and behavioral variables were investigated with a standardized questionnaire that was completed independently; answers were checked by a trained interviewer. The questionnaire consisted of the following items: occupation, status in the work place, years since first employment, number of co-workers, and changes in job content during the follow-up period. The following categories were included under the occupation item: security guard (n=3), service (104), transport (5), construction (77), production (132), merchant (60), clerk (28), and professional (49). The first five and last three categories were designated blue- and white-collar occupations, respectively.

The Japanese version of the WHO-MONICA Psychosocial

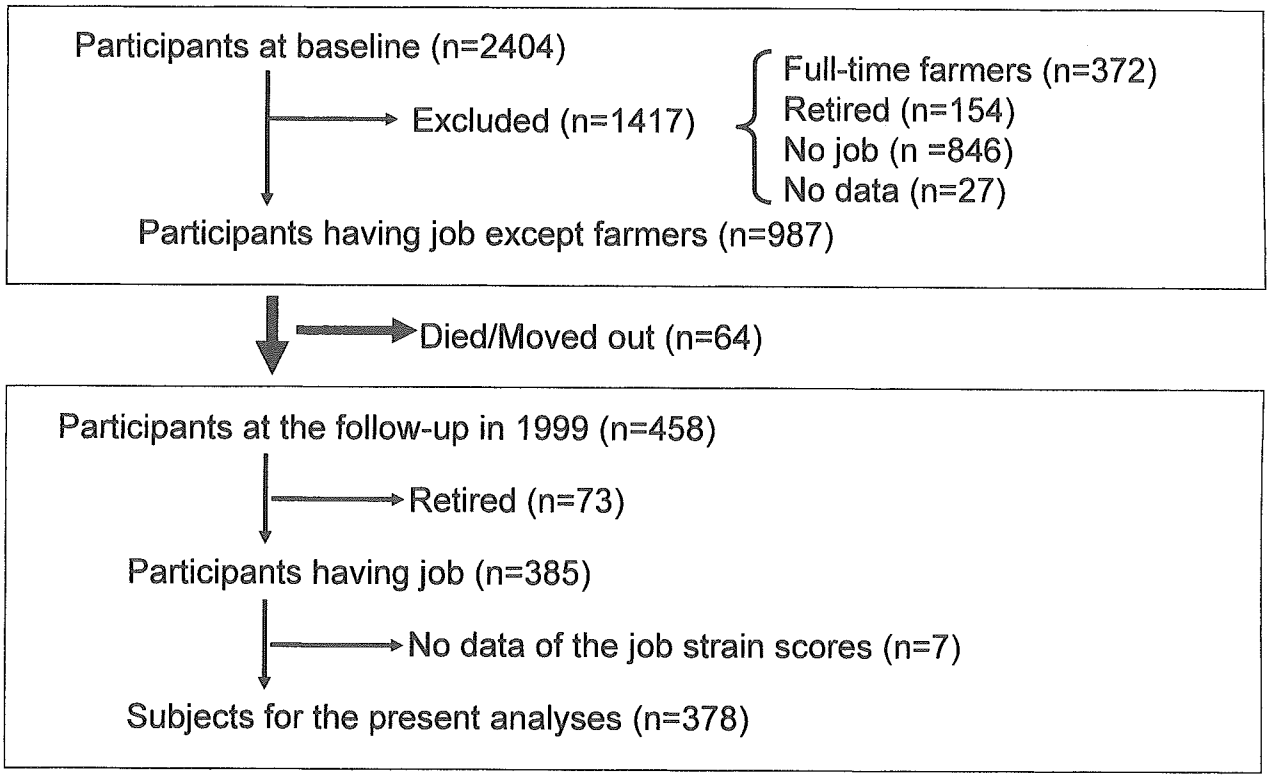

Figure 1. Outline of the subjects selection in the present analyses.

Study Questionnaire[10] was used to evaluate job strain levels at baseline examination (from 1992 through 1995) and follow-up in 1999. The questionnaire consists of two scales, decision latitude and psychological job demands. Decision latitude is defined as the sum of two subscales given equal weight: (a) skill discretion, measured by four elements (the continuous need to acquire new knowledge, skill requirements, creativity requirements, and repetitiveness [reversed score]), and (b) decision authority, measured by two elements (freedom to make decisions and choice in the approach to work). Higher scores indicate a higher level of decision latitude. Psychological job demands are defined by five elements (the need to work fast, the need to work hard, demands for extra work, insufficient time to do work, and conflicting demands). Higher scores indicate higher demand status. All questions were scored on a Likert scale of 1 to 4. The psychometric properties of the Japanese version of the demand-control questionnaire were reported previously.[14,15] Cronbach's coefficient alpha for the decision latitude and psychological demands scores were 0.80 and 0.79, respectively, with the baseline data obtained from the present subjects.

Descriptive parameters are shown as arithmetic means with standard deviations and percentage. The unpaired student's t-test and chi-square test were used to compare the baseline characteristics of participants and those of non-participants at the follow-up examination. The stability of the job characteristics scale measurements at baseline and follow-up was evaluated by calculating intraclass correlation coefficients and their 95% confidence intervals (CIs) using the two-way mixed effects model with absolute agreement. Differences in scores between baseline and follow-up were tested using a paired t-test. A general linear model was used for comparisons between the no job change group and other groups. Significance was defined as $p<0.05$. All statistical analyses were performed using the SPSS® statistical package 11.5j for Windows (SPSS, Chicago, Illinois, USA) with default settings.

RESULTS

The baseline characteristics of individuals who participated in the 1999 follow-up and those who did not are shown in Table 1. Compared to the non-participants, participants were more likely

Table 1. Baseline characteristics of the study population according to those who participated in the follow-up examination and those who did not.

	Follow-up examination:				
	Participants		Non-participants		p-value
No.	458*		529		
Sex, females (%)	259	(56.6)	261	(49.3)	<0.05
Age (years)**	46.7	11.4	45.2	12.9	n.s.
Education status (%)					n.s.
Elementary and junior high school	248	(54.4)	288	(55.2)	
High school	154	(33.8)	167	(32.0)	
University or other	54	(11.8)	67	(12.8)	
Years since first employment (%)					n.s.
Quartile 1 (12-15 years)	95	(20.9)	103	(19.6)	
Quartile 2 (16-17 years)	117	(25.7)	121	(23.0)	
Quartile 3 (18-19 years)	141	(31.0)	168	(31.9)	
Quartile 4 (≥20 years)	102	(22.4)	134	(25.5)	
No. of co-workers (%)					
Quartile1(1-2)	136	(30.6)	123	(24.8)	n.s.
Quartile2(3-5)	122	(27.4)	141	(28.4)	
Quartile3(6-10)	103	(23.1)	120	(24.2)	
Quartile4(≥11)	84	(18.9)	112	(22.6)	
Job category (%)					n.s.
White-collar occupations	137	(29.9)	176	(33.3)	
Blue-collar occupations	321	(70.1)	353	(66.7)	
Status at work (%)					n.s.
Administrative	70	(15.5)	91	(17.5)	
Non-administrative	383	(84.5)	430	(82.5)	
Job strain scores**					
Decision latitude†	15.6	±3.2	15.7	±3.4	n.s.
Psychological job demands‡	11.8	±2.7	11.4	±2.8	<0.05

* : This includes a number of subjects retired.

**: Values represent the mean ± standard deviation.

† : Higher scores indicate higher levels of decision latitude.

‡ : Higher scores indicate higher levels of demand.

n.s. not significant

to be women (56.6 vs. 49.3%, p<0.05) and to have a slightly higher job demands score (11.8±2.7 vs. 11.4±2.8, p<0.05). No statistically significant differences were observed with regard to age, education level, job-related variables, and decision latitude score.

Of the 458 participants of the follow-up in 1999, 73 retired during the follow-up period. A further 7 were excluded because of missing job strain score values at follow-up examination. Data of a total of 378 workers were therefore analyzed.

Intraclass correlation coefficient of the decision latitude scores was 0.629 (95% CI: 0.564 to 0.686) and that of the job demands scores was 0.551 (95% CI: 0.476 to 0.617) (Table 2 and Figure 2). Subgroup analyses according to age, sex, education level, years since first employment, number of co-workers, and job category and status at baseline revealed similar results (Table 2). A high correlation coefficient for decision latitude score was observed for workers with a higher education level (0.894, 95% CI: 0.818 to 0.939). Correlation coefficients for scores at baseline and follow-up examinations of decision latitude scale and of job demands scale among the 63 subjects who experienced position changes within the same enterprise or changed jobs were lower than those for subjects who experienced no changes (Table 2).

Decision latitude scores tended to increase after position (mean difference: 1.6, 95% CI: -0.1 to 3.3) and job changes (0.9, 95%CI: -0.1 to 1.9), although these results were not statistically significant. No meaningful interpretations were found with regard to changes in job demands scores.

Table 2. Intraclass correlation coefficients (ICC) of decision latitude and job demands scores between baseline and 5-year follow-up.

	Decision latitude			Job demands		
	N*	ICC	95% confidence interval	N	ICC	95% confidence interval
Whole subjects	377	0.629	0.564 - 0.686	378	0.551	0.476 - 0.617
Age(year)						
19-29	32	0.503	0.186 - 0.723	32	0.415	0.076 - 0.666
30-39	92	0.678	0.546 - 0.777	92	0.608	0.461 - 0.722
40-49	130	0.674	0.568 - 0.758	129	0.531	0.394 - 0.644
50-59	76	0.556	0.378 - 0.694	76	0.595	0.429 - 0.722
60-69	47	0.567	0.335 - 0.734	49	0.532	0.298 - 0.706
Sex						
Men	181	0.582	0.476 - 0.670	182	0.612	0.513 - 0.696
Women	196	0.587	0.487 - 0.671	196	0.410	0.286 - 0.520
Education status						
Elementary or Junior High school	191	0.593	0.492 - 0.677	192	0.572	0.469 - 0.660
High school	137	0.561	0.434 - 0.665	137	0.457	0.314 - 0.579
University or other school	48	0.894	0.818 - 0.939	48	0.661	0.466 - 0.794
Years since first employment (year)						
Quartile1 (12-15)	79	0.600	0.438 - 0.724	79	0.525	0.344 - 0.669
Quartile2 (16-17)	100	0.619	0.482 - 0.727	99	0.625	0.488 - 0.731
Quartile2 (18-19)	123	0.580	0.450 - 0.686	123	0.425	0.268 - 0.560
Quartile4 (20-)	74	0.736	0.611 - 0.825	76	0.629	0.470 - 0.748
Number of co-worker						
Quartile1(1-2)	120	0.478	0.327 - 0.605	119	0.575	0.441 - 0.684
Quartile2(3-5)	103	0.586	0.443 - 0.699	103	0.571	0.425 - 0.688
Quartile3(6-10)	85	0.704	0.579 - 0.797	86	0.651	0.510 - 0.757
Quartile4(≥11)	59	0.646	0.468 - 0.774	59	0.349	0.104 - 0.554
Job category						
White-collar occupations	118	0.632	0.510 - 0.729	117	0.549	0.409 - 0.664
Blue-collar occupations	259	0.622	0.542 - 0.691	261	0.543	0.451 - 0.623
Job status						
Administrative	63	0.553	0.356 - 0.703	64	0.574	0.384 - 0.717
Non-administrative	310	0.595	0.517 - 0.663	310	0.513	0.426 - 0.590
Change of job contents						
No change	315	0.678	0.613 - 0.733	316	0.620	0.548 - 0.684
Position change	22	0.195	-0.182 - 0.545	23	0.170	-0.210 - 0.523
Job change	40	0.431	0.151 - 0.649	39	0.302	-0.021 - 0.561

* : For some variables, the numbers do not total 378 because of missing values.

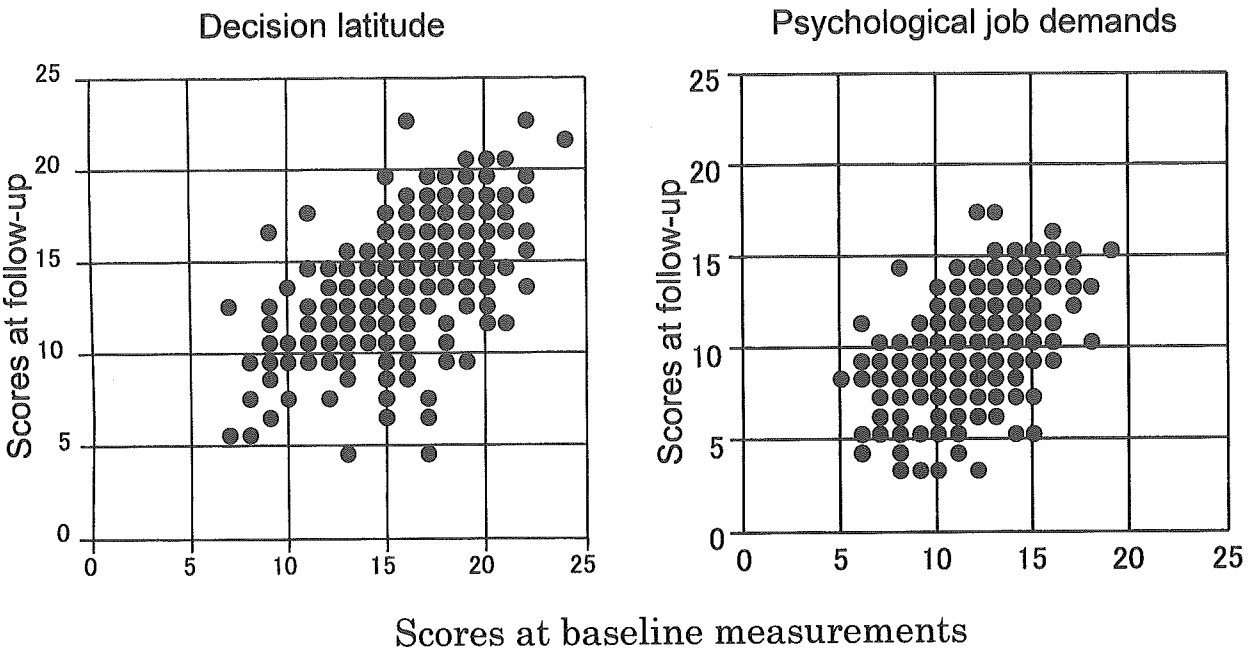

Figure 2. Correlation of decision latitude and job demand scores between baseline and follow-up. Whole subjects.

Table 3. Age-adjusted scores of the decision latitude and the job demands scale at the baseline examination by the job status changes.

Job change status	N	Adjusted mean*	SE	Estimated difference*	95% confidence interval	
				Decision latitude score		p<0.0001
No change	316	16.2	3.1	Reference		
Position change	23	14.4	2.5	-2.0	-3.3 -	-0.7
Job change	40	14.5	3.1	-1.9	-2.9 -	-0.9
Retired	72	13.8	3.0	-2.2	-3.0 -	-1.3
				Job demands score		p=0.064
No change	317	12.0	2.5	Reference		
Position change	24	10.8	3.0	-1.1	-2.2 -	0.0
Job change	39	11.4	2.9	-0.6	-1.4 -	0.3
Retired	71	11.5	3.0	-0.7	-1.4 -	0.1

* : Estimated with multivariate generalized linear model.
SE: standard error of the mean

To explore bias due to the healthy worker effect, decision latitude and job demands scores at baseline were compared according to job change status, including retirement, using a multivariate generalized linear model. After adjusting for age, the no job change group showed a statistically significant higher decision latitude score at baseline than other groups (Table 3).

DISCUSSION

Of the workers who participated in both baseline and follow-up examination, 84% did not change their job or job status during the study period, and their job strain scores showed moderate correlation coefficient levels. Results varied with age, sex, education status, years since first employment, and number of co-workers, and job category and status at baseline. Subgroups that experienced changes showed lower coefficients and the decision latitude

scores at follow-up examination tended to be higher than those at baseline.

To the best of our knowledge, this is the first study to evaluate the long-term reproducibility of the job characteristics scale in a large-scale population-based study in Japan. Two US studies previously reported the reproducibility of this scale. As part of the Work Site Blood Pressure Study in New York City, the 3-year test-retest correlation coefficient was shown to be 0.64 for job decision latitude and psychological job demands.[6] A four-year follow-up study of female nurses showed a moderate degree of stability with correlation coefficients for job control and job demands of 0.60 and 0.54, respectively.[16] These results are similar to those obtained here.

When compared with other behavioral factors, the coefficients for leisure-time physical activity in a Finnish study ranged from 0.41 to 0.43.[17] Regarding biomedical factors in the present population, we previously reported[18] that the coefficients for job strain scores were lower than those for body mass index (0.93), total and high-density lipoprotein cholesterols (0.73 and 0.75, respectively), and blood pressure (0.65). The job characteristics scores in our study seemed to have similar reproducibility compared with other behavioral and biomedical factors in the population-based studies.

Education is known as an important determinant of workers' health.[19] Higher correlation coefficients were observed for those with higher educational attainment. This is probably because they would have achieved a more stable job position than those with lower education levels.

Workers who experienced changes in their job or job status showed a weaker correlation between baseline and follow-up job strain scores and their decision latitude levels tended to increase. Although the small number of subjects who experienced job changes limits interpretation of the results, the job characteristics scales adopted seem responsive to change.

While some studies in Europe and North America have shown a significant relationship between high job strain and ischemic heart disease,[1] considerable numbers of studies, including a study of Japanese immigrants in Hawaii, have failed to show a significant positive association.[20] One reason is suggested to be misclassification of job characteristics due to the lack of information on cumulative exposure to high job strain.[2,21] Instability of job strain levels during study periods could also result in underestimations of the association between job characteristics and health problems. Our results estimating the responsiveness of the job characteristics scale to changes in job strain levels could support this partly.

In previous studies examining the relationship between behavioral work characteristics and health, subjects have mainly included workers from large enterprises with a narrow job category range. Studies on employees in small-sized firms, who tend to have diverse job categories, are scarce.[2] Moreover, the annual statistics of the Japanese labor force survey[22] reported that 97% of enterprises employ ≤50 members of staff, and 62% of the total work force work for small enterprises with ≤50 employees. In this study, 95% of the subjects worked for small-size enterprises (≤50 employees), and 69% were categorized as blue-collar workers. Our findings are unique in that they were derived from workers with diverse occupations, and therefore they are valuable with regard to Japanese workers' health.

This study has some limitations that need to be addressed in future research. First, most subjects in the present analysis were middle aged with relatively high levels of job security. The results displayed in Table 3 suggest that most subjects developed job adaptation skills prior to the baseline examination. This healthy workers effect could have biased our results. Secondly, the small number of subjects who experienced changes in their job circumstances lowered the power to detect the responsiveness of score changes. Thirdly, categorization of workers into job groups defined on the basis of self-administered questionnaire scores could induce misclassification. This study probably underestimated differences of stability of the job strain scores between job categories. Finally, the results of this study were restricted to information from workers living in a local municipality and therefore we should be cautious in generalizing the study findings to other municipal urban populations.

Despite these limitations, however, the findings of this study have important implications. The Japanese version of the WHO-MONICA Psychosocial Study Questionnaire showed statistically significant long-term stability and was supposed to be to some extent responsive to change in job strain levels.

ACKNOWLEDGMENTS

The authors are indebted to the public health nurses and health officers of Yamato (currently, Minami-Uonuma city) Health Examination Center, Niigata prefecture, for their contribution to data collection.

REFERENCES

1. Karasek R, Brisson C, Kawakami N, Houtman I, Bongers P, Amick B. The Job content Questionnaire (JCQ): an instrument for internationally comparative assessments of psychosocial job characteristics. J Occup Health Psychol 1998; 3; 322-55.
2. Schnall PL, Landsbergis PA, Baker D. Job strain and cardiovascular disease. Annu Rev Public Health 1994; 15: 381-411.
3. Kawakami K, Haratani T, Kobayashi F, Ishizaki M, Hayashi T, Fujita O, et al. Occupational class and exposure to job stressors among employed men and women in Japan. J Epidemiol 2004; 14: 204-11.
4. Tsutsumi A. Psychosocial factors and health: Community and workplace study. J Epidemiol 2005; 15: 65-9.
5. Tsutsumi A, Kayaba K, Tsutsumi K, Igarashi M, Jichi Medical School Cohort Study Group. Association between job strain and prevalence of hypertension: a cross sectional analysis in a Japanese working population with a wide range of occupations: the Jichi Medical School cohort study. Occup

Environ Med 2001; 58; 367-73.
6. Landsbergis PA, Schnall PL, Pickering TG, Schwartz JE. Validity and reliability of a work history questionnaire derived from the Job Content Questionnaire. J Occup Environ Med 2002; 44; 1037-47.
7. Williams RM, Sundelin G, Schmuck ML. Reliability of the Demand-Control Questionnaire for sewing machine operators. Work 2001; 16; 71-5.
8. Kawakami N, Fujigaki Y. Reliability and validity of the Japanese version of Job Content Questionnaire: replication and extension in computer company employees. Ind Health 1996; 34; 295-306.
9. Cheng Y, Luh WM, Guo YL, Reliability and validity of the Chinese version of the Job Content Questionnaire in Taiwanese workers. Int J Behav Med 2003; 10: 15-30.
10. Uehata T. Stress and life style. Bull Inst Public Health 1993; 42: 385-401. (in Japanese)
11. The WHO MONICA Project: Geographical variation in the major risk factors of coronary heart disease in men and women aged 35-64 years. WHO Health Stat Quart 1984; 41: 115-40.
12. Tsutsumi A, Kayaba K, Yoshimura M, Sawada M, Ishikawa S, Sakai K, et al. Association between job characteristics and health behaviors in Japanese rural workers. Int J Behav Med 2003; 10: 125-42.
13. Ishikawa S, Gotoh T, Nago N, Kayaba K, and the Jichi Medical School (JMS) Cohort Study Group. The Jichi Medical School (JMS) Cohort Study: design, baseline data and standardized mortality ratios. J Epidemiol 2002; 12: 408-17.
14. Sugisawa A, Uehata T, Pin H, Sekiya E, Ishihara N, Yamazaki Y, et al. Mental health, work environment, and health practices among middle-aged male workers. Jpn J Ind Health 1993; 35: 7-18. (in Japanese)
15. Tsutsumi A. The reliability and validity of the Karasek occupational stress scale (extended Karasek model) in a Japanese working population- the JMS cohort study. Jpn J Stress Sci 1994; 9: 109. (in Japanese)
16. Cheng Y, Kawachi I, Coakley EH, Schwartz J, Colditz G. Association between psychosocial work characteristics and health functioning in American women: prospective study. BMJ 2000; 320: 1432-6.
17. Kujaja UM, Kaprio J, Sama S, Koskenvou M. Relationship of leisure-time physical activity and mortality: the Finnish Twin cohort. JAMA 1998; 279: 440-4.
18. Kayaba K, Ishikawa S, Gotoh T, Nago N, Kajii E, Nakamura Y, et al. Five-year intra-individual variability in C-reactive protein levels in a Japanese population-based Study: the Jichi Medical School Cohort Study at Yamato, 1993-1999. Jpn Cric J 2000; 64: 303-8.
19. Godin I, Kittel F. Differential economic stability and psychosocial stress at work: associations with psychosomatic complaints and absenteeism. Soc Sci Med. 2004 ; 58: 1543-53.
20. Reed DM, LaCroix AZ, Karasek RA, Miller D, MacLean CA. Occupational strain and the incidence of coronary heart disease. Am J Epidemiol 1989; 129: 495-502.
21. Hlatky MA, Lam LC, Lee KL, Clapp-Channing NE, Williams RB, Pryor DB, et al. Job strain and the prevalence and outcome of coronary artery disease. Circulation 1995; 92: 327-33.
22. Statistics bureau, Ministry of public management, home affaires, posts and telecommunications. Labour Force Survey 2001.

ELSEVIER

Journal of Affective Disorders 85 (2005) 267–273

JOURNAL OF AFFECTIVE DISORDERS

www.elsevier.com/locate/jad

Research report

Personality of seasonal affective disorder analyzed by Tri-dimensional Personality Questionnaire

Nobuhisa Maeno[a,b,*], Kazunori Kusunoki[b], Tsuyoshi Kitajima[b], Nakao Iwata[b], Yuichiro Ono[b], Shuji Hashimoto[b], Makoto Imai[c], Lan Li[a], Yuhei Kayukawa[d], Tatsuro Ohta[a], Norio Ozaki[a]

[a]*Department of Psychiatry, Nagoya University Graduate School of Medicine, Nagoya 466-8550, Japan*
[b]*Department of Psychiatry, Fujita Health University School of Medicine, Toyoake, Japan*
[c]*Department of Psychiatry, Shiga University of Medical Science, Otsu, Japan*
[d]*Department of Health Administration Center, Nagoya Institute of Technology, Nagoya, Japan*

Received 11 March 2004; accepted 15 October 2004

Abstract

Background: Although there have been numerous reports in personality of mood disorders, there have been few reports in regard with personality of winter seasonal affective disorder (SAD). Furthermore, no reports have been published concerning summer SAD personality characteristics. Thus, this study was conducted to assess the personality of winter and summer SAD using Tri-dimensional Personality Questionnaire (TPQ) that have been used in a variety of mental disorders.
Methods: A total of 6135 Japanese were evaluated with TPQ, the Seasonal Pattern Assessment Questionnaire (SPAQ) and the Self-rating Depression Scale (SDS). Winter, summer and non-SAD groups were classified by SPAQ. We compared the difference of personality trait among these three groups in consideration of gender, age and SDS score influence.
Results: Winter SAD demonstrated higher "Novelty Seeking" and "Harm Avoidance"; summer SAD showed higher "Harm Avoidance" than the non-SAD group. "Harm Avoidance" in both SAD groups was re-analyzed using SDS score as a covariate, and "Novelty Seeking" in winter SAD using age as a covariate. As a result, the significance of high "Novelty Seeking" and high "Harm Avoidance" in winter SAD was excluded. However, "Harm Avoidance" remained the significant difference between summer and non-SAD.
Limitation: SAD was diagnosed only by SPAQ and not by interview. The state-dependency of "Harm Avoidance" was not confirmed in identical patients over lapse of time.
Conclusion: Patients with winter SAD have high "Harm Avoidance" dependent on the depressive state that is in accordance with non-seasonal depression. Patients with summer SAD have high "Harm Avoidance" possibly independent from the depressive state.

Keywords: Seasonal affective disorder; Personality; Harm avoidance; Depressive state; TPQ

* Corresponding author. Department of Psychiatry, Nagoya University Graduate School of Medicine, Nagoya 466-8550, Japan.
E-mail address: n-maeno@med.nagoya-u.ac.jp (N. Maeno).

0165-0327/$ - see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.jad.2004.10.005

1. Introduction

In cases of seasonal affective disorder (SAD), winter SAD is characterized as being accompanied by atypical depressive symptoms, including hypersomnia, hyperphagia and weight gain. Light therapy has been reported to be effective for winter SAD, although antidepressant drugs are not as effective as in general depression (Rosenthal et al., 1984). By comparison, little literature is available regarding the summer SAD, although this condition reported to be substantially influenced by temperature (Wehr et al., 1987). It is required to clarify the differences and similarities between winter and summer SAD, and non-seasonal depression to elucidate the pathophysiology of each mood disorder. For example, it is of interest whether the characteristics of SAD personality traits are similar to the characteristics of typical personality traits in general depression.

The Tri-dimensional Personality Questionnaire (TPQ) or Temperament and Character Inventory (TCI) (TCI is a revised variation of TPQ) has frequently been used in the assessment of personality traits for mental disorders including mood disorders. TPQ is an instrument of self-report developed by Cloninger (1987) composed of a hereditary factor, "Temperament" and an environmental factor "Character". Furthermore, "Temperament" is classified into following the three dimensions of neurotransmitter: "Novelty Seeking" based on dopamine; "Harm Avoidance" based on serotonin; and "Reward Dependence" based on norepinephrine. According to the results of patients with major depressive disorder evaluated by TPQ, the consensus is that there is a high level of "Harm Avoidance" before treatment and a decrease in "Harm Avoidance" associated with the level severity of depressive state by successful treatment (Chien and Dunner, 1996; Joyce et al., 1994). Moreover, our previous study with TCI is consistent with these results (Hirano et al., 2002).

Reports on the personality traits of SAD are essentially limited to winter SAD, in which conventional reports have mainly been performed with Neuroticism–Extraversion–Openness to discuss Personality Inventory results (NEO-PI-R; Costa and McCrae, 1988). According to the results, winter SAD is reported to demonstrate a significantly elevated level of "Openness" as compared with major depression (Bagby et al., 1996) and bipolar disorder (Jain et al., 1994). In addition, "Conscientiousness" is indicated to be significantly higher while "Extroversion", "Agreeableness" and "Neuroticism" are significantly lower than in controls (Lingjaerde et al., 2001). Furthermore, it has been reported that the use of light therapy results in decreased "Neuroticism," elevated "Extroversion" and "Agreeableness", although no noticeable change in "Openness" can be observed (Sachs et al., 1996; Jain et al., 1994).

The assessment of SAD personality traits with TPQ or TCI is limited to a report by Reichborn-Kjennerud and Lingjaerde (1996), which assessed the correlation between TPQ and response to light therapy in winter SAD. The report showed that "Harm Avoidance" remained high in the non-responder, although decreasing after light therapy in the responder. However, the assessment exclusively deals with the relationship of TPQ and response to light therapy, without comparison of SAD and control groups. Furthermore, to our knowledge, an assessment of personality traits in summer SAD has not been reported.

Thus, we compared the personality traits of winter and summer SAD patients with those of non-SAD individuals on the basis of TPQ in a population that we performed a SAD epidemiological survey (Imai et al., 2003). Because previous reports showed that "Harm Avoidance" is influenced by depressed state, "Novelty Seeking" is lower among the elderly, and "Reward Dependence" is higher in females, we made a comparative assessment of TPQ in consideration of these reports, namely by factors such as age, depressed state, and gender serving as the covariates.

2. Subjects and methods

The study consisted of the participation of 15,188 subjects from collaborating institutions in twelve locations throughout Japan. Namely, Asahikawa and Sapporo located in the northernmost island of Hokkaido (average latitude 43.27°N); prefectures in the main island of Honshu, including Akita, Kanazawa, Fukui and Tottori, located in along the Sea of Japan (average latitude 36.76°N), Chiba, Yamanashi, Nagoya, Osaka and Kurume, located in Pacific coastal zone (average latitude 36.68°N) and Kagoshima,

which is located in South Kyushu (31.36°; the southernmost of the four major islands). The subjects were evaluated with the Japanese versions of TPQ (Cloninger, 1987; 100 items), Seasonal Pattern Assessment Questionnaire (SPAQ; Rosenthal et al., 1984) and the Self-rating Depression Scale (SDS) (Zung et al., 1965), which were completed by the participating subjects. The distribution and collection of questionnaires were conducted in schools, companies and nursing homes by universities and research institutions in the 12 aforementioned locations, during the period of July–October 1997. After collection, 8769 (57.7%) subjects (n=15,188; age range: 18 to 69 years) whose personality traits were considered to be applicable to this research were initially selected. Of these, 6135 (70.0%) were selected for this study (3002 women [48.9%] and 3133 men [51.1%]). The other subjects were excluded from this study due to reasons such as failing to report their age and gender, and/or the TPQ, SDS and SPAQ were incomplete.

The diagnosis of SAD was performed according to criterion of Kasper et al. (1989). Specifically:

(1) SAD was defined as seasonality score on SPAQ being greater than or equal to 11 points, and seasonal change in behavior and mood was problematic in their lives at least to a moderate degree.
(2) (a) Sub-syndromal-SAD was defined as seasonality score on SPAQ being 9 or 10 points, and seasonal change in behavior and mood was problematic in their lives at least to a mild degree. (b) Seasonality score on SPAQ was greater than or equal to 11 points, and seasonal change in behavior and mood was not problematic in their lives or only to a mild degree.
(3) The determination of winter and summer type was defined in the subjects diagnosed as SAD or sub-syndromal-SAD; winter type was defined as those who feel worst in January and/or February, summer type was defined as those who feel worst in July and/or August.

Statistical analyses: Subjects were divided into three groups as follows.

(1) Winter SAD group; a total of winter and sub-syndromal winter SAD.
(2) Summer SAD group; a total of summer and sub-syndromal summer SAD.
(3) Non-SAD group.

First, to compare age difference, SDS score and score of each dimension on TPQ in these three groups, we performed a one-way analysis of variance (ANOVA) that made the diagnosis into an independent variable. Next, we analyzed Pearson's correlation coefficient regarding factors such as age, score of SDS and gender that may influence the score of each dimension on TPQ. Final comparison of the score of each dimension on TPQ was made by one-way analysis of covariance (ANCOVA), in which the diagnosis groups served as the independent variable, and the factors that had significant correlation to each dimension on TPQ served as the covariate. The three groups were compared using the multiple comparison test by Bonferroni's correction in the present study.

3. Results

The data in this study was identical to the data previously published by Imai et al.; therefore, the difference of the prevalence rate of each SAD by age, gender and latitude had been reported already (Imai et al., 2003). Our research identified the following: Of 6135 subjects of aged 18 to 69 who were considered to be pertinent to the purpose of the study, the winter SAD group (winter and sub-syndromal winter SAD) consisted of 117 subjects (1.9%) (winter SAD: 31 (0.5%); sub-syndromal winter SAD: 86 (1.4%)); the summer SAD group (summer and sub-syndromal summer SAD) was comprised of 98 subjects (1.6%) (summer SAD: 38 (0.6%), sub-syndromal summer SAD: 60 (1.0%)); and the non-SAD group totaled 5920 subjects (96.5%), respectively. Table 1 indicates the subjects' attributes, the result of each score on SPAQ, SDS and each dimension on TPQ in both SAD and non-SAD groups. Furthermore, the results of each dimension on TPQ variance and multiple comparisons test analyses using Bonferroni's correction in three groups are as follows:

(1) "Novelty Seeking": winter SAD group>non-SAD group (F=5.8, df=2, p=0.003), winter

SAD vs. non-SAD (Bonferroni's correction: p=0.011).

(2) "Harm Avoidance"; winter SAD group=summer SAD group>non-SAD group (F=29.2, df=2, p<0.001), both winter SAD vs. non-SAD and summer SAD vs. non-SAD (Bonferroni's correction: p<0.001).

(3) The other dimension showed no statistically significant difference.

Next, with regards to the score on "Novelty Seeking" and "Harm Avoidance", which showed a statistically significant difference between winter and non-SAD groups, and the score on "Harm Avoidance", which showed a statistically significant difference between summer and non-SAD groups, we compared correlative factors such as age, depressed state (score of SDS), and gender since they may influence these scores (Table 2). As is shown in Table 2, the score on "Novelty Seeking" showed a significant negative correlation with increased age, and the score on "Harm Avoidance" showed a significant positive correlation with SDS. This fact suggests that age is a confounding factor; therefore, we performed analysis of covariance regarding score on "Novelty Seeking" by statistical control of the influence of age. As a result, the statistically significant difference in score on "Novelty Seeking" disappeared (p>0.05). Similarly, SDS was presumed to be a confounding factor, and we performed an analysis of covariance concerning score on "Harm Avoidance" by statistical control of influence of depressed state. As a result, the statistically significant difference in score on "Harm Avoidance" remained between only summer and non-SAD groups (Table 1).

Table 1
The results of age, sex, latitude, SPAQ, SDS, TPQ in winter SAD group, summer SAD group and non-SAD group

	Winter SAD group, n=117	Summer SAD group, n=98	Non-SAD group, n=5920
Age (mean±S.D.)	34.4±13.02	35.7±16.15	39.0±14.37
Sex (M/F)	64/53	40/58	3197/2723
Latitude (northern/southern)	82/35	47/51	3004/2916
SPAQ total (mean±S.D.)	12.5±2.55	12.2±2.13	4.2±3.47
SDS (mean±S.D.)	43.1±8.20	43.9±7.72	37.4±8.49
Novelty Seeking[a] (mean±S.D.)	17.5±4.03	17.1±4.72	16.4±4.11
Harm Avoidance[b] (mean±S.D.)	19.8±5.80	21.0±6.13	17.2±5.96
Reward Dependence (mean±S.D.)	19.4±4.60	19.2±3.96	19.6±4.29

[a] In "Novelty Seeking", a significant difference disappeared as follows when we added age as covariate in ANCOVA. Winter SAD group=non-SAD group (F=2.602, df=2, p=0.074).

[b] In "Harm Avoidance", a significant difference showed results of as follows when we added SDS as covariate in ANCOVA. Summer SAD group>non-SAD group (F=3.7, df=2, p=0.025), summer SAD group vs. non-SAD group (Bonferroni's correction: p=0.032).

Table 2
The results of Pearson's correlation coefficient between age and "Novelty Seeking" and, the results of Pearson's correlation coefficient with SDS of "Harm Avoidance" in three groups

	Winter SAD group, n=117 (r)	Summer SAD group, n=98 (r)	Non-SAD group, n=5,920 (r)
"Novelty Seeking" and age	−0.522	−0.462	−0.293
"Harm Avoidance" and SDS	0.415	0.434	0.532

All the correlation coefficients of each group are p<0.001.

4. Discussion

The present study showed that the winter SAD group had higher scores in "Novelty Seeking" and "Harm Avoidance", and the summer SAD group demonstrated a higher score of "Harm Avoidance" than the non-SAD group. Furthermore, because "Harm Avoidance" showed positive correlation with depressed state, and "Novelty Seeking" showed negative correlation with increased age, "Harm Avoidance" exhibited depressed state serving as the covariate, and "Novelty Seeking" likewise constituted the covariate for age. As a result, "Novelty Seeking" was excluded as the statistically significant difference between the winter and non-SAD groups. Moreover, "Harm Avoidance" remained the statistically significant difference between only summer and non-SAD groups, and eliminated the statistically significant difference between winter and non-SAD groups.

The independence of high "Harm Avoidance" in summer SAD from the influence of depressed state is very peculiar in comparison with previous findings

that showed high "Harm Avoidance" being commonly influenced by state in depressive patients as discussed later in this section. There is a clear need for further studies to conclude whether high "Harm Avoidance" in summer SAD is independent from the influence of depressed state, since no report on the personality traits of summer SAD has been published to the knowledge of the authors.

Our study also demonstrated that winter SAD shows that high "Harm Avoidance" depends on depressed state. These results are consistent with the previous report that the assessment of changes of TPQ in pre- and post-light therapy in winter SAD shows that "Harm Avoidance" decreases with the reduction of depressed state, although the study did not compare the outcome with control subjects (Reichborn-Kjennerud and Lingjaerde, 1996). In addition, to date, many reports regarding personality traits of winter SAD patients are assessed by NEO-PI-R. Our results make the assumption that "Novelty Seeking" in TPQ (TCI) and "Extraversion" in NEO-PI-R compare to the respective correlation of "Harm Avoidance" in TPQ (TCI) and "Neuroticism" in NEO-PI-R (Cloninger et al., 1994). The report that "Neuroticism" decreased with reduction of depressed state in pre- and post-light therapy of winter SAD is also consistent with our results (Sachs et al., 1996; Jain et al., 1994). Conversely, in the only other report that compares personality traits of winter SAD with healthy persons, significantly lower "Extraversion" and "Neuroticism" is reported as compared with the control group, and thereby inconsistent with our results (Lingjaerde et al., 2001). Whether this inconsistency may be attributed to certain differences in Japanese and Norwegian subjects, or difference in diagnosis between groups based on the information extracted by SPAQ and clinical symptoms, is a subject that has yet to be clarified.

High "Harm Avoidance" dependent on the depressive state in winter SAD is also consistent with findings of previous reports in non-seasonal depression. For example, in our previous study, before and after antidepressant treatment in patients with major depression, a high score on "Harm Avoidance" before treatment decreased when treatment had been effective, and the score on "Harm Avoidance" correlated with the score on the Hamilton Rating Scale of Depression (Hirano et al., 2002). Therefore, it is considered that the association between high "Harm Avoidance" and dependence of "Harm Avoidance" on depressed state are not only a peculiar to phenomenon in winter SAD, but also a common phenomenon in depressive state.

High "Harm Avoidance" subjects phenomenally show "anticipatory worry and pessimism" and "fear and fret to uncertainty." Therefore, depressive patients show high "Harm Avoidance" during depressed state, resembling negative automatic thoughts, a target of cognitive behavior therapy. Actually, according to a comparison dealing with the cognitive profile of winter SAD patients, non-seasonally depressed and normal controls, the SAD group reported significantly more negative automatic thoughts and dysfunctional attitudes than the non-depressed control group, but did not differ from the group with non-seasonal depression (Hodges and Marks, 1998).

Furthermore, it has been reported that negative automatic thoughts of winter SAD patients change seasonally, and become the most remarkable during the course of the transition from autumn to winter (Rohan et al., 2003). According to these facts, it is thought that in general depression and winter SAD, negative automatic thoughts appear when they are accompanied by depressed state, and although negative automatic thoughts contribute to high "Harm Avoidance", negative automatic thoughts decrease with the reduction of depressed state, thereby "Harm Avoidance" also decreases. In the future, the association between high score on "Harm Avoidance" in depressive episode and negative automatic thoughts should be assessed.

The following points are acknowledged as limitations of the present study. In the present study, SAD subjects were extracted by SPAQ on a large-scale epidemiological survey; thereby we did not perform a psychiatric interview for the diagnosis of SAD, and questions remain as to whether we could correctly identify and extract true clinical SAD. Moreover, SDS was designed to evaluate usual depressive symptoms not atypical depressive symptoms that most SAD patients have. Therefore, the underestimation of the depressive state using SDS might contribute to High "Harm Avoidance" independent from the depressive state in summer SAD. In addition, although high "Harm Avoidance" dependent on depressed state was confirmed, to prove true state dependency, it is

necessary to confirm the degree to which a change of depressed state has an influence on "Harm Avoidance" score with the lapse of time in identical patients.

5. Conclusions

We performed an epidemiological survey of 15,188 Japanese and assessed the difference of personality traits of winter SAD, summer SAD and healthy persons with TPQ in consideration of influences such as age and score of SDS. As a result, we confirmed that the winter SAD group showed a high score on "Harm Avoidance" dependent on depressed state, equivalent to an evaluation in patients with general depression. Furthermore, the study revealed that a high score on "Harm Avoidance" in the summer SAD group was influenced less than the depressed state on "Harm Avoidance" in winter SAD.

Acknowledgements

The authors appreciate Dr. Norman Rosenthal's helpful comments to this article. This work was supported in part by research grants from the Ministry of Education, Culture, Sports, Science and Technology, and the Ministry of Health, Labor and Welfare. In addition, we extend our thanks to the teachers of universities and research institutions for their cooperation in the distribution and collection of questionnaires for the present study.

Collaborating research institutions: Matsumoto Miki (Asahikawa Medical University), Honma Hiroshi (Hokkaido University), Kobayashi Riko (Hokkaido University), Shimizu Tetsuo (Akita University), Mishima Kazuo (Akita University), Furuta Hisakazu (Kanazawa University), Nakagawa Hiroki (Fukui Mental Health Center), Ishizuka Yoshikazu (Yamanashi Medical University), Shirakawa Shuichiro (National Center of Neurology and Psychiatry), Inoue Yuichi (Tottori University), Sugita Yoshiro (Osaka University), Sakamoto Tetsuro (Kurume University), Kamei Kenji (Kagoshima University) and Fukusako Hiroshi (Kagoshima University).

References

Bagby, R.M., Schuller, D.R., Levitt, A.J., Joffe, R.T., Harkness, K.L., 1996. Seasonal and non-seasonal depression and the five-factor model of personality. J. Affect. Disord. 38, 89–95.

Chien, A.J., Dunner, D.L., 1996. The Tridimensional Personality Questionnaire in depression: state versus trait issues. J. Psychiatr. Res. 30, 21–27.

Cloninger, C.R., 1987. A systematic method for clinical description and classification of personality variants. Arch. Gen. Psychiatry 44, 573–588.

Cloninger, C.R., Przybeck, T.R., Svrakic, D.M., Wetzel, R.D., 1994. The Temperament and Character Inventory (TCI): A Guide to Its Development and Use. Center for Psychology of Personality, St. Louis, MO.

Costa, P.T., McCrae, R.R., 1988. Personality in adulthood: a six-year longitudinal study of self-reports and spouse ratings on the NEO Personality Inventory. J. Pers. Soc. Psychol. 54, 853–863.

Hirano, S., Sato, T., Narita, T., Kusunoki, K., Ozaki, N., Kimura, S., Takahashi, T., Sakado, K., Uehara, T., 2002. Evaluating the state dependency of the Temperament and Character Inventory dimensions in patients with major depression: a methodological contribution. J. Affect. Disord. 69, 31–38.

Hodges, S., Marks, M., 1998. Cognitive characteristics of seasonal affective disorder: a preliminary investigation. J. Affect. Disord. 50, 59–64.

Imai, M., Kayukawa, Y., Ohta, T., Li, L., Nagakawa, T., 2003. Cross-regional survey of seasonal affective disorders in adult and high-school students in Japan. J. Affect. Disord. 77, 127–133.

Jain, U., Blais, M.A., Otto, M.W., Hirshfeld, D.R., Sachs, G.S., 1994. Five-factor personality traits in patients with seasonal depression: treatment effects and comparisons with bipolar patients. J. Affect. Disord. 55, 51–54.

Joyce, P.R., Mulder, R.T., Cloninger, C.R., 1994. Temperament predicts clomipramine and desipramine response in major depression. J. Affect. Disord. 30, 35–46.

Kasper, S., Rogers, S.L., Yancey, A., Schulz, P.M., Skwerer, R.G., Rosenthal, N.E., 1989. Phototherapy in individuals with and without subsyndromal seasonal affective disorder. Arch. Gen. Psychiatry 46, 837–844.

Lingjaerde, O., Foreland, A.R., Engvik, H., 2001. Personality structure in patients with winter depression, assessed in a depression-free state according to the five-factor model of personality. J. Affect. Disord. 62, 165–174.

Reichborn-Kjennerud, T., Lingjaerde, O., 1996. Response to light therapy in seasonal affective disorder: personality disorders and temperament as predictors of outcome. J. Affect. Disord. 41, 101–110.

Rohan, K.J., Sigmon, S.T., Dorhofer, D.M., 2003. Cognitive-behavioral factors in seasonal affective disorder. J. Consult. Clin. Psychol. 71, 22–30.

Rosenthal, N.E., Sack, D.A., Gillin, J.C., Lewy, A.J., Goodwin, F.K., Davenport, Y., Mueller, P.S., Newsome, D.A., Wehr, T.A., 1984. Seasonal affective disorder. A description of the syndrome and preliminary findings with light therapy. Arch. Gen. Psychiatry 41, 72–80.

Sachs, G.S., Jain, U., Truman, C.J., Blais, M.A., Otto, M.W., Hirschfeld, D., 1996. Seasonal Affective Disorder and personality characteristics: assessing personality traits of pretreatment and post-treatment phases of seasonal depression. Soc. for Light Treatment and Biological Rhythms, Abstract, vol. 8, p. 36.

Wehr, T.A., Sack, D.A., Rosenthal, N.E., 1987. Seasonal affective disorder with summer depression and winter hypomania. Am. J. Psychiatry 144, 1602–1603.

Zung, W.W., Richards, C.B., Short, M.J., 1965. Self-rating depression scale in an outpatient clinic. Further validation of the SDS. Arch. Gen. Psychiatry 13, 508–515.

Intern. J. Neuroscience, 115:367–378, 2005

ISSN: 0020-7454 / 1543-5245 online
DOI: 10.1080/00207450590520984

Taylor & Francis
Taylor & Francis Group

EFFECTS OF FLUVOXAMINE ON LEVELS OF DOPAMINE, SEROTONIN, AND THEIR METABOLITES IN THE HIPPOCAMPUS ELICITED BY ISOLATION HOUSING AND NOVELTY STRESS IN ADULT RATS

H. MIURA
H. QIAO
T. KITAGAMI
T. OHTA
N. OZAKI

Department of Psychiatry
School of Medicine
Nagoya University
Nagoya Aichi, Japan

The authors investigated the effects of fluvoxamine on neurochemical changes in the hippocampus elicited by isolation housing and novelty stress. Male F344 rats (11 w) were housed one per cage for four weeks. On each day of the last week (7 days) they were s.c. injected with fluvoxamine (20 mg/kg), and then subjected to novelty stress. Isolation housing significantly increased dihydroxyphenylacetic acid (DOPAC) and 5-hydroxyindoleacetic acid (5-HIAA) levels, whereas fluvoxamine significantly decreased them. Isolation housing significantly increased the DOPAC/DA ratio. Fluvoxamine significantly decreased the DA level, and partially restored the DOPAC and 5-HIAA levels increased by isolation housing.

Keywords dopamine, fluvoxamine, hippocampus, isolation housing, novelty stress, serotonin

Received 16 April 2004.

Address correspondence to H. Miura, Department of Psychiatry, School of Medicine, Nagoya University, Tsuruma-cho, Showa-ku, Nagoya, Aichí 466-8550, Japan. E-mail: hmiura@med.nagoya-u.ac.jp

INTRODUCTION

In humans, major depression is thought to occur due to a disturbance of the brain monoamine system (Delgado, 2000; Hirschfeld, 2000; Leonard, 2000), and most patients become ill in middle- or older age after adverse life events, such as interpersonal loss (separation, etc.) (Paykel, 1994). Further, absence of social support appears to be associated with an onset and relapse of depression (Paykel, 1994). Kendler showed that genetic factors cooperate with environmental factors to induce the onset of depression in humans (Kendler et al., 1993). Thus, environmental risk factors in cooperation with genetic factors cause disturbances of the brain monoamine system in cases of depression in adulthood.

The authors previously investigated whether or not an animal model based on general environmental risk factors of depression (acute environmental change, i.e., an adverse life event; and social isolation, i.e., absence of social support) would be useful for future research into the expression of specific genes related to major depression. They therefore have proposed an animal model that simulated two known environmental risk factors (novelty stress and isolation housing) (Miura et al., 2002a, 2000b). In almost all previous studies investigating separation from a social group, isolation started soon after weaning (Gárzon et al., 1981; Gentsch et al., 1982; Holson, 1986; Wright et al., 1991; Hall et al., 1998; Paulus et al., 1998; Varty et al., 1999; Whitaker-Azmita et al., 2000; Muchimapura et al., 2002; Schrijver et al., 2002; Lapiz et al., 2003). These studies have all regarded isolation as a stressor, and the influence of isolation on the development of the central nervous system (CNS) was investigated in each of these studies. However, as mentioned earlier, the ordinary clinical onset of human depression is in middle- or older age for individuals with no prior developmental disturbance or social maladjustment. In other words, most of the data regarding the clinical onset of human depression suggests that the normally developed CNS becomes disorganized in adulthood. Thus, the authors have investigated the influence of isolation housing on normally developed adult rats, because they consider that this model more nearly resembles the clinical course of human depression than a model employing isolation soon after weaning.

Fluvoxamine, a selective serotonin (5-HT) reuptake inhibitor (SSRI), is a clinically effective antidepressant. The pharmacological effect of fluvoxamine is thought to be blockage of the serotonin transporter (SERT). Due to the straightforward mechanism of action of fluvoxamine, the possibility was considered that evaluating the effects of fluvoxamine on the neurochemical changes elicited by two environmental risk factors would be facilitated, in

comparison with the evaluation of other classical antidepressants. The aim of the present study was thus to investigate the effects of fluvoxamine on neurochemical responses elicited by isolation housing and novelty stress. Furthermore, whether or not isolation housing in adult rats had potential use as an animal model of depression was considered.

MATERIAL AND METHODS

Animals

The animals used in the present experiments were 11-week-old male F344 rats. The animals were divided into two groups (Figure 1). Rats in the isolation-housing group were housed individually in cages, whereas those in the group-housing group were housed three per cage. Cages (38 × 36 × 20 cm) were of the hanging type and had wire-mesh bottoms to minimize the influence of handling procedures, for example, cage exchange. Food and water were provided ad libitum. A 12-h light/12-h dark cycle was maintained, and room temperature was kept at 21–23°C. These rats were reared 4 weeks before the novelty stress experiment (Figure 1). All efforts were made to minimize the pain or discomfort of the animals and to reduce the number of animals used, and the experiments were conducted in accordance with the "Principles of Laboratory Animal Care" determined by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

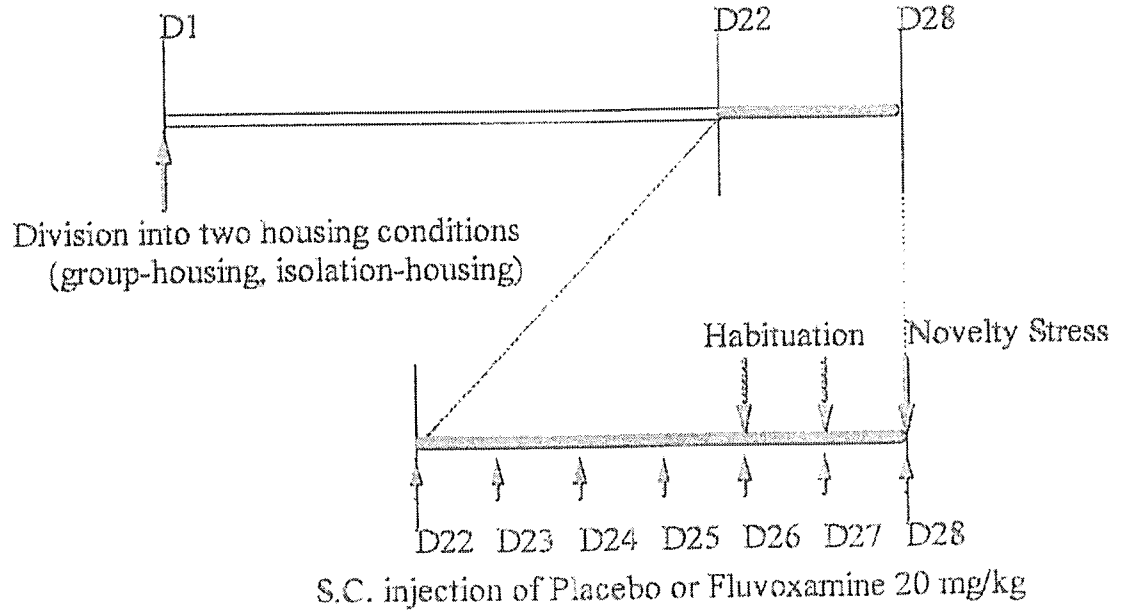

Figure 1. The time schedule of experiments. Rats were divided into eight groups as described in Materials and Methods.

Materials

Solvay Pharmaceuticals (Brussels, Belgium) kindly donated the fluvoxamine, which was suspended in distilled water. In the final week, rats were given 20 mg/kg fluvoxamine or distilled water (control) every day (7 days) by s.c. injection (Figure 1). Thus, the rats were further divided into control and fluvoxamine groups.

Novelty Stress Test

Four weeks after having been divided into two rearing groups, the animals were further divided into a stress and a non-stress group. Rats in the stress group received exposure to an unpredictable novelty stress (Figure 1): they were placed for 20 min in a semitransparent plastic cylinder (height, 40 cm; diameter, 31 cm) underlaid with a black resin sheet. Rats in the non-stress group underwent a 10-min habituation session in the apparatus on days 26 and 27 preparatory to a 20-min session on day 28 (Figure 1); thus, for these animals the session on day 28 represented an exposure to a somewhat familiar environment rather than to a novel environment that they had not previously encountered. Finally, the rats were divided into eight groups: group-housed, fluvoxamine (–), non-stress; group-housed, fluvoxamine (–), stress; group-housed, fluvoxamine (+), non-stress; group-housed, fluvoxamine (+), stress; isolation-housed, fluvoxamine (–), non-stress; isolation-housed, fluvoxamine (–), stress; isolation-housed, fluvoxamine (+), non-stress; and isolation-housed, fluvoxamine (+), stress. The number of rats in each group was 9, and the total number of rats was 72. All 72 animals underwent the session on day 28.

Sample Preparation

All 72 rats were killed by cervical dislocation immediately after exposure to the session on day 28. The brains were removed and, as soon as possible, dissected on glass plates over ice. The hippocampus was prepared for the following analyses. The samples were weighed and treated with 1000 μl of an ice-cold 0.2 M perchloric acid (PCA) solution containing 0.2 mM sodium pyrosulfite, 0.01% EDTA2Na, and 0.5 μM isoproterenol (ISO) as an internal standard per 100 mg wet tissue. This solution was sonicated and then centrifuged at 10,000 g for 20 min at 4°C. The supernatant was filtered through a Millipore HV filter (0.45 μm pore size) and then subjected to high-performance liquid chromatography (HPLC) with electrochemical detection (ECD).