Table 2
Chi-Squares and Fit Indices of All Models, Controlling for Gender, Income, and Chronic Conditions

Model	Parameter constraints[a]	χ^2	*df*	χ^2_{diff}[b]	GFI	AGFI	CFI	AIC
Saturated		50.96	48		.976	.954	.997	136.963
Stability	a = b = 0	58.70	50	7.74*	.973	.950	.992	140.702
Depression-to-step	a = 0	56.83	49	5.86*	.973	.951	.993	140.827
Step-to-depression	b = 0	52.83	49	1.87	.975	.954	.997	136.833

Note. GFI = goodness-of-fit index: AGFI = adjusted goodness-of-fit index; CFI = comparative fit index; AIC = Akaike information criterion.
[a] The letters a and b denote cross-lagged parameters. [b] Comparison with the saturated model.
* $p < .05$.

depressive symptoms at Wave 2 in both age groups) was compared with the following three possible models:

1. The non-age-specific model stipulated that the cross-lagged effect of steps on depressive symptoms was identical across age groups (Parameter a in Figure 1 was constrained to be equal between the middle-aged and the older groups).

2. The middle-aged-specific model stipulated that the steps were effective only on the middle-aged group (Parameter a in the older group was constrained to be zero, whereas Parameter a in the middle-aged group was freely estimated).

3. The older-specific model stipulated that the steps were effective only on the older group (Parameter a in the middle-aged group was constrained to be zero, whereas Parameter a in the older group was freely estimated).

Table 3 indicates the results of testing. Although all models, including the saturated model, could be rejected as statistically different from the observed data, the fit indices indicated that each model provided a good fit. Differences in fit among the models revealed that the non-age-specific model, $\chi^2(1, N = 1{,}151) = 5.70$, $p < .05$, and the middle-aged-specific model, $\chi^2(1, N = 1{,}151) = 5.73$, $p < .05$, provided significantly worse fits than the saturated model. The older-specific model, however, was statistically comparable to the saturated model, $\chi^2(1, N = 1{,}151) = 0.53$ (*ns*). The inference from these results is that the older-specific model fits the data best.

Parameter estimates of the older-specific model indicated that the two lagged effects (autoregressive paths from walking steps at Wave 1 to walking steps at Wave 2, and depressive symptoms at Wave 1 to depressive symptoms at Wave 2) were strong in both age groups, indicating that walking steps and depressive symptoms remained fairly stable over the 2 years (βs = .64 and .71 for walking steps and .62 and .74 for depressive symptoms in middle-aged and older groups, respectively, $p < .01$ in each case). Additionally, the older group showed a significant cross-lagged effect ($\beta = -.11$, $p < .05$) of walking steps at Wave 1 on depressive symptoms at Wave 2, suggesting that older participants who walked more at baseline reported fewer depressive symptoms at follow-up.

Discussion

In this study we used longitudinal data from a large community sample in Japan to examine the relationships between physical activity and psychological well-being. Cross-lagged panel analyses demonstrated that the baseline daily walking activity estimated by a pedometer was associated with depressive symptoms at the 2-year follow-up in older adults, even after adjusting for potential confounding variables. This is in line with the results of other studies conducted in Western countries (e.g., Camacho et al., 1991; Hassmen et al., 2000; Herzog et al., 1998, Lampinen et al., 2000; Ross & Hayes, 1988). In contrast, the analyses did not support the antidepressant effect of physical activity in middle-aged adults. Thus, as we predicted, the findings provide evidence for age

Table 3
Multigroup Testing of the Step-to-Depression Model, Controlling for Gender, Income, and Chronic Conditions

Model	Parameter constraints[a]	χ^2	*df*	χ^2_{diff}[b]	GFI	AGFI	CFI	AIC
Saturated		145.43	95		.981	.964	.987	319.43
Non-age-specific	m = o	151.13	96	5.70*	.981	.963	.986	323.13
Middle-aged-specific	o = 0	151.16	96	5.73*	.981	.963	.986	323.16
Older-specific	m = 0	145.96	96	0.53	.981	.964	.988	317.96

Note. GFI = goodness-of-fit index; AGFI = adjusted goodness-of-fit index; CFI = comparative fit index; AIC = Akaike information criterion.
[a] Alphabetic notations indicate age groups: m = middle-aged, o = older. [b] Comparison with the saturated model.
* $p < .05$.

differences in the beneficial effect of physical activity on psychological well-being.

In general, people become less active as they age (Shephard, 1997), as demonstrated in our study: Participants from the older group accumulated fewer walking steps than participants from the middle-aged group. However, it is unclear whether a decrease in habitual activity is a normal part of aging (Shephard, 1997), because studies have also reported that older adults can achieve excellent exercise adherence and maintenance (Emery, Hauck, & Blumenthal, 1992; McAuley, Jerome, Elavsky, Marquez, & Ramsey, 2003). In other words, it is likely that older adults' physical capacity may be underestimated because they are ostensibly inactive in their daily lives. Consequently, one possible explanation for the age difference we saw in this study is that individuals who are far below physical capacity in fitness (i.e., older adults) gain greater benefit from exercise. Our results may also suggest that the daily walking activity was too mild to affect the depressive symptoms of midlife adults. In fact, some studies (McGowan, Pierce, & Jordan, 1991; Rehor, Dunnagan, Stewart, & Cooley, 2001) have reported that vigorous aerobic exercise (e.g., running) or resistance training (e.g., weight lifting) improves psychological well-being in younger persons. Thus, the results in the present study suggest that a reasonable match between age and the type of exercise may be necessary for there to be an antidepressant effect.

Although some studies have suggested that older people can improve their psychological well-being by vigorous aerobic and resistance training (Blumenthal et al., 1991, 1999; Singh et al., 1997), too much physical activity can provoke cardiac risks or cause musculoskeletal injury, especially for an older person (Shephard, 1997). In addition, Penninx et al. (2002) found that a walking exercise intervention was more effective than a resistance exercise intervention for reducing depressive symptoms in older adults. In this regard, modest activity such as walking would be a secure and effective exercise for preventing depressive symptoms in older persons.

One of the greatest limitations in the present study is that the antidepressant effect of walking was not extremely strong ($\beta = -.11$). It should also be noted that the model comparisons using SEM revealed that the step-to-depression model was better, but the stability and depression-to-step models also fit the observed data well. Future analyses should attempt to refine our findings. For example, according to Williamson and Schulz (1992, 1995), illness and its resultant pain are related to depression because they restrict patients' routine activities. Although we excluded possibly disabled individuals from the data and adjusted for the effect of chronic health conditions in the analyses, prior health factors may still play an important role in the relationship between walking and depressive symptoms. It should also be noted that although the final model, predicting depression from baseline walking scores, fit the data the best, all of the models provided an adequate fit to the data on the basis of the goodness-of-fit indices. As such, the final model was based on the best-fitting model, within the context of a number of good-fitting statistical models.

It would also be valuable to consider the factors that mediate the relationship between walking and depressive symptoms. Both physiological and psychosocial pathways have been hypothesized as mediating the antidepressant effect of physical activity (Brown, 1992; Paluska & Schwenk, 2000). For example, physical activity is believed to have an effect by enhancing brain aminergic synaptic transmission (Ransford, 1982) or by reducing activity of the hypothalamic–pituitary–adrenal axis (van der Pompe, Bernards, Meijman, & Heijnen, 1999). The psychosocial explanation posits that individuals who exercise improve their psychological well-being by increasing self-efficacy (McAuley, Blissmer, Katula, Duncan, & Mihalko, 2000) or because the activity acts as a diversion from unpleasant stimuli (Hill, 1987). Modeling complex multistep pathways that consider these and other factors (e.g., gender) would be a fruitful approach for improving the predictive effect of physical activity on psychological well-being.

Nevertheless, an advantage of the present study is that it showed the availability of a simple measure of walking steps for predicting depressive symptoms in community-dwelling adults. Although there is increasing evidence regarding the importance of physical activity in maintaining mental health in older people, past findings were generally based on subjective, self-report measures of physical activity (e.g., Herzog et al., 1998; Lampinen et al., 2000) or on experimental works using small samples (e.g., McNeil et al., 1991; Singh et al., 1997). The use of an objective, low-cost, and user-friendly measure such as a pedometer makes assessing physical activity easier and thus more feasible to consider as a mental health factor in large community surveys.

Furthermore, a recent study (Talbot, Gaines, Huynh, & Metter, 2003) reported that a pedometer-driven walking program with a self-management educational program increased physical activity, muscle strength, and functional performance in older adults with osteoarthritis, as opposed to the educational program alone. This implies that a pedometer can also be used as a motivator for exercise adherence. From this viewpoint the results in the present study are small but important steps that warrant further research to clarify the availability of this tool to promote psychological well-being in older adults.

In conclusion, the present study partially confirmed the protective effect of physical activity on depressive symptoms in community-dwelling adults. The findings suggest that age should be taken into account when incorporating a walking exercise in research and daily practice for mental health.

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Brief Research Communication

Association of Cholecystokinin-A Receptor Gene Polymorphisms and Panic Disorder in Japanese

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Several lines of evidence have suggested that naturally occurring alterations in cholecystokinin (CCK) systems could contribute to the development of panic disorder (PD). Among recent investigations, polymorphisms of the CCK and CCK-B receptor (R) genes were investigated, but the results were inconclusive. We recently cloned the genomic structures of human CCK-AR, and determined the transcriptional start site of the human CCK-AR gene. Two sequence changes were detected in the promoter region: a G to T change in nucleotide −128 and an A to G change in nucleotide −81 (GenBank database under accession number D85606). The frequencies of the genotypes and haplotypes of these two polymorphisms were compared in 109 Japanese patients with PD and 400 age- and gender-matched normal Japanese control subjects. The frequency of variant genotypes (−81A/G, −128G/T; G/G, G/T, and G/G, T/T) having variant haplotype (−81G/−128T) was significantly higher in PD than in controls ($P < 0.0001$, OR = 2.81, 95% CI = 1.74–4.39). The statistical differences between the haplotype distributions in the PD and control groups were highly significant: the frequency of variant haplotype (−81G/−128T) was higher in the former group than in the latter ($P < 0.0001$). This association was not affected by clinical characteristics such as age, gender, and age at onset of PD. In this study, the first to report the positive association of the CCK-AR polymorphisms and PD, haplotype analyses further strengthened the association based on our comparison of genotype distributions. The CCK-AR gene polymorphism may be involved in the neurobiology of PD.

KEY WORDS: **panic disorder; cholecystokinin; CCK-A receptor; gene; polymorphism**

Panic disorder (PD) is a common anxiety condition, characterized by unprovoked anxiety attacks distinguished by such symptoms as palpitations, chest pain, dyspnea, choking, tremors, faintness, and sweating, in addition to fear of dying, losing control, or going crazy [American Psychiatric Association, 1987]. The carboxy-terminal tetrapeptide of cholecystokinin (CCK-4) induces panic-like attacks when administered as an intravenous bolus in healthy volunteers, and in patients with PD [De Montigny, 1989; Bradwejn et al., 1991].

CCK is a classical gastrointestinal hormone and one of the most abundant neurotransmitter peptides in the brain. CCK receptor (R)s have been classified into two subtypes, CCK-A and CCK-B, on the basis of their affinities for a structurally and functionally related family of peptides that have identical COOH-terminal pentapeptide sequences but differences in sulfation at the sixth (gastrin) and seventh (CCK) tyrosyl residues [Wank, 1995]. Among recent investigations [Wang et al., 1998; Kennedy et al., 1999; Hamilton et al., 2001; Hattori et al., 2001a,b; Yamada et al., 2001] examined polymorphisms of the CCK and CCK-BR genes, but the results were inconclusive. There has been only one study to determine the CCK-AR gene polymorphism with no association [Kennedy et al., 1999], which was 5′ area of the 3′ untranslated region, and its functional role is unknown.

We recently cloned the genomic structures of human CCK-AR [Funakoshi et al., 2000], and determined the transcriptional start site of the human CCK-AR gene. Two sequence changes were detected in the promoter region: a G to T change in nucleotide −128 and an A to G change in nucleotide −81 [GenBank database under accession number D85606, Funakoshi et al., 2000]. Six genotypes, including a wild type (−81A/A, −128G/G) and five other variants, have been identified [Funakoshi et al., 2000; Shimokata et al., 2000]. The homozygote (−81G/G, −128T/T) showed a significantly higher percent body fat, although the real mechanism has not been clarified. In this study, we investigated a possible association between the CCK-AR gene and PD by evaluating the distribution of not only the genotypes but also the haplotypes of the two polymorphisms.

The subjects consisted of 109 Japanese patients with PD (64 males, 18–63 years old; 45 females, 21–71 years old), all of whom met DSM-III-R criteria for PD on the PD part of the Structured Clinical Interview for DSM-III-R (SCID) assessment. The age- and gender-matched control group consisted of 400 unrelated Japanese. The controls were employees and students in Kurihama National Hospital and in the Tokyo Metropolitan Institute of Gerontology. Nobody shows signs of

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psychiatric disorders (234 males, 20–62 years old; 166 females, 21–71 years old). The Ethics Committees of the National Alcoholism Center, Kurihama Hospital, and Tokyo Metropolitan Institute of Gerontology approved this study. Written informed consent was obtained from each subject. Genomic DNA was extracted from peripheral leucocytes.

Examination of the polymorphism in the promoter region of the CCK-AR gene was accomplished using a mismatch PCR-RFLP method [Funakoshi et al., 2000]. Briefly, a pair of primers (sense primer = 5′-GCATATGTACACATGTGTGT-AAAAAGCAGCCAGAC-3′, and anti-sense primer = 5′-GCC-CTTTCCTGGGCCAGACT-3′) were used to amplify the 103-bp product, which was subsequently digested with restriction enzyme *Hinf* I and fractionated by 12% polyacrylamide gel electrophoresis.

Statistical differences between PD and control subjects were assessed using Fisher's exact test. An odds ratio with 95% confidence intervals was calculated to evaluate the difference in genotype frequencies between the groups. Probability differences of $P < 0.05$ were considered statistically significant. To assess linkage disequilibrium between the two polymorphisms of the CCK-AR gene, we calculated the D value and its significance, using the ASSOCIAT program downloaded from the web site of Dr. J. Ott (ftp://linkage.rockefeller.edu/software/utilities/). All statistical computations were carried out using the Statistical Analysis System package, version 6.12 [SAS Institute Inc, 1988].

Comparison of the genotype and haplotype distributions of the CCK-AR gene −81A to G and −128G to T polymorphism in PD patients and control subjects (Table I) revealed frequencies among the controls that were quite similar to those reported in community-dwelling individuals. Three kinds of genotypes (−81A/A, −128T/T), (−81A/A, −128G/T), and (−81A/G, −128T/T) were not detected in the previous cohort studies [Funakoshi et al., 2000; Shimokata et al., 2000] and in the present study. Therefore, haplotype −81A/−128T was not present, either. These polymorphisms were in linkage disequilibrium (PD samples, D = 0.1495, $P < 0.0001$: controls, D = 0.0865, $P < 0.0001$). Both genotypic frequencies of distributions were in Hardy–Weinberg equilibrium.

TABLE I. Genotype and Haplotype Frequencies of the −81A to G and −128G to T Polymorphisms in Patients With Panic Disorder and Controls

	Polymorphisms		Panic disorder N (%)	Controls N (%)
	−81	−128		
Genotype[a]			N = 109	N = 400
	A/A	G/G	48 (44.0%)	238 (59.5%)
	A/G	G/G	13 (11.9%)	71 (17.8%)
	A/G	G/T	36 (33.0%)	75 (18.8%)
	G/G	G/G	1 (0.9%)	6 (1.5%)
	G/G	G/T	9 (8.3%)	6 (1.5%)
	G/G	T/T	2 (1.8%)	4 (1.0%)
OR (95% CI)[b]			2.81 (1.74–4.39)	
Haplotype[c]			N = 218	N = 800
	A	G	145 (66.5%)	622 (77.8%)
	A	T	0 (0.0%)	0 (0.0%)
	G	G	24 (11.0%)	89 (11.1%)
	G	T	49 (22.5%)	89 (11.1%)

[a]Percentages may not total 100 due to rounding. Three genotypes (−81A/A, −128T/T), (−81A/A, −128G/T), and (−81A/G, −128T/T) were not present. $P < 0.0001$ (df = 5), $P < 0.0001$ (with −81G/−128T haplotype vs. without −81G/−128T haplotype, df = 1) when analyzed by Fisher's direct test.

[b]Ratio of odds (genotypes with −81G/−128T haplotype/genotypes without −81G/−128T haplotype) and 95% confidence interval.

[c]Haplotype (−81A/−128T) was not detected. $P < 0.0001$ when analyzed excluding −81A/−128T haplotype (df = 2), $P < 0.0001$ when compared between subjects with and without −81G/−128T haplotype (df = 1).

The frequency of variant genotypes (−81A/G,−128G/T; G/G, G/T, and G/G, T/T) having variant haplotype (−81G/−128T) was significantly higher in PD than in controls ($P < 0.0001$, OR = 2.81, 95% CI = 1.74–4.39). The statistical differences between the haplotype distributions in the PD and control groups were highly significant: The frequency of variant haplotype (−81G/−128T) was higher in the former group than in the latter ($P < 0.0001$; Table I).

Stratification of the PD samples and controls with respect to age and gender did not alter these relationships. Nor did the age at onset of PD affect the distributions of the CCK-AR gene polymorphisms (data not shown).

The frequencies of both the variant genotypes and haplotypes of the −81A to G and −128G to T polymorphisms of the CCK-AR gene were higher in our PD group than among our control subjects, suggesting that this gene is involved in the development of PD.

CCK-AR is expressed in specific brain regions such as the amygdala, nucleus tractus solitarius, posterior nucleus accumbens, ventral tegmental area, hypothalamus, substantia nigra, hippocampus, area postrema, and raphe nucleus, whereas CCK-BR is widely distributed throughout the central nervous system [Wank, 1995]. The expression patterns of these receptors overlap in the brain, and the cross-reactivity of each antagonist could not be excluded in pharmacological studies. Therefore, the functional differences of these two receptors remain unclear. Recently, we developed CCK-AR, BR, and ARBR gene knockout (−/−) mice and found that CCK-AR and BR may exert opposite influences on anxiety-related behaviors [Miyasaka et al., 2002a]. These evidences suggest that CCK-AR might be involved in induction of panic like attacks, although CCK-4 is a ligand of CCK-BR.

Our research has focused on two neighboring polymorphisms in the 5′ regulatory region of the CCK-AR gene, which shares the region involved in the regulation of the human CCK-AR promoter function [Takata et al., 2002]. We have examined CCK-AR gene polymorphisms in 50 patients with gallstone and 300 patients with diabetes mellitus before the establishment of RFLP method [Funakoshi et al., 2000]. We found one case with G to A in the intron 1, and another case C to G in the exon 3 without change in amino acid (Thr). The polymorphisms of promoter region (between −351 and +176) were also examined and no polymorphisms besides −81A to G and −128G to T were detected. Therefore, although various kinds of CCK-AR polymorphisms have been reported [Inoue et al., 1997; Tachikawa et al., 2001; Okubo et al., 2002], these may occur sporadically.

Although our recent investigation using the STC-1 murine neuroendocrine cell line showed that neither the −81A to G nor the −128G to T polymorphism affects luciferase activities [Takata et al., 2002], limitations in the experimental conditions suggest that those findings should be interpreted as inconclusive, because no human cell lines have been available. In a recent examination of the correlation of demethylation of the CCK-AR gene and its expression, we found significantly higher gene expression when the methylation level of the gene was low [Matsusue et al., 1999; Miyasaka et al., 2002b]. We observed many GC-rich segments in the CCK-AR promoter region, and the nucleotide position at −128 was methylated. Thus, a G to T replacement at the −128 position might be capable of altering CCK-AR gene expression.

In this study, the first to report the positive association of the CCK-AR polymorphisms and PD, haplotype analyses further strengthened the association based on our comparison of genotype distributions.

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PAPER

Differences in the relationship between lipid CHD risk factors and body composition in Caucasians and Japanese

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OBJECTIVES: To examine differences in the relationship between fat distribution and lipid coronary risk factors in Caucasian and Japanese population and further to determine whether the cut-points for body mass index (BMI) and waist circumference (WC) proposed by WHO and NHLBI are applicable to Japanese population as a predictor of a lipid risk factor abnormality or not.
RESEARCH METHODS AND PROCEDURES: Subjects were 895 participants of the Baltimore Longitudinal Study of Aging in the US (BLSA) and 1705 participants of the Longitudinal Study of Aging by the National Institutes for Longevity Science in Japan (NILS-LSA). Subjects were divided into four demographic groups as younger (age <65 y) men and women, and older (age ≥ 65 y) men and women. Blood total cholesterol, triglycerides, LDL- and HDL-cholesterol and anthropometry were measured. Regression coefficients of BMI and WC on risk factors, sensitivity and specificity of the BMI and WC cut-points for blood lipid abnormality, and mean values of blood lipids at BMI or WC cut-points were computed in both populations.
RESULTS: Height, weight, WC and BMI were significantly greater in the BLSA than those in the NILS-LSA subjects. Total cholesterol, HDL- and LDL-cholesterol were significantly greater in the NILS-LSA than in the BLSA subjects. Sensitivities of BMI and WC cut-points were much lower in the NILS-LSA than in the BLSA subjects. Specificities of BMI and WC cut-points were higher in the NILS-LSA than in the BLSA subjects. Mean values of triglycerides, total cholesterol, HDL- and LDL-cholesterol at BMI $=25$ were significantly greater in the NILS-LSA than in the BLSA subjects. At the WC cut-point (94 cm for men, 80 cm for women), mean values of all lipids were significantly greater in the NILS-LSA than in the BLSA subjects with the exception of triglycerides in younger women.
CONCLUSIONS: The Japanese subjects have smaller BMI and WC, worse total and LDL-cholesterol levels and better HDL-cholesterol levels compared to Caucasians. Sensitivities of BMI and WC for predicting lipid risk factor abnormality are much lower in Japanese. The cut-points for BMI and WC proposed by WHO and NHLBI may be too high for predicting an abnormality in triglycerides, total and LDL-cholesterol in Japanese. For detecting an abnormal HDL-cholesterol level, the BMI and WC cut-points may not be as beneficial for the Japanese population as for Caucasians.
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Keywords: racial difference; BMI; waist circumference; lipids; coronary risk factor

Introduction

The prediction and prevention of coronary heart disease (CHD) are of great importance, especially in industrial countries. The National Cholesterol Education Program (NCEP)[1] recommended that a fasting lipoprotein profile (total cholesterol, LDL-cholesterol, HDL-cholesterol and triglyceride) should be obtained once every 5 y in all adults aged 20 y or older. LDL-cholesterol was defined as the primary target of cholesterol-lowering therapy. Therefore, detecting an abnormality in blood lipids and initiating early treatment is essential to decrease the incidence of CHD.

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It has been established that obesity, especially central distribution of body fat, is associated with many chronic diseases.[2–6] Although imaging techniques such as magnetic resonance imaging (MRI) and computerized tomography (CT) have been the 'gold standard' methods for quantification of visceral fat, these methods are inconvenient and costly for routine clinical use. Therefore, several surrogates of intra-abdominal fat measurement have been examined.[7–9] The body mass index (BMI) has long been used as a convenient, useful index of overweight and obesity. Studies have shown that waist circumference (WC) could be used to predict risk factor abnormalities as a surrogate of body fat distribution.[9–11] Han *et al*[12] indicated the linear relationship between WC and intra-abdominal fat. The World Health Organization (WHO)[6] and the National Heart, Lung, and Blood Institute (NHLBI)[5] issued comprehensive recommendations for classifying abnormalities in body weight and body fat distribution. Both reports recommended the BMI and the WC as measures of obesity and fat distribution, and concluded that risk of disease increases at a BMI of 25 kg/m^2 in both men and women; the WHO report noted increased risk at a WC of 94 cm for men and 80 cm for women.

It has been well known that obesity and fat distribution are influenced by complex factors including social, behavioral, cultural, physiological, metabolic and genetic factors. Differences in the relationships among BMI, WC and waist–hip ratio (WHR) in 19 populations, including Beijing Chinese, were reported by Molarius *et al*.[13] They concluded that the optimal screening cutoff point of WC and BMI may be population specific. Also, Hu *et al*[14] showed that a rural Chinese population in developing countries has a different relationship between BMI and CHD from Western populations. However, NHLBI and WHO reports did not propose population-specific cut-points for either BMI or WC. Although it was shown that the cut-points proposed by WHO and NHLBI for BMI and WC were useful predictors for coronary risk factors in Caucasian younger and older men and women in our previous studies,[15,16] it is still not clear whether or not these cut-points are applicable to relatively short stature and lighter weight populations in an industrial country such as Japan.

The purposes of the present study are (1) to examine the relationship between plasma lipid coronary risk factors and indices of body composition (BMI and WC) in Caucasian and Japanese populations; (2) to test whether recently proposed cut-points of BMI and WC can be applied to the younger and older Japanese population as well as to Caucasians.

Methods

Subjects

The subjects of this study consisted of 566 men and 329 women who participated in the Baltimore Longitudinal Study of Aging (BLSA) in USA, and 868 men and 837 women who participated in the National Longevity Sciences-Longitudinal Study of Aging (NILS-LSA) in Japan. Subjects of both

Table 1 Characteristics of BLSA and NILS subjects

	Younger (40–64 y)				*Older (65–80 y)*			
	BLSA		*NILS*		*BLSA*		*NILS*	
	N	*Mean*	N	*Mean*	N	*Mean*	N	*Mean*
Men								
Height (cm)	318	178.6	598	166.8**	248	174.3	270	160.9**
Weight (kg)	318	84.7	598	64.0**	248	77.1	270	57.5**
BMI (kg/m^2)	318	26.5	598	23.0**	248	25.3	270	22.2**
WC (cm)	318	93.8	598	81.9**	248	92.8	270	80.6**
Total cholesterol (mg/dl)	316	191.7	594	212.8**	248	188.4	268	211.1**
Triglycerides (mg/dl)	316	135.8	587	133.5	248	115.0	259	122.0
HDL-cholesterol (mg/dl)	316	41.1	596	57.9**	248	44.0	269	57.3**
LDL-cholesterol (mg/dl)	316	123.3	582	128.6*	248	121.3	257	130.5**
Women								
Height (cm)	183	163.6	620	153.7**	146	159.4	217	147.3**
Weight (kg)	183	65.9	620	53.4**	146	64.2	217	49.4**
BMI (kg/m^2)	183	24.6	620	22.6**	146	25.2	217	22.6**
WC (cm)	183	76.3	620	73.4**	146	79.9	217	75.6**
Total cholesterol (mg/dl)	180	188.5	615	221.9**	145	204.0	216	234.6**
Triglycerides (mg/dl)	180	98.6	596	98.0	145	112.8	211	118.8
HDL-cholesterol (mg/dl)	180	52.9	616	67.9**	145	55.4	217	64.4**
LDL-cholesterol (mg/dl)	179	115.8	595	135.1**	145	126.0	210	147.3**

**$P<0.01$, significant difference in mean values between BLSA and NILS-LSA subjects. *$P<0.05$, significant difference in mean values between BLSA and NILS-LSA subjects.

Table 2 Regression coefficient and trend analysis for BMI and WC

	Men				Women			
	Younger		Older		Younger		Older	
	BLSA	NILS	BLSA	NILS	BLSA	NILS	BLSA	NILS
(a) BMI								
Total cholesterol	1.33	1.39	−0.44	0.36	1.98	0.68	0.01	0.07
Triglycerides	7.14	8.74	8.05	4.47	4.04	5.25	3.13	4.47
HDL-cholesterol	−0.61	−1.75**	−1.33	−1.49	−0.40	−1.65**	−1.02	−1.72
LDL-cholesterol	0.51	1.39	−0.75	0.93	1.58	1.21	0.40	1.09
(b) WC								
Total cholesterol	0.43	0.42	−0.03	0.28	1.30	0.49*	−0.01	0.24
Triglycerides	2.71	3.65	2.44	1.77	2.53	2.40	1.46	2.08
HDL-cholesterol	−0.24	−0.74**	−0.45	−0.49	−0.30	−0.72**	−0.42	−0.74*
LDL-cholesterol	0.08	0.42	−0.16	0.39*	1.10	0.69	0.12	0.56

**$P<0.01$, significant difference in the coefficient between BLSA and NILS-LSA subjects. *$P<0.05$, significant difference in the coefficient between BLSA and NILS-LSA subjects.

cohorts were aged between 40 and 80 y old. The populations were dichotomized at age 65 y into younger and older age groups for each sex. The BLSA subjects were Caucasian and the NILS-LSA subjects were Japanese. Details of the selection process and procedures of the baseline examination in the BLSA and the NILS-LSA have been published previously.[17,18] The subjects in the NILS-LSA were randomly selected from resident registrations in cooperation with the local government. The subjects in the BLSA were self-recruited, community-dwelling volunteers. Table 1 shows some descriptive statistics of the population.

Subjects who were being treated for hyperlipidemia that could influence the level of the risk factors were excluded. Measurements from women who were pregnant at the visit or who had had a baby less than 1 y prior to the visit were also excluded from these analyses.

Anthropometry

Height and weight were measured after an overnight fast with subjects wearing a light-weight hospital gown and without shoes. As an index of obesity, BMI was calculated as weight (kg) divided by the square of the height (m).

WC was used as the index of the body fat distribution. The waist was defined as the minimal abdominal circumference between the lower edge of the rib cage and the iliac crests in the BLSA, and as the circumference at the middle point between the lower edge of the rib cage and the iliac crests in the NILS-LSA. The circumferences were obtained with a flexible, metal tape measure, while maintaining close contact with skin and without compressing the underlying tissues. Subjects were in a standing position and breathing normally. The same small group of trained personnel made these measurements for the entire study in both the BLSA and the NILS-LSA.

Plasma lipids

After an overnight fast, an antecubital venous blood sample was drawn. The concentrations of plasma triglycerides and total cholesterol were determined by enzymatic method (Abbott Laboratories ABA-200 ATC Biochromatic Analyzer, Irving, TX 75015 for BLSA; Hitachi 7145 Automatic Analyzer, Hitachi Co., Ltd Japan for NILS-LSA). HDL-cholesterol was determined by dextran sulfate-magnesium precipitation procedure[19] in the BLSA and enzymatic methods in NILS-LSA (Hitachi 7145 Automatic Analyzer, Hitachi Co., Ltd Japan). LDL-cholesterol concentrations were estimated by the Friedewald formula[20] in both BLSA and NILS-LSA.

Cut-points for abnormalities of BMI, WC and risk factors

Cut-points for BMI and WC abnormalities were determined according to NHLBI[5] and WHO[6] guidelines. The BMI and WC categories were dichotomized at the lower recommended cut-points due to the small number of subjects in the obese and high WC groups. In addition, the designation of the risk factor cut-points that define an abnormal level was derived from the 1994 recommendations of the National Cholesterol Education Program.[21]

BMI	25 kg/m^2
WC	80 cm for women, 94 cm for men
Total cholesterol	240 mg/dl
Triglyceride	200 mg/dl
HDL-cholesterol	35 mg/dl
LDL-cholesterol	160 mg/dl

Sensitivity and specificity of WC and BMI cut-points for risk factor abnormality

To examine the applicability of cut-points for WC and BMI proposed by WHO and NHLBI, the sensitivities and specificities of WC or BMI cut-points were calculated in the BLSA

and NILS-LSA subjects. By using cut-points both for risk factors and for BMI (or WC), subjects were divided into four groups as shown.

	Normal	Abnormal
Normal BMI (or WC)	A	B
Abnormal BMI (or WC)	C	D

Sensitivity is defined as D over the sum of B and D, and specificity is defined as A over the sum of A and C according to the general definition of these terms.[13]

Statistical methods

All data were analyzed using Statistical Analysis System (SAS) version 6. Standard methods were used to compute means and standard errors of the mean. *P*-values below 0.05 were regarded as indicating statistical significance. ANOVA was used to test for the presence of statistically significant differences in BMI, WC and risk factors between the BLSA and the NILS subjects. A test of whether or not the regression coefficients (slopes) of BMI (or WC) and the risk factors are consistent between the two populations was performed using general linear models. χ^2 analysis was performed for analyzing effects of population in the percentage of subjects with abnormal levels of BMI, WC and risk factors. Adjusted mean lipid values were computed using ANCOVA by setting the covariates (BMI or WC) to the appropriate cut-point value.

Results

Differences in BMI, WC and risk factors between the BLSA and NILS-LSA subjects

Height, weight, WC and BMI were significantly higher in the BLSA than those in the NILS-LSA subjects, regardless of the sex/age group (Table 1). The subjects in the NILS-LSA had significantly greater total and LDL-cholesterol in younger and older men and women. HDL-cholesterol was significantly greater in the NILS-LSA than that in the BLSA subjects for all demographic groups (younger and older men and women). There was no significant difference in triglycerides between BLSA and NILS-LSA.

Associations between BMI, WC and risk factors

The only lipid/anthropometric association that was consistently different between the two populations was that of HDL-cholesterol with both BMI and WC. In all cases, the regressions were negative, but the impact of the body composition variables was greater in the NILS population; in five of the eight regressions, these differences were statistically significant. These population differences were especially striking in the younger men and women.

There was also a consistent very large effect of both BMI and WC on the triglyceride levels, but there were no significant differences in the slope between the two populations. The only other statistically significant slope differences were WC–total cholesterol in the younger women and WC–LDL-cholesterol in the older men, but these population differences were inconsistent in the other three demographic (age/sex) groups (Table 2).

Table 3 Percentage of subjects with an abnormal level in BMI, WC and lipid risk factors

	Men				*Women*			
	Younger		*Older*		*Younger*		*Older*	
	BLSA	*NILS*	*BLSA*	*NILS*	*BLSA*	*NILS*	*BLSA*	*NILS*
BMI	63.9	23.2**	48.8	17.9**	35.6	17.6**	44.1	21.8**
WC	49.4	5.2**	45.2	7.8**	31.7	19.0**	45.5	28.7**
Total cholesterol	8.2	20.5**	7.7	17.5**	12.2	30.9**	15.2	43.5**
Triglyceride	17.1	13.6	10.1	8.6	4.4	5.2	6.2	7.9
HDL-cholesterol	31.0	2.7**	23.4	2.2**	5.0	0.3**	6.2	0.0**
LDL-cholesterol	11.7	15.8*	10.1	11.2	11.7	20.8**	15.2	29.6**

**$P<0.01$, significant difference between BLSA and NILS by χ^2 analysis.
*$P<0.05$, significant difference between BLSA and NILS by χ^2 analysis.

Percentage of subjects with an abnormal risk factor status

Table 3 shows the percentages of subjects with an abnormal level of BMI, WC or risk factors for each age/sex group in the BLSA and NILS-LSA subjects. The percentage of subjects with an abnormal BMI as well as an abnormal WC was significantly greater in the BLSA than that in the NILS-LSA subjects in younger and older men and women. Consistent with these population differences, there was a significantly higher percentage of subjects with an abnormal HDL-cholesterol level in the BLSA than that in the NILS subjects in all age/sex groups. The percentage of subjects with an abnormal level of total and of LDL-cholesterol was significantly higher in NILS-LSA subjects than those in BLSA subjects with the exception of LDL-cholesterol in younger men. Abnormal triglyceride levels were similar in the two populations.

Sensitivity of BMI and WC

Table 4a shows the sensitivity of BMI cut-points proposed by WHO and NHLBI (BMI $<25\ kg/m^2$) for predicting risk factor abnormality. Sensitivities of BMI were very much lower in the NILS-LSA than in the BLSA. Also, sensitivities of WC (Table 4b) were lower in the NILS-LSA than those in the BLSA subjects.

Specificity of BMI and WC

Specificity of BMI and WC is shown in Table 5a and b. Higher specificities of BMI were found in younger and older men

Table 4 Sensitivity of BMI and WC cut-point for lipid risk factor abnormality

	Men				Women			
	Younger		Older		Younger		Older	
	BLSA	NILS	BLSA	NILS	BLSA	NILS	BLSA	NILS
(a) BMI								
Total cholesterol	69.2	27.1**	63.2	17.0**	45.5	17.7**	31.8	20.7
Triglycerides	88.9	37.4**	84.0	29.2**	62.5	50.0	77.8	23.5**
HDL-cholesterol	78.4	12.5**	70.7	16.7**	75.0	—	75.0	—
LDL-cholesterol	70.3	33.0**	44.0	20.0**	42.9	16.4**	40.9	21.9
Mean	76.7	27.5	65.5	20.7	56.5	28.0	56.4	22.0
(b) WC								
Total cholesterol	50.0	8.2**	47.4	10.6**	45.5	24.1*	36.4	26.1
Triglycerides	75.9	14.5**	72.0	20.8**	62.5	59.4	66.7	41.2
HDL-cholesterol	65.0	6.3**	67.2	16.7**	75.0	50.0	75.0	—
LDL-cholesterol	46.0	9.6**	40.0	10.0**	42.9	23.4 (0.06)	40.9	31.6
Mean	59.2	9.6	56.7	14.5	56.5	39.2	54.7	33.0

**$P<0.01$, significant difference in sensitivity between BLSA and NILS-LSA subjects. *$P<0.05$, significant difference in sensitivity between BLSA and NILS-LSA subjects. —: there was no NIL-LSA subject in some categories that were used for calculation of sensitivity.

Table 5 Specificity of BMI and WC cut-point for lipid risk factor abnormality

	Men				Women			
	Younger		Older		Younger		Older	
	BLSA	NILS	BLSA	NILS	BLSA	NILS	BLSA	NILS
(a) BMI								
Total cholesterol	36.6	77.8**	52.4	81.9**	65.8	82.4**	53.7	76.3**
Triglycerides	41.2	79.2**	55.2	83.4**	65.7	84.2**	58.1	77.7**
HDL-cholesterol	42.5	76.6**	57.9	82.1**	66.3	82.3**	57.3	77.6**
LDL-cholesterol	36.9	78.7**	50.7	82.4**	65.4	82.0**	55.3	77.4**
Mean	39.3	78.1	54.0	82.5	65.8	82.7	56.1	77.3
(b) WC								
Total cholesterol	50.7	95.6**	55.0	92.8**	70.3	82.8**	52.9	67.8*
Triglycerides	56.1	96.2**	57.9	93.2**	69.8	83.0**	55.9	71.5**
HDL-cholesterol	58.0	94.8**	61.6	92.4**	70.4	80.8**	55.8	70.5**
LDL-cholesterol	50.5	95.5**	54.3	92.1**	69.8	81.8**	53.7	71.2**
Mean	53.8	95.5	57.2	92.6	70.0	82.1	54.5	70.3

**$P<0.01$, significant difference in sensitivity between BLSA and NILS-LSA subjects. *$P<0.05$, significant difference in sensitivity between BLSA and NILS-LSA subjects.

and women in the NILS-LSA subjects compared to the BLSA subjects. Specificities of WC were also higher in the NILS-LSA subjects than those in the BLSA subjects, especially in men.

Mean values of risk factors at cut-points of BMI and WC

At the cut-point of BMI, mean values of triglycerides, total and LDL-cholesterol were significantly greater (worse) in the NILS-LSA than those in the BLSA subjects regardless of demographic groups (Table 6a). Mean values of HDL-cholesterol in the NILS-LSA subjects were significantly higher (better) than in the BLSA subjects.

At the cut-points of WC, mean values of triglycerides, total and LDL-cholesterol were significantly greater (worse) in the NILS-LSA than those in the BLSA subjects in all groups with the exception of triglycerides in younger women (Table 6b). The mean values of HDL-cholesterol in younger and older men and women were greater (better) in the NILS-LSA than in the BLSA subjects.

Discussion

Our previous reports on a Caucasian population[15,16] showed that BMI and WC independently were significant predictors of coronary risk factors in the blood pressure, glucose–

Table 6 Mean lipid values

	Men				Women			
	Younger		Older		Younger		Older	
	BLSA	NILS	BLSA	NILS	BLSA	NILS	BLSA	NILS
(a) BMI (25 kg/m²)								
Total cholesterol (mg/dl)	189.6	215.6**	188.5	212.1**	189.2	223.5**	204.0	234.8**
Triglyceride (mg/dl)	124.8	151.3**	112.4	134.7**	100.0	110.4*	112.1	129.1*
HDL-cholesterol (mg/dl)	42.0	54.3**	44.4	53.2**	52.7	63.9**	55.6	60.4**
LDL-cholesterol (mg/dl)	122.5	131.4**	121.5	133.1**	116.4	138.0**	125.9	149.9**
(b) WC (94 cm for men, 80 cm for women)								
Total cholesterol (mg/dl)	191.8	217.9**	188.3	214.9**	193.3	225.1**	204.0	235.7**
Triglyceride (mg/dl)	136.4	177.8**	117.9	145.7**	108.0	113.7	112.9	127.7*
HDL-cholesterol (mg/dl)	41.0	49.0**	43.4	50.8**	51.8	63.1**	55.4	61.2**
LDL-cholesterol (mg/dl)	123.3	133.7**	121.2	135.7**	119.9	139.6**	126.0	149.7**

**$P<0.01$, significant difference between the BLSA and NILS-LSA subjects. *$P<0.05$, significant difference between the BLSA and NILS-LSA subjects.

insulin and plasma lipid domains. Furthermore, the gradation of BMI into normal, overweight and obese zones according to NHLBI[5] and WHO[6] recommendations was supported. Also, the sex-specific WHO cut-points for WC that provided three zones (NHLBI standards provided two zones) were also found to be applicable to the risk factors in the four age–sex categories in Caucasians. However, it was pointed out that the BMI and/or WC in Asian populations are much lower than those in Caucasians.[22] Therefore, the important questions that remain are whether BMI and/or WC associated with coronary risk factors in relatively short and light-weight Asian populations as well as in Caucasians, and whether the BMI and WC cut-points proposed by NHLBI and WHO are applicable to Asian populations as a predictor of risk factor abnormality.

In the present study, in order to examine these questions, the relationship between BMI, WC and lipid risk factors (regression) and the applicability (sensitivity, specificity) of the BMI and WC cut-points for these risk factors were compared between the BLSA (Caucasian) and the NILS-LSA subjects (Japanese).

Height, weight and BMI were lower in the NILS-LSA than in the BLSA subjects regardless of the age/sex groups. There was a methodological difference in the measurement of WC between BLSA and NILS-LSA (see the Methods section). Although the minimal circumferences between the lower edge of the rib cage and the iliac crests were measured as WC in the BLSA subjects, the circumference at the middle point between the lower edge of the rib cage and the iliac crests was measured in the NILS-LSA subjects. Therefore, the measured WC in the NILS-LSA subjects may not be minimal as was the BLSA measurement. Despite this, WC in the NILS-LSA is still much smaller than that in the BLSA. In addition, WC of the NILS-LSA subjects was as highly correlated to BMI and to lipids as WC of the BLSA subjects (data not shown). Therefore, we compared the data of WC between the BLSA and the NILS-LSA directly.

It is well known that greater BMI or WC results in higher lipid risk factor levels. However, Japanese subjects (NILS-LSA) had higher levels in total cholesterol and LDL-cholesterol with smaller weight, BMI and WC, compared to Caucasians (BLSA). This result may indicate that associations between BMI, WC and lipid levels in Japanese differ from those in Caucasians. In the present study, the relationship (slope of regression) between BMI, WC and total cholesterol, triglycerides and LDL-cholesterol was similar, with the exception of the relationship between WC and LDL-cholesterol in older men, and between WC and total cholesterol in younger women. However, relationships between BMI, WC and HDL-cholesterol in most demographic groups were different in the two populations. Although relationships between BMI, WC and risk factors (triglycerides, total and LDL-cholesterol) were similar in the two populations, the mean values of total and LDL-cholesterol, and the percentages of subjects with an abnormal level of total and LDL-cholesterol in the NILS-LSA were higher than the levels of these variables in the BLSA subjects. In addition, the mean values at the BMI and WC cut-points in triglycerides, total and LDL-cholesterol were also higher (worse) in the NILS-LSA than those in the BLSA subjects. The mean plasma lipids are different between Japanese and Caucasians, although Japanese and Caucasians have similar relationships between BMI, WC and triglycerides, total and LDL-cholesterol. Because Japanese have higher levels of plasma lipids (excepting HDL-cholesterol) with a smaller BMI and WC, a normal BMI and WC defined by WHO and NHLBI does not indicate a lower risk in triglycerides, total and LDL-cholesterol in the Japanese population. The BMI and WC cutoff points seem to be too high as a predictor of risk abnormality to detect an abnormality in triglycerides, total and LDL-cholesterol for the Japanese population. Present data of very low sensitivities of the BMI and WC cut-points in the NILS-LSA support these results. For example, 83% of older men in the NILS-LSA who had an abnormal total cholesterol level had a normal

BMI, and 89.4% older men in the NILS-LSA with an abnormal total cholesterol had a normal WC.

Thus, the cut-points for BMI and WC proposed by WHO and NHLBI may not be ideal or even useful predictors of risk abnormality in the Japanese population. If these cutoff points of abnormality for BMI and WC are defined at lower levels, they may become a useful index for the Japanese population because BMI and WC still correlate with lipid risk factors in the Japanese subjects (data not shown). Further examinations are needed for the selection of the specific cutoff points for BMI and WC in the Japanese population.

In the present study, different relationships between BMI, WC and HDL-cholesterol in the two populations were found in most demographic groups. Although the magnitudes of the decrease in HDL-cholesterol with the increases of BMI and WC were greater in the NILS-LSA than in the BLSA subjects, mean values of HDL-cholesterol at the BMI and WC cut-points were still greater (better) in the NILS-LSA subjects. In the present study, there was a difference in the lipid methodologies between the two populations (see the Methods section). However, accuracy of both methods has been certified by the Center for Disease Control and Prevention (CDC). In addition, mean HDL-cholesterol levels were very similar in the BLSA and NHANES III,[23] and also in NILS-LSA and the National Nutrition Survey (Japan).[24] Therefore, we do not believe that these significant differences in HDL-cholesterol between BLSA and NILS-LSA subjects were caused by the methodological difference in HDL-cholesterol measurement. Thus, we compared HDL-cholesterol levels between BLSA and NILS-LSA subjects directly. Our result shows that the Japanese population with a normal BMI or WC has a remarkably higher level of HDL-cholesterol. NCEP noted that a high HDL-cholesterol level appears to be protective against CHD, and a level of ≥ 60 mg/dl can even be called 'a negative risk factor'. The mean values of HDL-cholesterol at the BMI cut-point in the Japanese population were 54, 53, 64 and 60 mg/dl in younger men, older men, younger women and older women, respectively. And the mean values of HDL-cholesterol at the WC cut-point were 49, 51, 63 and 61 mg/dl in these groups. Mean HDL-cholesterol levels in Japanese women were close to being 'a negative risk factor', even if their BMI levels exceeded 25 kg/m^2 or their WC levels exceeded 80 cm.

From our results, it may seem that the BMI and WC cut-points proposed by WHO and NHLBI are at levels too low for detecting HDL-cholesterol abnormality in the NILS-LSA subjects. However, it should be taken into account that most Japanese have relatively small BMI and WC (percentage of subjects with an abnormal BMI and WC in the four age/sex groups are only 5–29). If cut-points of BMI and WC are set at higher levels, almost no Japanese will have an 'abnormal' WC or BMI. In this Japanese population, lowering the cut-points for BMI or WC will provide very low specificity and rising the cut-points will yield very low sensitivity. The only other solution would be to redefine the level of HDL-cholesterol abnormality for the Japanese population.

Accumulation of intra-abdominal fat has been shown to be associated with risk factor abnormalities.[3,25,26] Although we did not quantify intra-abdominal fat using CT scans in the present study, the distribution of intra-abdominal fat might well be different in the two populations. This may underlie the fact that the BMI and WC cut-points do not have the same level of applicability for predicting risk abnormality in Caucasian and Japanese populations. Therefore, further study is needed to better understand the relation between abdominal fat distribution (CT scan) and risk factor abnormality; it should however be noted that Takami *et al*[27] reported that BMI and WHR are better predictors of metabolic abnormalities than abdominal fat measured by CT.

Also, the reason for the differences in blood lipids between the Japanese and Caucasian populations was beyond the scope of the present study. Diet, exercise, body composition or genetics might be expected to contribute to these differences.[28–32]

In the present study, there was an interesting finding that correlations between BMI, WC and lipids (total and LDL-cholesterol) in older people were weak or not significant regardless of populations, although BMI and WC were still highly correlated with triglycerides and HDL-cholesterol in older people. We have previously reported the effects of age on the relationship between body composition and risk factors in Caucasians[15,16,33] and these effects are also seen in the Japanese population.

In conclusion, the Japanese subjects have higher total and LDL-cholesterol levels with smaller mean BMI and WC measurements compared to Caucasians. Although mean values in triglycerides, total and LDL-cholesterol at the recommended cut-points of BMI and WC (BMI = 25 kg/m^2, WC = 94 cm for men 80 cm for women) are obviously high (worse) in the Japanese, the mean HDL-cholesterol level at the cut-point is higher (ie, better) in Japanese. Thus, these cut-points for BMI and WC proposed by WHO and NHLBI may be too high for predicting an abnormality in triglycerides, total and LDL-cholesterol in Japanese. Predicting an abnormal HDL-cholesterol level using the cut-points for BMI and WC may not be as beneficial for the Japanese population as for Caucasians.

It must be noted that direct analyses of the predictive power of the cut-points for BMI and WC on the development of CHD itself in Japanese and Caucasian populations would be instructive, since the variables examined are risk factors for CHD in the present study. We must also note that direct examinations of the relationship among the characteristics in plasma lipids, nutrition intake, and morbidity and mortality of CHD in the Japanese and Caucasians are desirable in future studies.

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The Impact of Health Problems on Depression and Activities in Middle-Aged and Older Adults: Age and Social Interactions as Moderators

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In this study, we compared the impact of health problems (HPs) on everyday activities and depressive symptoms between middle-aged and older adults. We also examined what type and source of social interactions moderate the noxious effects of HPs. Longitudinal analyses of data with 1,802 Japanese community-dwelling adults indicated that HPs were significantly related to (a) an increase in depressive symptoms among middle-aged adults and (b) a decline in everyday activities among older adults. The former was buffered by emotional family support, whereas the latter (b) was buffered by instrumental family support and, surprisingly, by negative interactions with family. In contrast, social interactions with other friends and acquaintances did not show any moderating effect.

MANY researchers have reported the relationship between health problems (HPs), such as disease or injury, and lower activities among older adults (Dargent-Molina, Hays, & Breart, 1996; Guccione et al., 1994; Mor et al., 1989). Yet, as aging per se is a normal phenomenon that leads to a limitation of activities (Dickerson & Fisher, 1993), the pathologic effects of disease on disability are sometimes confused with the results of normal aging (Pearson, 2000). However, the decline of physical function that is due to normal aging is relatively small and should not interfere with the ability of older adults to live an autonomous and high-quality life (Ferrucci et al., 2002). In fact, a noticeable percentage of persons who reach extreme longevity are still able to perform activities of daily living (ADLs; Franceschi et al., 2000). Consequently, we could expect older adults to live primarily free of disability if they do not suffer from HPs.

This assumption does not mean that the role age plays in the disablement process is negligible. For instance, Pohjasvaara, Erkinjuntti, Vataja, and Kaste (1997) examined whether ischemic strokes have an equivalent negative impact on the daily activities of younger versus older patients. They found that ADL functions deteriorated more significantly among the older patients than the younger patients after the stroke. The results suggest that older adults are more likely than younger adults to decrease their activities because of HPs. However, although most prior studies have statistically controlled for age when estimating the impact of HPs, the question of how age and HPs interact and influence everyday activities has rarely been addressed.

Psychosocial stress theory also considers HPs to be influential life events leading to a decline in psychological well-being such as depression (Holms & Rahe, 1967; Murrel, Norris, & Hutchins, 1984). Although little is known about the role of age in the stress process (Folkman, Lazarus, Pimley, & Novacek, 1987; Martin, Gruendahl, & Martin, 2001), theoretical and empirical findings suggest that HPs exert less impact on well-being in older adults than in younger adults. For example, although HPs affect middle-aged adults' well-being by producing social role strain regarding work or parenting (Karasz & Ouellette, 1995), the number of such social roles decreases as people age (Aldwin, Sutton, Chiara, & Spiro, 1996). As Krause (1994) argued, stressors will be more strongly associated with well-being when they arise in important social roles. Thus, the fewer social roles of older adults may make dealing with HPs psychologically less challenging for them than it is for middle-aged adults. Indeed, Aldwin and colleagues (1996) found that older adults were not more likely to appraise HPs in terms of loss or threat, despite the fact that they were actually dealing with HPs.

Furthermore, according to the normative life events theory, events that are not expected for a particular period in life will have a greater impact on the well-being of individuals during that particular period than on individuals during other periods (Pearlin & Lieberman, 1979). Following the logic, the higher morbidity in older adults (Bowling & Grundy, 1997; Kriegsman, van Eijk, Penninx, Deeg, & Boeke, 1997) may attenuate the psychological impact of HPs on the age group, compared with younger groups. In fact, Hurwicz, Durham, Boyd-Davis, Gatz, and Bengtson (1992) found that, although over 30% of the older adults tended to report "ill health" as the event that had had the greatest impact on them, compared with 21% of the middle-aged and 16% of the younger adults, a significant association between the ill health and depressive symptoms was revealed only in the younger adults.

Taken as a whole, the primary purpose of the present study was to examine age differences in the impact of HPs on everyday activities and depressive symptoms among middle-aged and older adults. However, disability and depression are not merely dependent on a person's HPs but are also subject to psychosocial factors. This study also focused on one such factor, social interactions, and its role in the relationships between HPs and outcomes.

An extensive body of research has demonstrated that positive social interactions, such as social support, contribute to the improvement of a person's psychological and physical well-being (Cohen & Willis, 1985). However, there is a growing consensus that social support is a multidimensional concept, and the type and source of support should be considered when its effect is estimated. Some studies have found that social support from friends is more effective for psychological well-being than that from family (Dean, Kolody, & Wood, 1990; Lee & Ishii-Kuntz, 1987). Others assert that family support is more effective than support from friends (Chi & Chou, 2001; Yanagisawa et al., 2002). The findings from Felton and Berry (1992) are more complicated: Emotional support was more beneficial for psychological well-being when provided by nonkin, whereas instrumental support was more beneficial when provided by kin. Regarding physical health outcomes, some researchers have found support to be beneficial in improving physical function and activities (Duke, Leventhal, Brownlee, & Leventhal, 2002; Seeman et al., 1995), whereas Mendes de Leon, Gold, Glass, Kaplan, and George (2001) have indicated that instrumental support was associated with an *increase* of disability risk among older adults.

Although the previous findings are not altogether consistent, a careful review of the literature by Crohan and Antonucci (1989) revealed that, whereas friends tend to play their largest role in the arenas of socialization and the provision of day-to-day companionship, support provided by family becomes important when long-term sick care or daily living help is needed. This suggests that support from family would be more beneficial than support from other relationships, at least for people suffering from HPs.

The mixed findings on the effect of support by type may be partly derived from the analytical designs. Most previous studies have focused, on one hand, on the *direct* effect of social support: the effect of improving well-being regardless of whether stressors, such as HPs, are present or not. The *buffering* effect, on the other hand, posits that support is related to well-being for persons under stress, as it protects persons from the potentially pathologic influence of stress events (Cohen & Willis, 1985). Indeed, Penninx and associates (Kriegsman et al., 1997; Penninx et al., 1997, 1998) have reported that instrumental support buffered the incidence of mobility difficulties for older people with chronic lung disease, whereas emotional support buffered the increase of depressive symptoms for older people with cardiac disease and arthritis. As Cohen and Willis (1985) argued, these findings suggest that there must be a reasonable match between the type of available support and the consequences of HPs in order for buffering to occur.

The present study also investigated how negative interactions, that is, interference and criticism dimensions of social interactions, may moderate the relationship between HPs and outcomes. Although negative interactions are theoretically assumed to exacerbate the noxious association of stressors with well-being (Shinn, Lehman, & Wong, 1984), this negative buffering, or stress-amplification hypothesis (Okun, Melichar, & Hill, 1990), has not been well established. For example, Finch, Okun, Barrera, Zautra, and Reich (1989) failed to confirm the effects of negative interactions to aggravate the associations between HPs and psychological distress in older adults. However, because their study had a cross-sectional analytical design using a relatively small sample ($N = 246$) and lacked attention to disability outcome, the results still have opened the door for further examination of the moderating effect of negative interactions on HPs and their consequences.

Hypotheses and Analytic Strategy

On the basis of the aforementioned grounds, this study examined the moderating effects of age and social interactions in the impact of HPs on everyday activities and depressive symptoms, using longitudinal data collected from Japanese middle-aged and older adults. In Japan, as in other Western countries, the population is aging rapidly, and estimating the influence of HPs on older adults' lives has become an important issue (Health and Welfare Statistics Association, 2002). This study would contribute to the available data for developing a cross-cultural view on the experience of HPs in later life.

The analysis was twofold. First, we addressed the question of whether the impact of HPs differed between middle-aged and older adults. We expected that the impact of HPs in decreasing everyday activities would be greater in older adults, compared with middle-aged adults. In contrast, compared with older adults, middle-aged adults would be more likely to increase their depressive symptoms because of HPs. To test the hypotheses, we conducted repeated measures analyses with a mixed procedure (SAS Institute Inc., 1996) to examine pattern differences of changes in activities and depression scores according to age group and HP experience.

Second, we examined what type and source of social interactions would moderate the negative consequences of HPs. To avoid problems associated with multicollinearity, we examined in separate analyses whether the effect of HPs is moderated by the level (high vs. low) of three types of social interactions (emotional support, instrumental support, and negative interactions), provided by the two interaction sources of family and others (friends or acquaintances). We expected that social interactions with family would more effectively buffer the negative consequences of HPs than interactions with others. Furthermore, we expected that emotional support would buffer the increase of depressive symptoms, whereas instrumental support would buffer the decline of everyday activities caused by HPs. We also predicted that negative interactions would amplify the noxious effects of HPs on activities and depressive symptoms.

Methods

Participants

The data for this study are taken from the baseline (Wave 1, from November 1997 to April 2000) and the follow-up (Wave 2, from April 2000 to May 2002) surveys of the National Institute for Longevity Sciences–Longitudinal Study of Aging (NILS–LSA). The average follow-up interval was 2.1 years. The NILS–LSA participants were Japanese community-dwelling adults between 40 and 79 years of age, randomly recruited from areas around the institute. Details of the NILS–LSA have been described elsewhere (Shimokata, Ando, & Niino, 2000). The study sample consisted of 1,802 men and women who had completed examinations at both Wave 1 and Wave 2. The average age for the entire sample was 58.3 ± 10.6 years. For

the analyses in this article, we divided the sample into two groups according to their age at Wave 1 (older adults: 60–79 years old, $n = 833$; middle-aged adults: 40–59 years old, $n = 969$).

Measures

Health problems.—We identified HPs by using a life event checklist at Wave 2. The trained interviewer presented participants with the checklist of 43 items and asked them to report the occurrence of each event between Wave 1 and Wave 2 periods. Participants who reported the occurrence of "major injury or disease," one of the listed items, were classified into the HP-present (HPP) group, whereas all others were classified into the HP-absent (HPA) group. Although information about the type of HP was collected from the HPP participants, no type-specific analyses were conducted in the study.

Everyday activities.—We measured everyday activities both at Wave 1 and Wave 2 by using the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIG-IC; Koyano, Shibata, Nakazato, Haga, & Suyama, 1987). This scale includes 13 items conceptually grouped into three categories: instrumental ADLs (using transportation, shopping, preparing meals, paying bills, and making bank deposits and withdrawals), intellectual or cultural activities (filling out forms, reading papers, reading books and magazines, and watching television), and social engagement activities (visiting a friend's home, helping others, going to see someone in the hospital, and talking to others). Acceptable reliability ($\alpha = .86$) and validity (association with mortality) of the index have been reported (Koyano, Shibata, Nakazato, Haga, & Suyama, 1991). Participants indicate whether or not they can perform each activity with a "yes" (= 1) or a "no" (= 0), and then the responses are totaled and used as an index of everyday activities (a higher score indicates better performance). In the study, the internal reliability of the scale was .72.

Depressive symptoms.—We measured depressive symptoms at both Wave 1 and Wave 2 by using a Japanese version of the Center for Epidemiologic Studies Depression (CES-D) scale (Radloff, 1977; Shima, Shikano, Kitamura, & Asai, 1985). Participants indicated how often during the previous week they had experienced any of the 20 depressive symptoms described in the scale. Each item was rated on a 4-point scale ranging from 0 (rarely or none of the time) to 3 (most or all the time). Four positively worded items were reverse scored. The points were added together so that a higher score represented a higher level of depressive symptoms. For our sample, the internal reliability of the scale was .91.

Social interactions.—We measured social interactions at Wave 2, using a scale developed by Noguchi (1991). This scale comprises three subscales: emotional support, instrumental support, and negative interactions, each of which consists of four items. Participants indicated whether there was someone to provide specific interactions such as "listening to them when they have worries or problems" (emotional support), "caring for them when they are confined to bed for several weeks" (instrumental support), or "being critical of them" (negative interactions). We rated the responses on a 4-point scale, ranging from 1 (none) to 4 (many), with higher scores indicating more social interactions. Each item was duplicated to refer to the two interaction sources of family and others (friends or acquaintances). Summing up item scores by type and source, we generated six social interaction measures (emotional support from family, emotional support from others, instrumental support from family, instrumental support from others, negative interactions with family, and negative interactions with others). The internal reliability of the measures ranged from .71 to .86. For analyses, participants with scores 1 *SD* below the age-specific mean of emotional support from family were classified into the low-emotional family support group and others were classified into the high-emotional family support group. We conducted the same operations for the other social interaction measures. However, for negative interaction measures, participants with scores 1 *SD above* the mean were classified into the high-negative interactions group and others were classified into the low-negative interactions group.

Control variables.—We used gender and annual family income at Wave 1 as control variables because of their significant associations with the outcome variables (data not shown). We measured annual family income by using a scale with 11 options (from 1 = income less than ¥1,500,000 to 11 = income greater than ¥20,000,000). In addition, in the analyses we considered the following information regarding participants' health status at Wave 1. Subjective health was assessed by a single self-reported question ("How would you rate your health?"), with five options (from 1 = very bad to 5 = very good). The presence and history of seven diseases (stroke, hypertension, cardiovascular disease, diabetes, bronchitis, arthritis, and cancer) were totaled as an index of participants' existing chronic conditions.

Results

Sample Characteristics

Table 1 presents the results of bivariate tests of age differences in the study variables. Male participants represented just over half of the individuals in both age groups. The older group had a significantly lower income than the middle-aged group. The older group also felt less healthy and was in worse condition than the middle-aged group, although the differences were not very large. Those who reported experiencing HPs between the surveys made up 13.9% of the older group and 11.6% of the middle-aged group, which was not significantly different. Regarding the HP subtypes, participants who reported disease outstripped those who reported injury and those who reported both disease and injury or malfunctions from an unknown cause such as indefinite complaint (categorized as "other" in Table 1) in both age groups. The outcome variables did not differ between the age groups, except for the TMIG-IC score at Wave 2, which was slightly lower in the older group. Regarding social interactions, older adults reported fewer negative interactions with both family and others. Furthermore, older adults reported slightly less emotional and instrumental support from others than did middle-aged adults.

Table 1. Descriptive Information for Study Variables and Age Differences

Variable	Older	Middle-Aged
Gender, male (%)	53.4	51.0
Income (*M*)	5.1 (2.4)	7.3 (2.0)***
Subjective health (*M*)	3.1 (0.6)	3.3 (0.7)***
Chronic conditions (*M*)	0.8 (0.8)	0.3 (0.5)***
HPP (%)	13.9	11.6
Disease	7.7	5.6
Injury	5.0	4.6
Other	1.2	1.3
TMIG-IC (*M*)		
Wave 1	12.3 (1.1)	12.4 (1.0)
Wave 2	12.2 (1.2)	12.3 (1.1)*
CES-D (*M*)		
Wave 1	7.0 (6.7)	6.9 (6.2)
Wave 2	7.4 (6.7)	7.3 (6.7)
Social interactions, source–type (*M*)		
Family–emotional	12.5 (2.3)	12.4 (2.1)
Family–instrumental	12.1 (2.2)	12.0 (2.0)
Family–negative	8.6 (2.4)	9.6 (2.2)***
Other–emotional	11.2 (2.7)	11.6 (2.5)***
Other–instrumental	9.0 (2.8)	9.3 (2.7)*
Other–negative	7.0 (2.3)	8.3 (2.3)***

Notes: Entries in parentheses are standard deviations. HPP = health problem present; TMIG-IC = Tokyo Metropolitan Institute of Gerontology Index of Competence; CES-D = Center for Epidemiologic Studies Depression (scale).

*$p < .05$; ***$p < .001$.

Age and the Impact of HPs

We conducted repeated measures analyses to examine pattern differences of changes in the TMIG-IC and CES-D scores according to age (middle-aged vs. older) and HP (HPP vs. HPA) groups. The design was a split plot, involving the main effects of age, HP, and time (Wave 1 vs. Wave 2), and their two-way and three-way interaction terms. Gender, income, subjective health, chronic conditions, and the baseline outcome (TMIG-IC or CES-D) were used as covariates.

The analysis indicated that, among between-subject factors, gender (female), $F(1, 1741) = 10.88$, $p < .001$, subjective health, $F(1, 1741) = 9.45$, $p < .01$, and the baseline outcome, $F(1, 1741) = 5751.82$, $p < .001$, had significant positive associations with the TMIG-IC score. No significant main effects were found for age, HP, and Age × HP interaction. Regarding within-subject factors, time, $F(1, 1743) = 13.32$, $p < .001$, and Age × Time, $F(1, 1743) = 6.73$, $p < .01$, were revealed to be significant, suggesting participants decreased their activities during the surveys, regardless of age or HP effects, and the decline was more rapid in the older group. However, a significant three-way interaction among Age × HP × Time, $F(1, 1743) = 5.34$, $p < .05$, was also revealed, suggesting that the change in the TMIG-IC score depended on the participant's age and HP experience.

We performed the same analysis with the CES-D outcome. The results indicated that, among between-subject factors, chronic conditions, $F(1, 1737) = 8.02$, $p < .01$, and the baseline outcome, $F(1, 1737) = 5271.15$, $p < .001$, had significant positive associations with the CES-D score, whereas income, $F(1, 1737) = 4.23$, $p < .05$, and subjective health, $F(1, 1737) = 18.44$, $p < .001$, had significant inverse associations with the CES-D score. Furthermore, significant main effects with regard to age, $F(1, 1737) = 12.53$, $p < .001$, and HP, $F(1, 1737) = 3.93$, $p < .05$, emerged, suggesting that those in the middle-aged group and those in the HPP group had more depressive symptoms compared with those in the older group and those in the HPA group, respectively. However, these effects are qualified by a between-subject factor, Age × HP interaction, $F(1, 1737) = 6.18$, $p < .05$, and within-subject factors, time, $F(1, 1701) = 8.90$, $p < .01$, and Age × HP × Time, $F(1, 1701) = 4.39$, $p < .05$. These results suggest that changes in depressive symptoms relating to HPs were not equivalent between the age groups.

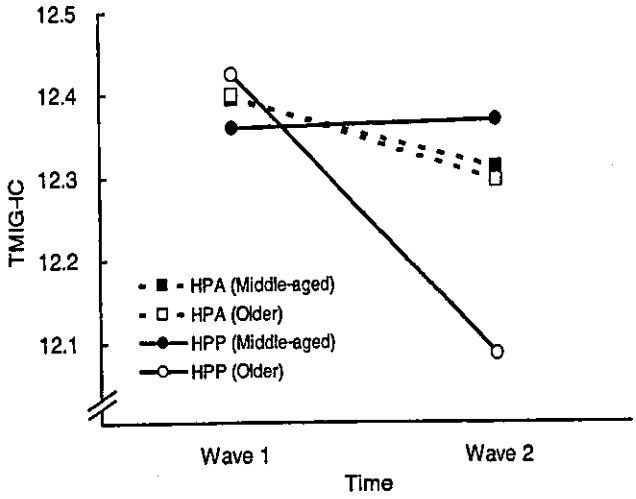

Figure 1. Changes in everyday activities (Tokyo Metropolitan Institute of Gerontology Index of Competence, or TMIG-IC) over time relating to age and health problem (HP) experience. HPA = HP absent; HPP = HP present.

Figure 1 and 2 illustrate the nature of the interactions by displaying the changes in the outcome scores over time by age and HP groups. We carried out further tests to examine simple main effects of time on each group by using the Tukey–Kramer adjusting method. After we controlled for gender, income, subjective health, chronic conditions, and the baseline outcome (TMIG-IC or CES-D), results revealed that the TMIG-IC score in older adults who had experienced HPs significantly decreased, $t(1743) = 3.64$, $p < .01$ (Figure 1), whereas the CES-D score in middle-aged adults who had experienced HPs significantly increased, $t(1701) = -3.14$, $p < .05$ (Figure 2), between the surveys. The HPA groups, in contrast, did not show any significant changes in their outcome scores, indicating stability of activities or mental health status over time irrespective of age group.

Moderating Effect of Social Interactions

Our second research goal was to determine the type and source of social interactions that moderate the noxious effects of HPs. On the basis of the results mentioned herein, we performed the analyses only on HPP participants. That is, for older adults with HPs, we carried out repeated measures analyses to determine whether the level (high vs. low) of each

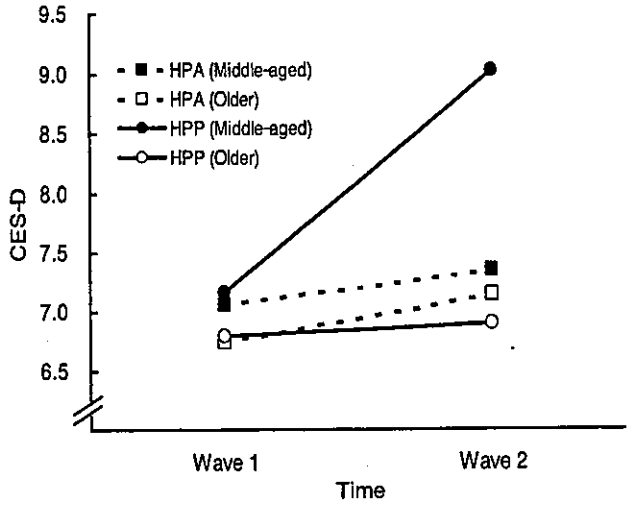

Figure 2. Changes in depressive symptoms (Center for Epidemiologic Studies Depression, or CES-D, scale) over time relating to age and health problem (HP) experience. HPA = HP absent; HPP = HP present.

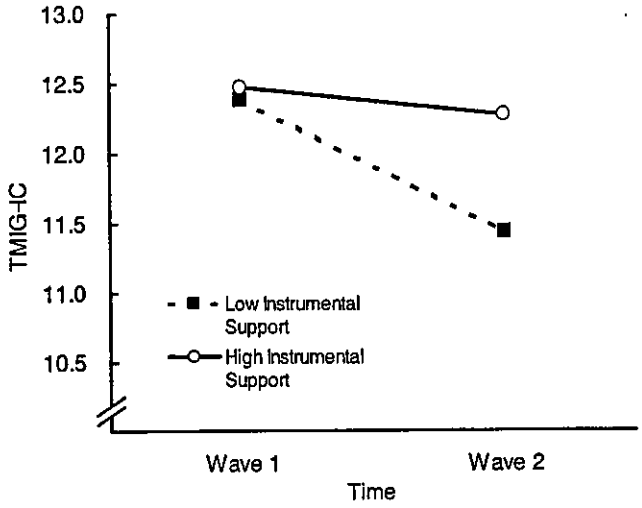

Figure 3. Changes in everyday activities (Tokyo Metropolitan Institute of Gerontology Index of Competence, or TMIG-IC) over time among older adults with health problems by the level of instrumental family support.

social interaction moderates (buffered or amplified) the change in TMIG-IC score over time. Similarly, for middle-aged adults with HPs, we examined whether the level of each social interaction moderates the change in CES-D score over time. The analyses tested the statistical significance of the main effect of each social interaction level and its interaction with time, controlling for gender, income, subjective health, chronic conditions, and the baseline outcome (TMIG-IC or CES-D).

The results were as follows. For older adults with HPs, significant main effects for levels of instrumental family support, $F(1, 104) = 11.09$, $p < .01$, emotional support from others, $F(1, 105) = 4.77$, $p < .05$, and negative interactions with family, $F(1, 104) = 4.45$, $p < .05$, emerged, with higher levels of these interactions increasing the TMIG-IC score. For middle-aged adults with HPs, significant main effects for levels of emotional family support, $F(1, 101) = 6.67$, $p < .05$, and instrumental family support, $F(1, 101) = 10.10$, $p < .01$, emerged, with higher levels of these interactions decreasing the CES-D score. No significant main effects were found for levels of other social interaction measures on both age groups, regardless of the outcome variable.

In addition to the main effects, three significant interactions emerged: Instrumental family support × Time, $F(1, 109) = 7.65$, $p < .01$, and Negative interactions with family × Time, $F(1, 109) = 5.55$, $p < .05$, in older adults, and Emotional family support × Time in middle-aged adults, $F(1, 104) = 3.97$, $p < .05$. The effects of these interactions are illustrated in Figures 3, 4, and 5. Among older adults with HPs, there was a significant decrease in the TMIG-IC score over time only when instrumental family support level was low, $t(109) = 3.89$, $p < .01$ (Figure 3). Surprisingly, there was also a significant decrease of the TMIG-IC score over time when the level of negative interactions with family was low, $t(109) = 3.95$, $p < .001$ (Figure 4). Among middle-aged adults with HPs, there was a significant increase of the CES-D score over time only when the emotional family support level was low, $t(104) = -2.72$, $p < .05$ (Figure 5).

Discussion

Age and the Impact of HPs

The three-way interaction of Age × HP × Time and the post hoc analyses indicated that the decline of everyday activities over time was statistically significant only for older adults who had experienced HPs between the surveys. The findings support our prediction that the impact of HPs in decreasing everyday activities would be greater in older adults, compared with middle-aged adults. As we noted earlier, aging per se is not so influential in limiting everyday activities of older adults (Dickerson & Fisher, 1993). However, although it is not inherently impaired, the reserve capacity to compensate for stress, metabolic derangement, and drug metabolism is increasingly limited with advancing age (Oskvig, 1999). Perhaps the age-related decline of reserve capacity in the human body allows HPs to have a greater impact on older adults, thus leading to limitations in the performance of everyday activities.

Another explanation for the difference is that the nature of HPs varies across age groups. Valderrama-Gama, Damian, Ruigomez, and Martin-Moreno (2002) argued that, whereas acute disease represents the main cause of HPs in young people, chronic conditions are more prevalent in older persons. Focusing on the type and, possibly, the severity of the HP would be the next step to developing and refining our findings.

In contrast, as we also expected, the increase of depressive symptoms over time was statistically significant only for middle-aged adults who had experienced HPs between the surveys. This is consistent with other studies (Aldwin et al., 1996; Hurwicz et al., 1992), including a Japanese one (Matsunaka, 2002), suggesting older adults are less emotionally reactive to HPs than younger adults. Thus, our results confirm the cross-cultural consistency in the psychological resilience of older adults with HPs. As we discussed earlier, because HPs threaten the salient social roles of middle-aged adults as parents or income earners (Karasz & Ouellette, 1995), they could become more critical for them and could lead to severe

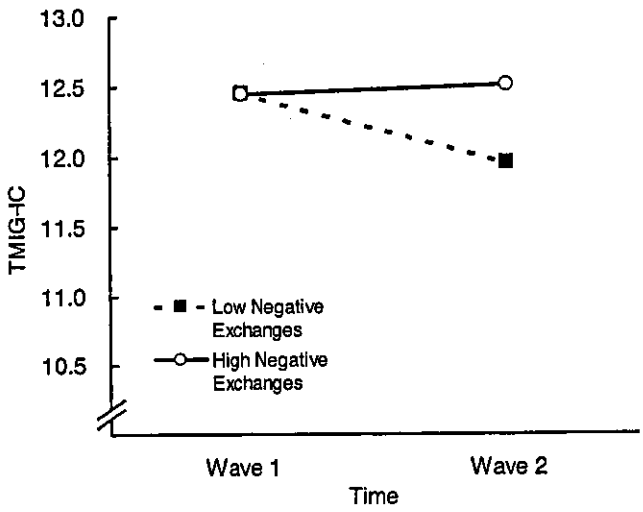

Figure 4. Changes in everyday activities (Tokyo Metropolitan Institute of Gerontology Index of Competence, or TMIG-IC) over time among older adults with health problems by the level of negative interactions with family.

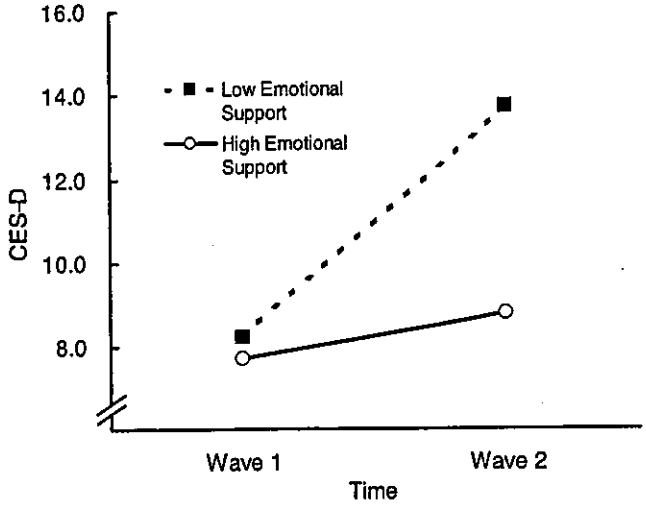

Figure 5. Changes in depressive symptoms (Center for Epidemiologic Studies Depression, or CES-D, scale) over time among middle-aged adults with health problems by the level of emotional family support.

psychological distress. In contrast, as disengagement theory (Cumming & Henry, 1961) implies, aging is a process whereby people gradually withdraw from society and are relieved of annoying obligations and social roles. The decreased demands from society may allow older adults to feel at ease and less stressed even when they are suffering from HPs.

Our findings would also be compatible with the normative life events theory, which posits that events that are expected for a particular period in the life span will have less impact on well-being (Pearlin & Lieberman, 1979). We found that the older group felt less healthy and was in worse condition even at the study entry, compared with the middle-aged group (see Table 1). As Norris and Murrell (1988) pointed out, the prior experience of a stressor provides "inoculation" against strong emotional reaction to a similar stressor experienced in later days. Thus, relatively worse health status at baseline in older adults might make provision against newly experienced HPs and attenuate the influence on psychological well-being.

Moderating Effect of Social Interactions

We found that instrumental family support buffered the decline of everyday activities in older adults, whereas emotional family support buffered the increase of depressive symptoms in middle-aged adults. In contrast, social support provided by other relationships (friends or acquaintances) did not show any buffering effect in either age group. One of the implications of the findings is that, as we expected, social support is more effective at preventing negative consequences of HPs when it comes from family rather than from other relationships. According to a hierarchical–compensatory model of social support (Cantor, 1979), people select supportive ties from a hierarchy of relationships, with family members always selected before nonfamily members. Additionally, as in other Asian countries such as China (Chi & Chou, 2001) and Korea (Mo, 1999), Japanese society maintains cultural values and traditional norms of caregiving in which the family provides care for its older members (Asahara, Momose, & Murashima, 2002). These values and norms may also strengthen the central roles of family as the support provider, especially for people suffering from HPs. However, because we aggregated friends and acquaintances into one support source category of "other relationships," the effects of key network nonkin members might be masked (Barrera, Chassin, & Rogosch, 1993). Distinguishing "other relationships" across levels of closeness would then be needed to further assess the beneficial effect of nonkin support.

Regarding the type of social support, the results also supported our predictions: Emotional support buffered the increase of depressive symptoms, whereas instrumental support buffered the decline of everyday activities. The results are in line with those of other cross-sectional findings (Kriegsman et al., 1997; Penninx et al., 1997, 1998) and the theoretical suggestion that posits that support closely linked to the specific need elicited by a stressor will exert the buffering effect (Cohen & Willis, 1985). For example, emotional support might reduce depressive symptoms caused by HPs because this type of support enhances the person's self-esteem, whereas instrumental support attenuates limitations of activities because it helps the person seek medical care for the HPs. However, contrary to our findings, Mendes de Leon and colleagues (2001) found that older adults with more instrumental support showed a decline of ADLs over time. They examined how baseline instrumental support predicts lower ADL functions at the follow-up, with no regard to the presence or absence of HPs in the study population, whereas we examined whether older adults with HPs maintain their activity level by instrumental support measured at the follow-up. The inconsistency between the studies would then be due to the differences in analytical designs.

An unexpected finding in the study is that negative interactions with family did not amplify but rather buffered the noxious effect of HPs on older adults' everyday activities. A possible explanation is that social network members may, by being critical and demanding of an older person, induce him or