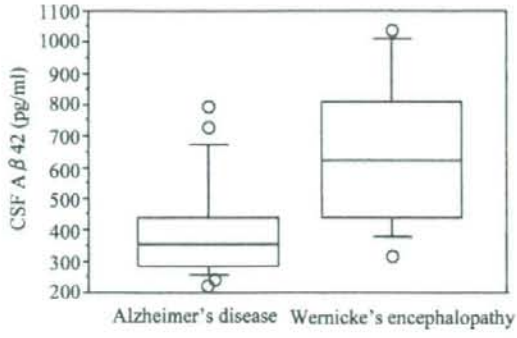

Fig. 4. CSF Aβ42 levels in acute Wernicke's encephalopathy and Alzheimer's disease. The horizontal lines within boxes indicate median values and the upper and lower hinges of the boxes indicate the 75th and 25th percentiles, respectively. The limit lines depict range; outliers are represented by open circles.

strongly suggest that extensive neuronal cell death occurred transiently in WE. As described above, CSF p-tau$_{181}$ increases and CSF Aβ42 decreases in patients with AD. Therefore, lower levels of CSF p-tau$_{181}$ and higher levels of CSF Aβ42 in WE than in AD suggest that the mechanisms of neuronal death differ between WE and AD. Moreover, the decline in total tau from the high levels found in acute WE coupled with the finding of normal levels of total tau in chronic WE, suggest that neuronal death is transient, not progressive, in WE. Transiently elevated CSF total tau and nonelevated CSF phospho-tau also characterize acute stroke (Hesse et al., 2001). These findings clearly suggest common mechanisms for CSF total tau elevation, i.e., extensive neuronal cell loss, in WE and acute stroke.

Our study indicates that in WD, neuronal cell death does not occur, or that the extent of neuronal damage is much less severe than in WE. Our WD subjects had normal total tau levels, with the exception of one case of borderline elevated total tau. On the other hand, our results demonstrate the potential clinical importance of CSF total tau levels as a biological marker of WE and KS. Although a diagnosis of WE can be made by the classic clinical triad of oculomotor abnormalities, gait ataxia and a global confusional state, the fact that two-thirds of patients with WE do not present the classic clinical triad (Victor et al., 1989) indicates that WE is difficult to diagnose during life. Thus, it is often difficult to distinguish WE from WD (Hersh et al., 1997). Most clinicians differentiate these clinical entities based on only patient symptoms and their response to thiamine administration, but a more accurate method of diagnosis is needed because of the frequently poor prognosis of patients with WE. Recent magnetic resonance imaging (MRI) results (Antunez et al., 1998) notwithstanding, the sensitivity and specificity of MRI diagnosis remains to be established as a clinically useful ante mortem diagnostic technique for WE (Antunez et al., 1998).

In KS patients, both memory disturbance and global cognitive impairment are frequent complications. The initial clinical manifestations of KS vary from acute coma to insidious onset of memory impairment. A history of WE is not invariably present in cases of KS (Kopelman, 1995). Similarly, differentiating KS from AD is frequently difficult, but early diagnosis of AD is needed to initiate symptomatic treatment with acetylcholinesterase inhibitors.

Our study has some limitations, including the small sample size and a lack of normal control subjects. However, CSF total tau has been intensively studied and according to recent review of CSF markers for AD, 36 different studies have used similar methods as our study, and these studies have included 2500 AD patients and 1400 controls (Blennow and Hampel, 2003). Therefore, we believe that a normal range for CSF total-tau level has been established.

In conclusion, this is the first study to describe the transient elevation of total tau levels in CSF of patients with WE, as well as the absence of elevated total tau in WD. These preliminary results remain to be confirmed in larger samples and to be extended in future investigations of autopsy-confirmed cases of WE.

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COMPETING INTERESTS

None.

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Addictive Behaviors

Short communication

Assessing multidimensional cognitions of drinking among alcohol-dependent patients: Development and validation of a drinking-related cognitions scale (DRCS)

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ABSTRACT

The aim of this study is to develop and validate the Drinking-Related Cognitions Scale (DRCS). The DRCS is a brief measure designed to assess multidimensional cognitions of drinking, including perception of drinking problems, perception of impaired drinking control, readiness to change, decisional balancing, and self-efficacy in alcohol-dependent patients. This study was carried out in Japan, with 132 alcohol-dependent patients (mean age (SD): 49.4 (7.5) years) admitted to an inpatient treatment program. On the basis of prior studies of the rating scales of drinking-related cognitions, DRCS items were selected. Factor analysis was carried out to assess the selection of DRCS items and the factor structure. The factor analysis of the 15 DRCS items showed three factors, "expectancy and resignation," "perception of impaired control," and "perception of drinking problem." The DRCS showed good reliability (Cronbach's α-coefficients for the entire scale and subscales were 0.80 or higher, and the analysis of variance intraclass correlation coefficient for the test–retest method was 0.81 for the total score). The total DRCS and subscale scores predicted abstinence status at a 3-month follow-up, and the DRCS was considered to have satisfactory predictive validity. It was suggested that the DRCS would be useful for the easy measurement of multidimensional cognitions of drinking in alcohol-dependent patients.

1. Introduction

Alcoholics' drinking-related cognitions such as perception of their drinking problems and impaired drinking control (Alcoholics Anonymous, 2001; Nowinski & Baker, 1992), readiness to change (DiClemente & Velasquez, 2002), decisional balancing (Miller, Zweben, DiClemente, & Rychtarik, 1995, Sobell et al., 1996) and self-efficacy (Larimer, Palmer, & Marlatt, 1999) play an important role in assessing therapeutic effect and outcome. The previous studies were used to develop the various rating scales of drinking-related cognitions, such as the Situational Confidence Questionnaire (SCQ; Annis, 1986), Alcohol Abstinence Self-Efficacy Scale (AASE; DiClemente, Carbonari, Montgomery, & Hughes 1994), Alcohol and Drug Consequences Questionnaire (ADCQ; Cunningham, Sobell, Gavin, Sobell, & Breslin, 1997), Alcohol Expectancy Questionnaire (AEQ; Brown, Christiansen, & Goldman, 1987), Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES; Miller & Tonigan, 1996), Readiness to Change Questionnaire: Treatment Version (RCQ-TV; Heather, Luce, Peck, Dunbar, & James, 1999), Impaired Control Scale (ICS; Heather,

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Tebbutt, Mattick, & Zamir, 1993), and Steps Questionnaire (Gilbert, 1991). However, alcohol-dependent patients' drinking-related cognitions are multidimensional, and not only one cognition affects a patient's treatment outcome. Some patients have poor self-efficacy for abstinence in spite of sufficient perception of drinking problems, whereas other patients have insufficient perception of impaired drinking control, although their balance sheets leaned towards the costs of drinking. Under such circumstances, we have developed a Drinking-Related Cognitions Scale (DRCS) for the simple and easy measurement of the multidimensional cognitions of drinking in alcohol-dependent patients, and assessed its reliability and validity.

2. Method

2.1. Participants

Among 153 patients admitted to the Middle-Aged and Elderly Male Alcohol-Dependence Ward, National Hospital Organization Kurihama Alcoholism Center, Kanagawa, Japan, who satisfied the DSM-IV (American Psychiatric Association, 1994) diagnostic criteria for "alcohol dependence," 132 patients (mean age (SD): 49.4 (7.5) years), excluding 16 who left the hospital on their own accord during the treatment program and 5 whose treatment outcome after discharge could not be followed up, participated in this study.

The details of this study were explained orally and in writing to the participants, and each participant's written informed consent to respond to a questionnaire and cooperate in a follow-up survey was obtained. Following the end of the inpatient treatment program, including assessment and feedback with regard to the patients' alcohol problems, education on alcoholism, motivational approaches, coping-skills training, and participation in a self-help group, the DRCS was conducted (this treatment program set a goal of continuing abstinence).

2.2. Item generation

First, 18 questionnaire items thought to be appropriate, content-wise, regarding the patients' drinking-related cognitions were chosen as candidate items by referring to the rating scales, such as the SCQ, AASE, ADCQ, AEQ, SOCRATES, RCQ-TV, ICS, and Steps Questionnaire. It was decided that all the responses to the questions were to be on a scale of 1 to 6 points. If "strongly agree" was chosen, this response was given a 1-point rating, and, following this, 2-, 3-, 4-, 5-, and 6-point ratings were given ("strongly disagree" being given a 6-point rating). Three of the 18 items were decided to be reversed items.

2.3. Consideration of item selection and factor structure

To consider item selection and factor structure of the DRCS, a factor analysis of all 18 items was conducted using the maximum likelihood method with promax rotation.

Table 1
Factor analysis of DRCS (maximum likelihood method, promax rotation)

Item (translated from Japanese)	Factor loading		
	ER	PI	PD
Expectancy and resignation (ER)			
1. I cannot give up drinking as long as I have stress.	**0.94**	−0.04	−0.06
4. When I get very irritated, I cannot help drinking.	**0.89**	0.02	−0.13
15. It is difficult to lead a pleasant life without drinking.	**0.79**	−0.06	0.14
7. I cannot control my urge to drink.	**0.63**	−0.02	0.00
10. Alcohol is my source of energy for life.	**0.58**	0.15	0.10
13. There are ways other than drinking to relieve my fatigue from work or housework. *	**0.44**	0.12	0.18
Perception of impaired control (PI)			
11. If I try to drink again and in moderation, the odds that I will succeed are high.	−0.07	**1.04**	−0.03
8. For low-alcohol beverages such as beer, I do not drink excessively.	0.13	**0.79**	−0.07
5. Even if I limit my alcohol consumption, I will eventually return to my previous pattern of drinking. *	−0.10	**0.65**	0.07
14. Now that I have known the harm of alcohol, I will be able to drink in moderation.	0.26	**0.60**	0.01
2. Even if I have an opportunity to drink again, I will not drink excessively.	0.04	**0.43**	0.16
Perception of drinking problem (PD)			
12. I have not caused as many problems related to my drinking as people around me say.	−0.17	0.12	**0.88**
3. I have not drunk so much as to cause trouble to my family or people around me.	0.20	−0.10	**0.72**
6. Drinking has not interfered with my work or finances.	0.05	−0.06	**0.70**
9. Drinking problems have interfered with my daily life. *	−0.01	0.11	**0.50**
Cumulative contribution rate (%)	40.20	50.94	58.20

* Reversed item.

2.4. Assessment of reliability

Regarding the reliability of the DRCS, Cronbach's α values for the entire scale and the subscales were calculated to assess internal consistency. The reproducibility of the DRCS was assessed by the test–retest method. To examine the test–retest reliability using the analysis of variance intraclass correlation coefficient (ANOVA ICC), 42 patients completed the DRCS twice following a 1-week retest interval.

2.5. Assessment of predictive validity

Three months after the participants had completed the inpatient treatment program, face-to-face interviews or interviews by telephone were conducted with the participants, their family or municipal welfare office staff. The treatment outcome at a 3-month follow-up was assessed by allotting (a) patients with the number of drinking days of "0" being the "abstinence group" and (b) those with the number of drinking days of 1 or more being the "drinking group." The relationship between DRCS score and treatment outcome was examined to assess the predictive validity of the DRCS, using the *t*-test.

3. Results

3.1. Consideration of item selection and factor structure

The factor analysis of the 18 DRCS items showed the following results. Three items, "Physical treatment rather than treatment of alcohol dependence is necessary for me," "I drink alcohol and enjoy it in a normal manner," and "I've been told that I can never be a good drinker, but I can't believe it," did not have a sufficient item load for any factor (less than 0.35). These items were considered inappropriate and were excluded. The factor analysis of the remaining 15 items was again conducted, and three factors were identified (Table 1). All the remaining items had a factor load of 0.40 or greater. The cumulative contribution of the three factors was 58.2%. Items that showed a high factor load for the first factor were considered to represent the patients' views "Alcohol is useful and necessary for me," and "I cannot give up drinking." This was interpreted as the "expectancy and resignation." Items that had a high factor load for the second factor were considered to represent the patients' views "I can control drinking," and "I don't drink too much." This was interpreted as the "perception of impaired control." Items that showed a high factor load for the third factor were considered to represent the patients' views "I have no drinking problem." This was interpreted as the "perception of drinking problem."

On the basis of the above results, the three items considered to decrease factor validity were excluded, and six items for the expectancy and resignation, five items for the perception of impaired control, and four items for the perception of drinking problem (15 items in total) were adopted as the final items of the DRCS.

3.2. Assessment of reliability

Cronbach's α values for the entire scale and subscales were 0.91 for the entire scale, 0.88 for the expectancy and resignation, 0.85 for the perception of impaired control, and 0.80 for the perception of drinking problem. These values were considered to indicate a good internal consistency of the DRCS.

In the test–retest method employed for 42 patients, the ANOVA ICC calculated on the basis of the score of the first and second tests were 0.81 for the entire scale, 0.84 for the expectancy and resignation, 0.66 for the perception of impaired control, and 0.79 for the perception of drinking problem, which is sufficiently high to confirm the reproducibility of the DRCS, except for the perception of impaired control.

3.3. Assessment of predictive validity

Table 2 shows the relationship between the treatment outcome at a 3-month follow-up and DRCS score (*t*-test). Both the total score and subscale scores were significantly higher in the abstinence group than in the drinking group. On the basis of these findings, the DRCS was considered to have a good predictive validity.

Table 2
Relationship between DRCS scale score and treatment outcome at a 3-month follow-up

	Abstinence group ($n=73$)	Drinking group ($n=59$)	*P*-value
Expectancy and resignation	32.8±4.6	29.6±5.8	0.001**
Perception of impaired control	26.0±5.2	23.5±6.7	0.019*
Perception of drinking problem	21.7±3.3	20.0±4.3	0.013*
Total	80.5±11.6	73.1±13.2	0.001**

*$P \leqq 0.05$; **$P \leqq 0.001$ (*t*-test).

3.4. Time required to complete the questionnaire

The time required to complete the DRCS was less than 5 min for 85.7% of the participants, 5 to less than 7 min for 11.9%, and 7 to 10 min for 2.4%.

4. Discussion

The factor analysis of the 15 DRCS items showed three factors. The subscale "expectancy and resignation" was interpreted as representing alcohol expectancies and self-efficacy for abstinence. It is suggested that the high alcohol expectancies generate the patients' belief "Alcohol is useful and indispensable for me," and that this belief leads to the thought "It is impossible to give up drinking." The subscale "perception of impaired control" is interpreted as representing the denial or unawareness of impaired drinking control. Patients who have poor perception of their impaired drinking control are thought to be unready to change their drinking-related behavior. The subscale "perception of drinking problem" is interpreted as representing the denial or unawareness of drinking problems. It is considered that patients perceiving their drinking problems also perceive that changing their drinking-related behavior will be beneficial for them.

The DRCS has been confirmed to have good reliability and validity, and has been suggested to be effective as a rating scale for the easy measurement of the multidimensional cognitions of drinking among alcohol-dependent patients. However, the assessment of the reliability and validity of the DRCS was limited in this study because the participants in this study were only middle-aged and older male alcohol-dependent patients who underwent hospital treatment. It will be necessary to conduct the DRCS questionnaire survey for mildly alcohol-dependent outpatients, females and young people for the assessment of the reliability and validity of the DRCS.

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Decrease in the Prevalence of Adolescent Alcohol Use and its Possible Causes in Japan: Periodical Nationwide Cross-Sectional Surveys

Yoneatsu Osaki, Takeo Tanihata, Takashi Ohida, Hideyuki Kanda, Kenji Suzuki, Susumu Higuchi, Yoshitaka Kaneita, Masumi Minowa, and Kenji Hayashi

Background: Trends in alcohol drinking prevalence were assessed among Japanese adolescents, and possible reasons for a decrease in drinking prevalence observed in 2004.

Methods: Cross-sectional nationwide surveys were conducted periodically. High schools were randomly sampled from throughout Japan in 1996, 2000, and 2004. All enrolled students in sampled schools were subjects of the surveys. Self-reporting anonymous questionnaires were collected from 115,814 students in 1996, 106,297 in 2000, and 102,451 in 2004. Questions about drinking prevalence of students and family members, proportion of students who have no friends, and sources of alcohol were included. Students who drunk at least one day of the 30 days preceding the survey were defined as the current drinkers.

Results: The drinking prevalence in 2004 was decreased in comparison to that in 1996 and 2000 in both sexes and in all school grades. The current drinking rate (monthly drinker) among junior high school boys was 29.4% in 1996, 29.0% in 2000, and 20.5% in 2004, while that among senior high school boys was 49.7%, 48.7%, and 36.2%, respectively. The respective prevalence among junior and senior girls was 24.0%, 25.5%, and 20.0% and 40.8%, 42.1%, and 34.1%. The prevalent sources of alcohol beverages were searching in home, stores (convenience store, supermarket, or gas-stand), liquor shops, and bars. An analysis of the reasons for this decrease identified a decrease in drinking prevalence in students' families, especially by fathers and older brothers, and an increase in the proportion of students who had no friends.

Conclusions: A decrease in drinking prevalence of male family members and a limitation of sources of alcoholic beverages may contribute to the decrease in adolescent drinking prevalence.

Key Words: Drinking Behavior, Alcohol Use, Adolescent Behavior, Japan.

CONSUMPTION OF ALCOHOL is one of the most important risk factors for noncommunicable diseases (A Joint WHO/FAO Expert Consultation, 2003; Hara et al., 2002; Inoue et al., 2005; Iso et al., 2004; Tsugane et al., 1999; Wakai et al., 2005). The drinking behavior of minors is not only a health concern due to the effects of the alcohol, but is also a major social issue related to a variety of health and social problems, including delinquency, traffic accidents, and sexually transmitted disease (Suzuki, 1995, 2001).

Traditionally, Japanese society has been relatively tolerant of alcohol consumption by adult males, while disapproving of such behavior among young people and women (Higuchi et al., 2006). However, these norms have been changing in recent years. Although Japan has the Act to Prohibit Minors from alcohol use enacted in 1990 prohibiting the consumption of alcohol by minors under age 20, it is thought that many adolescents nevertheless often drink before reaching 20 years of age (Osaki et al., 2003; Suzuki et al., 2003). Alcohol use is one of most important health-related behaviors among adolescents as well as cigarette smoking [Centers for Disease Control and Prevention (CDC), 2006a; Currie et al., 2004]. In Western countries, health-related behaviors including alcohol use among adolescents have been monitored periodically for several decades (CDC, 2006a,b; Currie et al., 2003; Hibell et al., 1996, 2000, 2004). Monitoring adolescent drinking behavior is necessary for establishing and evaluation of the national policy to prevent adolescent drinking. A nationwide survey was conducted on adolescent alcohol use in Japan in 1996, 2000, and 2004. In order to reveal trends in adolescent alcohol use in Japan, the results from the surveys were compared. This comparison revealed the actual situation of the

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drinking behavior among adolescents and related factors of alcohol use and possible causes of the change in drinking prevalence observed in 2004 survey. In addition, the results from the surveys will provide the baseline and mid-term values for adolescent drinking prevalence for "Healthy People Japan 21," i.e., national health plan for the 21st century. These data are expected to contribute to the development of the national policy on preventing drinking by minors.

MATERIALS AND METHODS

Subjects

The survey was a cross-sectional random sampling survey which used the single-stage cluster sampling methodology (Cochran, 1977). The survey targeted junior and senior high school students from schools selected throughout Japan using the National School Directory. The number of schools sampled for the 1996 survey was 122 of 11,274 junior high schools (selection rate: 1.1%) and 109 of 5,501 senior high schools (2.0%). The survey period was December 1996 to the end of January 1997. Respective values for the 2000 and 2004 surveys were 132 of 11,200 junior (1.2%) and 102 of 5,315 senior high schools (1.9%) from December 2000 to the end of January 2001; and 131 of 11,060 junior (1.2%) and 109 of 4,627 senior high schools (1.9%) from December 2004 to the end of January 2005. All students enrolled in the sampled schools were subjects of the study.

Procedures

The cooperation of the principals of these schools was requested and questionnaires were sent to each. The students' teachers were instructed to inform them of the voluntary nature of their participation and to urge them to answer honestly. Anonymous questionnaires and envelopes were handed to the students for completion during school time. Upon completion, the questionnaires were sealed in envelopes by the students themselves, collected by their teachers, and returned unopened. This survey was approved by the Ethics Committee of the National Institute of Public Health.

Measures

The questionnaire focused on their experience, frequency of alcohol use, drinking with peers, age (by school grade) when the respondent first tried drinking, amount of alcoholic beverages consumed by drinkers, sources of alcoholic beverages, alcohol-related problems, and drinking status of the student's family. Experimenting drinkers, current drinkers, and weekly drinkers were defined as those who had tried drinking at least once, those who had drunk at least once during the previous 30 days, and those who had responded as "every weekend," "several times a week," and "every day" in the question asking for the average frequency of alcohol use. Daily drinkers were defined as those who had drunk every day during the previous 30 days.

Response Rate

For the 1996 survey, responses were obtained from 80 junior (response rate 65.6%) and 73 senior high schools (67.0%), with a total of 115,814 responses accounting for 64.1% of all junior and 62.5% of all senior students enrolled in the sampled schools. Respective values for 2000 were 99 (75.0%) and 77 schools (75.5%), with 106,297 responses accounting for 66.1% and 59.3% of enrolled students; and for 2004, 92 (70.2%) and 87 schools (79.8%), with 102,451 responses accounting for 60.7% and 67.7% of students. The proportion of responded students by school grade among junior high school was not significantly different. The number of responded students of third grade of senior high school was less than that of other grades, however, the proportion of third grade students did not change significantly over the surveys. We compared subtotal prevalence of junior or senior high schools after combining each grade's data without weighting. The characteristics of the responding schools, such as the proportion of private schools, vocational schools, or general schools were chosen to be representative of the study population. The average number of enrolled students in responding schools was not significantly different from that of nonresponding schools. The urban junior high schools were less likely to respond to these surveys, but this trend was not observed in senior high schools.

Data Analysis

The percentages and 95% confidence intervals in the tables were calculated by a weighting method based on one-stage stratified cluster sampling (Cochran, 1977). The proportions in tables were compared using statistical testing for rate differences. Multiple logistic analyses were applied to calculate relative risks and population attributable risk percent of students' current drinking with family's (father, mother, senior brother, and senior sister) drinking or those of current drinking without friend. The data were analyzed using the SPSS for Windows (version 13.0) software program (SPSS Inc., Chicago, IL).

RESULTS

Prevalence of Alcohol Use

Lifetime drinking rate, current drinking rate, and weekly drinking rate increased with age. Although the prevalence of daily alcohol use was quite low, more than half of junior high school students had already experienced drinking alcohol. The current drinking rate of junior high school students already exceeded 20% for both boys and girls. The proportion of habitual drinking, such as current and weekly drinking, for senior high school students was found to be about 2 times more prevalent in comparison with that for junior high school students. The prevalence of lifetime, current, and weekly alcohol use decreased in 2004 survey in comparison to the 1996 and 2000 surveys for both sexes and type of school (junior or senior high school). Since the degree of decrease was greater in boys than in girls, the lifetime drinking experience rate was rather higher in girls than that in boys in the 2004 survey (Table 1).

Type of Alcoholic Beverage Consumed by Current Drinkers

Popular alcohol beverages among current drinkers were alcopop (ready mixed soft drinks containing 4% to 7% alcohol by volume), beer, and shochu (a rough Japanese spirit distilled from sake dregs and other ingredients). The prevalence of alcopop increased whenever surveyed and became the top 1 type of beverage for both sexes and type of school (junior or senior high school) in the 2004 survey. The proportion was much higher among junior high school students in comparison to senior high school students for boys, whereas the proportion was rather high in senior high school for girls. In contrast, the prevalence of beer, Japanese-sake, and spirits decreased (Table 2).

Table 1. Prevalence of Alcohol Use (1996, 2000, 2004)

Gender	High school	Year	Lifetime alcohol use	Experience drinking with peer	Experience drinking alone	Current alcohol use	Weekly alcohol use	Daily alcohol use	Sample size (*n*)
Boy	Junior	1996	73.5 ± 0.2	16.7 ± 0.1	10.3 ± 0.1	29.4 ± 0.2	6.4 ± 0.1	0.6 ± 0.0	21,471
		2000	64.5 ± 0.2	13.5 ± 0.1	8.5 ± 0.1	29.0 ± 0.2	5.9 ± 0.0	0.3 ± 0.0	25,348
		2004	53.3 ± 0.2	9.1 ± 0.1	5.8 ± 0.1	20.5 ± 0.2	3.9 ± 0.0	0.4 ± 0.0	20,679
	Senior	1996	87.2 ± 0.1	59.5 ± 0.3	28.7 ± 0.2	49.7 ± 0.3	13.8 ± 0.1	0.8 ± 0.0	35,645
		2000	83.5 ± 0.1	56.2 ± 0.2	27.0 ± 0.1	48.7 ± 0.3	14.4 ± 0.1	0.6 ± 0.0	29,228
		2004	75.3 ± 0.2	42.0 ± 0.2	32.6 ± 0.2	36.2 ± 0.3	10.0 ± 0.1	0.5 ± 0.0	35,319
Girl	Junior	1996	71.5 ± 0.2	14.2 ± 0.1	6.9 ± 0.1	24.0 ± 0.1	3.9 ± 0.0	0.4 ± 0.0	21,327
		2000	64.3 ± 0.2	12.2 ± 0.1	6.1 ± 0.0	25.5 ± 0.2	4.1 ± 0.0	0.2 ± 0.0	21,898
		2004	56.7 ± 0.2	9.8 ± 0.1	6.3 ± 0.1	20.0 ± 0.2	2.9 ± 0.0	0.2 ± 0.0	18,706
	Senior	1996	86.7 ± 0.1	54.5 ± 0.4	16.7 ± 0.1	40.8 ± 0.3	6.3 ± 0.1	0.3 ± 0.0	37,371
		2000	84.1 ± 0.2	51.2 ± 0.3	15.6 ± 0.1	42.1 ± 0.3	7.8 ± 0.1	0.2 ± 0.0	29,823
		2004	77.3 ± 0.2	39.6 ± 0.4	27.9 ± 0.3	34.1 ± 0.3	6.5 ± 0.1	0.3 ± 0.0	27,747

Values given are percentages (mean ± SE).
SE, standard error.
Lifetime alcohol use = students who had tried alcohol drinking at least once.
Current alcohol use = students who had drunk ≥1 day of the 30 days preceding the survey.
Weekly alcohol use = students who drink every weekend, several times a week, or every day.
Daily alcohol use = students who had drunk every day for the 30 days preceding the survey.

Sources of Alcohol Beverages

The major sources of alcohol beverages among current drinkers were in home, stores (convenience store, supermarket, gas-stand), and they received them from someone. Those among senior high students were in home, stores, and bars. The proportion of stores, liquor shops, vending machines, and bars decreased with the year of survey. In the 2004 survey, the proportion of current drinkers who drank at bars was higher for girls than boys (Table 3).

Characteristics of Drinking Behavior

The proportion of students who drank alcohol before age 13 decreased with the year of survey, and the figure in girls became higher than that in boys after the 1996 survey. The proportion of students who drank with friends before age 13 also decreased, whereas the proportion was still higher in boys except for in junior high school in 2004. The proportion of current drinkers who drank 3 drinks more in a drinking occasion decreased for senior high school students in the 2004 survey in comparison to that in the 2000 survey, whereas that for junior high school students slightly increased. A "binge drink" was defined as current drinkers who drank 6 drinks or more in a drinking occasion. The prevalence of binge drinking was much higher among senior students, and the figure decreased in 2004 in comparison to 2000 for senior students, whereas it tended to increase among junior boys and girls (Table 4).

Alcohol-Related Problems

Alcohol-related problems, namely vomiting, fighting, blacked out, trouble with police, and scolding by parents were assessed from the first survey. The prevalent problems were blacking out, vomiting, and scolding by parents for junior high drinkers. Prevalent problems among current drinkers in senior high school were also vomiting and blacking out, but the prevalence was much

Table 2. Modality of Alcohol Beverages Consumed by Current Drinkers

Gender	High school	Year	Beer	Japanese sake	Wine	Shochu	Alcopop	Spirits	Current drinker (*n*)
Boy	Junior	1996	66.7 ± 0.2	25.3 ± 0.2	28.6 ± 0.2	21.6 ± 0.2	53.3 ± 0.2	15.9 ± 0.1	6,332
		2000	56.9 ± 0.2	21.7 ± 0.2	33.8 ± 0.2	28.7 ± 0.2	49.8 ± 0.2	8.2 ± 0.1	7,215
		2004	44.0 ± 0.2	19.4 ± 0.1	24.2 ± 0.2	36.4 ± 0.3	68.9 ± 0.5	4.7 ± 0.1	4,246
	Senior	1996	79.4 ± 0.2	26.6 ± 0.2	21.6 ± 0.2	30.7 ± 0.4	47.6 ± 0.3	22.5 ± 0.2	17,942
		2000	68.4 ± 0.2	23.7 ± 0.2	25.3 ± 0.2	44.9 ± 0.3	54.0 ± 0.2	13.3 ± 0.1	14,245
		2004	53.3 ± 0.2	19.3 ± 0.1	18.3 ± 0.1	48.5 ± 0.2	57.2 ± 0.2	10.0 ± 0.1	12,783
Girl	Junior	1996	54.3 ± 0.2	18.6 ± 0.2	30.5 ± 0.2	24.8 ± 0.2	72.3 ± 0.2	12.0 ± 0.1	5,139
		2000	42.4 ± 0.2	14.0 ± 0.1	34.7 ± 0.2	33.4 ± 0.2	67.6 ± 0.2	6.2 ± 0.1	5,617
		2004	30.2 ± 0.2	12.9 ± 0.1	23.0 ± 0.2	36.4 ± 0.3	68.9 ± 0.3	4.7 ± 0.1	3,733
	Senior	1996	56.5 ± 0.3	15.5 ± 0.2	24.7 ± 0.2	34.8 ± 0.4	75.0 ± 0.2	11.5 ± 0.1	15,132
		2000	43.8 ± 0.3	12.6 ± 0.2	26.1 ± 0.2	47.9 ± 0.3	75.9 ± 0.3	5.7 ± 0.1	12,428
		2004	30.1 ± 0.2	10.7 ± 0.1	20.2 ± 0.3	50.9 ± 0.4	75.3 ± 0.1	5.7 ± 0.1	9,471

Values given are percentages (mean ± SE).
Percentages add up to more than 100%, as some students mentioned more than 1 type of alcoholic beverage.

Table 3. Sources of Alcoholic Beverages Among Current Drinkers

Gender	High school	Year	Searched in home	Received from someone	Convenience store, super market	Liquor shop	Vending machine	Bar	Other	Current drinking (*n*)
Boy	Junior	1996	70.5 ± 0.2	10.5 ± 0.1	25.4 ± 0.2	12.0 ± 0.2	18.5 ± 0.2	9.5 ± 0.1	11.7 ± 0.1	6,332
		2000	72.4 ± 0.1	10.5 ± 0.1	19.4 ± 0.2	8.6 ± 0.1	12.2 ± 0.1	7.9 ± 0.1	11.6 ± 0.1	7,215
		2004	72.0 ± 0.2	10.9 ± 0.1	12.0 ± 0.2	7.6 ± 0.2	9.7 ± 0.2	6.8 ± 0.1	12.6 ± 0.1	4,246
	Senior	1996	57.5 ± 0.3	20.1 ± 0.1	64.9 ± 0.3	38.0 ± 0.3	40.0 ± 0.3	37.4 ± 0.4	4.5 ± 0.0	17,942
		2000	58.7 ± 0.2	21.7 ± 0.1	65.9 ± 0.2	32.7 ± 0.2	28.2 ± 0.2	35.9 ± 0.4	5.0 ± 0.1	14,245
		2004	60.7 ± 0.2	21.7 ± 0.1	48.5 ± 0.3	31.2 ± 0.2	20.0 ± 0.2	27.9 ± 0.3	6.3 ± 0.1	12,783
Girl	Junior	1996	75.8 ± 0.2	9.1 ± 0.1	27.0 ± 0.3	11.6 ± 0.2	11.4 ± 0.2	11.8 ± 0.2	13.4 ± 0.1	5,139
		2000	76.0 ± 0.1	12.3 ± 0.1	23.7 ± 0.3	9.0 ± 0.1	9.5 ± 0.1	10.7 ± 0.1	9.4 ± 0.1	5,617
		2004	75.2 ± 0.2	13.8 ± 0.2	15.7 ± 0.2	7.5 ± 0.1	8.9 ± 0.2	10.1 ± 0.1	11.2 ± 0.1	3,733
	Senior	1996	61.2 ± 0.3	16.8 ± 0.2	61.7 ± 0.4	30.3 ± 0.3	25.4 ± 0.3	37.5 ± 0.4	3.8 ± 0.1	15,132
		2000	62.4 ± 0.3	19.3 ± 0.1	62.2 ± 0.3	23.2 ± 0.2	15.4 ± 0.2	38.9 ± 0.4	4.4 ± 0.0	12,428
		2004	68.0 ± 0.3	20.9 ± 0.2	45.7 ± 0.4	22.5 ± 0.2	10.9 ± 0.1	34.5 ± 0.4	5.8 ± 0.1	9,471

Values given are percentages (mean ± SE).
Percentages add up to more than 100%, as some students mentioned more than 1 type of alcoholic beverage.

Table 4. Proportion of Students Who Drank Alcohol Before 13 years of Age and of Binge Drinking

Gender	High school	Year	Drank alcohol before age 13	Drank with friends before age 13	3 drink and over[a]	6 drink and over[a]
Boy	Junior	1996	65.4 ± 0.2	16.3 ± 0.1	18.0 ± 0.2	6.4 ± 0.2
		2000	49.0 ± 0.1	11.2 ± 0.1	16.3 ± 0.2	6.0 ± 0.2
		2004	41.3 ± 0.2	9.7 ± 0.1	18.8 ± 0.2	7.2 ± 0.2
	Senior	1996	46.8 ± 0.2	6.9 ± 0.1	55.9 ± 0.1	27.8 ± 0.1
		2000	33.3 ± 0.1	5.6 ± 0.1	55.2 ± 0.1	25.6 ± 0.1
		2004	31.6 ± 0.1	5.5 ± 0.0	50.5 ± 0.2	21.3 ± 0.2
Girl	Junior	1996	63.4 ± 0.2	13.0 ± 0.0	11.3 ± 0.2	4.2 ± 0.2
		2000	51.5 ± 0.1	10.5 ± 0.0	14.9 ± 0.2	4.8 ± 0.2
		2004	44.9 ± 0.2	9.9 ± 0.1	15.8 ± 0.2	5.6 ± 0.2
	Senior	1996	45.2 ± 0.2	6.2 ± 0.1	37.8 ± 0.1	13.4 ± 0.1
		2000	35.9 ± 0.2	4.8 ± 0.0	41.5 ± 0.2	14.4 ± 0.2
		2004	33.6 ± 0.1	4.7 ± 0.1	38.8 ± 0.2	12.1 ± 0.2

Values given are percentages (mean ± SE).
Binge drink: Had ≥ 3 or 6 drinks of alcohol in a drinking occasion.
[a]Proportion in current drinker (Had at least one drink of alcohol on ≥1 of the 30 days preceding the survey).

higher than that in junior high school. These proportions slightly decreased in the 2004 survey in comparison to the 2000 survey. The rate difference between experience of problems and scolding by parents was small in junior high drinkers, whereas that in senior high drinkers was relatively high (Table 5).

Table 5. Experience Rates of Alcohol-Related Problems Among Current Drinkers

Gender	High school	Year	Vomiting	Fighting	Blacked out	Trouble with police	Scolding by parents	Current drinker (*n*)
Boys	Junior	1996	10.8 ± 0.1	4.6 ± 0.1	12.8 ± 0.1	2.2 ± 0.0	10.5 ± 0.1	6,332
		2000	10.6 ± 0.1	2.9 ± 0.0	11.8 ± 0.1	1.0 ± 0.0	8.4 ± 0.1	7,215
		2004	10.0 ± 0.1	3.5 ± 0.1	12.3 ± 0.2	1.9 ± 0.0	10.0 ± 0.1	4,246
	Senior	1996	34.3 ± 0.4	6.7 ± 0.1	23.8 ± 0.2	2.7 ± 0.0	9.2 ± 0.1	17,942
		2000	35.9 ± 0.3	5.9 ± 0.1	22.6 ± 0.2	2.3 ± 0.0	7.9 ± 0.1	14,245
		2004	28.4 ± 0.2	4.9 ± 0.1	18.0 ± 0.1	2.0 ± 0.0	7.5 ± 0.1	12,783
Girls	Junior	1996	6.9 ± 0.1	2.6 ± 0.1	9.8 ± 0.1	1.4 ± 0.0	7.7 ± 0.1	5,139
		2000	8.3 ± 0.1	1.7 ± 0.0	12.4 ± 0.1	0.6 ± 0.0	6.7 ± 0.1	5,617
		2004	7.8 ± 0.1	2.8 ± 0.1	13.0 ± 0.2	0.8 ± 0.0	8.7 ± 0.1	3,733
	Senior	1996	20.9 ± 0.3	2.4 ± 0.0	21.2 ± 0.2	1.0 ± 0.0	6.7 ± 0.1	15,132
		2000	23.0 ± 0.3	2.0 ± 0.0	21.4 ± 0.2	0.9 ± 0.0	6.0 ± 0.1	12,420
		2004	20.1 ± 0.2	2.2 ± 0.0	19.5 ± 0.2	0.9 ± 0.0	6.6 ± 0.1	9,471

Values given are percentages (mean ± SE).

Table 6. Prevalence of Family's Alcohol Use Reported by Students and Relative Risks and Population Attributable Risk of Students' Current Drinking With Family's Drinking

			Prevalence of alcohol use (mean ± SE)			*p*-value	Relative risk (95% CI)			Population attributable risk percent		
Student' sex	High school	Family	1996	2000	2004	2000 vs. 2004	1996	2000	2004	1996	2000	2004
Boy	Junior	Father	74.1 ± 0.1	74.2 ± 0.1	70.4 ± 0.1	*	1.27 (1.18–1.37)	1.42 (1.32–1.52)	1.37 (1.26–1.49)	16.7	23.8	20.7
		Mother	44.8 ± 0.1	49.0 ± 0.2	47.0 ± 0.2	*	1.64 (1.54–1.75)	1.75 (1.65–1.85)	1.72 (1.60–1.85)	22.3	26.9	25.3
		Older brother	15.2 ± 0.0	14.4 ± 0.1	12.3 ± 0.1	**	1.71 (1.58–1.85)	1.82 (1.67–1.96)	2.06 (1.87–2.25)	9.7	10.6	11.5
		Older sister	10.5 ± 0.1	10.7 ± 0.0	10.3 ± 0.1	**	1.81 (1.65–1.98)	2.04 (1.88–2.22)	2.05 (1.86–2.26)	7.8	10.0	9.8
		No friend[a]	3.4 ± 0.0	2.6 ± 0.0	5.2 ± 0.0	**	0.77 (0.87–1.20)	0.70 (0.58–0.84)	0.85 (0.73–1.00)	−0.8	−0.8	−0.8
	Senior	Father	75.8 ± 0.1	74.8 ± 0.1	70.8 ± 0.1	*	1.27 (1.20–1.33)	1.31 (1.24–1.39)	1.23 (1.17–1.30)	17.0	18.8	14.0
		Mother	45.7 ± 0.1	49.1 ± 0.2	48.5 ± 0.1	*	1.63 (1.56–1.70)	1.65 (1.57–1.73)	1.78 (1.70–1.87)	22.4	24.2	27.4
		Older brother	23.8 ± 0.1	23.0 ± 0.1	22.2 ± 0.1	**	1.45 (1.38–1.52)	1.44 (1.36–1.52)	1.53 (1.45–1.61)	9.7	9.2	10.5
		Older sister	18.2 ± 0.1	18.8 ± 0.1	18.6 ± 0.1	*	1.53 (1.45–1.62)	1.57 (1.47–1.66)	1.56 (1.48–1.65)	8.8	9.7	9.4
		No friend[a]	3.3 ± 0.0	3.1 ± 0.0	5.1 ± 0.0	**	0.38 (0.34–0.44)	0.30 (0.26–0.35)	0.35 (0.31–0.39)	−2.1	−2.2	−3.4
Girl	Junior	Father	76.7 ± 0.1	75.4 ± 0.1	72.1 ± 0.1	*	1.14 (1.05–1.24)	1.11 (1.03–1.20)	1.09 (1.00–1.19)	9.7	7.7	6.1
		Mother	51.2 ± 0.1	53.8 ± 0.1	52.5 ± 0.2	*	2.11 (1.97–2.26)	1.96 (1.83–2.09)	2.09 (1.93–2.27)	36.2	34.1	36.4
		Older brother	17.3 ± 0.1	16.5 ± 0.1	14.2 ± 0.0	**	1.63 (1.51–1.76)	2.86 (1.72–2.01)	1.83 (1.66–2.01)	9.8	23.5	10.5
		Older sister	12.6 ± 0.1	13.3 ± 0.1	12.6 ± 0.1	**	1.94 (1.78–2.12)	2.14 (1.97–2.32)	2.20 (2.00–2.42)	10.6	13.2	13.1
		No friend[a]	2.0 ± 0.0	1.3 ± 0.0	2.7 ± 0.0	**	0.96 (0.75–1.22)	0.79 (0.59–1.06)	0.72 (0.56–0.92)	−0.1	−0.3	−0.8
	Senior	Father	76.7 ± 0.1	76.4 ± 0.1	73.9 ± 0.1	*	1.13 (1.07–1.19)	1.15 (1.08–1.22)	1.17 (1.10–1.24)	9.1	10.3	11.2
		Mother	51.1 ± 0.1	54.0 ± 0.2	54.0 ± 0.1		1.75 (1.68–1.83)	1.90 (1.81–1.99)	1.89 (1.79–1.99)	27.7	32.7	32.5
		Older brother	25.6 ± 0.1	24.8 ± 0.1	24.3 ± 0.1	*	1.37 (1.43–1.58)	1.43 (1.36–1.51)	1.58 (1.49–1.67)	8.7	9.6	12.4
		Older sister	22.0 ± 0.1	22.2 ± 0.1	21.6 ± 0.1	*	1.50 (1.16–1.22)	1.55 (1.47–1.64)	1.56 (1.46–1.65)	9.9	10.9	10.8
		No friend[a]	1.1 ± 0.0	1.0 ± 0.0	2.1 ± 0.0	**	0.68 (0.55–0.84)	0.53 (0.41–0.69)	0.47 (0.38–0.57)	−0.4	−0.5	−1.1

Relative risks were calculated by adjusting with other family members and school grade using multiple logistic regression analysis.
CI, 95% confidence interval.
[a]Proportion of students who have no friend.
*or ** result of statistical testing between 2000 and 2004, *$p < 0.05$, **$p < 0.01$.

Possible Causes for the Decrease in Drinking Prevalence

The data were analyzed to identify reasons for the decrease in drinking prevalence among Japanese adolescents. The reported drinking status of family members showed some decrease in family drinking, especially that by fathers and older brothers, but drinking by older sisters and friends did not show a significant and persistent decrease. In contrast, drinking by mothers of junior high school boys increased (Table 6). In the results of multiple logistic regression analyses, family drinking was detected as an important risk factor for adolescent drinking in every survey. Especially, the magnitude of the relative risk of an older brother's drinking, older sister's drinking, and mother's drinking on adolescent drinking was relatively larger than that of father, and the influence of a mother's drinking on the population attributable risk percent was largest. The population attributable risk percent by a father's drinking for boys decreased in 2004 in comparison to that in 2000 (Table 6).

The proportion of students who reported that they had no friends was initially quite low, but suddenly increased in 2004 (Table 6). In the multiple logistic regression analyses, the factor was observed as a preventive factor for adolescent drinking. Although the magnitude of the population attributable risk percent was low, the relative risks were statistically significant.

DISCUSSION

Although Japan enacted the Act to Prohibit Minors from alcohol use enacted in 1990 prohibiting the consumption of alcohol by minors under age 20 years, some nationwide surveys have observed many adolescent drinkers among high school students (Osaki et al., 2003; Suzuki et al., 2003). On the other hand, the prevalence of alcohol use among adolescents in Japan is at an extremely low level in comparison to that in European and North American countries (CDC, 2006a; Currie et al., 2004; Hibell et al., 1996, 2000, 2004; Johnston et al., 2002; King et al., 1996; National Centre for Social Research, 2006).

This study provides the first evidence of a decrease in drinking prevalence among Japanese adolescents. The 2000 survey showed a decrease in lifetime drinking rate among junior high school boys only, and no decrease was observed in the lifetime drinking prevalence among girls or in regular drinking prevalence among both sexes. This study confirmed a decrease in lifetime, current, and weekly drinking rates in both sexes among junior and senior high school students in the 2004 survey. The results of this study show that the low drinking rate became lower.

Since drinking behavior is closely related to the culture, religion, or other social factors, the prevalence of alcohol use is much different from country to country. In recent years, a decrease in drinking prevalence among adolescents has been observed in some countries, including the United States, Finland, and Sweden. However, the majority of the world has not observed any decrease in drinking prevalence (CDC, 2006a; Hibell et al., 2004).

In the analyses for the causes of the change in prevalence, some change was observed in the characteristics of drinking behavior. Many researchers have reported a relationship between adolescent drinking behavior and drinking by parents or friends (Latendresse et al., 2008; Scholte et al., 2008; Seljamo et al., 2006; Webb and Baer, 1995; van der Vorst et al., 2006; Yeh, 2006). This study, also observed that family drinking behavior was closely related to students' alcohol use, and the drinking prevalence among male family members (father and senior brother) decreased with survey by survey. Since the population attributable risk percents of family members were high in this study, the decrease in the drinking prevalence among family probably contribute to the change in drinking prevalence among students. Some other surveys observed the decrease in the drinking prevalence of adults in the Japanese general population. The decrease includes an age-effect where the drinking prevalence decreases with aging and a cohort effect where the drinking prevalence of the younger generation is lower at a specific age. The observation on cohort effect indicates the decrease of drinking prevalence among the parents of high school students. Thus, health education on alcohol use toward adult population is continuing important to prevent drinking by minors.

The limitations of sources of alcohol beverages also contributed to the decrease of the drinking prevalence. The proportion of current drinkers who buy their alcohol beverages from a supermarket, convenience store, liquor shop or vending machine, or drink at a bar has decreased survey by survey. According to the revision of the Act to Prohibit Minors from alcohol use in 2000, the penalty for selling alcoholic beverages to minors was reinforced. Besides, the law was revised again in 2001 for the reinforcement of the age confirmation by the liquor distributors. After 2000, the number of alcohol vending machines has decreased by the self-regulation of the alcohol industry (Higuchi et al., 2006). These factors may have contributed to the limitation of the sources of alcohol beverages.

In 2004 survey, the proportion of students who had no friends increased. Since many researchers reported that drinking behavior of friends was strongly associated with adolescent drinking behavior (Epstein et al., 1999; Heeb et al., 2003; Johansen et al., 2006; Scholte et al., 2008), the increase with proportion of students who had no friends may mean the decrease of peer pressure to initiate drinking. This may also contribute to the decrease in the drinking prevalence among students.

This study indicated some encouraging changes in the surveys, however, some remaining problems were also observed. One problem is that the difference in drinking prevalence between fathers and mothers has shrunk survey by survey. Since the relative risk of mother's drinking on adolescent drinking was large, the influence on the adolescent drinking behavior may overcome the influence by other family

members before long. Other problem is the spreading inequity of health related behaviors among adolescents. The smoking prevalence among current drinkers did not change during the surveys, whereas that among nondrinkers decreased. The lifestyle of nondrinkers has become healthier, whereas that of drinkers has not changed in spite of the decrease in the number of adolescent drinkers. Besides, the prevalence of alcohol-related problems among adolescent drinkers has not changed. Problem drinking during adolescence is considered to be an important predictor for the onset of alcoholism. Therefore, both preventing alcohol use among minors and intervention for adolescents with problematic drinking behavior are necessary to improve their lifestyle and to prevent future adult alcohol-related problems and increased rates of alcoholism.

In addition, a rapid change of type of popular alcoholic beverages among adolescents was observed. In other words, the proportion of drinkers who drink alcopop or shochu has increased survey by survey. This may be indirect evidence that adolescents are more likely to be affected by the marketing of alcoholic beverages by the companies.

In Japan, there are still some problematic situations concerning minors drinking, such as the low price of alcohol beverages (less than 1 US$ for the cheapest beer or alcopop), the popularity of alcopop among both sexes, and many TV commercials for alcoholic beverages. It is expected that the alcohol consumption among adolescents will increase with the reduction in the price of alcohol beverages (Heeb et al., 2003). Periodical nationwide surveys on adolescent drinking and survey of environmental factors (TV CM, drinking scenes in TV drama, comics or movie, advertisements in magazines, and sponsorship of many events by the alcohol industry) are necessary to deal with the social problems of adolescent drinking.

A limitation of this study is the possible biased subjects, namely 30 to 35% of sampled schools did not respond to these surveys. However, characteristics of responding schools did not seriously different from those of nonresponding schools. It is difficult to estimate the effect of the relatively low response rate in urban schools in the junior high school. Since this tendency was consistent over the surveys, a major problem does not occur to interpret trends in study findings. Moreover, the response rate of these surveys did not have inferiority in comparison with the response rate of surveys in Western countries (CDC, 2006a). It is important and significant to continue conducting the periodical nationwide survey, even if the survey includes some methodological problems.

COMPETING INTERESTS

None declared.

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Association Between Personality Traits and ALDH2 Polymorphism in Japanese Male Alcoholics

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Background: Alcoholics who have developed alcoholism despite a strong negative risk factor, that is, the inactive form of aldehyde dehydrogenase-2 (ALDH2), are considered advantageous for studying predisposing factors for alcoholism. This study aimed to compare personality profiles and clinical characteristics between alcoholics with active and inactive ALDH2.

Methods: Subjects were 460 male Japanese alcoholics hospitalized in Kurihama Alcoholism Center. All patients underwent Cloninger's Tridimensional Personality Questionnaire and semi-structured interviews 4 to 8 weeks after admission to obtain data on personalities and clinical characteristics. ALDH2 genotypes were determined by polymerase chain reaction-RFLP. Sixty-six patients had the inactive form of ALDH2 (ALDH2*1/2*2) and 394 had the active form (ALDH2*1/2*1).

Results: Alcoholics with inactive ALDH2 had significantly higher novelty-seeking (NS) and lower harm-avoidance (HA) scores compared with those with active ALDH2. The inactive ALDH2 group experienced delirium tremens significantly less frequently than the active ALDH2 group.

Conclusions: These results suggest that high NS and low HA scores in alcoholics with inactive ALDH2 are associated with an increased risk for developing alcoholism, despite a low enzymatic ability to eliminate toxic acetaldehyde in these subjects. A study of alcoholics with inactive ALDH2 is useful for detecting environmental or personality factors related to alcoholism.

Key Words: Aldehyde Dehydrogenase, Polymorphism, Personality, Tridimensional Personality Questionnaire, Alcohol Dependence.

ALCOHOLISM IS A heterogeneous and multifactorial disorder consisting of several subtypes associated with different genetic, environmental, and temperamental backgrounds. Identifying predisposing factors for alcoholism can help prevent alcohol-related problems, lead to individualized treatments, and elucidate the mechanisms underlying the disease.

Studies have shown an association between personality and alcohol use disorders (Mulder, 2002). Most studies used dimensional scales that assess several aspects of personality, for example, Eysenck's Personality Questionnaire (EPQ) and Cloninger's Tridimensional Personality Questionnaire (TPQ) (Cloninger, 1987b). Both EPQ and TPQ are self-rating questionnaires that yield 3 scores to describe personality dimensions. EPQ provides scores for neuroticism, extraversion, and psychoticism, and TPQ provides scores for novelty-seeking (NS), harm-avoidance (HA), and reward-dependence (RD). Such dimensional studies have provided much-needed information about alcoholism. First, case–control studies show that NS and sensation-seeking are generally higher in alcoholics than non-alcoholics (Grucza et al., 2006; Heath et al., 1997; Ravaja and Keltikangas-Jarvinen, 2001; Van Ammers et al., 1997). However, some studies that compared children of alcoholics with children without a family history of alcoholism failed to show significant differences in these personality factors (Howard et al., 1997; Zaninelli et al., 1992). Second, HA and neuroticism are associated with alcoholism, but results of studies are mixed. Neuroticism, which is similar to HA in concept, is typically higher in alcoholics than in non-alcoholics (Mullan et al., 1986). Compared with controls, HA scores are lower in early onset alcoholism (Cloninger et al., 1988; Wills et al., 1994) or those with adolescent substance use (Masse and Tremblay, 1997). However, some studies suggest high HA scores are associated with alcoholism (Meszaros et al., 1996). Finally, results regarding RD and extraversion in alcoholics are unclear; most studies have reported no differences between alcoholics and controls.

Thus, in spite of the number of studies, a personality profile associated with alcoholism is not well established. One of the major obstacles in identifying such a personality profile is that alcoholism is a heterogenic disease. The variety of subtypes

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associated with different personality characteristics makes it difficult to identify a particular factor related to alcoholism.

A study using a population of alcoholics with the inactive form of aldehyde dehydrogenase-2 (ALDH2), a characteristic that should lead to less drinking, may address the heterogeneity problem. The polymorphism of ALDH2 is a well-known genetic determinant of the risk for alcoholism. Inactive ALDH2 causes a high acetaldehyde level after drinking, resulting in symptoms such as flushing, nausea, and headache, which suppress drinking behavior (Higuchi et al., 1996; Muramatsu et al., 1995) and the occurrence of alcoholism (Harada et al., 1982; Higuchi et al., 1994). The homozygotes of the inactive type of ALDH2 allele (ALDH2*2) prevent individuals from becoming alcoholics, and the incidence of alcoholism among heterozygotes of the ALDH2 allele is much lower than among homozygotes of the active ALDH2 allele (ALDH2*1). Patients with the inactive ALDH2 who develop alcoholism must have some other factors that drive them to drink. It would be advantageous to study personality factors among these subjects because they show reduced heterogeneity and possess factors conferring susceptibility to alcoholism.

We hypothesized that personality traits associated with alcoholism could be elucidated by finding characteristics of alcoholics with inactive ALDH2. This study aimed to identify the clinical and personality profile of alcoholics with inactive ALDH2 compared with those with active ALDH2.

SUBJECTS AND METHODS

Subjects

This study was approved by the Ethics Committee of the National Hospital Organization, Kurihama Alcoholism Center. All subjects gave informed consent. Subjects were 460 Japanese male alcoholics (mean age ± SD: 50.3 ± 8.5 years). All subjects were hospitalized at Kurihama Alcoholism Center. First, 444 subjects participated in this study regardless of ALDH2 genotype (mean age ± SD: 50.2 ± 8.4 years). An additional 16 alcoholics with the inactive form of ALDH2 genotype were recruited to increase the statistical power of the study. These 16 subjects were also patients hospitalized at Kurihama Alcoholism Center (mean age ± SD: 53.3 ± 10.6 years).

All patients underwent semi-structured interviews between 4 and 8 weeks after admission to obtain personal and familial information. The Structured Clinical Interview for DSM-IIIR assessment was also performed, and all subjects met DSM-IIIR diagnostic criteria for alcohol dependence.

Measure of Personality

Personality traits were assessed using the TPQ. TPQ is a self-rating questionnaire that consists of 100 true-false items. The patients completed a written Japanese-translated TPQ questionnaire between 4 and 8 weeks after admission. All patients were fully abstinent from alcohol for at least 4 weeks before completing the questionnaire.

Genotyping

Aldehyde dehydrogenase-2 genotyping was performed by a previously described polymerase chain reaction (PCR)-restriction fragment length polymorphism method (Crabb et al., 1989). Briefly, peripheral blood was obtained from each subject and leukocyte DNA was extracted. Portions of exon 12 of the ALDH2 gene were amplified using PCR, digested with *Mbo*II, electrophoresed on 12% acrylamide gel, and viewed with the aid of ethidium bromide staining.

Statistical Analysis

Differences in clinical backgrounds were tested using the chi-squared test. Differences in TPQ scores and age were tested using the *t*-test. Data were considered statistically significant if the $p < 0.05$.

RESULTS

In the first 444 subjects, 50 had ALDH2*1/2*2 genotype (inactive ALDH2) and 394 had ALDH2*1/2*1 (active ALDH2); none of them had ALDH2*2/2*2. After the 16 subjects with ALDH2*1/2*2 genotype were added, the total number of inactive and active ALDH2 group were 66 and 394, respectively.

Comparisons of TPQ scores in each group are shown in Table 1. NS score was significantly higher in the inactive ALDH2 group than in the active ALDH2 group ($p = 0.022$). In contrast, the HA score was significantly lower in the inactive ALDH2 group than in the active ALDH2 group ($p = 0.017$). There were no differences in RD scores between groups.

The clinical backgrounds of subjects with active and inactive ALDH2 are shown in Table 2. The mean age of onset of alcoholism did not differ significantly between groups. The percentage of patients with first-degree relatives with alcohol-related problems was lower in the inactive ALDH2 group (6.1%) than in the active ALDH2 group (13.7%), but the difference did not reach statistical significance ($\chi^2 = 3.0$, df = 1, $p = 0.083$). Significantly fewer patients in the inactive ALDH2 group had experienced delirium tremens com-

Table 1. Tridimensional Personality Questionnaire Scores of Alcoholic Subjects With Active and Inactive ALDH2

	Inactive ALDH2 ($n = 66$)	Active ALDH2 ($n = 394$)	p
Novelty seeking*	20.6 ± 5.0	19.0 ± 5.2	0.022
Harm avoidance**	18.8 ± 6.0	20.7 ± 6.3	0.017
Reward dependence	14.7 ± 3.9	14.6 ± 3.5	0.92

ALDH, aldehyde dehydrogenase. *$t = 2.3$, df = 458, $p = 0.022$; **$t = 2.4$, df = 458, $p = 0.017$.

Table 2. Clinical Backgrounds of Alcoholic Subjects With Active and Inactive ALDH2

	Inactive ALDH2 ($n = 66$)	Active ALDH2 ($n = 394$)	p
Age of onset, mean ± SD, years	41.0 ± 10.0	39.3 ± 10.7	0.23
Familial alcohol-related problems, %	6.1	13.7	0.083
Antisocial personality disorder, %	1.5	3.6	0.38
History of delirium tremens*, %	22.7	36.0	0.035

ALDH, aldehyde dehydrogenase. *$\chi^2 = 4.5$, df = 1, $p = 0.035$.

pared with patients in the active ALDH2 group (22.7% vs. 36.0%; $p = 0.035$). The frequency of comorbid antisocial personality disorder (ASPD) did not differ between groups.

DISCUSSION

Results of this study show that high NS and low HA scores were associated with an increased risk for alcoholism in alcoholics with inactive ALDH2. A low activity of acetaldehyde elimination causes toxic effects after alcohol intake; these effects tend to prevent people with inactive ALDH2 from drinking heavily. Patients who continue drinking despite these toxic effects are considered to have stronger factors that induce alcoholism. Our results imply that high NS and low HA scores are predisposing factors for alcoholism in subjects with active ALDH2 as well as in those with inactive ALDH2.

High NS and low HA scores reflect impulsive, danger-seeking, and aggressive personalities, which are considered to be associated with addiction-related behavior. People with such personality profiles would seek intoxicating activities and risk-taking behavior and be less likely to mind the suffering induced by the flushing response caused by drinking. These results support other studies that indicate that high NS and low HA scores are related to behaviors associated with alcoholism. High NS scores or sensation-seeking has been reported to be associated with alcoholism and substance use disorders (Grucza et al., 2006; Heath et al., 1997), but the association between HA and alcoholism is less clear. Cloninger proposed 2 prototypic groups of alcoholism: type I and type II. Type I alcoholism is defined by late onset, low familial alcoholic history, guilt related to alcohol use, and minimal criminality; type II alcoholism is associated with an earlier onset, a high genetic influence, spontaneous alcohol-seeking behavior, and frequent criminality (Cloninger, 1987a). They assessed TPQ scores among each type and reported that type II alcoholism was characterized by higher NS and lower HA scores.

The personality profile of the inactive ALDH2 group in this study revealed a similar pattern to Cloninger's type II alcoholism, but some features differed between type II alcoholics and inactive-ALDH2 alcoholics. Although type II alcoholics are characterized by young onset, frequent familial history, and high co-occurrence of ASPD, the age of onset and occurrence of ASPD among the inactive ALDH2 group was the same as the active ALDH2 group. The frequency of familial alcohol-related problems tended to be lower in the inactive ALDH2 group. These results suggest that alcoholics with inactive ALDH2 represent a different group from type II alcoholics. This hypothesis is supported by a study that showed no differences in ALDH2 genotype distribution between type I and type II alcoholism (Chai et al., 2005).

This study also presents new information on the different clinical backgrounds of alcoholics with active and inactive ALDH2. Little is known regarding clinical and temperamental characteristics of ALDH2-inactive alcoholics. A recent study compared alcohol outcome expectancies, assessed by the Alcohol Expectancies Scale, between active and inactive ALDH2 genotypes. Results showed that the negative alcohol expectancies scale was lower and the positive alcohol expectancies scale was higher in alcoholics with inactive ALDH2 than in those with active ALDH2 (Hahn et al., 2006). Murayama et al. (1998) reported that the development of alcoholism was delayed among patients with inactive ALDH2 compared with patients with active ALDH2, but our results failed to show a significant difference in the age of onset between groups. Our study did show that the inactive ALDH2 group less frequently experienced delirium tremens and were less likely to have a history of familial alcohol-related problems compared with the active ALDH2 group. It is possible that the difference in frequency of delirium tremens might be caused by a decreased quantity of alcohol consumption in the inactive ALDH2 group. It is well known that inactive ALDH2 reduces alcohol consumption in healthy people; however, a recent study of alcoholic patients suggested there was no difference in alcohol consumption between those with active and inactive ALDH2 (Hahn et al., 2006). However, the study's sample size was so small that it could only be considered a preliminary study. More research is necessary on alcohol consumption among alcoholics with each ALDH2 genotype.

The most likely explanation for lower tendency of familial history in inactive ALDH2 compared with active ALDH2 is that the relatives of patients with inactive ALDH2 also have a higher frequency of the inactive ALDH2 genotype rather than the active ALDH2 genotype; however, it is unlikely that alcoholics with inactive-ALDH2 have a stronger genetic predisposition even if the hereditary effect is discounted.

Results that alcoholics with the inactive ALDH2 genotype have different characteristics from those with active ALDH2 support the hypothesis that alcoholics with inactive ALDH2 are an advantageous model—with higher homogeneity—for studying risk factors associated with alcoholism. A typology of substance-related disorders should meet with 4 criteria: (1) homogeneity within categories (2) stability over time (3) comprehensive coverage of the alcoholic population (4) high constructive, discriminative, and predictive validity (Babor et al., 1992; Epstein et al., 2002) Typologies using a genetic polymorphism such as the ALDH2 active/inactive model are considered stable over time and easy to discriminate. The drawback of this classification is that it includes a limited alcoholic population. Only 10% of Asian alcoholics have inactive ALDH2, and there are no individuals with inactive ALDH2 in Caucasian populations (Agarwal and Goedde, 1992). In contrast to our expectation that this model might be a useful method for determining genetic factors associated with alcoholism, our results indicated that alcoholics with inactive ALDH2 had a lower family history of alcoholism than those with active ALDH2. It is more likely that alcoholics with inactive ALDH2 represent a promising model for detecting environmental or personality factors related to alcoholism as opposed to genetic factors.

The classification by ALDH2 as active or inactive might help predict treatment outcome and individualize treatment. Recent studies reported an association between gene variation and treatment outcome of psychosocial therapies and medication (Anton et al., 2008; Bauer et al., 2007). The application of genetic variants to selection of treatment is a hopeful way to improve the efficacy of treatment for alcoholism. If personality characteristics are different between alcoholics with active and inactive ALDH2, outcomes for different treatments, such as psychosocial treatments or medications, may vary as well. For example, the personality pattern of high NS and low HA scores, seen in alcoholics with inactive ALDH2 in this study, might reduce the efficacy of disulfiram or cyanamide, which blocks the catalytic activity of ALDH. Patients with such personality traits are likely to try to drink even though they are being treated with disulfiram or cyanamide, similar to the way that alcoholics with inactive ALDH2 continue to drink despite the uncomfortable experience induced by high acetaldehyde concentrations in the blood. Little is known about the treatment outcome among patients with inactive ALDH2 and the association between disulfiram efficacy and patients' background. Further study is needed to select the best treatment for each patient type.

There are several limitations to the generalization of these results. First, this study does not compare alcoholics with normal controls. A number of case–control studies have tried to determine the personality that makes people vulnerable to alcoholism, but results have been inconsistent. One of the possible reasons for these inconsistencies is that groups of patients and normal controls contain heterogenic subjects with different personalities. Furthermore, some studies recruit control subjects from a specific area, for example, students or hospital employees; these control populations could differ from the general population. The comparison of alcoholics with active and inactive ALDH2 could highlight differences in the personalities that predispose subjects to alcoholism because both groups contain hospitalized alcoholics. However, results do not necessarily reflect other general populations. Second, this study includes only male, Japanese subjects. Characteristics of alcoholics differ between male and females and among ethnic groups. Thus, our findings cannot be generalized to all alcoholics. In addition, the information on personality and clinical background obtained in this study was limited. Further study that includes female subjects and detailed analyses are necessary.

In conclusion, high NS and low HA scores were associated with an increased risk for alcoholism in alcoholics with inactive ALDH2, which suggests high NS and low HA might be predisposing factors for alcoholism. Alcoholics with inactive ALDH2 revealed a low familial history of alcoholism and a low incidence of delirium tremens. These results suggest that a model of alcoholics with inactive versus active ALDH2 is useful for detecting environmental or personality factors related to alcoholism.

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