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Association between lower estimated premorbid intelligence quotient and smoking behavior in patients with schizophrenia

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ABSTRACT

Aim: We aimed to investigate the involvement of premorbid intelligence quotient in higher prevalence of smoking in patients with schizophrenia.

Methods: Participants included 190 patients with schizophrenia (mean ± standard deviation age: 37.7 ± 10.8 years; 88 males and 102 females) and 312 healthy individuals (mean ± standard deviation age: 38.1 ± 13.8; 166 males and 146 females), matched for age, sex, and ethnicity (Japanese). Premorbid intelligence quotient was estimated using the Japanese Adult Reading Test and distress symptoms were assessed using the Hopkins Symptom Check List. Current smoking information was collected according to self-declarations.

Results: As expected, the smoking rate was higher, while mean education level and Japanese Adult Reading Test scores were significantly lower, in patients with schizophrenia than in healthy individuals ($p < 0.01$). The mean education level and Japanese Adult Reading Test scores were significantly lower in the smoker group than in the non-smoker group in both patients and healthy individuals ($p < 0.05$). In the patient group alone, Hopkins Symptom Check List subscale and total scores were significantly higher in the smoker group than in the non-smoker group ($p < 0.05$). A multivariate regression analysis showed that the Japanese Adult Reading Test score was a significant and negative predictor for smoking ($p < 0.001$, odds ratio = 0.97; 95% confidence interval: 0.96–0.99).

Conclusion: Our results suggest that lower estimated premorbid intelligence quotient is an important variable in elucidating smoking behavior in humans and may be associated with higher prevalence of smoking in patients with schizophrenia.

1. Introduction

Health risk behaviors, including cigarette smoking, have been suggested to be associated with symptoms or level of functioning in patients with schizophrenia (Cerimele and Katon, 2013). A higher prevalence of smoking has been reported in mental disorders (Leonard et al., 2001; Graham et al., 2007), especially in schizophrenia (De Leon and Diaz, 2005). Concerning the higher prevalence of smoking in schizophrenia, several hypotheses have been presented in neuropharmacological and psychosocial literature (Mobascher and Winterer, 2008; Sagud et al., 2009; Winterer, 2010; Peckham et al., 2016); however, the reason remains still unclear. As smoking habits have been reported to be associated with medical morbidity and mortality in patients with schizophrenia (Goff et al., 2005a, 2005b; Dickerson et al., 2018), it is important to consider any approach to minimalize the habit.

Gender, age, marital status, use of alcohol and typical antipsychotics, duration of illness, hospitalizations, and negative symptoms were associated with current smoking behaviors in Chinese inpatients with schizophrenia (Xu et al., 2014). In a French cohort, positive symptoms and antipsychotic dose were positively associated, while

Abbreviations: ANCOVA, Analysis of covariance; CI, Confidence interval; HSCL, Hopkins Symptom Check List; IQ, Intelligence quotient; JART, Japanese Adult Reading Test; MANCOVA, Multivariate analysis of covariance; NART, National Adult Reading Test; OR, Odds ratio; PANSS, Positive and Negative Syndrome Scale; PSQI, Pittsburgh Sleep Quality Index

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education level, negative symptoms, and anticholinergic agents were negatively associated, with the frequency of tobacco use (Mallet et al., 2017). Among the patients with schizophrenia, smokers showed lower cognitive functions (Zhang et al., 2012; Dickerson et al., 2016), although a possible effect of premorbid intelligence quotient (IQ) was not accounted for. However, when premorbid IQ and years of education were controlled for, no differences were observed in the analysis of cognitive function between smokers and non-smokers among first-episode psychosis patients (Hickling et al., 2018). Furthermore, lower white matter fractional anisotropy in the smoking group of patients with schizophrenia was not observed if lower IQ was corrected for as a covariate (Cullen et al., 2012). These suggest potential associations between IQ status and smoking.

There are numerous risks contributing to the vulnerability of schizophrenia onset, including tobacco use, low education level (Fusar-Poli et al., 2017), and premorbid IQ (Davis et al., 2016). The prevalence of smoking was associated with lower IQ at ages 18 to 20, which disappeared after adjustment for mental and social circumstances in early-life (Hemmingsson et al., 2008). In patients with schizophrenia, poor premorbid school performance (Riala et al., 2005) and social adjustment (Kelly and McCreadie, 1999) were associated with later smoking habits, although the studies did not include information about IQ. Lower education level in schizophrenia was also associated with current smoking behavior (Tang et al., 2007; Dickerson et al., 2013). Interestingly, initiation of regular smoking was earlier than age of schizophrenia onset in male patients (Ma et al., 2010) and the first frank episode of psychotic symptoms (Hickling et al., 2018).

Although several studies have suggested that earlier functioning is involved in smoking habits in patients with schizophrenia (Kelly and McCreadie, 1999; Riala et al., 2005), the relationship between estimated premorbid IQ and smoking behavior has not been examined using an objective tool such as the Japanese Adult Reading Test (JART). To elucidate the fact that habitual smoking is often comorbid with schizophrenia, we aimed to investigate the association between JART-predicted premorbid IQ and smoking. Moreover, we examined whether smoking behavior was associated with psychic symptoms and other clinical features in patients with schizophrenia and healthy individuals. Here we tested the hypothesis that estimated premorbid IQ and psychic symptoms were associated with the smoking behavior in patients with schizophrenia.

2. Methods

2.1. Participants

Participants comprised 190 patients with schizophrenia (mean ± standard deviation age: 37.7 ± 10.8 years; 88 males and 102 females) and 312 healthy individuals (mean ± standard deviation age: 38.1 ± 13.8; 166 males and 146 females), matched for age, sex, and ethnicity (Japanese). Information with respect to smoking was based on self-reports of those who were currently smoking. All participants were enrolled through recruitment forms at the National Center of Neurology and Psychiatry, advertisements in free magazines, and our website announcement. The participants were screened for axis I psychiatric disorders by trained psychiatrists using the Japanese version of the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998; Otsubo et al., 2005). The diagnosis was made according to the Diagnostic and Statistical Manual of Mental Disorders (fourth edition) criteria (American Psychiatric Association, 1994), based on the information from the Mini-International Neuropsychiatric Interview and medical records, if available. All healthy individuals were confirmed to have no axis I psychiatric disorders and had never received psychiatric services, while those who exhibited nicotine dependence were not eliminated. Participants with a medical history of neurological diseases, severe head injury, substance abuse, or mental retardation were excluded. All participants signed consent forms after explanation of the study content. The study protocol was approved by the ethics committee at the National Center of Neurology and Psychiatry and complied with the Declaration of Helsinki (World Medical Association, 2013).

2.2. Clinical and psychological assessments

Premorbid IQ was estimated by trained psychologists using the JART, which was developed as an alternative version of the National Adult Reading Test (NART) (Matsuoka et al., 2006). We used the face-to-face version consisting of 100 Kanji compound words. The Hopkins Symptom Check List (HSCL) (Derogatis et al., 1974; Lipman et al., 1979) and the Japanese version of Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989; Doi et al., 2000) were used to evaluate self-rated distress symptoms and sleep quality, respectively. Psychotic symptoms of patients were evaluated by trained psychiatrists using the Japanese version of the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987; Igarashi et al., 1998) and were represented by the scores of the five-factor model (van der Gaag et al., 2006a, 2006b). Daily doses of antipsychotics were converted to chlorpromazine-equivalent doses, in accordance with the Japanese guideline (Inada and Inagaki, 2015).

2.3. Statistical analyses

Continuous and categorical variables were compared between the patients and healthy individuals, or between smoker and non-smoker groups using unpaired *t*- and χ^2-tests, respectively. Correlations between the JART scores and clinical variables were assessed with Pearson's and Spearman's correlation coefficients for continuous and categorical variables, respectively. Among continous variables, the mean education level and JART, HSCL, PSQI, and PANSS (only for patients) scores were compared between smoker and non-smoker groups using a multivariate analysis of covariance (MANCOVA), controlling for age, sex, and psychotropic medication use (only for patients). Then, the mean education level and JART scores were compared using a two-way (diagnosis × smoking) analysis of covariance (ANCOVA), controlling for age and sex. For all participants, a logistic regression analysis was performed using the forced entry method, in which smoking was an objective variable and schizophrenia diagnosis, age, sex, mean education level, JART score, and HSCL total score were explanatory variables. Then, separate logistic regression analyses, based on diagnostic group, were performed using a stepwise (forward selection) method, in which smoking was an objective variable and all the clinical variables of the diagnostic group were explanatory variables. Effect sizes were calculated by r for the *t*-test, φ for the χ^2-test, and η^2 for the MANCOVA and ANCOVA tests. Goodness of fit for the logistic regression analysis was assessed using the Hosmer-Lemeshow test. Statistical analyses were performed using the Statistical Package for the Social Sciences version 25.0 (SPSS Japan, Tokyo, Japan). All statistical tests were two-tailed, and a p value < 0.05 was deemed significant.

3. Results

Demographic and clinical characteristics of the participants are shown in Table 1. As expected, the rate of smoking was significantly higher in patients with schizophrenia compared to healthy individuals ($p = 0.0014$, odds ratio [OR] = 2.03, 95% confidence interval [CI]: 1.31–3.14). The mean education level and JART scores were also significantly lower in the patients than in the healthy individuals ($p < 0.001$). PSQI and all HSCL scores were significantly higher in the patients than in the healthy individuals ($p < 0.001$).

Correlations between JART scores and clinical variables in patients with schizophrenia are shown in supplementary Table S1. Smoking was significantly and negatively correlated ($p = 0.005$), while mean

Table 1
Demographic and clinical characteristics of the participants.

	Patients with schizophrenia (n = 190)		Healthy individuals (n = 312)		
	Mean ± standard deviation	Range	Mean ± standard deviation	Range	Statistical comparison
Age (years)	37.7 ± 10.8	18–77	38.1 ± 13.8	18–75	Welch's t (468.8) = 0.39, p = 0.70, r = 0.02
Sex, female (%)	102 (53.7)		146 (46.8)		$\chi^2(1)$ = 2.24, p = 0.13, φ = −0.07
Smoking (%)	53 (27.9)		50 (16.0)		$\chi^2(1)$ = 10.20, $\boldsymbol{p}$ = **1.4.E-3**, φ = 0.14, odds ratio = 2.03, 95% confidence interval: 1.31–3.14
Education (years)	13.8 ± 2.4	6–20	15.2 ± 2.3	9–22	Student's t (500) = 6.58, $\boldsymbol{p}$ = **1.2.E-10**, r = 0.28
Japanese Adult Reading Test	71.6 ± 16.6	25–98	80.4 ± 11.4	39–100	Welch's t (299.3) = 6.43, $\boldsymbol{p}$ = **5.0.E-10**, r = 0.35
Pittsburgh Sleep Quality Index	7.9 ± 3.7	0–20	5.3 ± 2.7	0–15	Welch's t (311.3) = −8.42, $\boldsymbol{p}$ = **1.4.E-15**, r = 0.43
Hopkins Symptom Check List					
Somatization	25.5 ± 8.0	1–49	19.2 ± 4.8	14–45	Welch's t (271.4) = −9.73, $\boldsymbol{p}$ = **2.1.E-19**, r = 0.51
Obsessive-compulsivity	22.4 ± 6.5	9–36	16.4 ± 5.4	9–36	Welch's t (348.0) = −10.60, $\boldsymbol{p}$ = **6.1.E-23**, r = 0.50
Interpersonal sensitivity	22.0 ± 6.7	10–38	15.8 ± 5.4	9–37	Welch's t (338.1) = −10.70, $\boldsymbol{p}$ = **3.4.E-23**, r = 0.50
Anxiety	16.8 ± 6.1	8–31	10.6 ± 3.4	8–28	Welch's t (260.7) = −12.82, $\boldsymbol{p}$ = **1.6.E-29**, r = 0.62
Depression	28.1 ± 9.1	13–86	19.1 ± 5.9	13–46	Welch's t (284.3) = −12.18, $\boldsymbol{p}$ = **9.3.E-28**, r = 0.59
Total	114.9 ± 32.0	54–217	81.2 ± 21.9	54–177	Welch's t (297.3) = −12.80, $\boldsymbol{p}$ = **3.5.E-30**, r = 0.60Welch's t (297.3) = −12.80, $\boldsymbol{p}$ = **3.5.E-30**, r = 0.60
Positive and Negative Syndrome Scale five factor					
Negative	16.5 ± 7.0	5–36			
Positive	15.1 ± 6.1	5–35			
Excitement	12.8 ± 4.1	8–32			
Emotional distress	15.5 ± 5.5	8–33			
Disorganization	19.8 ± 6.2	10–42			
Age of onset (years)	23.5 ± 7.7	5–56			
Duration of illness (years)	14.0 ± 9.4	0.5–47			
Chlorpromazine-equivalent dose (mg/day)					
Typical antipsychotics	131.9 ± 258.9	0–2845.5			
Atypical antipsychotics	357.7 ± 427.5	0–1362.5			
Total antipsychotics	493.5 ± 467.2	0–2845.5			
Antiparkinson medication use (%)	74 (38.9)				
Minor tranquilizer use (%)	117 (61.6)				
Any psychotropic medication use (%)	168 (88.4)				

Significant p-values are shown in bold exponents.

education level was significantly and positively correlated ($p < 0.001$), with the JART score. For psychotropic medications, the use of chlorpromazine-equivalent atypical and total antipsychotics, minor tranquilizers, and any psychotropics was significantly and negatively correlated with the JART score ($p < 0.01$). Correlations between JART scores and clinical variables in healthy individuals are shown in supplementary Table S2. Sex and smoking were significantly and negatively correlated (p = 0.020 and 0.046), while mean education level was significantly and positively correlated ($p < 0.001$), with the JART score.

Comparisons of clinical variables between the smoker and non-smoker groups in patients with schizophrenia are shown in Table 2. As expected, there were significantly fewer female participants in the smoker group compared to the non-smoker group (p = 0.034, OR = 0.49, 95% CI: 0.25–0.95). Notably, MANCOVA revealed that the mean education level and JART scores were significantly lower in the smoker group than in the non-smoker group (p = 0.049 and 0.007; Fig. 1). HSCL somatization, obsessive-compulsivity, anxiety, depression, and total scores were significantly higher in the smoker group than in the non-smoker group ($p < 0.05$), while there were no significant differences regarding PSQI and PANSS five factor scores. Comparisons of clinical variables between the smoker and non-smoker groups in healthy individuals are shown in Table 3. Female participants were also significantly fewer in the smoker group compared to the non-smoker group ($p < 0.001$, OR = 0.25, 95% Cl: 0.13–0.49), and this difference was more marked in this group compared to the patient group. The MANCOVA revealed that the mean education level and JART scores were also significantly lower in the smoker group than in those in the non-smoker group (p = 0.021 and 0.00025; Fig. 1). There were no significant differences in PSQI and any HSCL scores. The mean education level and JART scores of the different groups are summarized in supplementary Table S3. As expected, both two-way ANCOVAs revealed that schizophrenia diagnosis and smoking had a significant and negative association with the mean education level and JART scores ($p < 0.01$).

Lastly, a logistic regression analysis regarding smoking using the forced entry method is shown in Table 4. Among the forced-entered explanatory variables, sex (p = 0.0000029, OR = 0.31, 95% CI: 0.19–0.51) and JART score (p = 0.00071, OR = 0.97, 95% CI: 0.96–0.99) were significant and negative predictors for smoking, while no significant association between smoking and schizophrenia diagnosis or mean education level was observed. Separate logistic regression analyses regarding smoking, based on diagnostic group, using the stepwise method are shown in supplementary Table S4. Among all the clinical variables observed in patients, sex (p = 0.046, OR = 0.50, 95% CI: 0.25–0.99) and JART score (p = 0.013, OR = 0.98, 95% CI: 0.96–1.00) were significant and negative predictors, while HSCL depression score (p = 0.045, OR = 1.04, 95% CI: 1.00–1.08) was a significant and positive predictor, for smoking. Similarly, among all the clinical variables observed in healthy individuals, sex (p = 0.00001, OR = 0.20, 95% CI: 0.10–0.41) and JART score (p = 0.00041, OR = 0.95, 95% CI: 0.93–0.98) were significant and negative predictors for smoking.

4. Discussion

As expected, the rate of smoking was higher, while the mean education level and JART scores were lower, in patients with schizophrenia

Table 2
Comparisons of clinical variables between the smoker and non-smoker groups in patients with schizophrenia.

	Patients with schizophrenia							
	Smoker (n = 53)				Non-smoker (n = 137)			
	Mean ± standard deviation			Range	Mean ± standard deviation			Range	Statistical comparison
Age (years)	39.3	±	9.7	26–68	37.1	±	11.2	18–77	Student's t (188) = −1.26, p = 0.20, r = 0.092
Sex, female (%)	18 (34.0)				70 (51.1)				$\chi^2(1)$ = 4.51, $\boldsymbol{p}$ = **0.034**, φ = 0154, odds ratio = 0.49, 95% confidence interval: 0.25–0.95
Education (years)	13.3	±	2.4	9–19	14.0	±	2.4	6–20	F(1, 185) = 3.92, $\boldsymbol{p}$ = **0.049**, η^2 = 0.021
Japanese Adult Reading Test	66.2	±	16.8	25–91	73.7	±	16.1	27–98	F(1, 185) = 7.45, $\boldsymbol{p}$ = **0.007**, η^2 = 0.037
Pittsburgh Sleep Quality Index	8.7	±	3.4	3–18	7.6	±	3.7	0–20	F(1, 185) = 2.84, p = 0.094, η^2 = 0.015
Hopkins Symptom Check List									
Somatization	27.5	±	8.0	14–43	24.7	±	7.9	1–49	F(1, 185) = 5.83, $\boldsymbol{p}$ = **0.017**, η^2 = 0.031
Obsessive-compulsivity	23.7	±	5.7	12–34	21.9	±	6.7	9–36	F(1, 185) = 3.90, $\boldsymbol{p}$ = **0.050**, η^2 = 0.021
Interpersonal sensitivity	22.8	±	6.5	10–34	21.7	±	6.8	10–38	F(1, 185) = 2.11, p = 0.15, η^2 = 0.011
Anxiety	18.0	±	5.7	8–29	16.3	±	6.2	8–31	F(1, 185) = 3.96, $\boldsymbol{p}$ = **0.048**, η^2 = 0.021
Depression	30.5	±	11.0	15–86	27.1	±	8.1	13–46	F(1, 185) = 6.52, $\boldsymbol{p}$ = **0.011**, η^2 = 0.034
Total	122.5	±	32.1	62–217	112.0	±	31.6	54–192	F(1, 185) = 5.62, $\boldsymbol{p}$ = **0.019**, η^2 = 0.029
Positive and Negative Syndrome Scale five factor									
Negative	17.1	±	7.0	5–36	16.2	±	7.0	7–35	F(1, 185) = 0.51, p = 0.48, η^2 = 0.003
Positive	16.2	±	6.3	5–27	14.7	±	5.9	6–35	F(1, 185) = 2.58, p = 0.11, η^2 = 0.014
Excitement	13.2	±	4.5	8–32	12.7	±	3.9	8–23	F(1, 185) = 0.56, p = 0.46, η^2 = 0.003
Emotional distress	16.4	±	5.4	8–27	15.2	±	5.5	8–33	F(1, 185) = 2.33, p = 0.13, η^2 = 0.013
Disorganization	20.1	±	5.5	11–32	19.7	±	6.5	10–42	F(1, 185) = 0.00, p = 0.99, η^2 = 0.001
Age of onset (years)	23.9	±	6.8	5–46	23.3	±	8.1	14–56	Student's t (187) = −0.47, p = 0.64, r = 0.035
Duration of illness (years)	14.6	±	8.7	4–39	13.8	±	9.7	0.5–47	Student's t (187) = −0.52, p = 0.60, r = 0.038
Chlorpromazine-equivalent dose (mg/day)									
Typical antipsychotics	99.6	±	202.6	0–903.0	145.0	±	278.2	0–2845.5	Welch's t (131.1) = 1.08, p = 0.22, r = 0.094
Atypical antipsychotics	399.9	±	422.8	0–2000	340.7	±	429.8	0–1362.5	Student's t (183) = −0.85, p = 0.40, r = 0.063
Total antipsychotics	499.5	±	449.5	0–2250	491.1	±	475.7	0–2845.5	Student's t (183) = −0.11, p = 0.91, r = 0.009
Antiparkinson medication use (%)	20 (37.7)				54 (39.4)				$\chi^2(1)$ = 0.13, p = 0.72, φ = −0.026
Minor tranquilizer use (%)	37 (69.8)				80 (58.4)				$\chi^2(1)$ = 1.52, p = 0.22, φ = 0.090
Any psychotropic medication use (%)	49 (92.5)				122 (89.1)				$\chi^2(1)$ = 0.49, p = 0.48, φ = 0.051

Significant p-values are shown in bold cases.

than in healthy individuals. For the patients, the mean education level and JART scores were lower and HSCL scores were higher in the smoker group than in the non-smoker group. For the healthy individuals, the mean education level and JART scores were lower in the smoker group than in the non-smoker group. Furthermore, a logistic regression analysis showed that JART score, but not the mean education level, was a negative predictor for smoking. To the best of our knowledge, these findings for the first time suggest that lower JART-predicted premorbid

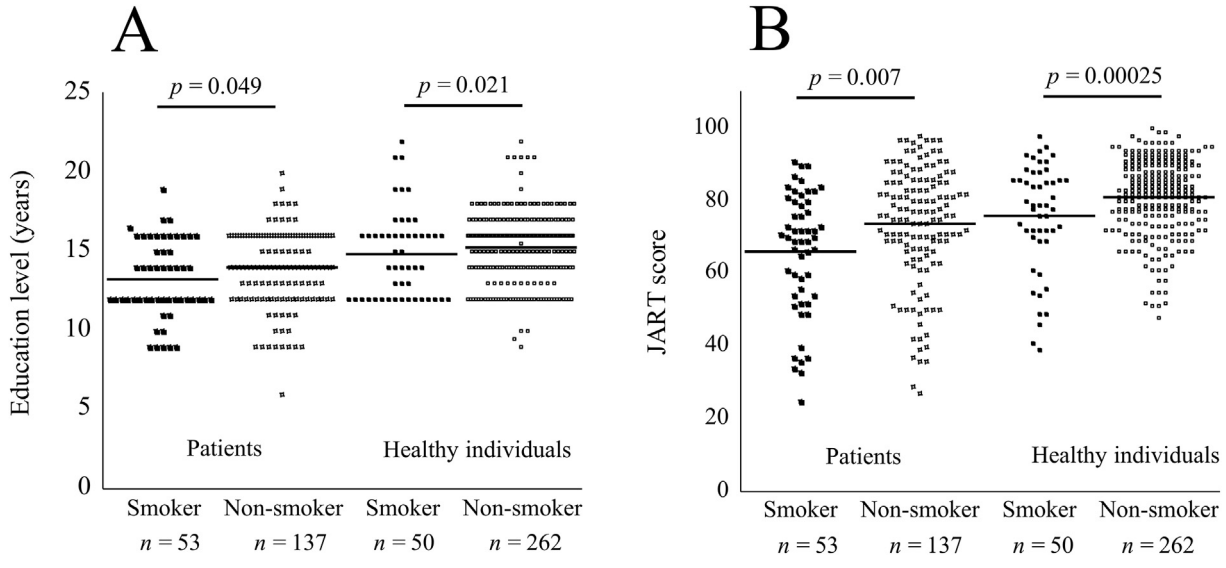

Fig. 1. Dot plots of comparisons in the education level and Japanese Adult Reading Test (JART) scores between smokers and non-smokers.
The education level was significantly lower in the smoker group than in the non-smoker group in both patients with schizophrenia and healthy individuals (η^2 = 0.021 and 0.016, A). The JART scores were also significantly lower in the smoker group than in the non-smoker group in both patients and healthy individuals (η^2 = 0.037 and 0.042, B). Horizontal lines in dot plots indicate mean scores.

Table 3
Comparisons of clinical variables between the smoker and non-smoker groups in healthy individuals.

	Healthy individuals							
	Smoker (n = 50)				Non-smoker (n = 262)			
	Mean ± standard deviation			Range	Mean ± standard deviation		Range	Statistical comparison
Age (years)	37.8	±	11.1	20–67	38.2	± 14.3	18–75	Welch's t (83.1) = 0.24, p = 0.81, r = 0.027
Sex, female (%)	13 (26.0)				153 (58.4)			$\chi^2(1)$ = 17.70, $\boldsymbol{p}$ = **2.6.E-5**, φ = −0.238, odds ratio = 0.25, 95% confidence interval: 0.13–0.49
Education (years)	14.8	±	2.7	12–22	15.3	± 2.2	9–22	F(1, 308) = 5.39, $\boldsymbol{p}$ = **0.021**, η^2 = 0.016
Japanese Adult Reading Test	76.0	±	14.9	39–98	81.2	± 10.5	48–100	F(1, 308) = 13.74, $\boldsymbol{p}$ = **2.5.E-4**, η^2 = 0.042
Pittsburgh Sleep Quality Index	5.1	±	2.6	0–11	5.4	± 2.7	0–15	F(1, 308) = 0.34, p = 0.56, η^2 = 0.002
Hopkins Symptom Check List								
Somatization	18.2	±	4.1	14–34	19.4	± 4.8	14–45	F(1, 308) = 0.84, p = 0.36, η^2 = 0.003
Obsessive-compulsivity	15.5	±	4.8	9–26	16.6	± 5.6	9–36	F(1, 308) = 1.86, p = 0.17, η^2 = 0.006
Interpersonal sensitivity	15.2	±	4.6	10–31	16.0	± 5.6	9–37	F(1, 308) = 0.41, p = 0.52, η^2 = 0.002
Anxiety	9.8	±	2.2	8–17	10.8	± 3.5	8–28	F(1, 308) = 2.41, p = 0.12, η^2 = 0.008
Depression	17.9	±	4.4	13–29	19.3	± 6.1	13–46	F(1, 308) = 0.73, p = 0.39, η^2 = 0.003
Total	76.7	±	16.9	55–119	82.0	± 22.7	54–177	F(1, 308) = 0.34, p = 0.56, η^2 = 0.005

Significant p-values are shown in bold cases.

IQ is associated with smoking behavior in humans, including the higher prevalence of smoking in patients with schizophrenia.

For patients, the mean education level and JART scores were lower, while the HSCL scores were higher, in the smoker group than in the non-smoker group. In addition to schizophrenia onset risks, such as lower educational level (Fusar-Poli et al., 2017) and premorbid IQ (Davis et al., 2016), among patients with schizophrenia who were smokers, the education level and estimated premorbid IQ was even lower. Our data are consistent with those of previous works, which state that lower education level (Tang et al., 2007; Dickerson et al., 2013; Mallet et al., 2017; Hickling et al., 2018) and premorbid functions (Kelly and McCreadie, 1999; Riala et al., 2005) in schizophrenia are associated with smoking habits, although some studies reported no difference in the education level (Ma et al., 2010; Zhang et al., 2012; Xu et al., 2014) and estimated premorbid IQ (Sanchez-Gutierrez et al., 2018) between smokers and non-smokers among patients with schizophrenia. The smokers in the patient group showed higher HSCL scores, suggesting more severe distress symptoms. This is in line with a study that reports higher Symptom Checklist-90 scores, a measure of psychiatric symptoms, were observed in patients with schizophrenia who were smokers (Li et al., 2017). In contrast, PANSS scores were not different between the smoker and non-smoker groups; this finding was inconsistent with those of other studies showing higher PANSS (Xu et al., 2014) and positive (Mallet et al., 2017) scores in patients with schizophrenia who were smokers.

For healthy individuals, the mean education level and JART scores were lower in the smoker group than in the non-smoker group. Our results are consistent with a lower education level observed in smokers (Winkleby et al., 1995; Azevedo e Silva et al., 2009). Since JART-predicted premorbid IQ nearly coincides with the current IQ in the normal population (Matsuoka et al., 2006), our results are also consistent with those of studies that report that higher prevalence of smoking is associated with the IQ status (Hemmingsson et al., 2008; Weiser et al., 2010; Modig et al., 2011). Moreover, two-way ANCOVAs revealed that schizophrenia diagnosis and smoking behavior were negatively associated with both the mean education level and JART scores. These suggest that smokers generally show lower education level and estimated premorbid IQ, which is particularly marked in patients with schizophrenia. In addition, our data showed that smokers have higher distress symptoms, but only in the patient group, suggesting that smoking may be a stress-coping behavior against higher psychological distress associated with more severe premorbid IQ limitations. Alternatively, it is also possible that smoking contributes to higher psychological distress. Taken together, these may result in a vicious circle.

A multivariate regression analysis revealed that JART scores, but not mean education level or schizophrenia diagnosis, was a significant predictor for smoking. This suggests that estimated premorbid IQ, rather than education level, is a significant index to explain smoking behavior, although JART scores positively correlated with the mean education level in both patients and healthy individuals. Schizophrenia diagnosis was also not significant in the regression analysis, suggesting that the association between estimated premorbid IQ and smoking is a trend commonly observed in humans, and not specifically relegated to patients with schizophrenia; this is in line with the earlier time-course of smoking initiation, rather than disease onset (Ma et al., 2010; Hickling et al., 2018). Stepwise regression analyses based on diagnostic group supported that JART-predicted premorbid IQ, but not education

Table 4
A logistic regression analysis regarding smoking using the forced entry method.

	B	p	Odds ratio	95% confidence interval	Hosmer-Lemeshow test
Schizophrenia diagnosis	0.17	0.56	1.18	0.67–2.10	$\chi^2(8)$ = 7.21, p = 0.51
Age (years)	0.00	0.77	1.00	0.99–1.02	
Sex	−1.16	**2.9.E-06**	0.31	0.19–0.51	
Education (years)	−0.06	0.28	0.94	0.85–1.05	
Japanese Adult Reading Test	−0.03	**7.1.E-04**	0.97	0.96–0.99	
Hopkins Symptom Check List total	0.00	0.42	1.00	1.00–1.01	
(Constant)	1.66	0.13	5.29		

Sex was coded as male: 1 and female: 2.
Significant p-values are shown in bold exponents.

level, is a significant predictor for smoking in both patients and healthy individuals. In addition, the male sex was the strongest predictor for smoking in the regression analyses, especially in healthy individuals. This is probably related to cultural factors, in that smoking behavior and its sex differences are diverse among ethnicities (Alvarado and Breslau, 2005; Harding et al., 2015; Higgins et al., 2015). This study presented data about smoking in patients with schizophrenia and healthy individuals of Japanese ethnicity, and the findings are consistent with a prior Japanese study which also reported that the male sex was most strongly associated with smoking (Shinozaki et al., 2011).

For treatment, smoking cessation may ameliorate physical comorbidity and premature mortality because patients with schizophrenia were able to receive the cessation advice (Tidey and Miller, 2015; Mitchell et al., 2015). However, nicotine dependence or addiction in schizophrenia has been an issue related to difficulty in smoking cessation (Dalack et al., 1998; Sharma and Vijayaraghavan, 2008; Aubin et al., 2012). Regarding mental health, medications targeted for nicotinic acetylcholine receptor have been mostly non-effective in improving cognitive function in schizophrenia (Rowe et al., 2015), which is reasonable considering the premorbid IQ limitations in schizophrenia. However, a prospective study reported poorer cognitive performance in smokers, with improved processing speed after smoking cessation in patients with schizophrenia, though information about premorbid IQ was not included (Vermeulen et al., 2018). In another study, parts of the PANSS score were improved after the use of varenicline, which decreased measures of smoking (Smith et al., 2016). Although this study seems to be less significant than our previous findings about cognition in schizophrenia (Hidese et al., 2018), it will be useful in elucidating the importance of smoking cessation in improving physical health, especially for patients with lower estimated premorbid IQ. Use of pharmacotherapy, for smoking cessation, will also be useful in promoting their physical health (Shawen and Drayton, 2018).

This study has several limitations. First, a large proportion of the patients had taken some form of psychotropic medication, which might have influenced their HSCL, PSQI, and PANSS scores, even though this was adjusted in the MANCOVA tests. Second, the JART is used as an equivalent to the NART, which has been validated to estimate premorbid IQ because reading ability is relatively intact during the progression of schizophrenia (Dalby and Williams, 1986; Morrison et al., 2000). However, there may be discrepacies between JART scores and early academic performance other than reading abilities, considering that the correlation between IQ at age 11 and NART score at elderly ages (McGurn et al., 2004) was lower than that between current IQ and JART score in elderly individuals (Matsuoka et al., 2006). As reported in a NART study (Schretlen et al., 2005), JART score can be used as a proxy for premorbid IQ, but will be relatively higher than the premorbid IQ itself. Additionally, JART-predicted premorbid IQ in schizophrenia may include cognitive deficits before the onset of frank psychosis as suggested in a meta-analytic review (Woodberry et al., 2008) and a prospective cohort study (Meier et al., 2014). Third, determinations of current smoking were based on participants' self-reports; therefore, our data did not include information about the onset and number of recurrences of smoking, and amount and lifetime use of tobacco. Finally, the design of this cross-sectional study cannot address the causality of the results; namely, although premorbid IQ is usually determined before the onset of smoking, it is difficult to confirm that lower estimated premorbid IQ is a reason why patients with schizophrenia habitually smoke. Moreover, multiple cross-sectional variables in this study, especially the education level, correlated with the JART score, suggesting the apparent interaction between educational attainment and estimated premorbid IQ. In addition to a previous study for the general population (Hemmingsson et al., 2008), future longitudinal studies in patients with schizophrenia will be required to draw conclusions on the causality.

5. Conclusion

In conclusion, the mean education level and JART scores were lower in the smoker group than in the non-smoker group among both patients with schizophrenia and healthy individuals. HSCL scores were higher in the smoker group than in the non-smoker group in only the patient group. In the logistic regression analyses, JART score, but not the mean education level, was a negative predictor for smoking behavior in both patients with schizophrenia and healthy individuals. These results suggest that the estimated premorbid IQ is an important variable in elucidating smoking behavior, and may be associated with the higher prevalence of smoking in patients with schizophrenia.

Conflicts of interest

All authors declare no conflicts of interest.

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Author contributions

SH designed, and HK supervised the study. JM, II, and MH assessed estimated premorbid IQ, distress symptoms, and sleep states by the JART, HSCL, and PSQI, respectively. SH, TT, MO, and KH determined psychiatric diagnoses and evaluated symptoms by the PANSS. SH performed the statistical analysis and wrote the draft of the manuscript. All authors have approved the final manuscript.

Disclosure statement

All authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scog.2018.09.003.

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