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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