Determinants of work outcome in neuroleptic-resistant schizophrenia and schizoaffective disorder: Cognitive impairment and clozapine treatment

Yasuhiro Kaneda a,⁎, Karuna Jayathilak b, Herbert Meltzer b

a Department of Psychiatry, Iwaki Clinic, Anan, Tokushima, Japan
b Department of Psychiatry, Vanderbilt University School of Medicine, Nashville, TN, USA

关键词:

文章历史:

接收 28 九月 2008
接收后修订 29 九月 2009
接受 15 四月 2009

目的

在神经科耐药性精神分裂症和双相情绪障碍中，认知障碍是工作和社交功能的重要决定因素。认知功能，特别是言语工作记忆，可能在治疗耐药性精神分裂症和双相情绪障碍患者中，更好地预测工作状况和工作能力的获得。治疗增强认知功能，特别是言语工作记忆，可能在治疗耐药性精神分裂症和双相情绪障碍患者中，更好地预测工作和社交功能。

1. 引言

在神经科耐药性精神分裂症和双相情绪障碍中，认知功能，特别是言语工作记忆，可能在治疗耐药性精神分裂症和双相情绪障碍患者中，更好地预测工作状况和工作能力的获得。治疗增强认知功能，特别是言语工作记忆，可能在治疗耐药性精神分裂症和双相情绪障碍患者中，更好地预测工作和社交功能。
verbal fluency and some types of verbal learning and memory and executive function, but not working memory (Hagger et al., 1993; Lee et al., 1994; Lee et al., 1999; Meltzer and McGurk, 1999). The goal of this prospective study was to test the hypotheses that (1) the clozapine treatment would improve employment outcome in treatment-resistant patients with schizophrenia or schizoaffective disorder, and (2) specific types of cognitive impairment but not psychotic symptoms in patients with schizophrenia would predict work status and that improvement in verbal memory and executive function in particular would predict improvement in employment status. In this study, treatment-resistant patients were chosen because clozapine use has generally been restricted to treatment-resistant patients with schizophrenia or schizoaffective disorder due to its ability to cause agranulocytosis.

2. Methods

2.1. Subjects
This study was conducted at Vanderbilt University. Data available from a prior prospective study (Gold et al., 2000) was used to test our hypotheses. Fifty-nine patients who met Diagnostic and Statistical Manual of Mental Disorders, third edition, Text Revision (DSM-III-R) (American Psychiatric Association, 1987) criteria for schizophrenia or schizoaffective disorder were included in this study. History of patients’ response to antipsychotic treatment was assessed at the outset through intensive interviewing of the probands, first-degree relatives and other informants, as well as a review of hospital records. Treatment–resistance status was determined according to the criteria of Kane et al. (1978). Patients with a significant current history of substance abuse/dependence, seizure or radiologically confirmed head injury/malformation were excluded from the study. The patients were interviewed with the Schedule for Affective Disorders and Schizophrenia Lifetime (SADS-L) and Change (SADS-C) versions (Endicott and Spitzer, 1978) to establish diagnoses. The Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962; Overall and Gorham, 1962;0 1978) was also employed to evaluate severity of psychopathology. Work status was defined as follows: 1. Employed = full-time (minimum of 30 h/week or full-time student status) or part-time (1–29 h/week or part-time student status); and 2. Unemployed = unemployed and not in school. Before admission to the study, informed written consent was obtained from all patients after the procedure had been fully explained. Demographic data are presented in Table 1.

Forty-eight (81.4%) patients were drug-free at least 5 days before baseline evaluation. Baseline assessments of the measures described above and cognitive function were performed. Patients were subsequently treated with clozapine. All patients were treated with the same measures after 12 months.

2.2. Treatment

2.2.1. Drug treatment
The drug treatment was carried out on an open basis because of the unreliability of maintaining masking during clozapine treatment. Thirty-nine of 59 (52.5%) patients required concomitant medications; 10 (16.5%) patients received benzotropine, 13 used lorazepam for psychomotor agitation, two received clozaepine and two received aminergic medications (metoclopramide and hydrochlorothiazide), one received chloral hydrate for insomnia, one received diclofenac for irritable bowel syndrome and one patient received ranitidine for ulcers. Four patients received fludrocortisone, two patients received divalproex, two patients received triptophan, one patient received sertraline and one patient received anafamid in addition to antipsychotic agents. The dosages of clozapine at 12 months were 422.4 mg/day (SD = 190.4 mg/day).

2.2.2. Psychosocial treatment
Patients received an intensive psychosocial treatment programme, which included group and multifamily therapy on a weekly basis throughout the course of the study. The nurse therapist who led these groups also provided a work readiness-training programme on both an individual and group basis for the treatment-resistant subjects. This included obtaining clerical tasks needed by the hospital and supervising the work of the patients in carrying out these jobs.

2.3. Cognitive tests
We used a cognitive test battery as described elsewhere (Kenny and Meltzer, 1991), consisting of the following measures: (1) a measure of psychomotor speed and attention (Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digit Symbol Substitution Test (DSST; Wechsler, 1981)); (2) verbal working memory (Consonant Trigram Test (CTT; Peterson and Peterson, 1959)); (3) verbal fluency (Controlled Word Association Test (CWAT; Benton et al., 1983) and the Category Instance Generation Test (CIGT; Talland, 1965)); (4) verbal learning and memory (Verbal List Learning (VLL); Immediate Recall (VLL-IR) and Delayed Recall (VLL-DR; Buschke and Fuld, 1974)); and (5) executive function (Wisconsin Card Sorting Test (WCST); category (CAT) and perseveration (PP; Berg, 1948); Wechsler Intelligence Scale for Children-Revised (WISC-R) Maze (Wechsler, 1974)). The neuropsychological tests were factor analysed into three factors: memory (CTT, VLL-IR, VLL-DR and WISC-R Maze), attention (DSST, CWAT and CIGT) and executive function (WCST) (Meltzer et al., unpublished results). These tests were administered by a psychologist who was not blind to the nature of drug treatment. An estimated intelligence score was obtained using WAIS-R.

2.4. Statistical methods
Data analysis was conducted using the SAS (Version 8.2, SAS institute, 1999) software. The comparison of categorical responses to employment groups was carried out using chi-square tests. T-test analyses for independent group comparisons were used to compare differences in psychopathology and cognitive variables on employment status at baseline and at 12 months between two groups of patients (patients who remained unemployed and patients who gained employment). Moreover, the differences in psychopathology and cognition variables at 12 months between three groups of patients (patients that remained unemployed, patients that remained gain non-competitive employment and patients that gained competitive employment) were compared by analysis of variance (ANOVA), followed by post hoc comparisons. Improvement of psychopathology and cognition over time across groups was analysed using a repeated-measure ANOVA model. A logistic regression model with forward selection criteria was used to predict employment status and change in employment at different time points (dichotomous response) using demographic variables, improvement in psychopathology and cognitive measures. A P-value of less than 0.05 was considered significant, and the statistical tests were two-sided.

3. Results

3.1. Changes in employment status
After 12 months, employment outcome had significantly improved from 20.3% (12/59) at baseline to 50.8% (30/59) [χ² = 12.0, df = 1, P = 0.001]. Out of 47 patients, 23 (48.9%) who were unemployed at baseline became employed during the 12 months period. One, eight and 12 patients gained paid full-time, paid part-time jobs and unpaid volunteer work respectively. One patient went back to school as a part-time student, and one patient undertook a vocational education programme. When the patients with unpaid employment (i.e., volunteer) were excluded, 15 (25.4% vs. 16.9% at baseline) patients had become competitively employed. Meanwhile, five of 12 (41.7%) patients employed at baseline became unemployed during the 12-month period.

3.2. Differences in baseline variables between unemployed and employed patients at baseline

Patients who were unemployed at baseline were significantly older [t = 2.64, df = 38, P = 0.01] and showed a trend towards a longer duration of illness [t = 1.99, df = 57, P = 0.05] than those who were employed (Table 2). Comparisons of these two groups revealed significantly better baseline scores in the employed group for the BPRS total [t = 2.02, df = 52, P = 0.04] and positive scores [t = 2.85, df = 52, P = 0.01]. There was a trend towards a higher WISC-R Maze score in the employed group [t = −1.65, df = 52, P = 0.10].

3.3. Predictors of work status at baseline

The logistic regression analysis used a forward stepwise procedure to predict work status at baseline from variables including baseline

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic information at baseline (n = 59).</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>35.6 (8.9)</td>
</tr>
<tr>
<td>Gender (Female/male)</td>
<td>35/64</td>
</tr>
<tr>
<td>Race (African American/Caucasian/others)</td>
<td>8/50/1</td>
</tr>
<tr>
<td>Age of illness onset (yrs)</td>
<td>19.6 (4.7)</td>
</tr>
<tr>
<td>Duration of illness (yrs)</td>
<td>16.0 (7.8)</td>
</tr>
<tr>
<td>Years of education (yrs)</td>
<td>12.4 (2.3)</td>
</tr>
<tr>
<td>Number of times hospitalised</td>
<td>8.6 (6.4)</td>
</tr>
<tr>
<td>IQ</td>
<td>90.8 (15.8)</td>
</tr>
</tbody>
</table>
دریافت فوری
متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات