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ORIGINAL RESEARCH

Symptom predictors of response to electroconvulsive therapy in older patients with treatment-resistant depression

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Background: Electroconvulsive therapy (ECT) has been used for treatment-resistant depression. However, predictors of response to ECT have not been adequately studied using the Montgomery and Åsberg Depression Rating Scale, especially in older patients with treatment-resistant depression.

Methods: This study included 18 Japanese patients who fulfilled the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition Text Revision criteria for a diagnosis of major depressive disorder or bipolar disorder with a current major depressive episode, and met the definition of treatment-resistant depression outlined by Thase and Rush, scoring ≥21 on the Montgomery and Åsberg Depression Rating Scale. The three-factor model of the Montgomery and Åsberg Depression Rating Scale was used for analysis. Factor 1 was defined by three items, factor 2 by four items, and factor 3 by three items, representing dysphoria, retardation, and vegetative symptoms, respectively. ECT was performed twice a week for a total of six sessions using a Thymatron System IV device with the brief pulse technique. Clinical responses were defined on the basis of a ≥50% decrease in total pretreatment Montgomery and Åsberg Depression Rating Scale scores.

Results: The mean pretreatment factor 2 score for responders (n = 7) was significantly lower than that for nonresponders (n = 11). Furthermore, a significant difference in mean factor 3 score between responders and nonresponders was observed one week after six sessions of ECT, indicating a time lag of response. No significant differences were observed for age, number of previous episodes, and duration of the current episode between responders and nonresponders.

Conclusion: This study suggests that a low pretreatment factor 2 score is a good predictor of response to ECT in older patients with major depression.

Keywords: factor analysis, electroconvulsive therapy, refractory depression, Montgomery and Åsberg Depression Rating Scale, predictors of response

Introduction

Electroconvulsive therapy (ECT) has been used for treatment-resistant depression. In a recent report, 50%–60% of patients with treatment-resistant depression responded to ECT.[1,2] Response rates have also been reported for older patients. For example, Tew et al reported that adult patients (≥59 years of age) had a significantly lower rate of response than young-older patients (60–74 years), while old-older patients (≥75 years) had an intermediate rate of response.[3] There has been some concern about factors predictive of response to ECT in the treatment for depression, and symptom predictors of response to ECT based on the Montgomery and Åsberg Depression Rating

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Scale (MADRS) have not been well studied, especially in old patients with treatment-resistant depression.

The MADRS is a 10-item clinical rating scale that measures the severity of several depressive symptoms.[4] Recently, Suzuki et al[5] analyzed pretreatment MADRS scores in 132 Japanese patients with major depressive disorder and followed the three-factor model of the MADRS: factor 1, defined by three items representing dysphoria, ie, reported sadness, pessimistic thoughts, and suicidal thoughts; factor 2, defined by four items representing retardation, ie, lassitude, inability to feel, apparent sadness, and concentration difficulties; and factor 3, defined by three items representing vegetative symptoms, ie, reduced sleep, reduced appetite, and inner tension.

Our recent preliminary research suggested that a higher score on factor 1 was a good predictor of response to ECT in patients with treatment-resistant depression.[6] We recruited a further group of old patients and reanalyzed the effects of differences in response to ECT in old patients with treatment-resistant depression (n = 18) by using the three-factor MADRS structure proposed by Suzuki et al.[5]

Methods

Subjects

This study was conducted at St Marianna University School of Medicine between March 2008 and January 2009. We included 18 Japanese patients who fulfilled the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition Text Revision (DSM-IV) criteria for a diagnosis of major depressive disorder (n = 16) or bipolar disorder (n = 2) with a current major depressive episode, and had a total pretreatment MADRS score ≥21. Patients with other axis I disorders (including schizophrenia, dementia, substance abuse, dysthymia, panic disorder, obsessive-compulsive disorder, and generalized anxiety disorder) and axis II disorders, as determined by a clinical interview, were excluded. Patients with severe nonpsychiatric physical disease were also excluded. Cognitive deficits were evaluated by mini-mental state examination, and patients with a pretreatment score ≤23 were also excluded.

Patients aged 60–83 years for whom ECT was planned were entered in the study. An independent psychiatrist recommended ECT because of drug resistance, according to clinical judgment. Drug resistance was defined as failure to respond to at least three courses of antidepressant medication of adequate dose and duration (ie, the stage 3 definition of Thase and Rush).[7] Patients were maintained on the same drug treatment for at least one week before ECT and during the entire study period. This study was approved by the bioethics committee of the St Marianna University School of Medicine. The purpose of the study and its methods were explained to all patients and their families, and written informed consent was obtained from all participants.

ECT treatment

A medical history and physical examination, together with routine blood and urine investigations, an electrocardiogram, a cerebral computed tomography scan, and a chest film were used to screen for general medical conditions. Patients were anesthetized with propofol 1.0–1.5 mg/kg, and muscle relaxation was achieved using suxamethonium 0.8–1 mg/kg. ECT was performed between 9.30 am and 11.30 am using a brief bipolar pulse from a constant-current Thymatron System IV machine (Somatics Inc, Lake Bluff, IL). ECT was given twice a week over six sessions. The number of ECT sessions was based on a report by Weiner et al.[8] If the response was inadequate at the end of the assessment period, further ECT sessions were added by the treating psychiatrist. Seizure threshold was determined at the first treatment using an empirical titration procedure.[9] Stimulus electrode placement was on the bifrontotemporal scalp. ECT treatment conditions were set up in a preset stimulation program to "Low 0.5," which delivers a 0.5 ms brief pulse that automatically adjusts the frequency to maximize stimulus train duration at each dose. Motor convulsion, electroencephalography, induced tachycardia, and electromyography were recorded during ECT. An ictal response was identified by convulsive motor activity and/or electroencephalographic changes. ECT was completed on the basis of the clinical judgment of the treating psychiatrist.

Data collection

The characteristics and severity of depressive symptoms were assessed by total and three-factor scores on MADRS. The patients were assessed pretreatment, following six sessions of ECT, and one week after the final ECT session. Clinical responses were defined on the basis of a ≥50% decrease in total pretreatment MADRS score. An independent psychiatrist not directly involved in clinical management of the patients completed the ratings. Data were collected for various demographic and illness variables, including gender, age, number of previous depressive episodes, duration of current episode, presence or absence of psychotic symptoms, age at onset of mental illness, medication history, and medication during the ECT course.

Statistical analysis

The clinical characteristics of the patients, including responders and nonresponders, were analyzed by Chi-square test or unpaired *t*-test, as appropriate. Two-way repeated-measures analysis of variance was used to compare total, factor 1, factor 2, and factor 3 MADRS scores in responders and nonresponders pretreatment, post-treatment, and one week after treatment. In addition, a receiver-operating characteristic (ROC) analysis was performed to estimate the cut point for factor 2.

Results

Patient characteristics are shown in Table 1. Seven patients were responders and 11 were nonresponders. Mean total MADRS score and three-factor MADRS scores pretreatment, post-treatment, and one week after completion of ECT for the responders and nonresponders are shown in Table 2. No significant difference was observed in total pretreatment ($F = 3.394$, $P = 0.0841$), factor 1 ($F = 0.211$, $P = 0.6525$), and factor 3 ($F = 1.149$, $P = 0.2998$) MADRS score between the responders and nonresponders. However, the mean pretreatment factor 2 score of the responders was significantly lower than that of nonresponders ($F = 9.001$, $P < 0.05$). The optimal cut point for the factor 2 score was 19 (sensitivity 0.91, specificity 0.71) on the ROC curve, for which the value of the area under the curve was 0.82 (95% confidence interval 0.64–1.01).

On completion of ECT, significant differences were observed in total ($F = 11.452$, $P = 0.0038$), factor 1 ($F = 7.258$, $P = 0.0160$), and factor 2 ($F = 14.732$, $P = 0.0015$) MADRS scores between responders and nonresponders. No significant difference was observed for post-treatment factor 3 ($F = 4.177$, $P = 0.0578$) MADRS score between responders and nonresponders.

One week after completion of ECT, significant differences were observed in total ($F = 16.345$, $P = 0.0009$), factor 1 ($F = 7.346$, $P = 0.0154$), factor 2 ($F = 18.536$, $P = 0.0005$), and factor 3 ($F = 12.726$, $P = 0.0026$) MADRS scores between responders and nonresponders. As a result, the mean value for factor 3 (vegetative symptoms) improved for the first time at this point, which indicates a time lag in response.

Discussion

The present study shows that the mean pretreatment factor 2 (retardation) score of responders was significantly lower than that of nonresponders. However, Hickey et al suggested that the response to ECT was associated with severe psychomotor disturbance in adult patients.[10] Buchan et al also suggested that adult patients who suffered from depression in which retardation and delusions were features had a significantly improved outcome at the end of four weeks of ECT treatment.[11] Therefore, it may be that a lower score for psychomotor retardation (factor 2) is a useful index for predicting efficacy of ECT in older patients with depression, but not in younger adult patients. The optimal cut point on factor 2 obtained using ROC analysis might be helpful for

Table 1 Clinical characteristics of total patients, responders and nonresponders

	Total (n = 18)	Responders (n = 7)	Nonresponders (n = 11)	Analysis	*P* value
Gender (male/female)	4/14	1/6	3/8	$x^2 = 0.57$	0.45
Age (years)	70.9 ± 6.91	72.3 ± 8.8	70.0 ± 0.6	$t = 0.67$	0.51
Number of previous depressive episodes	4.2 ± 2.7	3.6 ± 2.0	4.6 ± 3.0	$z = -0.54$	0.59
Duration of current episode (months)	8.0 ± 14.4	2.7 ± 2.0	11.4 ± 17.8	$z = -1.22$	0.22
MADRS scores	44.7 ± 7.5	40.9 ± 9.4	47.1 ± 5.0	$z = -1.40$	0.16
MMSE scores	25.8 ± 2.5	25.8 ± 3.1	25.8 ± 2.2	$z = -0.26$	0.80
Psychotic symptoms (%)	66.67	71.43	63.63	$x^2 = 0.12$	0.73
Age at onset of mental illness (years)	55.72 ± 13.70	58.29 ± 13.64	54.09 ± 14.15	$t = 0.62$	0.54
Antidepressants administered		Clomipramine 25–75 mg (n = 4) Dosulepin 50 mg (n = 1) Mianserin 20 mg (n = 1) Paroxetine 10 mg (n = 1)	Clomipramine 25–75 mg (n = 2) Dosulepin 100 mg (n = 1) Mianserin 20–60 mg (n = 3) Milnacipran 50 mg (n = 2) Paroxetine 10–20 mg (n = 2) Sertraline 100 mg (n = 1)		

Notes: Data are expressed as mean ± SD; comparisons were made between the responders and nonresponders using the χ^2 test, unpaired *t*-test, and Mann–Whitney U test.
Abbreviations: MMSE, minimental state examination; MADRS, Montgomery and Åsberg Depression Rating Scale; SD, standard deviation.

Table 2 Mean total, factor 1, factor 2, and factor 3 MADRS scores in responders (n = 7) and nonresponders (n = 11) to electroconvulsive therapy

	Pre-ECT	Post-ECT	One week after ECT
Total MADRS			
Responders	40.9 ± 9.4	12.3 ± 7.2	7.1 ± 2.9
Nonresponders	47.1 ± 5.0	24.9 ± 8.0	19.4 ± 7.6
P	0.0841	0.0038[b]	0.0009[b]
Factor 1			
Responders	12.1 ± 2.6	3.7 ± 2.2	2.4 ± 1.3
Nonresponders	12.7 ± 2.6	6.7 ± 2.4	5.4 ± 2.7
P	0.6525	0.0160[a]	0.0154[a]
Factor 2			
Responders	17.3 ± 4.2	5.6 ± 3.3	3.6 ± 1.8
Nonresponders	21.5 ± 1.6	12.7 ± 4.1	10.2 ± 3.8
P	0.0085[a]	0.0015[a]	0.0005[b]
Factor 3			
Responders	11.4 ± 3.0	3.0 ± 2.2	1.1 ± 0.9
Nonresponders	12.9 ± 2.8	5.5 ± 2.7	3.8 ± 1.8
P	0.2998	0.0578	0.0026[b]

Notes: [a]$P < 0.05$; [b]$P < 0.01$.
Abbreviations: ECT, electroconvulsive therapy; MADRS, Montgomery and Åsberg Depression Rating Scale.

clinicians when deciding whether to use ECT in older patients with treatment-resistant depression.

Our recent report suggested that a higher score for factor 1 (dysphoria) is a good predictor of efficacy of ECT.[7] In contrast with our previous study, the mean factor 1 score was not significantly different between responders and nonresponders in this study. The reason for this discrepancy is unknown. The effect of small sample is undeniable. Salzman reported that the cardinal sign of depression in older patients may be the absence of positive affect rather than the presence of dysphoria.[12] Therefore, this discrepancy may be due to the absence of prominent dysphoria in depressed older patients.

There have been several studies of predictors of efficacy of ECT. Some have found that a shorter duration of the current episode is associated with a better response to ECT,[1,13] whereas others have found no relationship between duration of the current episode and responsiveness.[14,15] Our present study found no significant effect of duration of the current episode. However, it should be noted that the duration of the current episode in responders was relatively short compared with that in nonresponders; the latter group included deviated samples, such as patients with chronic depression or dysthymic disorder, so may not have been suitable for analysis. A long duration of depressive symptoms could explain lack of response to ECT. No significant difference was found between responders and nonresponders for psychotic symptoms. Some studies have suggested that psychotic features respond well to ECT, and that responsiveness to ECT decreases with increasing severity of depression,[10,11,16] while others do not.[17,18] We also failed to identify differences in age between responders and nonresponders with treatment-resistant depression. Petrides et al[19] and O'Connor et al[20] reported that ECT was more effective in older than in younger adult patients. Therefore, it may be difficult to identify significant age-related differences between responders and nonresponders within only a group of older patients and with no patients under 60 years old.

In conclusion, the mean pretreatment factor 2 (retardation) MADRS score may be an important predictor of efficacy of ECT in older patients with severe treatment-resistant depression. One limitation of the present study was its small sample size, so we cannot generalize our findings to a larger population. To confirm and generalize our findings, more detailed clinical studies in larger numbers of patients are needed to identify symptoms which predict response to ECT in older patients with severe treatment-resistant depression.

Disclosure

The authors report no conflicts of interest in this work.

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