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The Relationship between Symptom Relief and Psychosocial Functional Improvement during Acute Electroconvulsive Therapy for Patients with Major Depressive Disorder

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Abstract

Background: We aimed to compare the degree of symptom relief to psychosocial functional (abbreviated as "functional") improvement and explore the relationships between symptom relief and functional improvement during acute electroconvulsive therapy for patients with major depressive disorder.

Methods: Major depressive disorder inpatients (n = 130) requiring electroconvulsive therapy were recruited. Electroconvulsive therapy was generally performed for a maximum of 12 treatments. Symptom severity, using the 17-item Hamilton Depression Rating Scale, and psychosocial functioning (abbreviated as "functioning"), using the Modified Work and Social Adjustment Scale, were assessed before electroconvulsive therapy, after every 3 electroconvulsive therapy treatments, and after the final electroconvulsive therapy. Both 17-item Hamilton Depression Rating Scale and Modified Work and Social Adjustment Scale scores were converted to T-score units to compare the degrees of changes between depressive symptoms and functioning after electroconvulsive therapy. Structural equation modeling was used to test the relationships between 17-item Hamilton Depression Rating Scale and Modified Work and Social Adjustment Scale during acute electroconvulsive therapy.

Results: One hundred sixteen patients who completed at least the first 3 electroconvulsive therapy treatments entered the analysis. Reduction of 17-item Hamilton Depression Rating Scale T-scores was significantly greater than that of Modified Work and Social Adjustment Scale T-scores at assessments 2, 3, 4, and 5. The model analyzed by structural equation modeling satisfied all indices of goodness-of-fit (chi-square = 32.882, P =.107, TLI = 0.92, CFI = 0.984, RMSEA = 0.057). The 17-item Hamilton Depression Rating Scale change did not predict subsequent Modified Work and Social Adjustment Scale change.

Conclusions: Functioning improved less than depressive symptoms during acute electroconvulsive therapy. Symptom reduction did not predict subsequent functional improvement. Depressive symptoms and functional impairment are distinct domains and should be assessed independently to accurately reflect the effectiveness of electroconvulsive therapy.

Keywords: major depressive disorder, electroconvulsive therapy, 17-item Hamilton Depression Rating Scale, Work and Social Adjustment Scale, structural equation modeling

Significance Statement

This is the first study to explore the relationships between depressive symptoms and psychosocial functioning (abbreviated as "functioning") for depressed patients receiving acute electroconvulsive therapy (ECT). As we know, it is generally assumed that an improvement in depressive symptoms is equal to an improvement in functioning. The first finding of this study was that psychosocial functional (abbreviated as "functional") improvement lagged behind rather than paralleled symptomatic improvement. The second was that symptom relief did not predict subsequent functional improvement after analysis. Our finding could help clinicians to understand the trajectories of symptomatic and functional changes across the acute electroconvulsive therapy. Actually, improvements in functioning are a highly desirable outcome from the patient's perspective. ECT added on some psychosocial treatments to enhance the functioning should be explored.

Introduction

Electroconvulsive therapy (ECT) is considered the most effective short-term treatment for patients with major depressive disorder (MDD) (UK ECT Review Group, 2003). According to the DSM-IV-TR (APA, 2000) or the DSM-5 (APA, 2013), psychosocial functional (abbreviated as "functional") impairment is a necessary criterion for major depressive episodes. However, efficacy of ECT has traditionally been determined on the basis of a change in depression rating scales, such as the Hamilton Depression Rating Scale (HAMD) (Hamilton, 1960) or Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979). These 2 scales do not directly assess functional impairment. Although achieving clinical response represents an important therapeutic milestone, it does not necessarily indicate a recovery from a major depressive episode, since many patients with clinical response will still have functional impairment (Mathew et al., 2007). Furthermore, functional impairment predicts poorer long-term outcomes (Solomon et al., 2004; Vittengl et al., 2010). The goal of treatment for MDD patients is not merely to control the depressive symptoms but, equally important, to restore the psychosocial functioning (abbreviated as "functioning"). The American Psychiatric Association (APA) guideline for the treatment of patients with MDD (APA, 2010) emphasizes the importance of adding functional measures to adequately capture the full impact of depression and its treatment.

ECT textbooks suggest that the therapeutic goal of acute ECT is symptomatic remission (Mankad, 2010; Waite and Easton, 2013). It is generally assumed that there is a bidirectional relationship between depression severity and functional impairment (McKnight and Kashdan, 2009). To date, there have been few studies on the functional outcome of depressed patients treated with ECT (Mathew et al., 2007).

Many studies have found that functioning may improve more slowly than depressive symptoms, regardless of whether depressed patients receive pharmacotherapy or psychotherapy (Hirschfeld et al., 2002; Vittengl et al., 2004; Dunn et al., 2012; Renner et al., 2014; Lin et al., 2015). These results suggest that improvements in functioning are not fully explained by improvements in depressive symptoms.

Recent studies have examined the reciprocal relationships between depressive symptoms and functioning for depressive patients receiving the psychotherapy (Dunn et al., 2012) or pharmacotherapy (Lin et al., 2015). Therefore, we aimed to extend the present research beyond depressed patients receiving psychotherapy or pharmacotherapy to those receiving acute ECT. There were 2 hypotheses about the relationship between depressive symptoms and functioning: (1) the degree of symptom reduction was greater than that of functional improvement, and (2) reduction of depressive symptoms predicted subsequent functional improvement, or vice versa. We first compared the degree of symptom relief to that of functional improvement after ECT. We later used a cross-lagged longitudinal model to examine the possible relationship between symptom relief and functional improvement across the course of acute ECT.

METHODS

Ethics

This study was part of our earlier prospective, observational study, which has been documented elsewhere (Lin et al., 2016). The study was approved by Kai-Syuan Psychiatric Hospital's institutional review board and conducted in accordance with Good Clinical Practice procedures and the current revision of the Declaration of Helsinki (project no. KSPH-2008-12). This study was registered on Clinicaltrials.gov (NCT02032576).

Subjects

As previously described in detail (Lin et al., 2016), Han Chinese inpatients with MDD requiring ECT were enrolled from the Inpatient Psychiatric Unit of Kai-Syuan Psychiatric Hospital, a major psychiatric center in south Taiwan. The study duration was from January 2008 to October 2013.

Subjects were eligible if they were aged 18 years or more, satisfied DSM-IV-TR criteria for MDD that was confirmed using the Structured Clinical Interview for DSM-IV Axis I (APA, 1994), had a HAMD-17 ≥18, and a Clinical Global Impression of Severity (Guy, 1976) ≥4 at baseline, had given written informed consent to participate in the study, and had not undergone ECT within the past 6 months. Exclusion criteria included histories of schizophrenia or other psychotic disorders, schizoaffective disorders, bipolar disorders, and mental disorders due to organic factors, pregnancy, or severe cognitive impairment. Patients with serious medical conditions or neurological illnesses that restricted the use of ECT were excluded from the study.

ECT Protocol

The practice of ECT was in accord with the APA Task Force on ECT (APA, 2001). All subjects and their past histories of medical illnesses, physical and neurological examinations, blood and urine tests, chest X-ray, EEG, and ECG were assessed to decide the patients' general medical conditions before ECT. Antidepressants, antipsychotics, and mood stabilizers were withdrawn before initiating ECT, and patients remained medication free during the ECT course. During the course of treatment, psychiatrists were allowed to prescribe benzodiazepines, up to a dosage equivalent to 3 mg/d of lorazepam, for severe anxiety or

insomnia as needed. However, benzodiazepines should be withheld 8 or more hours before an ECT treatment. Only lorazepam, oxazepam, estazolam, or brotizolam were allowed. For our ECT protocol, anesthesia was induced by thiopental or thiamylal, both at doses of 1.5 to 2.0 mg/kg i.v. Neuromuscular blockade was induced by succinylcholine at a dosage of 0.5 to 1.0 mg/kg i.v. ECT was performed using the Thymatron System IV machine (Somatics, Inc.) with a bipolar brief pulse square wave. Standard bitemporal ECT was used. Physiological monitoring during ECT included an EEG, an electromyogram, an ECG, and a pulse oximetry. The stimulus parameters of ECT were: a constant current of 0.9 A, a pulse width of 0.5 ms, and a frequency of 60 Hz. Stimulus intensity was first established according to the patient's age and gender (Petrides and Fink, 1996; Abrams and Swartz, 2002). Seizure duration was regarded as effective when it continued for at least 20 seconds, as measured by electromyogram, and for at least 25 seconds, as measured by EEG (Sackeim et al., 1987; Coffey et al., 1995; Mankad, 2010). If the seizure duration was insufficient, restimulation was performed with a higher electrical dosage. Treatment was given 2 or 3 times weekly, with all ECTs administered in the morning. Prior to August 2009, ECT was given 3 times/wk, but to decrease complaints of memory impairment from some patients, and to adjust clinicians' workloads, ECT was later given 2 times/wk. The number of ECT treatments was determined by the treating psychiatrist if remission (HAMD-17 ≤7) had been reached, if patients could not tolerate the side effects (APA, 2001), or if patients decided to discontinue ECT. The maximum number of ECT treatments was 12.

Outcome Measures and Subjective Memory Impairment following the ECT

Symptom severity was assessed by independent raters using HAMD-17. All the raters were board-certified psychiatrists. Higher HAMD-17 scores (ranging from 0 to 52) indicate more severe depression. Among the raters using HAMD-17, the intraclass correlation coefficient of reliability approached 0.95.

The Work and Social Adjustment Scale (WSAS) (Mundt et al., 2002) is a self-rating scale consisting of 5 items. It assesses an individual's perception of work and social functioning, with higher scores representing greater impairment of functioning. Each item is scored from 0 (not affected at all) to 8 (severely affected). WSAS has been shown to be a reliable and valid measure of functional impairment. Item 1 assesses the work ability, but it may be difficult to demonstrate a high level of work functioning while in the hospital when patients' jobs are outside of the hospital, or for those patients who have retired. Therefore, Item 1 has been omitted. We renamed the Work and Social Adjustment Scale, without item 1, as the Modified Work and Social Adjustment Scale (MWSAS) in the present study and used it to assess functioning. MWSAS was used to assess functioning of depressed patients in our earlier study (Lin et al., 2015). Symptom severity and functioning were assessed using HAMD-17 and MWSAS before ECT, after every 3 ECT treatments, and after the final ECT treatment. Therefore, if a patient received a total of 10, 11, or 12 ECT treatments, he or she was assessed 5 times (i.e., assessments 1, 2, 3, 4, and 5). To prevent post-ECT confusion from influencing the assessment, HAMD-17 and MWSAS were conducted 1 to 2 days after treatment.

Subjective memory impairment that had not been present before ECT, either first observed by the psychiatrist at each visit or first reported spontaneously by the patient, indicated a patient with the side effect of subjective memory impairment following the ECT.

Statistical Analyses

Analysis was on a modified intent-to-treat basis for subjects reporting at least one postbaseline assessment. We first carried out descriptive statistics to summarize the data (i.e., percentages, means, and SDs). Pearson's χ^2 test was used to compare categorical variables; independent t test was used for continuous variables. Effect size (d) was used to demonstrate the level of improvement at endpoint. Effect size was defined as the mean of difference between baseline and posttreatment scores for each measure, divided by the SD of difference (Morris and DeShon, 2002). A d-value of 0.20 indicates a small effect size, 0.50 a medium effect size, and 0.80 a large effect size (Cohen, 1988). Large effect sizes indicate clinically relevant improvements at the end point.

HAMD-17 and MWSAS have different metrics. To compare the degrees of changes between depressive symptoms and functioning after ECT, both the HAMD-17 and MWSAS scores were converted to T-score units (mean = 50, SD = 10). This transformation has been used before (Vittengl et al., 2004; Dunn et al., 2012). The T score was calculated by the following formula (Minium et al., 1993):

$$X_T = [(X_{raw} - X_{pre\text{-}treatment}) / SD_{pre\text{-}treatment}] \times 10 + 50.$$

The generalized estimating equations method, with the first-order autoregressive working correlation structure (Zeger and Liang, 1986), was applied to compare degrees of symptom relief to those of functional improvement at assessments 2, 3, 4, and 5. That is, the generalized estimating equations method was used to compare the differences in T-score changes between HAMD-17 T-scores and MWSAS T-scores at assessments 2, 3, 4, and 5.

Correlations between variables were analyzed by Pearson's correlation coefficients. We replicated the methods from the study by Dunn et al. (2012) and our own recent study (Lin et al., 2015). The cross-lagged longitudinal model was analyzed by structural equation modeling to test whether symptom reduction could predict subsequent functional improvement, or vice versa. Path coefficients in the structural equation modeling model represented the strength of the path between 2 measured variables and were calculated using standardized regression coefficients (i.e., β values). The null hypothesis for structural equation modeling was that the model fits the data. The goodness-of-fit of the model was judged using the chi-square statistic ($P > .05$ indicates a good fit with the data) (Bollen, 1989; Tabachnick and Fidell, 2007), the Tucker-Lewis Index (TLI) (values > 0.95 indicates a good fit), the Comparative Fit Index (CFI) (values >0.90 indicates a good fit), and the Root Mean Square Error of Approximation (RMSEA) value (values <0.08 indicates a good fit) (Bentler and Bonett, 1980; Bentler, 1990; Bollen and Long, 1993; Kline, 2011). Missing data were handled by full information maximum likelihood (Schafer and Graham, 2002; Enders, 2011). This method uses all available data to estimate the structural equation modeling model and maximize statistical power. Data were analyzed using the SPSS version 17.0 for Windows and the Analysis of Moment Structures version 17 (SPSS Inc.). Statistical significance was defined as an alpha <0.05.

RESULTS

Characteristics of Subjects

One-hundred and thirty inpatients with MDD participated in the study. Fourteen of the 130 patients, who did not complete the first 3 ECT treatments and thereby failed to have at least

one posttreatment assessment, were excluded. The remaining 116 (89.2%) patients entered the analysis. Twenty-seven (29.3%) were male and 82 (70.7%) were female. The mean (SD) age was 46.9 (12.3) years and their mean (SD) age of MDD onset was 38.1 years (12.8). The mean (SD) number of ECT treatments was 8.9 (2.5). There were 23 patients treated with thrice-weekly ECT and 93 twice-weekly. Forty-eight (41.4%) patients reported subjective memory impairment following the ECT. Patients treated with thrice-weekly ECT experienced significantly higher rates of subjective memory impairment than did those treated with twice-weekly ECT (65.3% = 15/23 vs 35.5% = 33/93; P = .010).

Degree of Symptom Reduction vs Degree of Functional Improvement

Table 1 contains raw scales, effect sizes, and T-scales of the HAMD-17 and MWSAS at each assessment. Acute treatment with ECT resulted in medium (d = 0.67) to large (d = 2.77) levels of changes in MWSAS and HAMD-17 scores at assessment 2, 3, 4, and 5. Reduction of HAMD-17 T-scores was significantly greater than that of MWSAS T-scores, which began at assessment 2 (estimate = -11.6, P < .001), and persisted through assessment 3 (estimate = -16.7, P < .001), 4 (estimate = -16.9, P < .001), and 5 (estimate = -16.04, P < .001) (Table 2). Figure 1 illustrates the HAMD-17 T-score and WMSAS T-score throughout acute ECT. These results suggest that HAMD-17 T-scores changed sooner than MWSAS T-scores at assessments 2, 3, 4, and 5. The trajectory of symptom reduction did not parallel that of functional improvement.

The Relationships between Depressive Symptoms and Functioning

The correlation coefficient between HAMD-17 and MWSAS scores at assessments 1, 2, 3, 4, and 5 were 0.20, 0.48, 0.51, 0.49, and 0.40, respectively (Table 3). These results reveal that the correlations between depressive symptoms and functioning may be bidirectional (van der Voort et al., 2015). However, they were only weak to moderate (McKnight and Kashdan, 2009), correlation before ECT being the lowest.

The cross-lagged longitudinal data analyzed using structural equation modeling satisfied all indices of goodness-of-fit (chi-square = 32.882, df = 24, P = .107, TLI = 0.92, CFI = 0.984, RMSEA = 0.057) (Fig. 2). The path between MWSAS at assessment 1 and HAMD-17 at assessment 2 (i.e., MWSAS at assessment 1→ HAMD-17 at assessment 2 in Fig. 2) was significant (P < .05), indicating that MWSAS score change at baseline (i.e., assessment 1) was significantly associated with subsequent HAMD-17 score change at assessment 2. However, HAMD-17 changes did not predict subsequent MWSAS change. The e1, e2, e3, e4, e5, e6, e7, and e8 indicate the error terms (Fig. 2). The error term represents variance unexplained by independent variables.

Discussion

To our knowledge, this is the first study to explore the relationships between depressive symptoms and functioning for depressed patients receiving acute ECT. The first finding of this study was that functional improvement lagged behind rather than paralleled symptomatic improvement. This finding was consistent with reports from depressed patients receiving psychotherapy, pharmacotherapy, or a combined treatment of psychotherapy and pharmacotherapy, that functioning may be more difficult to change than depressive symptoms (Hirschfeld et al., 2002; Vittengl et al., 2004; Bech, 2005; Dunn et al., 2012; Renner et al., 2014; Zu et al., 2014; Lin et al., 2015). Functioning should therefore be regarded as a distinctive domain of depression (Hirschfeld et al., 2002; McKnight and Kashdan, 2009; Lam et al., 2011; Lin et al., 2015; van der Voort et al., 2015; Vittengl et al., 2016).

The factors beyond symptoms, for example residual depression, neurocognitive impairment, or comorbidity, may be important in determining functional improvement (Kennedy et al., 2007). Is the asynchrony between symptomatic improvement and functional improvement reflecting self-rating vs observer-rating scales? Observer-rating scale has been reported to be more sensitive in detecting symptom or functional change than self-rating scale (Lin et al., 2014). In the preset study, functioning was also rated by the Global Assessment of Functioning (GAF) (Endicott et al., 1976) before ECT, after every 3 ECT treatments, and after the

Table 1. Raw Scores, Effect Sizes, and T Scores of HAMD-17[a] and MWSAS[b] at Each Assessment

	Assessment 1 (n = 116)	Assessment 2 (n = 116)	Assessment 3 (n = 107)	Assessment 4 (n = 73)	Assessment 5 (n = 61)
HAMD-17, mean ± SD	30.9 ± 7.0	18.3 ± 7.6	11.1 ± 6.3	8.4 ± 5.9	7.1 ± 5.2
Effect size		1.59	2.34	2.76	2.77
MWSAS, mean ± SD	23.5 ± 7.3	18.9 ± 8.0	15.2 ± 8.5	12.2 ± 8.4	10.7 ± 7.8
Effect size		0.67	1.11	1.26	1.67
HAMD-17 T-score, mean ± SD	50.0 ± 10.0	32.0 ± 10.8	21.8 ± 9.0	17.9 ± 8.4	16.0 ± 7.5
MWSAS T-score, mean ± SD	50.0 ± 10.0	43.7 ± 11.0	38.6 ± 11.8	34.5 ± 11.5	32.4 ± 10.8

[a]HAMD-17 = 17-item Hamilton Depression Rating Scale.

[b]MWSAS = Modified Work and Social Adjustment Scale = Work and Social Adjustment Scale (WSAS) without Item 1.

Table 2. Differences (= Estimate) between HAMD-17 T-Scores Reduction and MWSAS T-Scores Reduction at Assessments 2, 3, 4, and 5 Using Generalized Estimating Equations Method

Scale × Time[a]	Estimate	Standard Error	P
Scale × Assessment 2	-11.6	1.4	<.001
Scale × Assessment 3	-16.7	1.5	<.001
Scale × Assessment 4	-16.9	1.7	<.001
Scale × Assessment 5	-16.4	1.8	<.001

[a]scale = HAMD-17 T-score vs MWSAS T-score (as reference scale).
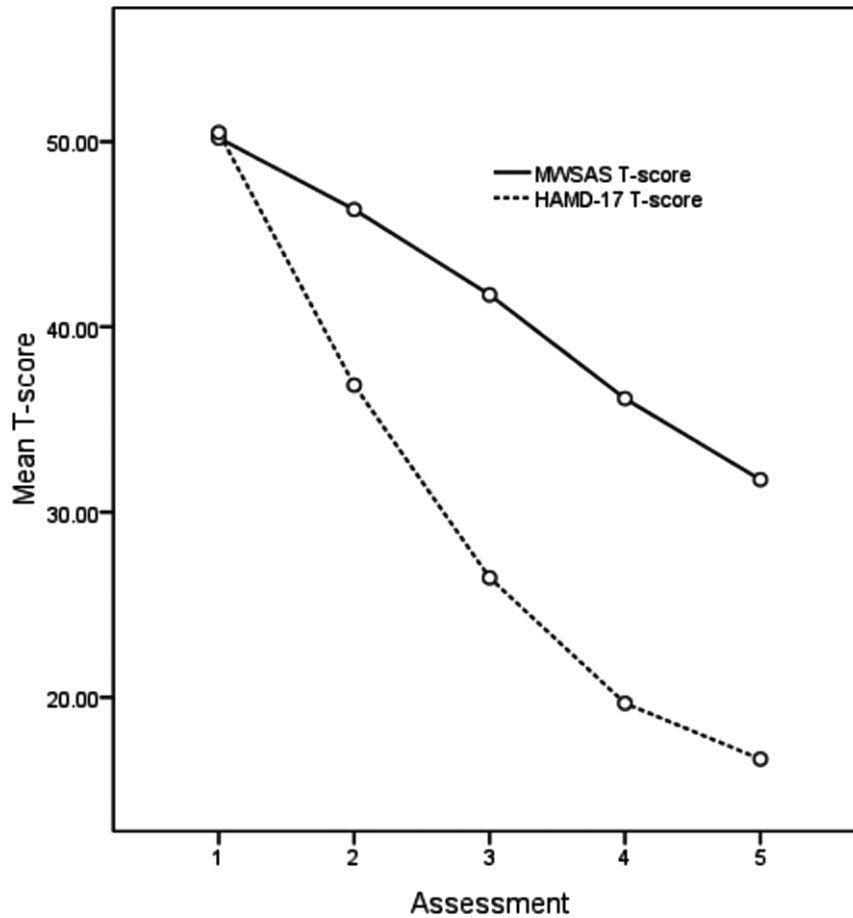
Figure 1. 17-item Hamilton Depression Rating Scale (HAMD-17) T-scores vs Modified Work and Social Adjustment Scale (MWSAS) T-scores at each assessment during acute electroconvulsive therapy (ECT). The symptom severity and functioning were assessed using the HAMD-17 and MWSAS before ECT, after every 3 ECT treatments, and after the final ECT.

final ECT. The GAF is commonly used to report a clinician's judgment of a patient's overall functioning, though the GAF confounds severity of symptoms with difficulty in functioning (Jones et al., 1995). The GAF is scored on a 1 to 100 scale, with a lower score indicating more functioning. The mean score ± SD of GAF at assessments 1, 2, 3, 4, and 5 were 38.3 ± 10.5 (n = 116), 47.9 ± 9.6 (n = 116), 59.7 ± 11.0 (n = 107), 65.3 ± 9.2 (n = 73), and 68.1 ± 9.4 (n = 61), respectively. The effect sizes were 0.98, 1.56, 2.15, and 2.21 at assessments

2, 3, 4, and 5, respectively. The effect sizes for GAF were less than for HAMD-17, but larger than for MWSAS at 4 post-ECT assessments (Table 1). These findings suggested that depressive symptoms improved more quickly than functioning during the acute treatment with ECT, regardless of functioning as rated by the GAF (i.e., an observer-rating scale) or MWSAS (i.e., a self-rating scale). Furthermore, as mentioned above, neurocognitive impairment may contribute to functional impairment and therefor hinder

Table 3. Pearson Correlation Coefficient Matrix of the Measured Variables

	HAMD1	HAMD2	HAMD3	HAMD4	HAMD5	MWSAS1	MWSAS2	MWSAS3	MWSAS4
HAMD1	1								
HAMD2	0.41**	1							
HAMD3	0.21*	0.72**	1						
HAMD4	0. 78	0.51**	0.79**	1					
HAMD5	0.15	0.32*	0.56**	0.81**	1				
MWSAS1	0.20*	0.26**	0.23*	0.13	0.15	1			
MWSAS2	0.17	0.48**	0.41**	0.30**	0.19	0.61**	1		
MWSAS3	0.05	0.439**	0.51**	0.46**	0.31*	0.53**	0.73**	1	
MWSAS4	0.08	0.27*	0.39**	0.49**	0.35*	0.36**	0.57**	0.81**	1
MWSAS5	-0.14	0.10	0.17	0.44**	0.40**	0.39**	0.46**	0.76**	0.84**

Abbreviations: HAMDn, HAMD-17 score at assessment n, n =1, 2, 3, 4, or 5; MWSASn, Modified WSAS score at assessment n, n = 1, 2, 3, 4, or 5.
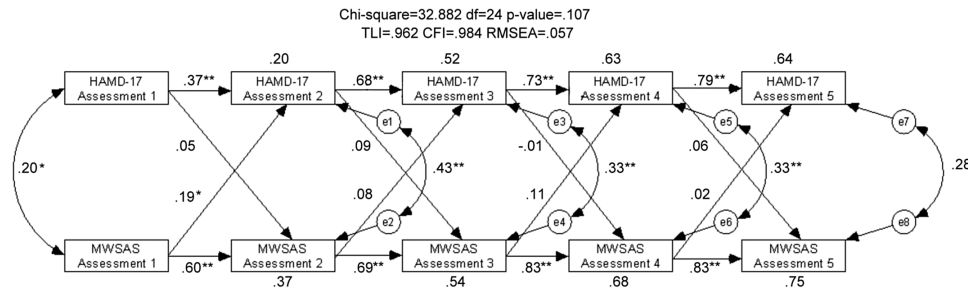*P<.05, ** P<.01.

Figure 2. The cross-lagged longitudinal model illustrates that the relationships between depressive symptoms and functioning during acute electroconvulsive therapy (ECT). Unidirectional arrows signify direct effects and bi-directional arrows represent correlations, *P < .05, **P < .01. e1-e8 = error term.

functional improvement (McIntyre et al., 2013). Neurocognitive impairment, particularly memory impairment, has long been recognized as a common side effect of ECT (Ingram et al., 2008). Whether neurocognitive impairment such as subjective memory impairment was associated with functional improvement should be assessed. In present study, there were no statistically significant differences in MWSAS (-11.9 ± 8.9 vs -12.8 ± 9.0, p = 0.616) and GAF (29.1 ± 15.3 vs 28.2 ± 15.5, p = 0.752) changes at endpoints between patients with subjective memory impairment following the ECT and those without (data not shown in the table). However, lack of any objective measure of memory impairment or other neurocognitive side effects in the present study limited to explain whether objective memory impairment or other neurocognitive side effects may influence functioning improvement after ECT. Further studies are needed to explore the potential factors, for example neurocognitive impairment measured using standardized and sensitive neuropsychological tests, related to functional improvement.

The second finding was that symptom relief did not predict subsequent functional improvement. This indicates that symptom reduction may not drive functional improvement. This finding correlated to those of other studies, regardless of whether the patients received antidepressants or cognitive psychotherapy (Vittengl et al., 2004; Trivedi et al., 2009; Dunn et al., 2012; Lin et al., 2015). However, only baseline MWSAS (i.e., assessment 1) predicted HAMD-17 at assessment 2. This finding was in agreement with our earlier study on depressed patients treated with fluoxetine that only baseline MWSAS predicted HAMD-17 at week 1. However, we cannot replicate the results from the study of Dunn et al. (2012), which asserted that improvements in functioning predict subsequent symptom reduction. Whether this inconsistent result is due to variations in the patient population (inpatients vs outpatients) or types of interventions (biological treatment vs cognitive therapy) requires further study.

Studies (Gorenstein et al., 2002; Hirschfeld et al., 2002; Dunn et al., 2012; Renner et al., 2014) have found that psychotherapy alone can improve functioning. The combination of ECT with psychotherapy may therefore confer additional and positive functional outcomes (McClintock et al., 2011). The efficacy of this combination on improvement in functioning needs to be explored in future well-designed, controlled trials.

Taken together, assessing both depressive symptom severity and functioning repeatedly throughout treatment is an important consideration when determining the efficacy of ECT. Functional impairment impacts not only the patients but also their families, friends, and society (McKnight and Kashdan, 2009). In fact, many depressed patients receiving treatment are more interested in functional improvement than symptom reduction (Zimmerman et al., 2006).

Several strengths of this study should be addressed. First, this was a repeated measure study. The longitudinal follow-up

data were obtained from the same subjects. The cross-lagged longitudinal model allows estimates of bidirectional causality between symptoms and functioning at various time points (e.g., to what extent earlier symptom reduction drives subsequent functional improvement, and vice versa) (Blalock, 2007). Using this method, prior symptoms and functioning predict subsequent changes in symptoms and functioning simultaneously. Second, treatment parameters (electrode placement, stimulus wave form, and stimulus intensity dosing procedures) and diagnoses were the same for all subjects. Because all of the subjects were from a single psychiatric center with a similar environment, the study required fewer patients to detect differences, due to the relatively lower variance. Third, standardized rating scales were used to assess ECT outcomes.

However, our findings have been constrained by several limitations. First, the patients were not blinded to treatment, nor was there a control group. Second, for structural equation modeling analysis, a minimum sample of 100 has been suggested (Hoyle, 1995; Loehlin, 2004). The current sample size (n = 116) was therefore too small to perform SEM analysis with many variables. There may be other models with larger case numbers that would fit the data better. Third, this trial used specific scales to assess depression and functioning. Other scales assessing such variables may yield different results. Fourth, given the hospital environment, changes in functioning might be limited to social roles rather than work ability within the inpatient setting. Fifth, all participants were treated with bitemporal ECT. Therefore, whether the present findings can be extrapolated to those treated with bifrontal or right unilateral ECT requires additional study. However, one study (Prudic et al., 1996) has concluded that ECT outcome appears to be independent of electrode placement. Additionally, 6 to 12 treatments are necessary for most patients in usual clinical practice (APA, 2001; Kellner, 2012), but a patient with poor response after 12 treatments is not likely to have a favorable response even after receiving more ECT treatments (Waite and Easton, 2013). However, the rate and quality of response to ECT are highly individualized. Some patients may need as many as 20 treatments to obtain maximal improvement (Mankad, 2010).

In conclusion, functioning improved more slowly than did depressive symptoms during acute ECT. Symptom reduction did not significantly predict subsequent functional improvement. Assessing both depressive symptoms and functioning repeatedly throughout treatment may provide various and complementary information (Lam et al., 2011). After all, improvements in functioning are a highly desirable outcome from the patient's perspective (Renner et al., 2014). Further research is warranted to explore the effectiveness of augmenting ECT with evidence-based psychotherapy and its long-term treatment outcomes (McClintock et al., 2011).

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Acknowledgments

Statement of Interest

None.

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