

The Influence of Age on the Natural History of Unipolar Depression when Treated with Electroconvulsive Therapy

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Summary. The influence of age on the natural history of unipolar depression when treated with electroconvulsive therapy (ECT) was studied using a naturalistic/archival study design. A sample of 125 patients who received no somatic treatment were compared with 128 patients who all received a course of ECT with at least four treatments. Patients were separated according to age at admission. Treated patients, aged 40 or older, who were clearly remitters showed no differences in previous episodes, subsequent episodes, subsequent hospitalizations, or likelihood of experiencing a period of full recovery when compared with a similar group of untreated patients. Hospitalization greater than 1 year and chronicity were significantly more common in the untreated older subjects. Treated patients aged 39 or younger, who also were clearly remitters, showed significant increases in subsequent episodes and subsequent hospitalizations when compared with a group of depressed patients of similar age who received no somatic treatment. Hospitalization greater than 1 year was also more common in the untreated younger patients. ECT clearly reduces the rate of chronicity in older patients but may be associated with an increase in episodes after treatment in the younger population.

Key words: Electroconvulsive therapy – Unipolar depression – Age

Introduction

The clinical presentation and natural history of depressive illnesses may be influenced by the age of the patient. Young depressives can expect an episodic

life-time course, whereas elderly patients may have a less episodic course with lengthy episodes and a high risk of chronicity (MacDonald 1918; Lundquist 1945; Angst et al. 1973). Symptomatically, depressive episodes may appear different at varying ages. For example, a patient may show psychomotor retardation when young but more agitation in later episodes when older (Avery and Silverman 1984). Young patients who are psychotic in early episodes may show a reduction or absence of psychosis during episodes in later life (Winokur et al. 1985). Additionally, there is evidence that episode length may increase with age (Angst et al. 1973).

The reasons for these differences are not clear. The poor prognosis associated with older patients may be a result of ongoing medical problems, failure to diagnose the illness properly, inadequate treatment or any combination of these (Post 1972; Murphy 1983; Burvill et al. 1986). The possibility that a separate late-onset affective disorder exists with characteristic symptoms, unique prognosis, and response to treatment remains at least partially viable and may, in part, account for differences in symptoms and outcome (Mendlewicz and Baron 1981; Brown et al. 1984; Meyers et al. 1984). Another possible explanation for these changes is that they may be more related to age at illness rather than the presence of separate illnesses, and there is some evidence for this (Pichot and Pull 1981; Rinieris 1982).

Since there are symptom and outcome differences related to age, then perhaps age also has some effect on response to treatment. Early literature on electroconvulsive therapy (ECT) suggested that patients over 40 years respond better to this therapy than younger patients (Kalinowsky and Hoch 1946). Three studies have found significantly better outcomes in older individuals, but follow-up was only 1–6 months

after treatment (Mendels 1965; Carney and Sheffield 1974; Coryell and Zimmerman 1984). It would be useful to follow treated patients for longer time periods to see if age influences the long-term response to ECT. This study examines the influence of age on the long-term response to ECT in a group of depressed inpatients.

Methods

As part of a naturalistic research project to study depression, 253 records were selected from the University of Iowa Psychiatric Hospital. One hundred twenty-five of the 253 records studied were taken consecutively from depressed patients admitted to the hospital between 1935 and 1938. The remaining 128 records were taken consecutively from depressed patients admitted between 1945 and 1946. One hundred one patients had a discharge diagnosis of involutional melancholia and the remaining 152 patients of manic depressive psychosis, depressed type. In the 1935 group there were 73 females and 52 males. In the 1945 group there were 73 females and 55 males. The 1935 group was designated the "no treatment" control group. These patients received psychotherapy, hydrotherapy, and occupational therapy during their hospitalization. The 1945 group was designated the "ECT treatment" group, and all these patients received a course of ECT. Each patient received at least four treatments.

Each record was carefully examined by RBW. The original, complete type-written records of all psychiatric and social service interviews, progress notes, laboratory studies, discharge summaries, and transcripts of interviews with the patients were available for examination. These records were kept by the same physicians and social workers as the record used in the Iowa 500, which is a high-quality archival study (Morrison et al. 1972). Eighty-seven of these records actually overlap with the Iowa 500.

Information on a variety of variables was obtained, including age at onset, age at admission, number of previous episodes, number of subsequent episodes and rehospitalizations. A previous episode was defined as any period of time lasting at least 1 month where the patient experienced a distinct change in the quality of life, characterized by typical depressive symptoms as described in DSM-III. Information on the number of previous episodes was obtained from the physician and social worker records. A subsequent episode was defined as a distinct, new, depressive period, lasting at least 1 month and clearly separated from any prior episode by at least 3 months. Any relapse within 3 months was counted as a continuation of the earlier episode. Rehospitalization was defined as any subsequent period of hospital confinement for the treatment of any depressive episode at any hospital.

Follow-up records were kept on most patients in the study. Eight (6.7%) and 20 (16.5%) were lost to follow-up in the 1935 and 1945 groups respectively. These follow-up records include notes by physicians and social workers as well as correspondence with the patient. A patient was considered recovered if one of two criteria were met: (1) the patient sustained a full remission of all presenting symptoms or (2) the patient sustained a near full remission of all presenting symptoms but was successful in returning to his/her previous occupation (from which he/she was originally incapacitated). A judgement about final outcome was made based on the last contact with the patient as

Table 1. Duration of follow-up

Group	N	Mean	SD	t	P
Those ill at last follow-up included					
1935, 40 years +	80	4.26	4.09		
1945, 40 years +	69	3.44	3.04	1.33	0.19
1935, 39 years -	32	3.11	3.52		
1944, 39 years -	32	3.80	3.63	-0.78	0.44
Those ill at last follow-up excluded					
1935, 40 years +	44	5.67	4.06		
1945, 40 years +	63	3.48	3.47	3.03	0.003
1935, 39 years -	29	3.32	3.63		
1945, 39 years -	32	3.80	3.63	-0.15	0.61

indicated in the chart. Outcome fell into one of three categories: (1) full recovery without evidence of recurrence, (2) full recovery with evidence of subsequent episodes, and (3) chronic course with no periods of clear remission. It was indicated in the records if the patient was transferred to a state institution, and frequently notes from the state hospital were included as part of the follow-up. Hospitalization greater than 1 year was defined as confinement to any hospital or series of hospitals for at least 1 continuous year for the purpose of treating a depressive illness.

The first author (RBW) was blind to the study hypotheses throughout the data collection and diagnostic process. DSM-III diagnoses were made by RBW, based on the information presented in the records. All data obtained were coded into a computer program. Chi-square, Fisher's exact tests and *t*-tests were performed where appropriate.

Only patients with a DSM-III diagnosis of major depressive disorder, with or without psychosis, were included in the analysis. Twelve patients met criteria for bipolar affective disorder and were dropped. The remaining 241 patients were used in the analysis. One hundred twenty patients were in the 1935 "no treatment group" and 121 patients were in the 1945 "treated group".

These groups were further subdivided by age at admission, which was defined as the age at which the patient was first admitted to University of Iowa Hospitals. A cut-off age of 40 was set to separate younger depressives from older ones. The result was four groups as follows: (1) untreated 1935, over 40 years of age; (2) untreated 1935, under 40 years of age; (3) treated 1945, over 40 years of age; and (4) treated 1945, under 40 years of age. The older untreated group was compared with the older treated group, and the younger untreated group was compared with the younger treated group.

These groups were compared with one another in two ways. First, all patients were analyzed regardless of follow-up status. Second, those who were judged to be chronically ill were excluded. Deleting the chronically ill produced a group of individuals who all had a remitting illness. Studying remitters alone could provide insights into how often patients relapse after ECT as compared with no treatment.

Mean follow-up times were calculated for each group and are given in Table 1. The mean follow-up times for the two younger groups were equal. This was true whether the chronically ill were included or not. The two older groups did show a statistically significant difference in the mean duration of follow-up when the chronically ill were excluded from the analy-

Table 2. Comparison of treated and untreated patients aged 40 and older

	All patients			Remitters only		
	Untreated N = 80	Treated N = 69	P	Untreated N = 44	Treated N = 63	P
	N (%)	N (%)		N (%)	N (%)	
One or more previous episodes	35 (40.23)	39 (47.56)	0.421**	20 (39.22)	36 (47.37)	0.47**
One or more subsequent episodes	21 (27.3)	35 (50.7)	0.006**	19 (43.2)	32 (50.79)	0.56**
Two or more subsequent episodes	4 (5.16)	6 (8.70)	0.517*	3 (6.82)	6 (9.52)	0.734**
One or more subsequent hospitalizations	20 (26.0)	24 (34.8)	0.328**	17 (38.64)	22 (34.92)	0.85**
Two or more subsequent hospitalizations	7 (9.1)	2 (2.9)	0.172*	5 (11.4)	2 (3.17)	0.12*
Hospitalized longer than 1 year	31 (35.63)	1 (1.22)	0.001**	8 (15.7)	1 (1.32)	0.003*
Chronically ill	36 (45.0)	6 (8.7)	0.001**	—	—	—

*Fisher's exact (two-tailed)

** χ^2 with Yate's correction**Table 3.** Comparison of treated and untreated patients aged 39 and less

	All patients			Remitters only		
	Untreated N = 29	Treated N = 32	P	Untreated N = 32	Treated N = 32	P
	N (%)	N (%)		N (%)	N (%)	
One or more previous episodes	12 (36.36)	22 (28.2)	0.627**	11 (36.7)	11 (28.2)	0.626**
One or more subsequent episodes	3 (9.7)	12 (37.5)	0.022**	3 (10.7)	12 (37.5)	0.036**
Two or more subsequent episodes	0 (0.0)	6 (18.75)	0.024*	0 (0.0)	6 (18.75)	0.026*
One or more subsequent hospitalizations	4 (12.9)	9 (28.13)	0.238**	4 (14.29)	9 (28.13)	0.325**
Two or more subsequent hospitalizations	0 (0.0)	7 (21.88)	0.011*	0 (0.0)	7 (21.88)	0.012*
Hospitalized longer than 1 year	6 (18.18)	0 (0.0)	0.007**	4 (13.3)	0 (0.0)	0.032*
Chronically ill	3 (9.4)	0 (0.0)	0.24*	—	—	—

*Fisher's exact (two-tailed)

** χ^2 with Yate's correction

sis. In that circumstance the mean duration of follow-up was longer for the older untreated group.

Results

The two cohorts of depressed inpatients were compared on clinical grounds. In general, the 1935 cohort was more severely ill. This group had significant increases in mood-congruent delusions ($P = 0.004$), mood-congruent hallucinations ($P = 0.01$), and mood-incongruent delusions ($P = 0.005$). Suicide attempts prior to admission ($P = 0.025$), neurotic depression ($P = 0.038$), chronicity ($P = 0.001$), and hospitalization greater than 1 year ($P = 0.001$) were also characteristic of the 1935 cohort. The 1945 cohort showed a significant increase in subsequent episodes whether compared for one or more ($P = 0.001$) or two or more ($P = 0.025$) episodes after index admission. The groups did not differ with respect to weight loss, diurnal variation, sleep disturbance, family history,

sex, age, or psychomotor activity (Wesner and Winokur 1988).

The results of treated versus untreated patients aged 40 years and older are given in Table 2. Taking all older subjects together, regardless of outcome status, no significant differences were seen in the number of previous episodes or subsequent hospitalizations. The older treated group did show an increase in one or more (50.7% vs 27.3%, $P = 0.006$) but not two or more episodes (8.7% vs 5.16%, $P = 0.517$). Hospitalization greater than 1 year was considerably more common in the untreated group (35.63% vs 1.22%, $P = 0.001$) as well as a high likelihood of becoming chronically ill (52.5% vs 23.2%, $P = 0.001$).

Examining the remitters only showed no differences in previous episodes, subsequent episodes, or subsequent hospitalizations during recorded follow-up. A significant increase in prolonged hospitalization was, however, again found in the untreated older group (15.7% vs 1.3%, $P = 0.003$).

The results of treated versus untreated patients aged 39 years and younger are given in Table 3. Taking all younger subjects together, regardless of outcome status, no difference was found in the number of previous episodes. The treated younger group did show significant increases when compared for one or more (37.5% vs 9.7%, $P = 0.022$) or two or more (18.75% vs 0%, $P = 0.024$) subsequent episodes. The treated younger group also showed an increase in two or more subsequent hospitalizations (21.88% vs 0%, $P = 0.011$). Hospitalization greater than 1 year was more common in the untreated group (18.18% vs 0%, $P = 0.007$), but the rates of chronicity were similar between the two groups ($P = 0.762$).

Examining the remitters only showed no differences in previous episodes. The treated younger group did continue to show an increase in subsequent episodes, when compared for one or more (37.5% vs 10.7%, $P = 0.036$) or two or more (18.75% vs 0%, $P = 0.026$) subsequent episodes. Again, the treated younger group showed an increase in two or more subsequent hospitalizations (21.88% vs 0%, $P = 0.012$), and prolonged hospitalization was more common in the untreated group (13.13% vs 0%, $P = 0.032$).

Within the group of remitters, 13 patients had a period of hospitalization lasting greater than 1 year. Although these patients clearly remitted during follow-up, they all had lengthy episodes and in that respect are similar to those who were chronically ill during follow-up. These patients were removed from the analysis along with the chronically ill. This produced a group of patients who were all remitters and had hospitalizations lasting less than 1 year.

Four of the 13 patients each had one subsequent episode of illness during follow-up. Four had one subsequent hospitalization and one had two subsequent hospitalizations during follow-up. A total of 6 patients accounted for all of these subsequent episodes and hospitalizations. The remaining 7 patients all remitted and remained well during follow-up.

Removing these patients from the analysis did not significantly change any of the results compared with those obtained when only eliminating the chronically ill. For remitted patients aged 40 and older, 16 (44.4%) of the untreated and 31 (50%) of the treated went on to have one or more subsequent episodes ($\chi^2 = 0.10$, NS). Thirteen (36.1%) and 22 (35.5%) of the untreated and treated older patients respectively went on to have one or more subsequent hospitalizations ($\chi^2 = 0.08$, NS). Four (11.1%) and 2 (3.2%) of the same groups respectively went on to have two or more subsequent hospitalizations (Fisher's exact, two-tail, $P = 0.12$). For remitting patients aged 39 and less, 4 (16.7%) of the untreated and 9 (28.1%) of the treated

patients went on to have one or more subsequent hospitalizations ($\chi^2 = 1.2$, NS). The remainder of the comparisons for all the groups were virtually unchanged.

Discussion

Our data indicate that age does influence the natural history of depression when treated with ECT. Treating older patients with ECT greatly reduces the need for prolonged hospitalization and reduces the risk of developing a chronic illness. These same older patients may go on to have more episodes of illness than untreated patients, but this is not entirely clear from the data. Since the elderly untreated patients in this study had a high risk of prolonged hospitalization and chronicity, it is possible that the extra episodes seen in the treated group were late relapses of earlier episodes. This idea is supported by the additional finding that when the remitters were analyzed alone, there was no observable increase in subsequent episodes. In summary, it appears that the natural history of depression in the older patient is altered by ECT, with its greatest impact on shortening the length of illness and reducing the rate of chronicity.

Treating the younger depressed patient also reduces the need for prolonged hospitalization, but in contrast to the older patient the overall rate of chronicity is much less in this group. None of the treated and only 3 (9.4%) of the untreated younger patients in this study were chronically ill throughout the follow-up period ($P = 0.24$). Chronicity is more common in the older depressed population. In this study 28.2% of the 40-year-old and older patients and 4.7% of the 39-year-old and younger patients were found to be chronically ill ($\chi^2 = 13.5$, $P = 0.001$). Since chronicity is not common in younger patients, ECT may only shorten episodes that would have remitted spontaneously.

The treated younger group clearly went on to have more episodes of illness as compared with the untreated group. This was true whether the groups were compared for one or more, or two or more subsequent episodes. When the remitters were analyzed alone, the same findings held true. Additionally, the same group went on to have two or more hospitalizations, suggesting that their subsequent episodes were incapacitating. This suggests that ECT not only fails to protect against further episodes but may be associated with an increase in total life-time episodes and that these illnesses are of sufficient severity to warrant hospitalization.

The aim of this study was to examine how age might effect the life-time course of unipolar depression when treated with ECT. This study is unique

from the standpoint that no selection bias was present as to who received ECT. No one in the 1935 group received ECT, while everyone in the 1945 group received a course of ECT with at least four treatments. We are unaware of any modern study that utilizes a similar design. Several years after the introduction of ECT, and well before the onset of neuroleptics and antidepressants, a few studies appeared that examined the rates of relapse and rehospitalization. In general, these studies report that ECT shortens depressive episodes and shortens hospital stays but does not prevent relapse. Huston examined the effect of ECT on the course of manic depressive psychosis and involutional psychosis. Some of his findings agree with ours. The manic depressives in his study, who were generally younger patients with a mean age at onset of 40 years, had a similar outcome to our younger groups. Huston's manic depressives who received ECT had the same rate of recovery as those untreated. This finding is very similar to the findings noted in our younger groups. Prolonged hospitalization was also dramatically reduced in his treated group. With respect to subsequent episodes, however, no difference was found between the treated and untreated patients (Huston and Locher 1948a). Huston's involutional psychotics were older patients with a mean age of onset of approximately 50 years. These patients are similar to the older groups in this study. Huston found his older patients showed a pronounced improvement or recovered completely 75%–85% of the time when treated. This compared with a recovery rate of only 46% of those untreated. This corresponds with our finding of a 91.3% recovery rate for the treated older subjects and a 55% rate of recovery for the untreated older subjects. Average hospital stay in Huston's study was 6 months for the treated group vs 21 months for the untreated group. Huston did not compare the rates of relapse in the involutional group (Huston and Locher 1948b).

Karagulla (1950) reported that depressed patients treated with ECT and discharged from the hospital as "recovered" show a higher percentage of relapse compared with those untreated. Oltman and Friedman (1950), however, presented data indicating that shock-treated patients showed a much lower rate of readmission than those untreated. Patients in their study, however, were treated either with ECT or metrazol.

Recently, Winokur and Kadrmas (1988) reported that bipolar patients who received convulsive therapy showed more episodes, both mania and depressions, in the life-time course of their illness. Additionally, in another study, they showed an early age at onset, a subacute onset, a family history of bipolarity and the administration of ECT during an index episode

were all associated with a polyepisodic course of illness. All of those variables appeared to be individually related to the course of illness (Winokur and Kadrmas, in press).

A potential criticism of this study is the use of a control group that was admitted 10 years before the treated group. It is possible that a cohort effect may, in part, account for these findings. Nowhere in this study did any group show an excess of episodes prior to index admission. If a cohort effect is present, one would expect a difference in the course of illness prior to admission, as well as a difference after discharge. The point that these patients showed a difference in the course of illness only after the introduction of treatment would argue against a cohort effect.

The finding that no group had an excess of previous episodes is also important because patients with many prior episodes tend to have multiple subsequent episodes. The treated younger group went on to have more episodes and this may indicate an association with treatment and not merely represent a group of patients who naturally have multiple episodes.

Another potential criticism of this study is that patients who lived at a time when effective treatment was not available, i.e. 1935, may not return to the hospital during subsequent illnesses, simply because no treatment was available. The results of this study do not support that argument, as older untreated depressives showed no significant difference in readmissions as compared with the treated older group (11.4% vs 3.2%, $P = 0.12$). The influence of age on this differential response to ECT is interesting. These data suggest that older patients have a treatment-responsive illness and that receiving treatment significantly increases the likelihood of full recovery and reduces the time spent in the hospital. Younger depressed patients may have their episodes and hospitalizations shortened by the use of ECT, but these data suggest that younger patients treated with ECT may be at some risk for having an increase in the number of subsequent episodes after treatment. This differential response to ECT, based on age, has clinical implications. It suggests that older depressives may benefit quickly and more permanently from the use of ECT, whereas younger patients may either remit spontaneously with no treatment or may be better candidates for medication therapy. Although these data are tentative and need to be replicated, they do point to a specific indication for ECT in the population over 40 years of age. This is encouraging, since ECT has been advocated in the elderly because it may be safer and have fewer side effects than medication (Benbow 1985). A prospective study is needed to confirm these preliminary findings.

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Received September 28, 1988