Learning and Memory in Bipolar and Unipolar Major Depression: Effects of Aging

*†Tal Burt, M.D., *‡Joan Prudic, M.D., *‡Shoshana Peyser, Ph.D., *§Jennifer Clark, M.A., and
*†‡Harold A. Sackeim, Ph.D.

*Department of Biological Psychiatry, New York State Psychiatric Institute; and Departments of †Psychiatry and
‡Radiology, College of Physicians and Surgeons of Columbia University, New York, New York

Objective: The goal of this study was to examine the effects of aging on neuropsychological functions in bipolar and unipolar major depression. Background: Earlier studies suggested that neurocognitive deficits in mood disorder patients correlate with duration and severity of illness and also that bipolar disorder has a more virulent course than unipolar disorder. We hypothesized that elderly patients with bipolar disorder will demonstrate greater neurocognitive dysfunction than young patients with bipolar disorder and elderly patients with unipolar disorder. Method: A battery of tests of general intelligence and learning and memory was administered to 79 inpatients with major depression referred for electroconvulsive therapy. With patients 60 years of age and older defined as elderly, there were 29 young and 24 elderly unipolar patients and 13 young and 13 elderly bipolar patients. Results: Unipolar and bipolar patients did not differ in measures of general intelligence or global cognitive status. Generally, across tests of memory, young bipolar patients exhibited the best performance and elderly bipolar patients exhibited the poorest performance. Conclusions: The results suggest that over the course of their illness, patients with bipolar disorder experience greater deterioration in memory functions than patients with unipolar disorder. Longitudinal studies are required to support the preliminary findings of this cross-sectional study. (NNBN 2000;13:246–253)

There have been repeated demonstrations that patients in an episode of major depression manifest disturbance across a variety of neuropsychological domains (1–5). Deficits in retrieval from episodic or declarative memory are particularly common (6–11) (see reviews by Burt et al [12] and Kindermann and Brown [13]). A recent meta-analysis of 22 studies of neurocognitive deficits in major depression found that the greatest impairment occurred in tests of episodic declarative memory function (14).

Bipolar and unipolar major depression differ in phenomenologic features (15), typical age at onset (16,17), family history (18,19), and optimal forms of pharmacologic treatment (20). Despite these differences, relatively few investigations have contrasted neuropsychological performance in bipolar and unipolar depressed patients (21–25). In a meta-analysis, Burt et al (12) noted that recall deficits were of greater magnitude in population samples that contained both bipolar and unipolar depressed patients compared with population samples restricted only to patients with unipolar major depression. Kindermann and Brown (13) reached the same conclusion.

There is conflicting evidence that patients with bipolar illness achieve higher educational and/or occupational levels compared with patients with unipolar illness or other psychiatric groups (26–30). This might suggest that premorbid intellectual abilities are superior in bipolar patients relative to unipolar patients. This suggestion has received mixed empirical support (31–33). Conversely, bipolar illness typically has an earlier age of onset and more frequent affective episodes and hospitalizations. In euthymic women with a history of major depression, there is evidence that recurrent episodes are associated with diminished hippocampal volume (34,35). The volume of
the hippocampus has been inversely associated with the total duration of depressive episodes and linked to deficits on tests of verbal memory (34). In euthymic unipolar and bipolar patients, several recent studies have found that the number of psychiatric hospitalizations and the amount of time spent in depressive or manic episodes were inversely related to neurocognitive performance (36–38). Given the more virulent course of bipolar illness, we predicted that compared with unipolar patients or young bipolar patients, elderly patients with bipolar disorder would be especially characterized by deficits in retrieval from episodic memory.

This study examined an inpatient sample referred for treatment with electroconvulsive therapy (ECT). The use of this treatment modality ensured that the sample was characterized by severe depressive symptoms with considerable uniformity. After a medication washout, a battery of tests of general intelligence and learning and memory was administered. We contrasted the performance of groups defined by mood disorder diagnosis (bipolar vs unipolar illness) and age (<60 years old vs ≥60 years old), testing the hypothesis that deficits in learning and memory would be more marked in the elderly bipolar disorder group.

**METHOD**

**Patients**

Patients were participants in a research protocol examining the affective and cognitive consequences of ECT. All met the research diagnostic criteria (39) for major depression (unipolar or bipolar) on the basis of semistructured interviews using the Schedule for Affective Disorders and Schizophrenia (40) and other diagnostic information. At baseline, patients had a score on the 24-item Hamilton Rating Scale for Depression (HRSD) (41) of at least 18. Patients with a history of schizophrenia, schizoaffective disorder, other functional (nonmood disorder) psychosis, rapid cycling bipolar disorder, central nervous system disease or insult (including possible or probable Alzheimer disease), alcohol or substance abuse (other than nicotine) within the past year, ECT in the past 6 months, or serious medical conditions were excluded.

Eighty patients entered the research protocol, and 1 patient was excluded from neuropsychological testing because of visual impairment. There were 29 patients in the young (<60 years old) unipolar group, 24 patients in the elderly (≥60 years old) unipolar group, 13 patients in young bipolar group, and 13 patients in the elderly bipolar group.

**Neuropsychological Evaluation**

With the exception of lorazepam, patients were withdrawn from all psychotropic medications at least 5 days before neuropsychological testing (Table 1). Across the sample, the average duration of medication washout before neuropsychological evaluation was 11.42 days (SD = 8.05, 30-day upper limit). Lorazepam, used for anxiolytic/hypnotic purposes, was given as needed and limited to 3 mg/day (see Table 1), with an average dose across the

**Table 1. Demographic and clinical features of unipolar and bipolar depressed patients as a function of age group**

<table>
<thead>
<tr>
<th></th>
<th>Unipolar</th>
<th>Bipolar</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Young (n = 29)</td>
<td>Elderly (n = 24)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>46.45 ± 9.00</td>
<td>71.09 ± 9.44</td>
</tr>
<tr>
<td><strong>Sex (% female)</strong></td>
<td>65.52</td>
<td>62.50</td>
</tr>
<tr>
<td><strong>Education (years)</strong></td>
<td>14.52 ± 2.92</td>
<td>13.08 ± 3.66</td>
</tr>
<tr>
<td><strong>Socioeconomic status</strong></td>
<td>2.28 ± 1.13</td>
<td>2.58 ± 1.18</td>
</tr>
<tr>
<td>Hamilton Rating Scale for Depression</td>
<td>31.14 ± 6.74</td>
<td>31.52 ± 8.86</td>
</tr>
<tr>
<td>Psychotic depression (%)</td>
<td>31.03</td>
<td>41.67</td>
</tr>
<tr>
<td>Duration current episode (weeks)</td>
<td>45.52 ± 29.62</td>
<td>40.50 ± 36.04</td>
</tr>
<tr>
<td>Age at onset (years)</td>
<td>33.66 ± 14.02</td>
<td>53.13 ± 14.62</td>
</tr>
<tr>
<td>Previous affective episodes*</td>
<td>2.38 ± 2.24</td>
<td>2.08 ± 2.21</td>
</tr>
<tr>
<td>Previous psychiatric hospitalization*</td>
<td>1.48 ± 2.20</td>
<td>1.96 ± 2.31</td>
</tr>
<tr>
<td>Past electroconvulsive therapy (%)</td>
<td>27.59</td>
<td>45.83</td>
</tr>
<tr>
<td>Psychotropic washout (days)†</td>
<td>11.24 ± 8.04</td>
<td>10.42 ± 8.04</td>
</tr>
<tr>
<td>Lorazepam (mg/day)</td>
<td>1.54 ± 1.10</td>
<td>1.16 ± 1.12</td>
</tr>
</tbody>
</table>

*Upper limit of 10 imposed.
†Upper limit of 30 days imposed.
sample of 1.44 mg/day (SD = 1.19). To assess general intellectual function, patients were administered the Wechsler Adult Intelligence Scale—Revised (42). Global cognitive status was assessed with the modified Mini-Mental State Examination (mMMS) (43). The mMMS is an expanded version (range, 0–57) of the original MMS (44) and contains additional items for digit span, forward/backwards, confrontation naming, more copying tasks, and other items. Reliability and validity have been established (45,46).

A series of learning and memory tasks were administered. The Buschke Selective Reminding Test (SRT) (47,48) was given using 12 words and 10 trials. Free recall was assessed after a 2-hour delay, and the full SRT procedure was then repeated. For this study, the dependent measures were total recall across the 10 trials at first administration, first trial delayed free recall, and total recall across the 10 trials at the second administration.

Recognition memory for verbal and nonverbal material was assessed with paired-word and paired-face tasks (49,50). The paired-word task involved presentation of 30 word pairs. After presentation of these items, acquisition was assessed by presenting a target and four foils (including the paired word). The paired-face task involved presentation of 20 face pairs in two sets of 10 pairs. Presentation of each set was followed by immediate recognition testing using a target and three foils (including the paired face). The stimuli (faces from 1950s high school yearbooks) for a given trial were matched for gender and perspective. After 4 hours, delayed recognition memory was assessed for both tasks. The number of correct responses at immediate and delayed testing served as the dependent measures. The order of the paired-face and paired-word tasks was randomized.

Complex figure copying and reproduction were tested, randomizing patients to the Rey-Osterrieth, Taylor, or Richie figure (51,52). Patients copied the figure, and reproduction from memory was tested after 3-minute and 20-minute delays. Copy and 20-minute delayed scores were used.

The complete Randt Memory Test was administered (53,54). Subtests included immediate and delayed memory for a word list (five items), verbal paired associates (six associates), story recall, and picture recognition (seven objects). The dependent measures were scores for immediate acquisition and 24-hour delayed recall. After the 24-hour delay, verbal recall was assessed for the picture objects.

Statistical Analyses

For continuous measures of demographic and clinical features, ANOVAs were conducted with diagnosis (unipolar vs bipolar disorder) and age group as between-subject terms. Significant interactions were followed by Newman-Keuls post hoc comparisons to identify the sources of difference between the four groups. Log-linear analyses were used for analysis of dichotomous variables with diagnosis (unipolar vs bipolar disorder) and age group as between-subject terms. To contrast the groups in terms of neuropsychological scores, ANCOVAs were conducted on each neuropsychological measure with diagnosis (unipolar vs bipolar disorder) and age group as between-subject terms and years of education as the covariate. In virtually all analyses, there were substantial covariate effects, which are not reported here. Post hoc comparisons of the diagnostic and age groups were based on t tests on least-squares adjusted means, without correction for multiple comparisons.

To test the main hypothesis, significant interactions should be obtained between diagnosis (unipolar vs bipolar disorder) and age group in the ANCOVAs on learning and memory scores. Power to detect such interactions was modeled assuming a moderate effect size for the main effect of age group ($f = 0.25$), no effect for diagnosis ($f = 0.0$), and $R^2 = 0.16$ for the covariate, education, with the dependent neuropsychological measure. Under these assumptions, and with a total sample size of 79, the effect size must be $f = 0.30$ or greater to have at least an 80% probability of detecting a significant interaction. This corresponds to an effect size considered to be between moderate and large in magnitude (55). Given its limited power and the exploratory nature of this study, statistical correction was not used for multiple comparisons.

RESULTS

Demographic and Clinical Features

Table 1 presents demographic and clinical features for the four groups. The ANOVA on age yielded a main effect of age group ($F[1,75] = 145.87, p < 0.0001$) and a trend for a main effect of diagnosis (unipolar vs bipolar disorder) ($F[1,75] = 3.10, p = 0.08$), with bipolar patients tending to be younger than unipolar patients. There were no effects regarding the distribution of gender. With respect to years of education, there was a main effect of diagnosis ($F[1,75] = 10.35, p = 0.002$) and a trend for an effect of age group ($F[1,75] = 3.87, p = 0.05$). Bipolar patients had more years of education than unipolar patients. Socioeconomic status, assessed with the Hollingshead four-factor index (56), did not differ between the groups.

Presence or absence of psychotic (delusional) depression and severity of depressive symptoms as assessed with the HRSD did not differ between the groups. Likewise, the groups were equivalent in the duration of the current episode of major depression. As expected, there was a main effect of diagnosis on age at onset of mood disorder ($F[1,75] = 16.17, p < 0.0001$) as well as a main effect of...
age group, \(F[1,75] = 28.50, p < 0.0001\). Bipolar and younger patients had an earlier age at onset. For number of prior affective episodes, there was a main effect of diagnosis \(F[1,75] = 25.20, p < 0.0001\), a trend for age group \(F[1,75] = 3.14, p = 0.08\), and a significant interaction \(F[1,75] = 5.16, p = 0.03\). Post hoc comparisons indicated that the elderly bipolar group had a greater number of prior episodes than the three other groups, which did not differ from one another. A similar pattern characterized the number of previous psychiatric hospitalizations. There were main effects of diagnosis \(F[1,75] = 8.43, p = 0.005\) and age group \(F[1,75] = 7.37, p = 0.008\) as well as a trend for an interaction \(F[1,75] = 3.82, p = 0.05\). Post hoc comparisons indicated that elderly bipolar patients had more prior hospitalizations than any other group. There was a main effect of age group on history of previous treatment with ECT, \(\chi^2[1] = 8.51, p = 0.004\), with older patients more likely to have received this treatment in the past.

There was no difference between the groups in the duration of medication washout before neuropsychological testing or in the amount of lorazepam administered at the time of testing.

Overall, these analyses suggest that at the time of evaluation, the patient groups were comparable in severity of illness. As expected, elderly bipolar patients had a history of more frequent episodes and hospitalizations. Independent of age, bipolar patients were better educated than unipolar patients.

### Neuropsychological Testing

**Intelligence and Global Cognitive Status**

There were no significant effects in the analysis of verbal IQ scores (Table 2). For performance IQ, there was a main effect of age group \(F[1,63] = 5.63, p = 0.02\), Older patients had lower scores. Similarly, for the mMMS, there was a main effect of age group \(F[1,74] = 10.59, p = 0.002\), with older patients having lower scores.

**Learning and Memory**

Table 3 presents scores for the four groups on the tests of learning and memory. Each of the ANCOVAs on the three scores for the Buschke SRT yielded a main effect of age group \((p \leq 0.002)\), with the older patients having lower scores. In addition, the ANCOVA on total recall at first administration produced a trend for interaction between diagnosis and age group \(F[1,71] = 3.30, p = 0.07\). This effect was significant in the ANCOVA on total recall scores at the second administration \(F[1,71] = 4.58, p < 0.04\). For both measures, elderly bipolar patients had the poorest scores. Post hoc comparisons indicated that for total recall at the first administration, elderly bipolar patients had poorer performance than young unipolar and young bipolar patients. For the second administration, elderly bipolar patients had significantly poorer performance than each of the three remaining groups.

There was a main effect of age group for immediate recognition scores on the paired-word task \(F[1,68] = 26.04, p < 0.0001\). This effect was greater in magnitude for delayed recognition scores \(F[1,68] = 33.19, p < 0.0001\). There were no effects involving the diagnostic group.

The ANCOVA on paired-face immediate recognition scores produced a main effect of age group \(F[1,68] = 22.44, p < 0.0001\) and a trend for an interaction between diagnosis and age group \(F[1,68] = 3.64, p = 0.06\). In adjusted means, young bipolar patients had superior performance and elderly bipolar patients had the poorest performance. For delayed recognition performance, there was a main effect of age group \(F[1,68] = 7.94, p = 0.006\) and an interaction between diagnosis and age group \(F[1,68] = 8.19, p = 0.006\). Post hoc comparisons indicated that the young bipolar patients had superior delayed recognition scores relative to each of the other three groups and that older bipolar patients had inferior performance relative to each of the other groups.

There was a main effect of age group on complex figure copying scores \(F[1,63] = 10.26, p = 0.002\), and there was an interaction between diagnosis and age group \(F[1,63] = 4.04, p < 0.05\). Post hoc comparisons indicated that the older bipolar patient group had poorer scores than the other three groups. The analysis of delayed reproduction scores also produced a main effect of age group \(F[1,63] = 27.24, p < 0.0001\) and an interaction

### TABLE 2. Wechsler Adult Intelligence Scale–Revised and modified Mini-Mental State Examination scores adjusted for education

<table>
<thead>
<tr>
<th></th>
<th>Unipolar</th>
<th>Bipolar</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Young</td>
<td>Elderly</td>
</tr>
<tr>
<td>WAIS-R verbal IQ</td>
<td>105.63 ± 12.47</td>
<td>103.91 ± 12.24</td>
</tr>
<tr>
<td>WAIS-R performance IQ</td>
<td>98.35 ± 12.15</td>
<td>91.69 ± 11.92</td>
</tr>
<tr>
<td>mMMS</td>
<td>51.76 ± 5.45</td>
<td>47.86 ± 5.61</td>
</tr>
</tbody>
</table>

WAIS-R, Wechsler Adult Intelligence Scale–Revised; mMMS, modified Mini-Mental State Examination.
### TABLE 3. Scores on tests of learning and memory adjusted for education

<table>
<thead>
<tr>
<th></th>
<th>Unipolar</th>
<th>Bipolar</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Young</td>
<td>Elderly</td>
</tr>
<tr>
<td><strong>Buschke Selective Reminding Test</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total recall: first administration</td>
<td>92.06 ± 19.51†</td>
<td>82.98 ± 20.04†</td>
</tr>
<tr>
<td>2-hour delayed free recall</td>
<td>9.01 ± 2.70</td>
<td>7.36 ± 2.77</td>
</tr>
<tr>
<td>Total recall: second administration</td>
<td>100.54 ± 21.60†</td>
<td>97.45 ± 22.19†</td>
</tr>
<tr>
<td><strong>Paired-word recognition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate</td>
<td>21.57 ± 5.85</td>
<td>14.55 ± 5.95</td>
</tr>
<tr>
<td>4-hour delay</td>
<td>19.44 ± 6.15</td>
<td>11.23 ± 6.25</td>
</tr>
<tr>
<td><strong>Paired-face recognition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate</td>
<td>13.76 ± 3.37†</td>
<td>11.30 ± 3.43†</td>
</tr>
<tr>
<td>4-hour delay</td>
<td>10.11 ± 2.84†</td>
<td>10.11 ± 2.88†</td>
</tr>
<tr>
<td><strong>Complex figure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Copy</td>
<td>32.75 ± 6.24†</td>
<td>30.69 ± 6.33†</td>
</tr>
<tr>
<td>20-minute reproduction</td>
<td>19.10 ± 7.38†</td>
<td>12.88 ± 7.49†</td>
</tr>
<tr>
<td><strong>Randt Memory Test</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Five items acquisition</td>
<td>10.69 ± 3.01</td>
<td>9.56 ± 3.10</td>
</tr>
<tr>
<td>Five items 24-hour delay</td>
<td>1.74 ± 1.58†</td>
<td>2.07 ± 1.62†</td>
</tr>
<tr>
<td>Paired-word acquisition</td>
<td>13.72 ± 3.71†</td>
<td>12.44 ± 3.81</td>
</tr>
<tr>
<td>Paired-word 24-hour delay</td>
<td>3.66 ± 1.82</td>
<td>3.42 ± 1.87</td>
</tr>
<tr>
<td>Short story immediate gist</td>
<td>4.84 ± 2.39</td>
<td>4.80 ± 2.46</td>
</tr>
<tr>
<td>Short story 24-hour gist</td>
<td>4.81 ± 2.33</td>
<td>3.55 ± 2.40</td>
</tr>
<tr>
<td>Picture recognition immediate</td>
<td>6.76 ± 0.95</td>
<td>6.37 ± 0.97</td>
</tr>
<tr>
<td>24-hour delayed verbal recall of pictures</td>
<td>3.57 ± 2.32</td>
<td>4.13 ± 2.38</td>
</tr>
</tbody>
</table>

*Probability value for the interaction between diagnosis (unipolar vs bipolar) and age group (young vs elderly) in the ANCOVA on the neuropsychological measure.

†Values differed significantly (\( p < 0.05 \)) in post hoc comparisons of least-squares adjusted means. Post hoc comparisons are only reported when the interaction between diagnosis and age group in the ANCOVA yielded a probability value less than or equal to 0.10.

between diagnosis and age group (\( F[1,63] = 4.51, p = 0.04 \)). The elderly bipolar patient group had markedly low reproduction scores and differed from each of the remaining groups. Elderly unipolar patients had poorer performance than young unipolar and bipolar patients.

The Randt five-item word test involved three trials of selective reminding. There was only a main effect of age group for immediate acquisition scores (\( F[1,66] = 7.95, p = 0.006 \)). In contrast, there was no interaction between diagnosis and age group for scores on 24-hour delayed recall (\( F[1,64] = 4.13, p < 0.05 \)). Older bipolar patients had significantly poorer recall than the patients in the other groups.

Paired associate acquisition used six word pairs and a restricted reminding procedure and three trials. The ANCOVA on acquisition scores only yielded a main effect of age group (\( F[1,66] = 6.54, p < 0.01 \)). In contrast, analysis of 24-hour delayed recall scores yielded a trend for a main effect of diagnosis (\( F[1,67] = 3.37, p = 0.07 \)). Although this trend reflected poorer scores among bipolar patients, this effect was principally due to poorer recall performance in the elderly bipolar patients (see Table 3).

There were no differences between the groups in immediate recall of the gist of the short story. At 24-hour delayed recall, elderly bipolar patients had the poorest scores. For this measure, only the main effect of age group was significant (\( F[1,62] = 8.75, p < 0.006 \)).

There were no differences between the groups in immediate picture recognition. At 24-hour delayed recall, the elderly bipolar group again had the poorest scores, but the interaction between diagnosis and age group was not significant (\( F[1,60] = 2.57, p = 0.11 \)), and there were no other significant effects.

### Regression Model

The elderly bipolar patients in this sample had more prior episodes of affective illness and more psychiatric hospitalizations than any other group. There is some evidence that lifetime duration of mood disturbance is related to neuropsychological deficits (34.36–38). We examined whether the number of affective episodes and severity of depression could account for the findings of neuropsychological impairment in the elderly bipolar group.

Delayed recognition performance on the paired-face task yielded the largest effect size for the interaction between diagnosis and age group. A simultaneous multiple regression analysis was conducted predicting these scores on the basis of diagnosis (1 = unipolar, 2 = bipolar), age, interaction between diagnosis and age, number of previous affective episodes, interaction between diagnosis and number of episodes, pretreatment HRSD score, and education. The results of this analysis are presented in Table 4.

The overall model was significant (\( F[7,65] = 3.61, p = 0.002 \)), accounting for 28% of the variance in delayed
TABLE 4. Simultaneous regression analysis predicting delayed recognition scores on the paired-face task

<table>
<thead>
<tr>
<th>Variable</th>
<th>Parameter estimate</th>
<th>SE</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>6.94</td>
<td>4.45</td>
<td>1.56</td>
<td>0.12</td>
</tr>
<tr>
<td>UPBP disorder</td>
<td>5.82</td>
<td>2.60</td>
<td>2.24</td>
<td>0.03</td>
</tr>
<tr>
<td>Age</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
<td>1.05</td>
</tr>
<tr>
<td>UPBP disorder x age</td>
<td>-0.10</td>
<td>0.05</td>
<td>-2.18</td>
<td>0.03</td>
</tr>
<tr>
<td>Episode number</td>
<td>0.18</td>
<td>0.41</td>
<td>0.43</td>
<td>0.67</td>
</tr>
<tr>
<td>UPBI disorder x episode number</td>
<td>-0.06</td>
<td>0.27</td>
<td>-0.23</td>
<td>0.82</td>
</tr>
<tr>
<td>HRSD score</td>
<td>-0.09</td>
<td>0.05</td>
<td>-2.05</td>
<td>0.04</td>
</tr>
<tr>
<td>Education</td>
<td>0.11</td>
<td>0.10</td>
<td>1.08</td>
<td>0.28</td>
</tr>
</tbody>
</table>

UPBP, unipolar versus bipolar; HRSD; Hamilton Rating Scale for Depression.

recognition scores. There was no evidence that the number of affective episodes, either alone or in interaction with diagnosis, was related to task performance. Greater depression severity was associated with poorer delayed recognition memory. Overall, bipolar patients had superior performance. Nevertheless, in line with the major hypothesis, there was a significant interaction between diagnosis and age, indicating that older age was associated with inferior recognition memory performance among bipolar patients. Adding the presence or absence of delusional depression to the model only strengthened the interaction between diagnosis (unipolar vs bipolar disorder) and age.

DISCUSSION

This study supports the notion that over the course of their illness, there is greater deterioration of memory function in patients with bipolar disorder compared with patients with unipolar disorder. With considerable consistency, the elderly bipolar patient group had the poorest performance in measures of delayed retrieval compared with each of the other groups. No differences were observed between bipolar and unipolar patients in verbal or performance IQ or in a measure of global cognitive status (mMMS). Similarly, the pattern of greater relative deficit in elderly bipolar patients was generally not observed in measures of learning. These findings suggest that the deficits in elderly bipolar patients show a degree of specificity and may be most marked for retrieval from declarative memory.

If these observations are valid, they suggest that age or factors associated with age exert a greater impact on neuropsychological function in bipolar patients compared with unipolar patients. It was noteworthy that bipolar patients attained higher levels of education than unipolar patients in this sample, independent of age group. This is compatible with the findings of some prior reports (26,29, 30,57) and may help to account for the trends of superior mnemonic performance in young bipolar patients. Conversely, elderly bipolar patients also had an educational advantage, especially in relation to elderly unipolar patients, and yet typically performed poorest on tests of delayed retrieval.

It is not known why elderly bipolar patients showed the greatest performance deficits. This group was distinguished by a greater number of prior affective episodes and hospitalizations than any of the other groups. As indicated, there is evidence from studies of euthymic unipolar and bipolar patients that deficits in attention, memory, and executive function are associated with frequency of psychiatric hospitalization and/or total duration of affective episodes (36–38). This would imply a toxic effect of acute episodes of mood disorder, a notion compatible with the finding that decreased hippocampal volume is correlated with total lifetime duration of depressive episodes (34,35,58). When we examined the relation between the number of episodes of mood disturbance and performance on the measure that showed the greatest deterioration with aging among bipolar patients, no evidence was obtained for an association. Conversely, it is also conceivable that some treatments used for mood disorders may exert long-term iatrogenic effects. For instance, it is likely that the elderly bipolar group differed from the other groups in terms of lifetime exposure to lithium (59–61). In this regard, it is noteworthy that elderly bipolar and unipolar patients did not differ in history of treatment with ECT.

Elderly patients with mood disorders show an excess of hyperintensities on magnetic resonance imaging, which is usually interpreted as a manifestation of cerebrovascular disease (62–65). In normal, neurologic, and mood disorder population samples, there is evidence that these abnormalities, when severe, are associated with cognitive deficits (63,64). There is no evidence that these magnetic resonance imaging abnormalities are more characteristic of elderly bipolar patients than of elderly unipolar patients, however. Indeed, the opposite may be the case (66).

These accounts of the neuropsychological patterns observed in this study imply that the differences between the groups would be maintained in the euthymic state. A toxic effect of prior episodes of depression, a long-term iatrogenic effect of treatment, or a consequence of structural brain abnormality should be observed independent of affective state. Clearly, this is an issue that requires further investigation.

This study had a number of limitations. There is the obvious limitation of using a cross-sectional design to examine a “course” hypothesis. Indeed, the lack of a positive finding for course variables (i.e., number of affective episodes) raises the possibility that noncourse features may be operating to produce the pattern of findings. The number of bipolar patients was relatively small, limiting
statistical power. The cutoff for age (<60 years or ≥60 years) was arbitrary, producing comparably sized young and elderly groups but not necessarily optimal for revealing aging effects. The neuropsychological measures primarily focused on episodic learning and memory, and broader neuropsychological assessment is needed to determine the specificity of interactions between mood disorder diagnosis and age. Although patients were free of almost all psychotropic medications at time of evaluation, they did receive low doses of a benzodiazepine, which can adversely affect memory (67). It is uncertain whether the elderly bipolar and unipolar groups were comparable in terms of other medical conditions that might affect cognition. Nonetheless, this study provides the first indication that among patients in an episode of major depression, age and mood disorder diagnosis interact in determining the magnitude of impairment in retrieval from declarative memory.

Acknowledgment: This study was supported in part by grant R37 MH35636 from the National Institute of Mental Health and by a young investigator grant from the Stanley-Vada Foundation to Dr. Burt.

REFERENCES


