Leukotomy and Aging in Chronic Schizophrenia: A Followup Study 40 Years After Psychosurgery

by Philip D. Harvey, Richard C. Mohs, and Michael Davidson

Abstract

Many followup studies have found that frontal leukotomy does not lead to marked changes in behavioral or cognitive functions in patients with chronic schizophrenia. However, these studies left open the issue of whether aging interacts with frontal lobe lesions in some way. This study examined 24 elderly schizophrenia patients who had experienced a bifrontal leukotomy and 48 subjects who were similar to the leukotomized patients in age, gender, chronicity, and overall severity of cognitive impairment. Clinical ratings of schizophrenic symptoms and cognitive deficits were obtained, as was a neuropsychological evaluation. Very few cognitive effects of leukotomy were noted, although clinically rated deficits in self-care were more severe in the leukotomized sample. These findings again suggest that the cognitive effects of frontal leukotomy procedures are limited and imply that aging does not interact substantially with leukotomy in patients with chronic schizophrenia.

A lack of demonstrable therapeutic efficacy has led to the abandonment of surgery of the frontal lobe as an intervention for chronic schizophrenia. Between 1947 and 1956, the peak period for this procedure, more than 10,000 psychiatric patients underwent some form of surgery affecting the frontal lobe. The most common forms were the bifrontal leukotomy procedure, which consisted of bilateral incisions introduced through holes cut with a burr in the lateral skull, and transorbital procedures, followed by a variety of alternative procedures that varied in the degree of tissue damage they induced. Like focal neurological lesions, frontal lobe surgery may constitute a “natural experimental paradigm” for understanding the functions of the frontal lobe in human subjects (Stuss et al. 1983; Goldberg et al. 1989a). Furthermore, this procedure could be of particular importance to the understanding of the pathophysiological processes active in schizophrenia, inasmuch as some of the behavioral abnormalities in schizophrenia have been attributed to malfunctions of the frontal lobe (Weinberger et al. 1986, 1992; Weinberger 1987, 1988; Buchsbaum 1990; Robbins 1990). Because the leukotomy procedure was virtually abandoned in the late 1950s, patients on whom its effects are studied today are typically quite old. Therefore, any conclusions have to be interpreted as reflecting the potential interactions between the lesion, schizophrenia, and aging.

If we borrow from neurodevelopmental models of schizophrenia (e.g., Weinberger 1987) in which a static lesion present at birth or before is expressed later, in the second or third decade of life, it may be hypothesized that the effects of frontal lobe lesions induced by a leukotomy could become more evident with aging. This field of study is particularly relevant because the frontal lobe is involved in most cognitive functions, and many elderly schizophrenia patients suffer from severe

Reprint requests should be sent to Dr. P.D. Harvey, Dept. of Psychiatry, Box 1229, Mt. Sinai School of Medicine, New York, NY 10029.
cognitive impairments. Finally, a recent study has suggested that cognitive deficits are very stable in schizophrenia patients between the ages of 18 and 65 (Goldberg et al. 1992). Consequently, the high prevalence of severe cognitive impairment in very elderly schizophrenia patients (Ciompi 1980; Harvey et al. 1992) must be associated with cognitive changes after the age of 65. Thus, a followup of leukotomized patients older than 65 might reveal more cognitive effects of leukotomy than would studies of younger patients.

The majority of previous research studies have reported that standard leukotomy procedures administered to schizophrenia patients fail to induce deficits in cognitive and intellectual functions relative to the individuals’ preprocedure level and to levels of control samples (Stuss and Benson 1986; Joschko 1985). The most comprehensive assessment efforts were from the Northampton series (Benson et al. 1981; Benson and Stuss 1982; Stuss et al. 1986); these studies reported that (1) lesioned subjects performed no more poorly than equivalently ill nonlesioned patients across the majority of measures of neuropsychological functions; (2) size of lesion failed to directly predict cognitive dysfunction, although larger frontal lobe lesions predicted better recovery; and (3) severity of schizophrenic illness was the best predictor of the severity of impairment on the neuropsychological indicators of frontal lobe dysfunction.

There are several methodological limitations in previous studies of the sequelae of leukotomy. The small sample sizes in the Northampton series introduce the possibility that the lack of statistically significant effects of the cortical lesion are related to low levels of statistical power. Other studies have used comparison samples that were very dissimilar from the psychosurgery patients (Mirsy and Orzack 1977). Not all schizophrenia patients received a leukotomy; aspects of selection for leukotomy may influence postprocedure test scores (Joschko 1985). Selection of tests is important as well. Many studies of cognitive functions in leukotomized patients have used either tests that are heterogeneous in nature (e.g., the Wechsler Memory Scales—WMS; Wechsler 1945; Mirsky and Orzack 1977; Stuss et al. 1983) or tests that measure functions that are subserved by other cortical areas (such as the temporal lobes). The one study that used measures of memory functions that are generally accepted to be dependent on the frontal lobes (Stuss et al. 1983) found an effect of leukotomy on performance. Finally, the level of recovery of the patients may be important as well, because the results of the Northampton studies suggested that leukotomized patients with a “good” level of recovery manifest postleukotomy intelligence scores that are higher than those of the nonsurgical comparison group (Stuss et al. 1983).

The present report describes a clinical and neuropsychological followup study of leukotomized patients approximately 40 years after the procedure, a period 15 years longer than any previous followup of such patients. Twenty-four elderly schizophrenia patients who had experienced a leukotomy were compared with 48 elderly nonleukotomized schizophrenia patients. Both groups were residents of the same long-term chronic psychiatric hospital. Patients in the comparison sample were selected for similarity to the leukotomy sample in medication status, gender, age at first admission to psychiatric care, length of current stay, and overall severity of cognitive impairments. We considered the possibility that the indications for leukotomy 40 years ago might have resulted in the selection of a particular group of patients with a characteristic behavior or pattern of psychiatric symptoms that would then be indistinguishable from the consequences of leukotomy. During the screening process we found five schizophrenia patients for whom the indications for leukotomy were established but who, owing to factors not related to medical or psychiatric variables, never received the procedure. These patients constitute a valuable comparison group. Their data were compared with those of the other two samples, with the understanding that a small sample may not be fully representative of patients for whom the indications for leukotomy were established.

All of the patients were assessed for current severity of clinical symptoms on the Positive and Negative Syndrome Scale (PANSS; Kay et al. 1987) and for severity of clinically rated cognitive impairment on the Clinical Dementia Rating (CDR) scale (Berg 1988). To examine the effect of surgery on specific areas of cognition, we examined all patients with a neuropsychological battery. The neuropsychological battery was designed to assess cortical functions that were (1) supposedly specific to the prefrontal cortex; (2) supposedly dependent on, but not specific to, the prefrontal cortex; or (3) supposedly specific to areas other than the prefrontal cortex. Between-groups analyses compared
the leukotomized and nonleukotomized samples on positive, negative, and general psychiatric symptoms; on the severity of six different clinically rated aspects of cognitive impairments; and on neuropsychological performance. These data provide information regarding the possibility that focal frontal lesions interact with aging to produce greater deterioration than has previously been found in shorter term followup studies. In addition, the sample size of the present study leads to greater power in statistical analyses than was achieved in previous studies of comprehensively assessed samples.

Methods

Subjects. The subjects were 72 geriatric inpatients at a State psychiatric center who were part of a larger study of cognition and clinical symptoms in elderly schizophrenia patients. Twenty-four of these patients had undergone a leukotomy between 1948 and 1956. A chart review was used to determine preprocedure DSM-III-R (American Psychiatric Association 1987) diagnoses for the patients who had received the procedure. Each patient’s chart was reviewed by a research psychiatrist who re-assessed the patient’s lifetime primary psychiatric diagnosis. Particular attention was given to historic data in the medical records or provided by informants: the patient’s entire lifespan was covered and whether or not the patient met DSM-III-R criteria was documented for each decade. Symptoms were not counted as present unless specific examples were given in the chart and unless their presence could be documented in more than one decade. To exclude developmental disorders, mental retardation, and presenile dementia, we excluded from the study patients in whom the primary psychiatric symptoms started before age 18 or after age 45. The diagnostic and assessment procedure for the larger study as a whole, which included 308 geriatric schizophrenia inpatients, is presented in Harvey et al. (1992).

All patients in the leukotomy sample had received bilateral prefrontal leukotomies performed with the Freeman and Watts (1942) procedure. The operative reports were in the charts of all patients who participated in this study, and these reports were read to confirm that the patients had in fact received the leukotomy and that they had all been operated on with the same procedure. There were a total of 51 patients in the sample of 308 who had received a leukotomy, according to hospital records. Patients were included in the detailed neuropsychological assessment only if their global cognitive impairment was found to be moderate or less (a CDR global score of $\leq 2$). This requirement led to the exclusion of 17 patients on the basis of excessive cognitive impairment; the charts of 10 more patients lacked the operative reports. When the 51 patients in the larger sample who had received a leukotomy were compared with the nonleukotomized patients on the Mini-Mental State Examination (Folstein et al. 1975), there was no significant difference ($t[306] = -0.48$). Thus, the overall sample of patients did not differ in global cognitive functioning status before selection of this subset for more detailed analysis.

The other 48 subjects were patients who also met lifetime diagnostic criteria for schizophrenia, as described above. Comparison patients were matched to the leukotomized patients for neuroleptic medication status, age (within 2 years), gender, and severity of global cognitive impairment. These patients were also selected for similarity to the leukotomy sample for year of initial admission to a psychiatric facility. No patients were accepted into the study if they had completed fewer than 6 years of education. These patients were matched in a ratio of 2 to 1 to the leukotomy patients so that the sample of subjects would be as representative as possible of the larger sample of inpatients.

An additional five patients constituted a special comparison sample. These patients had received a diagnosis of schizophrenia and had been approved for leukotomy but had not undergone the procedure, either because of administrative errors or because their relatives withdrew consent immediately before the procedure. This group represents a control for the aspects of clinical presentation that led to the decision to perform a leukotomy.

Two-thirds of all patients in the samples were receiving minimal doses of neuroleptic medication, and they were tested while receiving this medication. Data on the medication status of the patients, as well as other descriptive data, are presented in table 1. The demographic information was tested across the samples with chi-square analyses and t-tests. None of the between-groups differences was significant.

Clinical Assessments. Current psychiatric symptoms were assessed with the PANSS, a 30-item scale that is divided into three
Table 1. Descriptive information on subjects

<table>
<thead>
<tr>
<th>Subject Group</th>
<th>Leukotomy (n = 24)</th>
<th>No leukotomy (n = 48)</th>
<th>Approved (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (mean/SD)</strong></td>
<td>76.0</td>
<td>78.1</td>
<td>72.6</td>
</tr>
<tr>
<td><strong>Gender (% female)</strong></td>
<td>66</td>
<td>66</td>
<td>60</td>
</tr>
<tr>
<td><strong>Length of current hospitalization (yrs) (mean/SD)</strong></td>
<td>42.2</td>
<td>42.8</td>
<td>42.0</td>
</tr>
<tr>
<td><strong>Years of education (mean/SD)</strong></td>
<td>10.1</td>
<td>9.4</td>
<td>9.6</td>
</tr>
<tr>
<td><strong>Neuroleptic medication (% receiving)</strong></td>
<td>75</td>
<td>75</td>
<td>80</td>
</tr>
<tr>
<td><strong>Daily dosage of medicated patients (CPZ equivalent) (mean/SD)</strong></td>
<td>294.8</td>
<td>301.0</td>
<td>312.50</td>
</tr>
</tbody>
</table>

Note.—SD = standard deviation; CPZ = chlorpromazine.

subscales that measure “positive,” “negative,” and “general” symptoms (Kay et al. 1987). To evaluate the reliability of these ratings in the overall study from which the present sample was selected, two raters who observed the same interview performed 54 assessments. Intraclass correlation coefficients were computed for the 30 items, and the correlations were found to be uniformly high, ranging from 0.86 to 1.00 (all p < 0.001). The dependent variables taken from the PANSS were the total severity scores from the positive, negative, and general subscales.

Cognitive impairment was assessed with the CDR scale (Berg 1988). The CDR is a staging scale for the severity of dementia that consists of six categories: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. Global severity of cognitive impairment is rated on a 5-point scale on which scores of 0 or 1 reflect the absence of dementia or mild dementia and scores of 2 to 5 reflect moderate to terminal dementia. The advantage of this scale is that it reflects a composite picture of a subject's functioning within his or her environment, partially eliminating the effects of motivation. The intraclass correlations of the individual CDR items ranged from 0.80 to 0.92; the global CDR rating was 0.86.

Neuropsychological Battery. The neuropsychological battery was designed to assess a variety of cognitive functions. The battery was administered to the subjects in a single assessment session whenever possible. None of the leukotomy patients who met the study's entry criteria for diagnosis, operative procedure status, or severity of cognitive impairment was untestable with the battery as a whole. It was impossible to ensure that testers were unaware of the leukotomy status of the patients because of the prominent cranial stigmata of some of these patients. The tests which performed the neuropsychological assessment were unaware of patients' level of cognitive impairment, as defined by the CDR, and specific PANSS symptom ratings.

Wisconsin Card Sorting Test (WCST). The WCST (Heaton 1981) is a measure of conceptual functions that has been demonstrated to be sensitive to frontal lesions, particularly in the dorsolateral aspects of the prefrontal cortex (Milner 1963). One previous report (Milsky and Orzack 1977) suggested that leukotomized patients show an increase in perseverative errors on this test. The dependent variables were the number of categories completed and the number of perseverative errors.

Spatial Delayed Response and Spatial Delayed Alternation. Spatial delayed response performance is reduced by lesions of the lateral frontal lobe in primates (Fuster 1989); studies in this area date back nearly 60 years (Jacobson 1935). In addition, delayed alternation paradigms are sensitive to functions of the frontal area, and there is some evidence that performance of delayed alternation tests activates the dorsolateral prefrontal cortex (Berman et al. 1991). In the delayed response task,
subjects were presented with a stimulus location that was randomly distributed between the right and left sides of two 3 × 3-cm monochrome cards placed in front of the subject. The ascending method of limits was used to determine the subject’s memory threshold for a nonverbal (i.e., pointing) response. The interval was altered in 1-second increments until a criterion of seven consecutive correct responses at that interval and fewer than seven at the next higher interval was met. For delayed response, the instructions were to identify the location of the stimulus; for delayed alternation, the instructions required the subject to point alternately to the location and to the contralateral location. For each condition the dependent variable was the memory threshold. This specific test has not previously been applied in patients who have undergone a leukotomy.

Verbal Recall and Recognition. Although verbal learning and memory abilities are generally agreed to be dependent on the functions of the left temporal cortex (Saykin et al. 1991), frontal lobe lesions may also be associated with specific deficits in the ability to recall serially presented information, while having a lesser impact on recognition performance (Goldberg et al. 1989b). Calev (1984) created psychometrically matched recall and recognition tasks that were of equal difficulty for normal subjects and demonstrated that chronicity in schizophrenia was associated with somewhat greater deficits in recall than in recognition performance. These two tasks were used in the present study. In the recall task, a 24-word list is presented, and free recall is immediately required of the subject. In the recognition task, the subject is presented with a single 24-item list, and recognition is immediately required. The recognition sheet contains the target words and 16 foils. The dependent variable in each task was the difference between recognition and recall performance. This test has not previously been applied in patients who have undergone a leukotomy.

Verbal Fluency. Tests of verbal fluency (i.e., controlled word association) are often used to assess language deficits associated with frontal lobe lesions. Left-sided lesions of the anterior brain regions lead to a greater loss of letter fluency than do right-sided lesions, but bilateral frontal lesions lead to an even greater deficit (Benton et al. 1983). In this study, the letters F, A, and S were used to assess fluency. The dependent measure was the total number of words produced in 3 minutes. Previous reports (e.g., Teuber et al. 1977) suggested that leukotomy had no effects on verbal fluency.

Digit Span. Digit span is a typical measure of short-term memory ability that has been demonstrated to be deficient in schizophrenic patients (Gruzelier et al. 1988). Performance on this task has been reported to be impaired by dysfunctions in the frontal and hippocampal areas of the brain (Mirska et al. 1991). In the present study the digit span items from the WMS-R were used, with standard instructions, and the digit span was the longest length at which the subject correctly reproduced one trial.

Supraspan Digit Learning. Practice-related improvement in supraspan learning is impaired substantially by dysfunctions in the temporal cortex and connecting hippocampal areas (Milner 1968). Gruzelier et al. (1988) demonstrated that schizophrenia patients also had less ability to acquire a repeated supraspan item than did normal and affective control subjects. In the present study a supraspan digit test, consisting of 13 supraspan digit trials, was administered to the subjects immediately after their digit spans were determined. Each string was one digit longer than the subject’s predetermined digit span. Every fourth trial was identical, yielding five repetitions of a single supraspan item and eight nonrepeated supraspan items. The dependent variable was the proportion of subjects who were able to recall the supraspan item at each successive repetition. This test has not been used previously with leukotomized patients.

Agraphesthesia. Agraphesthesia is commonly associated with lesions of the parietal cortex and occasionally with lesions of the temporal lobe; it is seldom associated with lesions of the frontal lobes (Lezak 1983). In the present study, we examined agraphesthesia with a skin writing test. The subjects were presented with a series of five letters and five numbers written on each palm; the order of palm and stimulus type was randomized. The subjects were asked to close their eyes and identify each stimulus verbally after presentation. After an initial practice number and letter on each palm, no repeated presentations of stimuli were allowed. The dependent variable was the total number of correct responses per hand. No data are available regarding the effects of leukotomy on agraphesthesia.
Raven Coloured Progressive Matrices. The Raven Coloured Progressive Matrices (Raven 1976) are used to assess “nonverbal intelligence.” The colored version is designed for use with children and the elderly. In this study, to reduce assessment time, form AB was used and the dependent variable was the total number of correct responses. Although no data are available about the specific effects of prefrontal leukotomy on performance on this test, previous data suggest that bilateral prefrontal leukotomy has minimal effects on other measures of intelligence (such as the Wechsler scales).

Results

Data Analytic Strategy. Because the nonleukotomized subjects were selected for similarity to the leukotomized subjects but were not matched on a case-by-case basis, independent-sample, rather than paired, t tests were used to compare these subjects. Because the number of subjects in the “approved but not operated on” sample was so much smaller than the numbers in the other two samples, they were compared with each group separately with planned contrasts. The Bonferroni correction procedure was applied to each of the three sets of data collected (PANSS ratings, individual CDR items, and neuropsychological measures). Bonferroni significance was set at 0.02 (0.05/3) for the PANSS ratings, at 0.008 (0.05/6) for the CDR items, and at 0.004 (0.05/13) for the cognitive battery. All results are reported in terms of their significance with both corrected and uncorrected tests.

Clinical Symptom Ratings. When clinical symptom severity for the two samples of subjects was compared with t tests, there were no differences in severity on the positive ($t(70) = 0.22$), negative ($t(70) = 1.33$), or general ($t(70) = 0.75$) PANSS symptom subscales. As would be expected from the fact that the samples were matched on global CDR scores, there was no difference between groups on any of the individual CDR item scores except for personal care, on which the leukotomized sample was significantly more impaired ($t(70) = 3.29 \, p < 0.002$; significant even with the Bonferroni correction applied).

Cognitive Measures. To examine the effects of leukotomy on performance on individual psychometric tests, we compared the leukotomized and nonleukotomized patients with t tests on all of the neuropsychological variables. The data for these comparisons are presented in table 2. There were significant differences between the groups on two variables: the number of perseverative errors on the WCST ($t(70) = 2.85, \, p < 0.05$) and the difference between recall and recognition performance on the verbal recall test ($t(70) = 2.20, \, p < 0.05$). Although these two differences were in the hypothesized direction, they would not have reached Bonferroni criteria for significance. None of the other differences between the groups reached significance at $p < 0.05$. The sample of subjects who were approved for a leukotomy but did not undergo the procedure did not perform differently from either of the other groups (planned contrasts with t tests were all nonsignificant at $p < 0.05$).

Correlational Analyses. To examine the relationships among the variables that discriminated the leukotomized and nonleukotomized groups, we computed Pearson product-moment correlations among those three variables (the difference between recall and recognition memory, WCST perseverative errors, and personal care). The correlations were computed separately for each of the two samples of subjects. For the nonleukotomized patients, none of the correlations were significant; in fact, none were larger than $r = 0.15$. For the leukotomized patients, the correlation between impaired personal care and WCST perseverative errors was significant ($r = -0.37, \, p < 0.05$) but the largest correlation between the difference between recognition and recall memory performance and either of the other two variables was $r = 0.10$.

Discussion

The results of this study indicate that in patients with chronic and severe schizophrenia, leukotomy has no aggravating or ameliorating effects on schizophrenic symptoms as these patients reach old age. Leukotomized patients were impaired on personal care, but this is not in itself a schizophrenic symptom and the impairment seen here may result from an interaction of brain lesion and aging that has little to do with the psychiatric disorder. These findings are in agreement with other, shorter interval, followup studies (Witton and Ellisworth 1962; McKenzie and Kaczanowski 1964) and are contrary to anecdotal reports, based on postoperative observations (e.g., Brown 1985), that suggested that leukotomy aggravates or exacer-
Table 2. Neuropsychological performance of subject groups

<table>
<thead>
<tr>
<th>Measure</th>
<th>Leukotomy Mean/SD (n = 24)</th>
<th>No leukotomy Mean/SD (n = 48)</th>
<th>Approved Mean/SD (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WCST categories</td>
<td>0.47 ± 0.61</td>
<td>0.48 ± 0.70</td>
<td>0.40 ± 0.60</td>
</tr>
<tr>
<td>WCST perseverative errors</td>
<td>89.71 ± 28.73</td>
<td>66.29 ± 38.47</td>
<td>74.00 ± 51.00</td>
</tr>
<tr>
<td>Difference of recall and recognition</td>
<td>4.00 ± 4.60</td>
<td>2.02 ± 4.00</td>
<td>1.84 ± 3.20</td>
</tr>
<tr>
<td>Spatial delayed response</td>
<td>37.87 ± 21.90</td>
<td>49.60 ± 19.09</td>
<td>39.00 ± 20.00</td>
</tr>
<tr>
<td>Spatial delayed alternation</td>
<td>30.00 ± 24.48</td>
<td>44.35 ± 23.27</td>
<td>34.00 ± 25.35</td>
</tr>
<tr>
<td>FAS verbal fluency</td>
<td>13.83 ± 11.30</td>
<td>10.83 ± 8.17</td>
<td>10.80 ± 7.92</td>
</tr>
<tr>
<td>Digit span</td>
<td>5.50 ± 1.41</td>
<td>5.51 ± 1.36</td>
<td>6.20 ± 1.10</td>
</tr>
<tr>
<td>Supraspan acquisition—trial 1</td>
<td>0.13 ± 0.34</td>
<td>0.23 ± 0.43</td>
<td>0.00 ± 0.00</td>
</tr>
<tr>
<td>Supraspan acquisition—trial 5</td>
<td>0.29 ± 0.46</td>
<td>0.38 ± 0.49</td>
<td>0.40 ± 0.55</td>
</tr>
<tr>
<td>Skin writing test—left hand</td>
<td>6.23 ± 3.16</td>
<td>6.58 ± 3.55</td>
<td>8.00 ± 4.95</td>
</tr>
<tr>
<td>Skin writing test—right hand</td>
<td>6.77 ± 3.33</td>
<td>6.17 ± 3.67</td>
<td>7.80 ± 4.92</td>
</tr>
<tr>
<td>Raven Progressive Matrices</td>
<td>5.38 ± 3.73</td>
<td>5.48 ± 3.10</td>
<td>5.75 ± 4.11</td>
</tr>
</tbody>
</table>

Note.—WCST = Wisconsin Card Sorting Test (Heaton 1981); Raven Progressive Matrices (Raven 1976).

*Leukotomized versus nonleukotomized, p < 0.05.*

Table 2. Neuropsychological performance of subject groups

<table>
<thead>
<tr>
<th>Measure</th>
<th>Leukotomy Mean/SD (n = 24)</th>
<th>No leukotomy Mean/SD (n = 48)</th>
<th>Approved Mean/SD (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WCST categories</td>
<td>0.47 ± 0.61</td>
<td>0.48 ± 0.70</td>
<td>0.40 ± 0.60</td>
</tr>
<tr>
<td>WCST perseverative errors</td>
<td>89.71 ± 28.73</td>
<td>66.29 ± 38.47</td>
<td>74.00 ± 51.00</td>
</tr>
<tr>
<td>Difference of recall and recognition</td>
<td>4.00 ± 4.60</td>
<td>2.02 ± 4.00</td>
<td>1.84 ± 3.20</td>
</tr>
<tr>
<td>Spatial delayed response</td>
<td>37.87 ± 21.90</td>
<td>49.60 ± 19.09</td>
<td>39.00 ± 20.00</td>
</tr>
<tr>
<td>Spatial delayed alternation</td>
<td>30.00 ± 24.48</td>
<td>44.35 ± 23.27</td>
<td>34.00 ± 25.35</td>
</tr>
<tr>
<td>FAS verbal fluency</td>
<td>13.83 ± 11.30</td>
<td>10.83 ± 8.17</td>
<td>10.80 ± 7.92</td>
</tr>
<tr>
<td>Digit span</td>
<td>5.50 ± 1.41</td>
<td>5.51 ± 1.36</td>
<td>6.20 ± 1.10</td>
</tr>
<tr>
<td>Supraspan acquisition—trial 1</td>
<td>0.13 ± 0.34</td>
<td>0.23 ± 0.43</td>
<td>0.00 ± 0.00</td>
</tr>
<tr>
<td>Supraspan acquisition—trial 5</td>
<td>0.29 ± 0.46</td>
<td>0.38 ± 0.49</td>
<td>0.40 ± 0.55</td>
</tr>
<tr>
<td>Skin writing test—left hand</td>
<td>6.23 ± 3.16</td>
<td>6.58 ± 3.55</td>
<td>8.00 ± 4.95</td>
</tr>
<tr>
<td>Skin writing test—right hand</td>
<td>6.77 ± 3.33</td>
<td>6.17 ± 3.67</td>
<td>7.80 ± 4.92</td>
</tr>
<tr>
<td>Raven Progressive Matrices</td>
<td>5.38 ± 3.73</td>
<td>5.48 ± 3.10</td>
<td>5.75 ± 4.11</td>
</tr>
</tbody>
</table>

Note.—WCST = Wisconsin Card Sorting Test (Heaton 1981); Raven Progressive Matrices (Raven 1976).

*Leukotomized versus nonleukotomized, p < 0.05.*

Bates aspects of behavior that are currently classified as negative symptoms. Although global differences in cognitive functioning could not be expected because patients were matched by CDR scores, it was expected, on the basis of data from patients with focal frontal lesions, that leukotomy would have detrimental effects on specific cognitive functions attributed to the frontal cortex or to the region of the frontal cortex lesioned during the procedure.

There were small performance differences on two cognitive tests and a more substantial difference on a behavioral measure of self-care. Deficits in self-care and basic behavioral organization are often reported in patients with lesions involving the frontal lobe (Eslinger and Damasio 1985). The correlation with WCST perseverative errors, although modest in size, supports the contention that these self-care deficits are related to dysfunctions of the prefrontal cortex in leukotomized patients. Although the patients in both study groups had obvious deficits in the area of independent functioning, as evidenced by their lengthy consecutive hospital stays, the overall matching on general level of dementia should minimize differences in all of the components of that global rating. This fact, and the level of significance of the difference, suggests that leukotomy-induced frontal lesions are associated with somewhat greater self-care deficits in elderly schizophrenia patients. It is, of course, not possible to determine from this cross-sectional study whether these deficits are of senescent onset or whether they had been present since the psychosurgery.

One of the psychometric differences found between the two samples was an inflation of approximately 50 percent in perseverative errors on the WCST in the leukotomized sample. Although earlier studies with the WCST have yielded somewhat inconsistent results (see Mirsky and Orzack 1977; cf. Teuber et al. 1977), the present data suggest differences in perseverative tendencies. Although the main damage associated with bilateral leukotomy is reported to be white matter lesions of the orbital cortex (Stuss and Benson 1986), performance on the WCST, a test that is putatively associated with dysfunctions in the dorsolateral frontal cortex (Milner 1964), was more impaired in leukotomized patients. One possible explanation for this finding, which is supported by the clinical frontal lobe lesion literature, is that leu-
sions throughout the frontal cortex, including the orbital regions (Stuss and Benson 1986), induce perseveration. It should be kept in mind that ability to complete the WCST, as indexed by the number of categories completed, was very poor in both patient samples and that a certain number of random responses generated by a subject who completely failed to understand the test would be scored as perseverative.

The other psychometric difference between the two samples was an exaggerated recall deficit, relative to recognition performance, in the leukotomized sample. Recall failures, as compared with recognition, were recently (Goldberg et al. 1989a) attributed to deficits in executive functioning and, by inference, to the functions of the prefrontal cortex. The group differences found in the present study are consistent with the idea that lesions of the frontal cortex tend to reduce recall performance more than recognition. This finding, similar to the perseverative error finding, should be viewed tentatively because of the large number of statistical tests performed and the relatively limited number of statistically significant group differences. A major limitation of this finding is that this deficit was unassociated with either of the other two discriminating variables, which were related to each other. A further limitation of this finding is a lack of information regarding how neurological patients with lesions in the temporal, as opposed to the frontal, cortex perform on this test. Such information would provide more conclusive information regarding the cortical localization of the measures.

Despite these few differences between the two samples, the main results are consistent with those of previous studies examining cognitive functions and leukotomy: there were more similarities than differences between schizophrenia patients who had undergone a leukotomy and those who had not. The patients in whom the indication for leukotomy was established but who did not receive it did not diverge in their performance from either of the other two samples. Clearly, aging for 40 years or more post leukotomy does not induce major psychometric and behavioral deficits beyond those found at shorter followup intervals. Statistical power concerns were less of an issue in the present study than in previous studies in which there were negative findings regarding cognitive differences between leukotomized and nonleukotomized samples: with the number of subjects in the present study a moderate effect size could have been detected at \( p < 0.05 \) with 95 percent power.

The question must be asked, however, whether there are additional consequences of leukotomy in chronic schizophrenia. The aim of the leukotomy was to reduce emotional behavior and the probable mechanism for this reduced emotionality was a severing of connections between the frontal cortex and the limbic region. There are a number of cortical-subcortical pathways that might be severed by a leukotomy, depending on its scope, including the mesocortical and mesolimbic tracts. It might be expected, therefore, that a cortical-subcortical neurotransmitter dysregulation, particularly of the dopaminergic system, might be induced by a leukotomy, even if this dysregulation were "silent" in terms of cognitive dysfunction in the typical state. It might be expected that probes with dopaminergic agonists and antagonists would have differential effects in leukotomized and nonleukotomized samples, and that these effects would occur both in the area of cognitive functions and in the byproducts of neurotransmission.

A variety of limitations must be kept in mind when examining the data from this study. The levels of chronicity manifested by these patients are extreme and are atypical in current clinical care. Patients who underwent a leukotomy and remained in the hospital may be different in many ways from those who were discharged, and earlier data are consistent with that idea (Stuss et al. 1986). The control sample may in fact reflect an even more deviant group, in that they have remained hospitalized for decades despite somatic treatment and without having experienced psychosurgery. In addition, the extreme deviance manifested by the nonleukotomized patients on a variety of measures of frontal cortical functions may obscure legitimate deficits induced by a leukotomy. A normal comparison sample was not examined, which made it impossible to perform a profile analysis of the relative deviance of the schizophrenia patients or to determine the potential effects of normal aging on these tests. Even though in the present study the leukotomized subjects were treated with the same surgical procedure, their lesions would be expected to vary to some extent, and the characteristics of these lesions were not examined neuroradiologically. It should be noted that lesion size following leukotomy has been noted to vary radically, although the variance in lesion size and location was consistent in earlier
studies within patients with similar levels of recovery (Benson et al. 1981).

References


Milner, B. Disorders of memory
after brain lesions in man. Neuro-
Mirsky, A.F.; Anthony, B.J.; Dun-
can, C.C.; Ahearn, M.B.; and Kel-
lam, S.C. Analysis of the elements
of attention: A neuropsychological
approach. Neuropsychology Review,
Mirsky, A.F., and Orzack, M.H. Fi-
nal report on the psychosurgery
pilot study. [Appendix] In: Psychos-
surgery: Report and Recommenda-
tions. Washington, DC: U.S. Gov-
Raven, J.C. The Raven Coloured
Progressive Matrices. London, Eng-
Robbins, T.W. The case for fron-
tostriatal dysfunction in schizo-
phrenia. Schizophrenia Bulletin,
Saykin, A.J.; Gur, R.C.; Gur, R.E.;
Mozley, R.D.; Mozley, L.H.;
Resnick, S.M.; Kester, D.B.; and
Stafiniak, P. Neuropsychological
function in schizophrenia: Selective
impairment in memory and learn-
ing. Archives of General Psychi-
Stuss, D.T., and Benson, D.F. The
Frontal Lobes. New York, NY:
Stuss, D.T.; Benson, D.F.; Clermont,
R.; Della Malva, C.L.; Kaplan, E.F.;
and Weir, W.S. Language function-
ing after bilateral prefrontal leuko-
tomy. Brain and Language, 28:66–70,
1986.
Stuss, D.T.; Kaplan, E.F.; Benson,
D.T.; Weir, W.S.; Chiulli, S.; and
Sarazin, F.F. Evidence for the
involvement of the orbitofrontal
cortex in memory functions: An
interference effect. Journal of Com-
parative and Physiological Psychol-
Teuber, H.L.; Corkin, S.; and
Twitchell, T. A study of cingu-
lotomy in man. In: Psychosurgery:
Report and Recommendations. [Ap-
pendix] Washington, DC: U.S. Gov-
Wechsler, D. A standardized mem-
ory scale for clinical use. Journal of
Weinberger, D.R. Implications of
normal brain development for the
pathogenesis of schizophrenia. Ar-
chives of General Psychiatry, 44:660–
Weinberger, D.R.; Berman, K.F.;
and Illowsky, B.P. Physiologic dys-
fuction of the prefrontal cortex in
schizophrenia: III. A new cohort
and evidence of a monoaminergic
mechanism. Archives of General
Weinberger, D.R.; Berman, K.F.;
Suddath, R.; and Torrey, E.F. Evi-
dence of dysfunction of a pre-
frontal-limbic network in schizo-
phrenia: A magnetic resonance
imaging and regional cerebral
blood flow study of discordant
monozygotic twins. American Jour-
Weinberger, D.R.; Berman, K.F.;
and Zec, R.F. Physiologic signifi-
cance of dorsolateral prefrontal
cortex in schizophrenia: I. Regional
cerebral blood flow evidence. Ar-
chives of General Psychiatry, 43:114–
124, 1986.
Witton, K., and Ellsworth, R.B. So-
cial and psychological (MMPI)
changes 5–10 years after lobotomy.
Diseases of the Nervous System,

Acknowledgments
The authors thank Corina
Vocisano, Suzanne McIntyre, and
Danya Vardi—the three testers
who examined these patients—as
well as the patients and staff at
Pilgrim Psychiatric Center.

The Authors

Philip D. Harvey, Ph.D., is Associ-
ate Professor of Psychiatry, Mt.
Sinai School of Medicine. Richard
C. Mohs, Ph.D., is Professor of
Psychiatry and Chief of the Divi-
sion of Psychology, Department of
Psychiatry, Mt. Sinai School of
Medicine. Michael Davidson, M.D.,
is Professor and Director of the
Division of Clinical Research, De-
partment of Psychiatry, Mt. Sinai
School of Medicine, New York,
NY.