

## Effects of ECT and Depression on Various Aspects of Memory

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**Summary:** Seventy severely depressed patients randomly assigned to receive 8 real or sham ECT were further subdivided on the basis of degree of recovery from depression afterwards. In comparison to a non-depressed control group the depressed patients were impaired on a wide range of tests of memory and concentration prior to treatment, but afterwards performance on most of the tests had improved. Real ECT induced impairments of concentration, short-term memory and learning, but significantly facilitated access to remote memories. At 6 month follow-up all differences between real and sham ECT groups had disappeared. On the majority of tests the previously depressed patients now performed at the same level as the control group. There was some evidence that a subgroup of treatment-resistant patients (poor outcome after real ECT) were significantly more likely to complain of memory problems 6 months later.

ECT is widely used as a treatment for severe depression, but there has been increasing disquiet about possible adverse side effects. In addition to the well known short term cognitive impairments some evidence suggests that impairments of memory and concentration may persist for several months. Haliday *et al* (1968) found evidence of deficits in some non-verbal learning tasks after three months and Cronin *et al* (1970) found that bilateral ECT was associated with greater deficit on the Wechsler memory scales than was unilateral ECT some four to six weeks after a standard course of treatment. On the other hand Bidder *et al* (1970) consider that performance returns to preECT levels within 30 days after treatment. Also Squire and Chace (1975) found no evidence of specific learning deficits 6 to 9 months after treatment, although patients who had received bilateral ECT were more likely to complain of problems with memory.

Interpretation of these results is complicated by the observation that memory impairments are associated with depression itself (Cronholm and Ottosson, 1963; Sternberg and Jarvik, 1976) and improve with improvements in mental state. As a consequence pre-treatment levels of functioning cannot be taken as representative of pre-morbid levels. Furthermore memory impairments at the end of treatment might reflect failure to recover from depression rather than adverse consequences of ECT. Thus to gain a better understanding of the effects of ECT on memory it is

crucial to be able to separate out the effects of the treatment from effects of changes in the level of depression.

Interpretation is also complicated by the difficulty of choosing appropriate comparison groups. Retrospective studies of patients who have received more or less ECT are confounded by the likelihood that the patients who received less ECT also had milder or less frequent episodes of depression. Prospective comparison studies tend to have compared bilateral and unilateral ECT. Such a comparison is very likely to underestimate the deficit in relation to an untreated group. In the study reported here 70 severely depressed patients were randomly assigned to two groups who received either a standard course of eight bilateral ECT or else an identical course of treatment in which only the shock was omitted. Any differences between these groups thus can be unequivocally related to shock. Furthermore there were enough subjects for it to be possible to look at outcome (i.e. degree of recovery from depression) as an independent factor contributing to changes in memory performance. Within this design we have looked both at the learning of new material and the recall of material learned long before the course of treatment.

In a series of recent studies in both depressed patients (Lloyd and Lishman, 1975) and normal subjects (Teasdale and Fogarty, 1979) an interesting relationship between mood and memory has been demonstrated: during depressed moods unpleasant

experiences are more readily recalled than pleasant ones. On the basis of these results it is possible to speculate that suppression of memory for unpleasant events might be an important part of the therapeutic process. We have tried to look at this aspect of memory in depressed patients by studying the recall of words varying in their emotional connotations.

### Method

Seventy patients diagnosed as suffering from a severe endogenous depression entered the trial. All patients fulfilled the following criteria: the MRC criteria for depressive illness (Medical Research Council, 1965), the Feighner criteria for primary depressive illness (Feighner *et al*, 1972), the Newcastle criteria for endogenous depressive illness and the Newcastle criteria for predicting a good outcome from ECT (Carney *et al*, 1965). There were 52 females and 18 males, with a mean age of 49.4 years and a range of 30 to 69 years. Fifteen patients had received ECT for previous episodes.

The patients were randomly allocated to a real and a simulated ECT group. Both groups received methohexitone 1.5 mg/kg, atropine 0.6 mg, and suxamethonium 0.5 mg/kg. No electricity was passed in the simulated ECT group, but in the real ECT group electrodes were placed in the bifrontal position and a current of 195 V duopulse wave form 1 was passed for 1.7 sec. To allow confirmation that a convulsion had taken place a sphygmomanometer cuff inflated above arterial pressure was applied to one arm before the injection. In this way the convulsion could be observed unmodified by muscle relaxants. No other anti-depressant treatment was given. The patients received two treatments per week for four weeks. Sixty two patients completed the full course of treatment. After the eighth treatment the patients were treated as the consultants in charge of them thought fit.

Assessments of memory were carried out by MS and CDF at times to be detailed below. Both assessors were unaware of the treatment allocation as were the psychiatrists assessing the severity of depression. This latter assessment was made using Hamilton depression ratings (Hamilton, 1967). These were conducted weekly throughout the course and at one month and 6 months after the completion of the course.

*Controls.* The controls were 10 attenders at a psychiatric outpatient clinic. They were matched for age and sex with the depressed patients, and had a mean age of 46 years. They were not depressed at the time of testing, had never had a severe depressive illness and had never received ECT. None had ever been diagnosed as psychotic. They were suffering from mild anxiety, transient situational disturbances or circumscribed phobias.

### Memory assessments

(a) *Subjective memory:* The patients were asked if they had any problems with memory and/or concentration, and their complaints were noted. This assessment was made pretreatment, post-treatment and at 6 months.

(b) *Concentration/vigilance:* Patients carried out the continuous processing task (Kornetsky and Mirsky, 1966) for 15 minutes. In this task a randomly selected letter of the alphabet appeared every second in the centre of a visual display unit. The subject was required to press a button every time the letter A appeared. The signal appeared at random at the rate of 3 per minute (i.e. 1 in 20 presentations was a signal). The total number of missed signals and false positive responses was recorded. This assessment was made pretreatment, half way through and at the end of the course of treatment, always on a non-treatment day.

(c) *Word list recall and recognition:* Patients were presented with a list of 20 words. Ten words had positive emotional connotations (e.g. warmth, prosperity, happiness) and 10 had negative connotations (e.g. crime, injury, bereavement). The two categories were matched for imagery, concreteness and meaningfulness (Paivio *et al*, 1968). The patients read through the list of words, rating them for pleasantness on a seven point scale. They then counted backwards in 7s for 30 seconds to prevent rehearsal of the material. They were then asked to recall as many of the words as they could. After this they were presented with a list of 40 words containing the 20 words they had seen before plus 20 new words chosen from the same two categories and had to indicate which words they recognized as coming from the list they had just seen. Two equivalent forms of the test were constructed. Assessments were made pretreatment, post-treatment and at 6 months. Half the patients received forms of the test in the order ABA and half in the order BAB. It was hoped that the seven month delay between retesting with the same form would minimise any carry over.

(d) *Learning labels for faces* (derived from Cronholm and Ottosson, 1963): The patients were shown five faces in succession and told the three verbal labels associated with each face; a name, a town and an occupation (e.g. this is Pauline who is a Barmaid from Oxford). Each face was shown for 5 seconds. There followed five trials in which the five faces were shown in random order and the subject was asked to recall the three labels. If there was a failure to recall a label a cue was given in the form of the first letter of the word. If the cue did not help the correct label was given. The number of correct responses on each trial was recorded. This assessment was made on the day before the third ECT and at 6 months. Two equivalent forms of the test were used in the order AB or BA.

(e) *Remote semantic memory* (Baddeley, 1979): Patients had to verify simple sentences (e.g. oranges can be bought in shops, oranges move about searching for food) by making a tick or a cross. The number of sentences verified in four minutes was recorded. To control for the effects of retardation on the motor aspect of this task the patients also made ticks and crosses against a random sequence of the words YES and NO. The number of marks made in this task in four minutes was also recorded. A sentence verification time was calculated which was the mean time to verify a sentence minus the mean time to make a tick or a cross. This assessment was made four times after the 3rd, 4th, 5th and 6th ECT.

(f) *Remote episodic memory*: The patient was presented with a large number of names, some of well known personalities (e.g. Agatha Christie) and some made up (e.g. Laura Whalen). Most of the famous personalities were chosen from people who had been very well known for a time in the past, but had then dropped out of the limelight (e.g. Lady Docker). The special feature of this latter group of famous people was verified by showing that a large number of normal subjects in their 20s did not usually recognise them (Stevens, 1979; after Warrington and Silberstein, 1970). The number of correct identifications and false positive identifications was noted and the signal detection measure, 'd', was calculated indicating the ability to distinguish between the once famous and the unknown. Two equivalent forms of this test were used. The assessment was made three times; pretreatment, post-treatment and at 6 months. Half the subjects received the forms in the order ABA and half in the order BAB.

For various reasons not all the patients gave usable results for all the tests and thus slightly different numbers are involved in the various comparisons as detailed in the results section. In addition for the comparisons at 6 months those patients who received ECT either before or after the experimental treatment are excluded. Thus only patients who had received only the eight trial ECT were included in the comparison.

*Outcome*: The index of outcome was the percentage decrease in Hamilton score after the eighth ECT as compared to the pretreatment score. The patients were divided into two groups on the basis of the median percentage improvement. (Poor outcome group; 21 per cent to 68 per cent improvement: good outcome group; 70 per cent to 100 per cent improvement).

### Results

*Outcome*: As we have reported elsewhere (Johnstone and others, 1980) there was a significantly

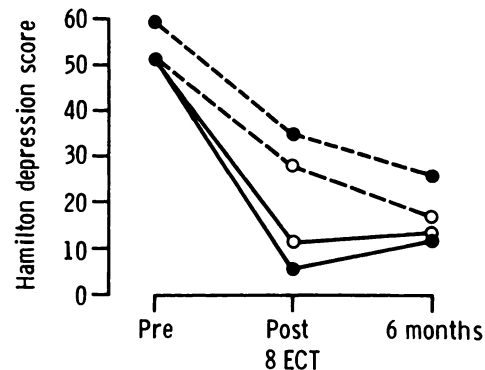


FIG 1.—Hamilton depression score (n = 62). ○---○ sham ECT, bad outcome; ○—○ sham ECT, good outcome; ●---● real ECT, bad outcome; ●—● real ECT, good outcome.

greater improvement in the real ECT than in the sham ECT group. As a consequence the numbers in the four groups defined by treatment and outcome were not equal. Twenty in the real ECT group had a good outcome and 11 had a bad outcome, while 11 in the sham ECT group had a good outcome and 20 had a bad outcome. In the analyses that follow these four groups will be compared using analysis of variance by the method of unweighted means (Winer, 1971) or a non-parametric equivalent (Meddis, 1980). Thus although there is clearly a relationship between treatment and outcome these methods allow us to study the effects of ECT and of changes in depression independently.

This method cannot, of course be entirely satisfactory since classification into outcome groups was carried out retrospectively and depends on an arbitrary cutoff. Fig 1 shows the mean Hamilton scores for the 4 groups; pretreatment, post-treatment and at 6 months follow up. Pretreatment—there are no significant differences between the groups. Post-treatment, by definition there is a big difference between the outcome groups and no difference between the treatment groups. At 6 months this difference between the outcome groups remains ( $P < 0.01$ ). At this point the difference is contributed almost entirely by the group who received real ECT, but had a poor outcome suggesting the possibility of a treatment resistant group. However the interaction of outcome with treatment fails to reach significance ( $P < .07$ ). We must thus conclude that after 6 months the poor outcome group is more depressed than the good outcome group whatever treatment they had.

*Subjective memory*: Fig 2 shows the percentage of subjects complaining of difficulties with memory and concentration pretreatment, post-treatment and at 6 months. There is no change in the number of

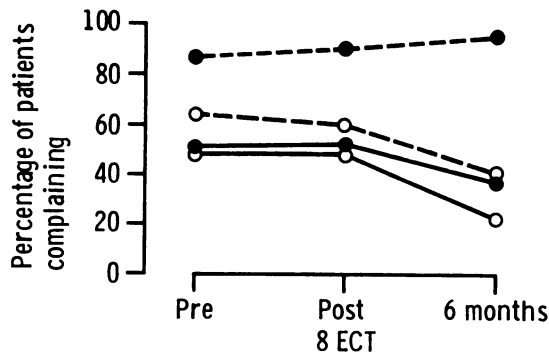


FIG 2.—Subjective problems with memory and concentration (n = 43). ○ - - - ○ sham ECT, bad outcome; ○—○ sham ECT, good outcome; ● - - - ● real ECT, bad outcome; ●—● real ECT, good outcome.

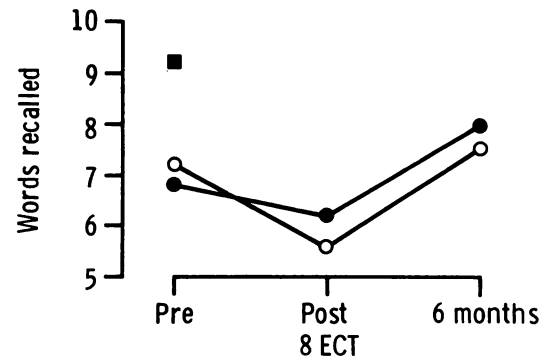


FIG 4.—Recall score (n = 39). ○—○ sham ECT; ●—● real ECT; ■ controls.

complaints pre and post-treatment, but there is a general reduction at 6 months. There is no effect of treatment on complaints, but there is a significant effect of outcome which is more marked at 6 months ( $P < .01$ ). As with the depression score this is most marked with the poor outcome group who received real ECT, although the interaction outcome by treatment again fails to reach significance ( $P < 0.06$ ).

**Vigilance:** Fig 3 shows the mean number of errors (misses + false positives) made by the real and sham ECT groups pre and post treatment. Pretreatment—there were no differences between the groups. There was a general improvement post-treatment which was greater in the sham ECT group than in the real ECT group, but this difference failed to reach significance ( $P < .10$ ). There was no significant effect of outcome on this task. In comparison with the reports of this task in the literature (Kornetsky and Mirsky, 1966) our patients were performing very badly prior to treatment.

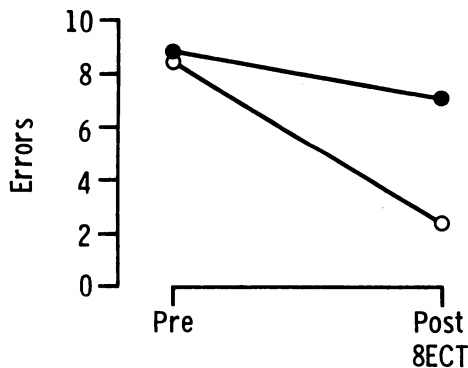


FIG 3.—Vigilance errors (n = 36). ○—○ sham ECT; ●—● real ECT.

**Word list recall and recognition:** The manipulation of the affective connotation of the words had no significant effect on performance. Subjects remembered as many pleasant as unpleasant words whether they were in the depressed group or in the control group. Furthermore there was no effect of treatment or recovery from depression for the relative recall of the two categories of word. The same was true for the recognition scores. Fig 4 shows the mean number of words recalled pretreatment, post-treatment and at 6 months for the real and sham ECT groups and also the performance of the non-depressed control group. The control group remembered marginally more words than the depressed patients on all three occasions ( $P < .07$ ). There was a slight decline in performance from pre to post treatment and a slight improvement from post-treatment to 6 months. However these changes were not significant and did not relate to treatment or outcome. Fig 5 shows the number of errors (misses + false positives) in the recognition task. The depressed patients made significantly more errors than the control group on all three occasions of testing ( $P < .01$ ). The real ECT group showed a significant increase in errors pre to post-treatment in comparison with the sham ECT group ( $P < .01$ ). By 6 months they had returned to the pretreatment level and did not differ from the sham ECT group. There was no effect of outcome on performance.

**Learning labels for faces:** Fig 6 shows the number of correct responses (uncued) per trial for the task learned during treatment. The performance of the depressed patients was worse than the controls at all stages of the task, particularly at the end ( $P < .001$ ). The two ECT groups did not differ on the first trial, but the sham ECT group learned faster and were significantly better on the 5th trial ( $P < .05$ ). Fig 7 shows the same data at 6 months. Here the differences between the two ECT groups and the control group have

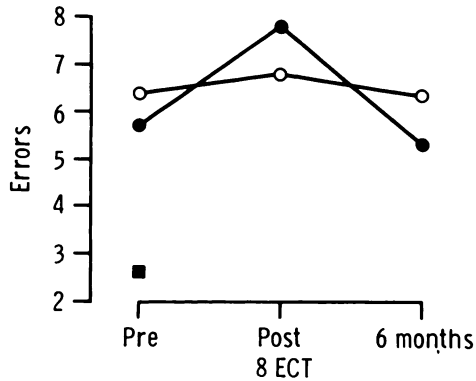


FIG 5.—Recognition errors (n = 39). ○—○ sham ECT; ●—● real ECT; ■ controls.

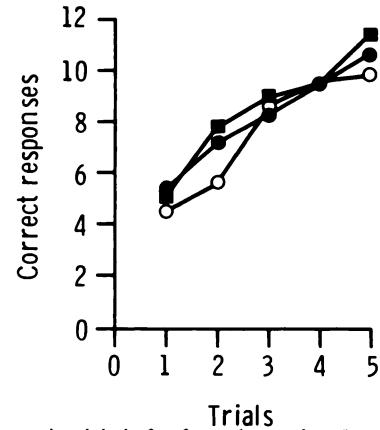


FIG 7.—Learning labels for faces 6 months after treatment (n = 51). ○—○ sham ECT; ●—● real ECT; ■ controls.

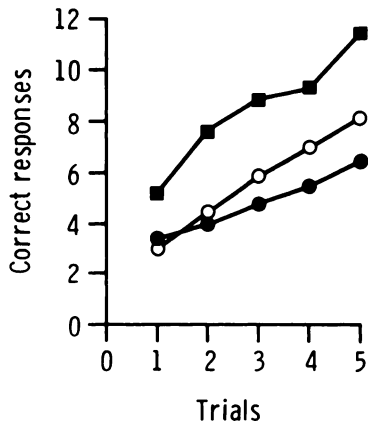


FIG 6.—Learning labels for faces post 3 ECT (n = 56). ○—○ sham ECT; ●—● real ECT; ■ controls.

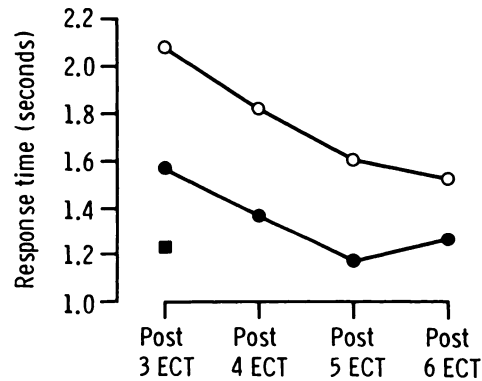


FIG 8.—Remote semantic memory, sentence verification time (n = 54). ○—○ sham ECT; ●—● real ECT; ■ controls.

completely disappeared. The effects of cueing and other manipulations involved in this task will be presented elsewhere (Frith *et al*, in preparation). There were no effects of outcome on this task.

**Remote semantic memory:** Fig 8 shows the mean sentence verification time, corrected for movement time, during the course of treatment. There was a general tendency for all patients to get faster over the four occasions of testing. There was no difference between the groups in the rate of improvement, but the real ECT group performed faster than the sham ECT group throughout ( $P < .05$ ). There was no effect of outcome on performance. The depressed patients performed significantly worse than the control group on the first occasion of testing ( $P < .05$ ), but did not differ from them on the fourth occasion of testing.

**Remote episodic memory:** Fig 9 shows the ability of the patients to distinguish between famous people from the past and made up names pretreatment, post-treatment and at 6 months. The ECT patients did not differ pretreatment, but post-treatment the real ECT group were significantly better than the sham ECT group ( $P < .05$ ). This difference had disappeared by 6 months. Over the course of treatment the real ECT patients improved their performance on this remote memory test whereas the sham ECT patients got worse. This is not a consequence of outcome which was controlled for and for which there was no effect. Pretreatment the depressed patients performed significantly worse than the controls ( $P < .05$ ), but this difference had disappeared at 6 months.

**Discussion**

From within this large group of subjects it was

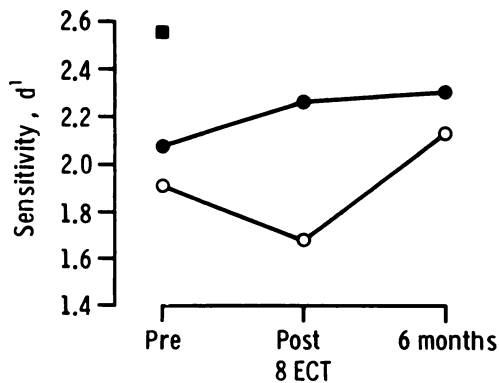


FIG 9.—Remote episodic memory, sensitivity to once famous names ( $n = 47$ ). ○—○ sham ECT; ●—● real ECT; ■ controls.

relatively easy to find anomalous patients who showed a good outcome after sham ECT or a bad outcome after real ECT. It was therefore possible to some extent to separate effects of treatment from effects of change in depression score. At the 6 month follow-up there was a trend (which failed to reach significance) for the two bad outcome groups to have diverged (see Fig 1). The group who received sham ECT had caught up with the two good outcome groups presumably because of the treatment they received subsequent to the trial. The group who received real ECT had not caught up in spite of the subsequent treatment they received. These patients thus form a “treatment-resistant” group.

When interpreting the results of the memory tests it is important to note that even at 6 month follow-up some of the patients in this group were still showing signs of depression. The mean of the three relatively well groups was 16 on the Hamilton depression scale and the treatment-resistant group had a mean of 26. Given the effects of depression on memory we have no reason to expect these patients to perform absolutely normally on memory tests at 6 months after the index episode of depression. On the other hand during the course of treatment there is a massive reduction in depression in all groups whatever their treatment and whatever their outcome. For this reason we might well expect to see large improvements in memory during the course of treatment.

Our depressed patients performed worse than control subjects on all the aspects of memory and concentration investigated before treatment. They also performed worse on the two tests given for the first time during treatment (learning labels for faces, and remote semantic memory), but this impairment might be a consequence of the repeated anaesthesia they had

already received by this time. In most cases the differences between the depressed patients and the controls had disappeared either post-treatment or at the 6 month follow-up.

The one exception to this was the word list recall and recognition which was impaired in comparison to the control group throughout. This might be a consequence of the moderate degree of depression shown by some of the trial patients, both post-treatment and at follow-up. It cannot be ascribed to ECT since it appeared in the sham ECT group to the same extent. Recovery was particularly striking in the learning test. Performance on this test was identical to the control group at the 6 month follow-up even though it had been markedly impaired for all groups during treatment. There were few significant effects of outcome. This was probably because the difference in depression scores between the good and bad outcome groups was relatively small compared to the overall decrease in depression during treatment.

The one exception was subjective memory which was significantly worse in the poor outcome groups both post-treatment and at 6 months. Thus complaints about the memory problems seem not to be associated with real ECT, but with a relatively high degree of depression and an unsuccessful treatment.

There were a number of significant immediate effects of ECT post-treatment. Vigilance was worse, word list recognition was worse and learning was less rapid post-treatment in the real ECT than in the sham ECT groups. However there were no significant differences on any test at the 6 month follow-up. Surprisingly the real ECT groups performed significantly better than the sham groups on the two tests of remote memory. For the semantic memory the result is equivocal since there was no pretreatment measure and there was no divergence as the trial continued. This result would clearly need to be replicated by looking at pretreatment performance and performance after the first ECT of a course. However these problems do not apply to the memory for famous names which was measured pre- and post-treatment. Had this facilitating effect of ECT appeared on just one of these tests of remote memory we would have been inclined to dismiss it as coincidence or sampling error, but since it appeared on both tests and since these tests were very different in form and content we are inclined to think this is a real effect.

There were no effects of any kind resulting from the manipulation of the affective connotations of words. This suggests that these effects are restricted to pleasant and unpleasant memories and experiences of subjects and cannot be investigated using the rather artificial paradigm involving single words which are assumed to have a general affective connotation.

### Conclusions

There are marked effects of depression on all aspects of memory and concentration which must be taken into account when investigating the effects of treatment on memory. This is particularly so at long term follow up when a number of patients either as a continuation from the initial episode or on a new recurrence may be showing at least a moderate degree of depression. Ideally follow-up patients should not be tested at a fixed time after treatment, but at a point when their depression is least evident. The subjective experience of memory problems in particular seems to be a function not of treatment, but of outcome, with the more depressed patients who have experienced an unsuccessful treatment making the most complaints.

There are clear immediate impairments due to real ECT, in comparison to sham, in secondary memory, in new learning and in concentration. However remote memory seems to be facilitated by real ECT. There is no evidence of any long term impairment of memory after one course of standard bilateral ECT.

### Acknowledgement

This trial was conducted under the auspices and according to the rules of the Ethical Committee of Northwick Park Hospital. We are grateful to Karalyn Patterson and Alan Baddeley for their help and advice.

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*(Received 24 September 1982)*