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Using ECT to Study Hemispheric Specialization for Sequential Processes

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SUMMARY Two studies are reported, citing the effects of unilateral versus bilateral electroconvulsive shock therapy on the performance of short cognitive tests. In Study 1, seven tests were administered before and after three treatment sessions The most interesting finding was that performance improved significantly on the Knox Cube Imitation test following right unilateral shock. Study 2 replicated this unexpected finding. These results were interpreted as demonstrating that the left cerebral hemisphere is specialized for the processing of sequential time-dependent information.

The fact that the two hemispheres of the human cortex differ in the functions they perform best is no longer in dispute. The evidence supporting such differences comes from three main sources: firstly, the study of patients following sectioning of the corpus callosum; secondly, the study of the effects of unilateral cerebral lesion; and thirdly, the study of lateralization of function in the normal intact human. The present paper presents evidence from a fourth source—the effects on performance of unilateral versus bilateral electroconvulsive therapy (ECT). The results to be reported shed some light on the actual *nature* of the functional difference between the two cerebral hemispheres.

Thus, whilst it may be a truism to say that the left hemisphere in most humans is concerned with processing linguistic information and the right with processing visuo-spatial material, this statement only takes account of the *type* of information processed. It does not involve any statement concerning the mechanisms which underlie such functional differences. Broadbent (1974) as well as Gordon and Bogen (1974) have speculated that the fundamental difference resides in the fact that the left hemisphere processes information in a sequential fashion, whilst the right employs a more holistic, non-sequential approach.

With reference to our independent variable, research into the effects of ECT on human cognitive activity has been, in the main, confined to the study of its effect upon learning and memory. This work has been recently reviewed (Horan, 1976; Robertson and Inglis, 1977). The spur for the present work was, however, curiosity about the effects of ECT on cognitive operations other than learning and memory, since information about these processes might extend our somewhat limited understanding of how the brain works.

The therapeutic use of both unilateral and bilateral ECT in therapy opens up the possibility of assessing which cognitive processes are lateralized—a possibility that was exploited by Kronfol, Hamsher, Digre and Waziri (1978). Since unilateral shock is preferentially delivered to the right hemisphere, interference with the linguistic processes of the left hemisphere should be minimized. When bilateral shock is administered, processes in both hemispheres would be disrupted. In the light of Broadbent's (1974) proposal, however, we would predict that right unilateral shock should not interfere with any cognitive activity dependent upon the sequencing capacity of the left hemisphere. Nevertheless, such shock would interfere with any activity requiring holistic processing. If humans normally employ both modes, viz—sequential and holistic, then interfering with the holistic

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mode should leave only the sequential. This latter mode could then be more apparent, as it would not be intermixed with or even masked by the holistic one. On the other hand, bilateral ECT would be expected to interfere with activities requiring both sequential and holistic processing.

STUDY 1

Method

Patients

Patients at three hospitals, for whom ECT had been prescribed, were selected for the sample on the following criteria: Age below 60 years, no evidence of neurological impairment, no ECT during the previous six months, no history of epilepsy, no clinical indication of general mental retardation. After the inevitable subject wastage inherent in the use of hospital patients, a sample of 20 was studied. They were aged from 22 to 59 years. Their diagnoses included: schizophrenic psychosis (7), paranoid reaction (1), agitated depression (1), paranoid schizophrenia (6), reactive depression (2), endogenous depression (3). There were eleven cases in the bilateral ECT group (8 males and 3 females) and nine cases in the right-unilateral ECT group (4 males and 5 females). Group assignment followed the predilection of the psychiatrist concerned; a particular psychiatrist in charge of a unit preferentially orders ECT in one mode and patients are assigned to a unit as an empty bed occurs. The experimenters were not involved in this process and thus, for our purposes, assignment was random, since one psychiatrist always gives unilateral ECT and another always bilateral.

For each patient, hemispheric dominance was determined using a modified version of the Zamora and Kaelbling (1968) examination technique. On this assessment, all patients in the sample were dextrals and were presumed to be left-hemisphere dominant for speech and language functions.

The test battery

The selected battery of seven sub-tests consisted of two from the WAIS Verbal Scale (Vocabulary and Digit Span) in conjunction with the five sub-tests (Knox Cube Imitation, Beads Test, Passalong, Pattern Matching and Form Assembly) which make up the Queensland Test (McElwain and Kearney, 1969). Collectively, the sub-tests are thought to measure four main areas of cerebral function, which are—verbal, memory, visuo-motor sequencing and visual-spatial. Because the most interesting finding concerned performance on the Knox Cube Imitation test, a description of this test follows. The Knox Cube Imitation test consists of four black cubes, which are spaced at equal intervals along a white base 18 cms long. The tester holds a detached cube, and the subject another. The tester then taps out a sequence, hitting the cubes in a prescribed order. The sequences become longer and more complex throughout the test.

Procedure

The Test Battery was individually administered to a patient on the afternoon before the first ECT, scheduled to be given the following morning.

Six days later, when the patient had received three ECTs he was tested again on the battery of tests, six to eight hours after the last electrical stimulation. The unit of three applications was chosen because this constituted a block of treatments, after which the patient's psychiatric condition was reviewed. If improvement warranted it, treatment was then terminated. Other investigators have also used three ECTs as the unit imposed between before and after measures, so that our findings should be comparable on this variable; Kronfol *et al* (1978), however, studied patients after eight treatments. Throughout the investigation, patients received antidepressant and anti-anxiety sedative drugs, as prescribed by their attending psychiatrists.

The administration and scoring of the tests was carried out without the investigator being aware of the site of stimulation, i.e. whether unilateral or bilateral, for a particular patient.

ECT administration

Treatment was given on Monday, Wednesday and Friday. There was thus an interval of two days between treatments, except for those

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occasions on which a weekend occurred, when the interval was three days.

Bilateral ECT was applied in the conventional bifronto-temporal manner. For unilateral ECT, the electrode placement was as described by Lancaster, Steinert and Frost (1958). In the latter case, the lower electrode was placed 4 cm above the centre of a line between the lateral angle of the orbit and the external auditory meatus; the upper electrode was 9 cm higher than the lower. In bilateral treatment, both electrodes were placed in positions corresponding to the lower electrode in unilateral treatment.

Premedication consisted of atropine, injected about one hour before treatment. The anaesthetic used was methohexitone sodium (Brietal) in conjunction with the muscle relaxant Brevidil. Oxygen was infused both before and after shock. The current was delivered by a Siemens Convulsator. The voltage applied was usually between 4 and 8 volts; the duration of the application of the current was individually determined, being used only until the start of generalized convulsions.

Results and Discussion

Deficits can be examined on a within-subjects basis by determining whether post-stimulation scores are significantly different from pre-stimulation scores. Or, on a between-groups basis, examination is in terms of whether there are different levels of change in performance from before to after stimulation, due to bilateral and right-unilateral ECT application respectively. One-tailed *t* tests of the difference scores (10 *df* for the bilateral group and 8 *df* for the right-unilateral group) were used in making these comparisons. The results, as shown in Table I, demonstrate that on a within-subjects basis, bilateral ECT significantly impairs performance on Vocabulary and Form Assembly, whereas right-unilateral application impairs performance on Form Assembly, and significantly *improves* performance on the Knox Cube Imitation test. Between-groups comparisons reveal significant differences for Vocabulary, Knox Cube Imitation, and Form Assembly.

The intra-group deficit in performance on Vocabulary for bilaterally treated, but not for right-unilaterally treated patients, was expected

TABLE I

Difference scores (from before to after ECT) for the bilateral and right-unilateral groups

Subtest	Group	Before shock score		After shock score		Difference score	SD	t value	p (one tailed)
		x̄	SD	x̄	SD				
Vocabulary	Bilateral	11.00	3.35	9.9	3.50	−1.1	0.51	6.88	< .0005
	R-Unilateral	11.78	1.71	11.78	2.22	0.00	0.00	0.00	N.S.
Digit span	Bilateral	10.00	2.32	10.27	2.14	0.27	2.03	0.41	N.S.
	R-Unilateral	10.56	2.55	10.11	2.25	−0.45	1.16	0.40	N.S.
Knox cube imitation	Bilateral	6.36	2.11	6.09	1.81	−0.27	2.25	0.36	N.S.
	R-Unilateral	5.33	2.3	6.89	2.65	1.56	1.41	3.12	< .01
Beads	Bilateral	2.82	1.94	3.45	1.96	0.64	1.26	1.69	N.S.
	R-Unilateral	3.11	2.08	3.33	2.71	0.22	1.13	0.37	N.S.
Passalong	Bilateral	4.64	1.62	4.64	1.62	0.00	0.00	0.00	N.S.
	R-Unilateral	5.22	1.09	4.88	1.16	−0.34	0.47	1.98	N.S.
Pattern matching	Bilateral	13.82	1.25	14.00	1.25	0.18	0.93	0.62	N.S.
	R-Unilateral	14.00	2.12	13.56	2.78	−0.44	0.68	1.83	N.S.
Form assembly	Bilateral	10.45	1.29	9.55	1.86	−0.90	1.09	2.57	< .02
	R-Unilateral	11.56	1.51	9.44	1.42	−2.12	1.84	3.26	< .01

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on the grounds that bilateral ECT would impair left hemispheric function. The vocabulary sub-test may therefore be considered to tap language abilities that are predominantly subserved by the left hemisphere. Six to eight hours after the third bilateral ECT, patients show impaired ability to define words; the definitions they give at this time are less adequate than those they gave before the first treatment. This lowered performance is not apparent after right-unilateral stimulation to the nondominant hemisphere. But when ECT has been applied to the nondominant hemisphere, as in both bilateral and right-unilateral stimulation, Form Assembly—a non-verbal test requiring the mental manipulation of space and form—shows impaired performance.

These findings of asymmetrical deficit are also implicit in some of the more recent ECT literature, where the implied left-right differentiation is characteristically associated with memory function. In extension of the ECT results on memory deficit, our results demonstrate that cognitive processes involving linguistic and spatial relationships are also affected (perhaps temporarily) by ECT. Tasks other than those specifically concerned with memory and learning, if they are mediated by verbal or spatial reasoning, are poorly executed for at least some eight hours after the third ECT treatment.

When short-term verbal and visual memory are considered, results in the present study are in close agreement with those in the literature (Horan, 1976; Robertson and Inglis, 1977). On the Digit Span test, four bilateral and two right-unilateral ECT patients showed improved performance, while overall results show no significant change. On this same test McAndrew, Berkey and Matthews (1967) found no impairment for any of their groups, Halliday, Davidson, Browne and Kreeger (1968) found improvement for right-unilateral treatment and 'no change' after bilateral ECT while Fromholt, Christensen and Stromgren (1973) demonstrated improved performance on Digit Span for both groups. Results on the Beads test show a tendency towards improved performance on this visual memory task, but averaged performance is unchanged by ECT. An increasing number of studies, using a variety of visual tests, have reached the same conclusion (e.g. Zamora and Kaelbling, 1968; Cronholm and Molander, 1957; Dornbush, Abrams and Fink, 1971) to the point where Fromholt *et al* (1973) comment that whatever the explanation may be, it seems certain that visual memory is not impaired by ECT.

On the Knox Cube Imitation test, performance remained unchanged for the bilaterally treated group, but showed significant improvement after right-unilateral ECT. The intergroup differences for this group were also significant, indicating increased performance after nondominant ECT, in comparative as well as in absolute terms. It would now seem from the significantly improved performance of the nondominant ECT group on this test that the visuo-motor-sequencing required for successful performance of this task is either under linguistic control, or else the left hemisphere is preeminent for time-dependent or sequential operations (such as those involved in the Knox Cube Imitation test) which may also underlie similar aspects of linguistic activity. The finding of an actual improvement in performance on the sequential task suggests that normally sequential (left hemisphere) and holistic (right hemisphere) processing both occur, but not to their individual full capacity. With the partial suppression of right hemisphere processing, left hemispheric sequencing operations are facilitated or enhanced. Obviously, word meanings, etc. would be independent of such sequential operations, and thus tasks that include a semantic component (Vocabulary and Digit Span) would not be expected to show any improvement after right-unilateral shock.

This second hypothesis is in accord with persuasive arguments that have pervaded the literature to the present day. Thus, Gordon and Bogen (1974) proposed, in a line of reasoning that stems from Hughlings Jackson's observations, that the left and right hemispheres may be distinguished by their specialization for time-dependent and time-independent operations respectively. Speech or language units (unlike spatial information), are sequential with respect to both input and output. So also is the Knox Cube Imitation task, in which a sequence

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of motor movements is copied by the subject. In the same vein, Kimura and her colleagues (Kimura, 1973; Kimura and Archibald, 1974) suggested that brain regions in the left parietal area are important for the production of motor sequences which lend themselves readily to communication or speech. This region of the brain is seen as an important part of a system controlling certain motor sequences, both vocal and manual; Lomas and Kimura (1976) concluded that the neural systems for speaking and for movement sequences of the right hand in right-handers thus appear to overlap considerably in the left hemisphere.

Since our subjects were all dextrals, the findings of improved performance on the Knox Cube Imitation test, following right-unilateral, but not bilateral ECT, would directly support the above interpretations. The Knox Cube Imitation tests would, therefore, seem to constitute a useful instrument for rigorous investigation of the 'sequential operations' hypothesis. Because of the possible importance of the present findings, however, the result must be replicated to ensure that a Type 1 error has not occurred during data analysis. Since the patients had to perform seven different tasks, some differences may have been found by chance. A final problem with the present results lies in the fact that our two groups of patients differed initially in their performance on the Knox Cube Imitation test before any treatment. Thus, the bilateral treatment group performed slightly better than the unilateral group before administration of the ECT. The possibility exists of a 'ceiling' effect, such that the only possible direction of change was down for the bilateral group.

With these problems in mind, another sample of patients was studied, using only the Knox Cube Imitation test.

STUDY 2

Method

Subjects

The 24 patients included in the study were obtained from two hospitals and were selected according to the criteria of the previous study. Ten were matched controls who received no ECT, seven received bilateral shock (3 males and 4 females) and seven received right-unilateral ECT (5 males and 2 females).

The diagnoses of the unilateral ECT sample were as follows: three psychotic depression, two severe depression; two schizophrenia with depressive symptoms. The bilateral sample were diagnosed as: one depressive psychotic; four endogenous depression; two schizophrenic-depressive symptoms. Diagnoses of the control patients were allowed to vary. Again, patients were continued on prescribed drugs.

Procedure

The test was given within 12 hours prior to the first ECT, dependent upon notification from the hospital staff of the availability of patients. Subjects were re-tested within six to eight hours of their receiving their third ECT, as in the previous study.

ECT administration

The ECT of subjects within this experiment was administered on the mornings of Monday, Wednesday, and Friday. Premedication with atropine was routinely administered on the morning prior to the treatment. In this study, the anaesthetics used were sodium methohexitone (for the unilateral sample) and thiopentone sodium (for the bilateral sample). The reason for this differentiation in anaesthetics is that sodium methohexitone has convulsant properties, and is thus the choice for unilateral electroconvulsive therapy, where seizure is sometimes more difficult to induce. Full muscle relaxation was secured with succinyl choline. Oxygen was infused through an airway before and after the convulsion was induced. The duration of the application of the current was individually determined, being applied only until the commencement of a generalized seizure.

The controls were similarly tested twice, with the second testing being given six days after the first, this time interval being equivalent to that intervening being tests for the treated patients.

Results

Pre- and post-test scores were determined for each subject and difference scores calculated. Results as shown in Table II indicate that on a

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TABLE II

Difference scores for the Knox Cube Imitation Test from before to after ECT for the right unilateral and bilateral group

Group	Before shock score	After shock score	Difference score	t value	p (one tailed)
R-Unilateral	5.86	8.00	2.14	2.352	< .05
Bilateral	5.71	6.57	0.86	.969	N.S.

The difference scores for the control group summed to zero.

within-subjects basis, right unilateral ECT significantly improves performance on the Knox Cube Imitation test ($P < .05$), whilst the bilateral ECT sample indicated no significant difference in pre- and post-test performance. The patients who did not receive any ECT similarly manifested no significant changes in test scores. Because the different scores for the control group summed to zero, no further statistics were applied to those data. The findings of the current experiment are in accord with those of Study 1.

General Discussion

Both the studies reported above have shown enhanced performance on the Knox Cube Imitation test, six hours after a third application of right-unilateral ECT. The finding of improved performance on this test, whilst surprising, appears to be a reliable phenomenon. This strongly suggests that the left hemisphere, when operating with reduced inference from the right, displays a preeminence for sequential motor operations. This operation may constitute the underlying mechanism involved in the prepotency of this hemisphere for language. An alternative explanation for the found improvement may be that the ECT lifted depression and this then led to improved performance. This was the hypothesis put forward by Kronfol *et al* (1978), but they used eight treatment sessions, and found improvements on most of their tasks. We, on the other hand, found differential effects after three treatments. Thus, lightening of depression does not account adequately for our findings, since enhanced performance occurred solely on a motor-sequencing task.

The test used in the present study (the Knox Cube Imitation test) would seem to be a quick, simple and valid test for investigating sequential-operation functions. One possible application of the Knox test would be in the realm of language development, where the test's simplicity recommends it for use with children of different ages. The prediction is, of course, that with older children, the right hand will manifest an increased proficiency over the left, as the left hemisphere became increasingly specialized for time-dependent functions.

Another important conclusion can be drawn from the present results, viz—ECT is a useful and powerful tool for investigating differential hemispheric functioning. Problems found in the use of ECT for investigations (Horan, 1976; Robertson and Inglis, 1977) may stem from an excessive concentration on memory functions. Our results suggest that other cognitive activities could be more profitably used as the dependent variable. This would augment information derived from normal, brain lesioned, or commisurotomized patients.

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