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Alterations in Cerebral Laterality during Acute Psychotic Illness

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A new dichotic listening test (fused rhymed words) was used to monitor changes in perceptual asymmetry (PA) in patients recovering from acute psychotic episodes; some were also given a dichotic nonsense syllables test, a dichotic tone test, and a single visual field dot localisation test. Contrary to expectation, PA on the word test decreased with recovery, while asymmetry on the tone and dot tests did not change; results cut across diagnosis, could not be related to medication, and were independent of changes in overall performance. More specific hypotheses are needed than those of generalised single hemisphere dysfunction in major psychiatric illness, but existing models and concepts are inadequate to explain the findings.

Numerous studies have examined putative indices of regional brain function (RBF) in psychotic illness, including perceptual asymmetry (PA), spontaneous and evoked electrical activity, and blood flow and metabolism (Flor-Henry, 1979; Gruzelier, 1981; Merrin, 1981, 1982; Newlin, 1981; Riederer, 1981; Wexler, 1980). Most purport to have found evidence of a single localised dysfunction, and suggest that this is characteristically associated with a particular clinical disorder.

However, many have been marked by the methodological shortcomings generally found in first-generation studies: measures of RBF have often been of limited reliability and/or validity; most studies have included patients of only one diagnostic group, making it necessary when attempting to compare different clinical disorders to compare data from different studies using different experimental measures and designs; and many have only compared patients and healthy controls, without assessment of severity of illness or sick/well repeated measures. (Such procedures are essential in differentiating state from trait abnormalities, and are potentially useful in further validating and defining the nature of an association between alteration in RBF and a clinical disorder). Finally, most studies have used only one measure of RBF. Problems resulting from the use of single measures are twofold: the degrees of freedom in drawing inferences from them about possible brain dysfunction are so great that specific conclusions cannot be drawn with any confidence; and the use of single measures biases conclusions toward single localised dysfunctions, since it is then impossible to see enough to assess integrative and interactive aspects of brain physiology (Wexler, 1986).

A new and improved language-related dichotic listening test was used here to assess RBF in acutely psychotic depressed and schizophrenic patients. Subjects were presented with dichotic pairs of single-syllable rhymed words, differing only in the initial consonant. Members of each pair fuse into a single auditory image, and subjects experience and report only one word on each trial. In a multi-centre study of right- and left-handed controls, this test proved to be very reliable and to approximate the validity criteria derived from neurological patients (70% right ear advantages (REA) in sinistrals and 95% in dextrals) as closely as any test currently available (Wexler & Halwes, 1983). Although developed specifically for this study, it is now being used world-wide.

The dichotic word test was used to follow-up an earlier finding of an increase in REA on a dichotic nonsense syllable test, as depressed and schizophrenic patients recovered from acute psychotic episodes (Wexler & Heninger, 1979). The nonsense syllable test was also a fused single response test, in which members of each pair differed in only one consonant and in which the set of such consonants was the same as those distinguishing the rhymed words. To facilitate comparison of the two studies, a sub-set of subjects in the present one also received the nonsense syllables test; sub-sets of patients also received two other PA measures. The four tests together constituted the current state of development of a multi-test battery. The first of these was a dichotic tones test, in which subjects receive a different tone in each ear and indicate which sounds louder; normal subjects show a highly reliable right ear bias (Wexler & Halwes, 1981). The last test was a visual dot localisation test, modelled on one of Levy

& Reid (1978). Dots are flashed briefly in either the right or left visual field, and subjects are required to indicate the position on a response key. Normal subjects typically have a left visual field advantage (LVFA), presumably because specialised final processing of these stimuli takes place in the right hemisphere. All tests were given to subjects twice—shortly after admission, when acutely symptomatic, and again after treatment and major improvement in symptoms; severity of symptoms was assessed at both times with a multidimensional nurses' rating scale (Heninger *et al*, 1970).

The recovery-associated increase in REA on the nonsense test, noted earlier, was hypothesised to reflect a breakdown in normal interhemisphere inhibitory processes during acute psychosis (Wexler & Heninger, 1979). The present project was designed to replicate the initial finding, and to determine whether results with other measures of PA were consistent with this hypothesis. It was predicted that because of the similarity between the word and nonsense tests, results from them should be comparable. The tone and dot tests, on the other hand, were different enough from the other two for their results to help define the limits of the pathological process reflected in them.

Method

Subjects

Patients admitted consecutively to the Connecticut Mental Health Center, who met research criteria for the diagnosis of schizophrenia or primary major depressive disorder (Spitzer *et al*, 1975), and were right-handed, participated in the study. One patient's test scores were markedly different from all the others', and he was excluded on this basis. The median age of the remaining 26 was 40 years, range of 19–64; 11 were men and 15 women. Seven were diagnosed as schizophrenic (four men, three women, median age 25 years, range 19–38) and 19 as primary major depressives (seven men, 12 women, median age 50 years, range 23–64). All 26 took the dichotic words test. Sub-sets of 15 took the dichotic nonsense test (three schizophrenic, and 12 major depressive disorder), 19 took the dichotic tones test (three schizophrenic and 16 major depressive disorder) and 16 took the visual dot localisation test (three schizophrenic and 13 major depresive disorder). All patients were without major illness other than their psychiatric disorders and none were taking non-psychiatric medications; none had any history of neurological illness or injury, language or learning disability, or excessive alcohol or drug use.

Control subjects were right-handed and without history of psychiatric, neurological or major medical illness, learning or language difficulties, or excessive drug or alcohol use. None were taking medication with CNS effects. There were 47 controls for the words test (23 men, 24 women, median age 27 years, range 17–56); 31 for the nonsense test (nine men, 22 women; median age 27 years, range 20–38); 16 for the tones test (eight men, eight women; median age 27 years, range 20–35); and 29 for the dot test (14 men, 15 women, median age 28 years, range 20–56).

Research design

Patients were tested initially seven to 14 days after admission, when actively symptomatic. Each PA test was given twice on the same day, and the results combined. Word and nonsense tests were given on separate days, with about half the subjects receiving the word test first and the other half receiving the nonsense test first. The dot and tone tests were often given on the same day, with a two hour break between tests, and were generally given after the word and nonsense tests. All tests given initially were then repeated 12 to 145 days later (median 50), when clinical staff considered that maximum expected clinical improvement had occurred. Fourteen patients were off all medication at the time of initial testing (median in hospital drug-free period was ten days, range seven to 14); eight of the remaining 12 were on the same or the same class of medication (e.g. antidepressant) on initial testing as they were on retesting. The remaining four patients discontinued or had a change in class of medication between the initial and final testing. The depressed patients were treated with TCAs and/or lithium carbonate, all within usual therapeutic dose-ranges. The schizophrenics were treated with haloperidol or chlorpromazine, within usual dose-ranges. All 23 controls for the nonsense test took the test repeatedly, 11 with a nine-week inter-test interval, and the remaining 12 with less than a one-week interval; 18 word test controls, all 16 tone test controls, and ten dot test controls were retested within one week of original testing.

Behavioural measures

Once during the 7 am–3 pm shift and once during the 3–11 pm shift, patients were rated by nursing staff on a 13-item clinical rating scale, identical to one described by Heninger *et al*, (1970), save for the elimination of an expressed anger rating. Ratings on the day prior to a PA test, the day of the test, and the day after the test (six ratings in all) were averaged for a clinical rating to correspond to each PA value.

Perceptual asymmetry tests

The dichotic word, nonsense, and tone tests have all been described elsewhere (Wexler & Halwes, 1981, 1983; Wexler & Heninger, 1979). The word test consists of 15 different single syllable word pairs, in which each member of every pair differs from the other only in the initial consonant, e.g. coat, goat. All words begin with one of six stop consonants, b, d, p, t, g, k, and are natural speech, spoken by a male voice. The initial consonant portion of one member of each pair was cross-spliced onto the vowel-final consonant portion of the other member on the DDP 224

Computer System at Haskins Laboratories. The members of each pair fuse into a single auditory image. Consequently, subjects are aware of hearing, and report only one word on each trial. Each pair is presented twice in 30 trial blocks, the second time with each word to the ear opposite that of the first presentation. Four such 30-item blocks make up the test, for a total of 120 trials. Subjects indicate what word they heard by making a line through it on an answer sheet that has four possible responses—both members of the dichotic pair and two other words differing from the dichotic stimuli only in the initial consonant. A score for each ear is determined by totalling the number of times the word presented to that ear is the one indicated: an error is scored when neither of the pair is chosen.

The nonsense test consists of dichotic pairs, made up of the six stop consonents, b, d, p, g, t, k, preceded and followed by the vowel 'a' (e.g. aba, aka). The stimuli are synthetic copies of natural speech. As in the word test, the members of each pair fuse into a single auditory image, and subjects expect, experience, and report only one response on each trial. Three of the 15 possible pairings of the six syllables were found to be subject to frequent phonemic blending errors (Halwes, 1969) and were therefore discarded. The remaining 12 pairs were presented twice in 24-pair sequences, the second time with each syllable to the ear opposite that of the first presentation. Four such blocks were combined to make a 96-trial test. Subjects indicate what syllable they hear by writing b, d, p, g, t, or k in a blank space between two a's on a prepared answer sheet. The text is scored as for the word test.

In the tone test, each dichotic pair consists of a 440 and a 450 Hz tone, differing in volume by 0–10 dB; subjects indicate which sounds louder. If subjects indicate that one ear signal was louder when in fact the opposite was true, the ear chosen is assigned a number of points equal to the number of decibles by which the stimuli differed in intensity. Right- and left-ear scores are combined to give a total error score. All test tapes were made at Haskins Laboratories in collaboration with Terry Halwes. Tapes were played on a Teac-2-track master recorder, and stimuli delivered through matched pairs of TDH-39 earphones. Calibration tones at the beginning of each tape were balanced to minimise channel effects, while remaining channel effects were controlled by reversing earphones after the first and third quarters of the tests. In all tests, subjects received practice trials before the start, to familiarise them with the procedure and to decrease anxiety and errors. On the words and nonsense tests, subjects were not told, and did not realise that they were getting different inputs in each ear on each trial. In the loudness test, they were told they would hear a different tone in each ear, and should indicate which sounds louder.

The visual dot localisation test was modelled after one developed by Levy & Reid (1978). Subjects are instructed that a single dot will appear in one of 40 possible positions within a circular frame, encompassing both the left and right fields; there are 20 different, randomly chosen positions, mirrored in the two visual fields. Stimulus slides are exposed for 120 msec. Subjects report the location of the dot from a hand-held response key. The circular frame extends to 3.5° lateral of fixation, with dot positions ranging from 0.7° to 2.7°. Subjects sit 30 inches from the screen, directly in front of the central fixation point.

A digit, 0–19 is presented in the centre of the field on each trial and subjects report this digit before indicating dot location; this central digit subtends an angle of 0.2°. The pre-stimulus fixation/post stimulus noise slides consist of an x in the centre for fixation, and several different types of visual noise in the remainder of the slide. Dots are presented once in every position in each visual field for a total of 40 trials, with a two-minute rest after 20 trials. Trials on which the central fixation number is incorrectly reported are not scored, and are repeated at the end.

The numbers of items correctly identified in each field constitutes the score for each; the numbers of items identified incorrectly in both, together constitute a total error score. Results from subjects who made more than 75% errors were discarded. Prior to the test, subjects were familiarised with the procedure and stimuli by being shown similar slides, and were required to identify the central number and to indicate whether or not a dot was present.

Auditory acuity was tested in each ear by the method of ascending and descending limits, using tones of 250, 500, 1,000, 2,000, and 4,000 cps; no subject had a difference in auditory acuity between the ears of more than 5 db on more than two of the five frequencies tested. Handedness was assessed by observing which hand was used in each of eight tasks: writing, throwing a ball, dealing cards, opening a jar, threading a needle, brushing teeth, cutting with scissors, and striking a match. All subjects wrote and did at least five of the other seven tasks with the right hand.

Data analysis

Laterality scores were calculated by subtracting left-ear (or visual field) scores from right-ear (or visual field) scores, and dividing the difference by the sum of the two. Independent t-tests were used to evaluate mean differences between groups, paired t-tests to evaluate change within subjects over time, and Pearson correlation coefficients to evaluate relationships among the variables.

Results

Patients compared to controls

On the dichotic nonsense and tone tests and on the visual dot test patients, when first tested, tended to be less lateralised than controls, but none of these differences reached the $P<0.05$ level of statistical significance. Mean laterality for the patients on the nonsense test was 0.03 ± 19, for the controls 0.12 ± 0.18, 2 tail $P<0.10$, on the tone test 0.07 ± 0.59 and 0.33 ± 0.45, $P<0.17$), and on the dot test 0.03 ± 0.17 and -0.08 ± 0.21 $P<0.09$. Asymmetry on the word test among patients when they were acutely symptomatic was essentially identical to that among controls; 0.13 ± 0.14 and 0.13 ± 0.15. Patients made more errors than controls did on the word test (pts. 5.4 ± 4.76, con. 1.8 ± 2.1, $P<0.001$) and on the nonsense test (pts. 2.5 ± 3.1, con. 0.38 ± 1.1, $P<0.05$), but patients and control error rates were not significantly different on either the

TABLE I
Changes in dichotic nonsense and dichotic words tests with recovery from acute psychotic episodes

Nonsense (n=15)	*Sick*	*Well*	*P value (2-tail)*
Laterality (PD index)	0.03±0.19	0.07±0.20	$P=0.10$
Errors	2.8±3.2	5.1±7.1	$P=0.13$
Word Test (n=26)	Sick	Well	P value (2-tail)
Laterality (PD index)	0.13±0.14	0.06±11	$P=0.001$
Errors	5.4±4.6	4.1±5.1	$P=0.28$

tone or the dot test. There were no significant correlations between error rate and asymmetry on any of the tests in either controls or patients. Results of each statistical comparison were essentially the same when sub-groups of the sample (depressives, schizophrenics, patients off and on medication) were examined separately.

Changes in asymmetry with clinical improvement (Table I)

Following treatment and clinical improvement there was a decrease in PA on the dichotic word test; initial mean laterality 0.13±0.14, retest 0.06±0.11, 2 tail $P<0.001$. The sub-set of 15 patients who also took the nonsense test showed the same increase in laterality noted in an earlier study; laterality means 0.03±0.19 and 0.07±0.20, one tail $P<0.05$. Changes in the tone test (0.07±0.59 and 0.02±0.06) and in the dot test (0.03±0.17 and 0.02±0.14) did not approach significance. The degree of change in PA in individual patients on the nonsense test was not correlated with the degree of change on the word test (Pearson correlation 0.08). Changes in all tests were similar in subgroups defined by diagnosis (schizophrenia or depression) or by medication status (group 1 off medication initial testing, on antidepressant medication second testing, group 2 on the same medication for both initial and repeat testing). Controls did not show significant changes with retesting on any of the four tests. Error rates on neither the word test nor the nonsense test changed significantly with clinical improvement.

When recovered, asymmetry on the word test in the patient group was significantly less than in the controls (pts 0.06±0.11, controls 0.14±0.16 $P<0.04$). Asymmetry on the nonsense test, which had been less than that of controls when patients were sick ($P<0.10$), moved closer to control values (pts. 0.07±0.20, controls 0.13±0.18, $P<0.26$). Asymmetry on both the tone and the dot tests moved farther from control values with recovery so that differences between recovered patients and controls were significant on both tests (tone test, pts 0.02±0.47, controls 0.33±0.45 $P<0.03$; dot test pts. 0.04±0.4, controls −0.08±0.21, $P<0.05$).

Correlation between PA and clinical symptomatology

Two sets of correlations between PA and symptomatology were calculated; between initial PA scores and initial clinical ratings, and between recovery-related changes in PA and degree of symptom improvement. The correlations between PA on the tone and dot tests and clinical ratings were not significant in either of the sets with a frequency greater than would be expected by chance alone. The same was true for initial PA scores on the word and nonsense tests and initial nurses' ratings. Errors on the word test when patients were acutely symptomatic were positively correlated with ratings of odd or unusual thoughts (0.58 $P<0.002$), anxiety (0.40 $P<0.04$), disorganised thinking (0.53 $P<0.006$), hallucinations (0.47 $P<0.01$), paranoia (0.44 $P<0.02$) and overall psychosis (0.57 $P<0.002$). Correlations between errors on the nonsense, dot and tone tests, and clinical ratings were not statistically significant.

The correlations between recovery-related changes in PA and errors on the word and nonsense tests, and recovery-related changes in nurses' ratings are presented in Table II. All change variables were calculated by subtracting initial values from time two values (repeat or well values). Thus, an increase in laterality on the nonsense test would lead to a positive change score, while a decrease in laterality on the word test, a decrease in test errors, or a decrease in symptomatology would lead to a negative change score. Correlations between changes in PA on the nonsense test and changes in severity of symptoms were consistent with the recovery-related increase in laterality in group mean scores. Those patients with larger increases in laterality on the nonsense test had greater improvement in ratings of odd and unusual thoughts, disorganised thinking, hallucinations, paranoia, and overall psychosis. Neither changes in the overall depression rating nor in specific aspects of depression (ie. anxiety, withdrawal, agitation, motor retardation, decreased energy) were correlated with changes in asymmetry. In contrast, on the word test, only changes in the magnitude of social withdrawal, motor retardation and decreased energy—all symptoms associated with depression—were significantly correlated with change in PA. However, the direction of correlation was opposite what might be expected from the group mean decrease in asymmetry on the word test with recovery: those patients with smaller decreases in laterality exhibited greater improvements in symptomatology.

Decrease in errors on the words test was positively correlated with improvement in ratings of psychotic symptomatology. Although change in laterality on the nonsense test was also correlated with change in most of the same symptoms as was change in words test errors, the correlation between change in laterality on the nonsense test and change in overall errors on the words test was not significant (0.23). The extent of change in errors on the other PA measures were not correlated with change in ratings of symptoms.

Separate analyses were conducted for patients off medication when ill, patients on medication both ill and well, schizophrenic patients, and depressed patients. In patients off medication, PA on the word and nonsense tests when ill tended to be more highly correlated with ratings of

TABLE II

Correlations between recovery related changes in dichotic variables and recovery related changes in clinical ratings

		NPD	*NERR*	*WPD*	*WERR*	*THO*	*ANX*	*WITH*	*AGIT*	*DIST*	*HOST*	*MRET*	*HALL*	*ENE*	*PAR*	*PSY*	*DEP*	*MAN*
Nonsense Test																		
Laterality	R	1.00	−0.19	0.08	−0.19	−0.59	−0.25	0.03	−0.09	−0.63	0.08	0.22	−0.68	0.14	−0.55	−0.61	0.14	−0.33
(PD index)	P	0.00	0.50	0.78	0.51	0.03	0.37	0.91	0.75	0.01	0.78	0.44	0.005	0.63	0.03	0.02	0.62	0.23
Errors	R	−0.19	1.00	−0.10	0.55*	−0.14	0.07	−0.23	−0.134	0.27	−0.02	−0.23	0.14	0.04	−0.07	−0.11	−0.12	0.21
	P	0.50	0.00	0.73	0.03	0.62	0.82	0.40	0.62	0.34	0.93	0.42	0.63	0.88	0.79	0.69	0.68	0.44
Words Test																		
Laterality	R	0.08	−0.10	1.00	−0.54	−0.11	−0.31	−0.36	0.02	−0.12	−0.30	−0.35	−0.06	−0.45	−0.21	−0.12	−0.26	−0.11
(PD index)	P	0.78	0.73	0.00	0.004	0.60	0.12	0.07	0.92	0.57	0.14	0.08	0.77	0.02	0.310	0.55	0.19	0.59
Errors	R	−0.19	0.55	−0.54	1.00	0.40	0.43	0.29	0.38	0.51	0.21	0.03	0.45	0.07	0.33	0.40	0.06	0.29
	P	0.51	0.03	0.004	0.00	0.04	0.03	0.15	0.05	0.007	0.30	0.88	0.02	0.74	0.10	0.04	0.76	0.15

symptoms than they were in the entire group, but patterns of correlation in other groups were similar to those of the entire sample.

Discussion

The recovery-related increase in PA on a dichotic nonsense test, noted by Wexler and Heninger (1979), was replicated here; in that study, the degree of increase in asymmetry on this nonsense test was correlated with the degree of decrease in clinical ratings of paranoia, and this correlation was confirmed. In addition, the degree of increase in asymmetry was found to correlate with the degree of improvement in ratings of odd and unusual thoughts, disorganised thinking, hallucinations, and overall psychosis. When ill, patients showed less asymmetry than healthy controls; the increase in asymmetry with recovery moved patients' asymmetry values closer to those of controls'.

Perceptual asymmetry on a dichotic word test decreased as patients recovered. Despite the fact that this test was very similar in task, structure, and stimulus characteristics to the nonsense test, the recovery-related change in PA on this test was opposite in direction to that on the nonsense test. Recovery-related changes moved patients' asymmetry away from control values, so that although patients' group mean asymmetry was essentially identical to that of controls when the patients were ill, when they recovered, their mean asymmetry was significantly less. Those patients with the greatest decreases in PA with recovery tended to show the smallest decrease in ratings of social withdrawal, motor retardation, and decreased energy—which can be related to depression and/or side-effects of medication. The decrease in PA on the word test was not related to the change in ratings of psychosis or of psychotic thought processes.

Errors on the dichotic word test were positively correlated with ratings of psychotic thought and behaviour when patients were ill, while recovery-related decreases in errors were positively correlated with improvement in these ratings. The relationships between errors on the word test and the clinical variables were very different from those between errors on the other tests and these variables. When ill, patients made significantly more errors than controls on the word and nonsense tests, but not on the dot or tone tests; it was only on the word test that errors were significantly correlated with clinical variables. In controls, the word test consistently yielded fewer errors than any of the others. Together, these observations suggest that the associations between errors on the word test and clinical

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variables reflect a specific aspect of brain dysfunction, and are not merely a reflection of the general decrement in performance associated with psychosis.

Data generated by the tone and dot tests were not robust: group mean values on neither test changed significantly as patients recovered, and neither asymmetry nor errors on either test correlated significantly with clinical ratings. However, when ill, patients tended to be less lateralised on both tests than were controls. With recovery, patients' values moved further from those of controls, and the differences became statistically significant.

Interpretation of these data is difficult: firstly, because recovery-related changes on different tests are in different directions, both with respect to initial illness values and controls, and secondly, because there are data from four different tests. It would be easier to consider those from only one or two, but such simplification would merely cause delay. Despite such efforts, however, an interpretation that incorporates all statistically significant findings has not so far been possible, but as the addition of new pieces to a complex puzzle provides places for those previously impossible to fit, future studies will perhaps allow interpretation of all current data.

Recovery-related changes in asymmetry

It is striking that asymmetry on two tests as similar as the dichotic word and nonsense tests would change in opposite directions with recovery. The fact that the change on the nonsense test has been replicated, together with the high statistical significance of change in the word test, suggests that the difference in direction is worthy of attention. There is also support from three other sources. Firstly, similar opposite changes in asymmetry on these same two tests have been noted in healthy subjects with administration of concurrent visual tasks (Wexler & Halwes, 1985). Secondly, the two tests fluctuate in opposite directions from day to day in depressed patients during the initial phase of ECT (Wexler *et al*, unpublished). Lastly, schizophrenics have greater asymmetry than controls on a dichotic word test (Lishman *et al*, 1978), and less on a dichotic nonsense test (Colburn & Lishman, 1979).

It seems unlikely that the differences between the word and nonsense tests result from merely procedural factors. In the previous recovery study, the nonsense test was given alone, and the same increase in PA with recovery noted; the nonsense test was given on successive days, as were the word and nonsense tests in the present study, and scores on each of the illness test days were lower than those on the well days. To control for test-order effects, in the present study, half the patients who received both tests received the word test first, and half the nonsense test first: those who did not take the nonsense test showed the same decrease in PA as did the entire group. Finally, an unpublished study found inter-correlations ranging from 0.52 to 0.70 ($n=40$, $P<0.001$) among four word tests, each modelled after the one used in this study but differing in the emotional quality of stimulus words. Together with the high test-retest reliability of the word and nonsense tests, this makes it unlikely that the differences observed here between them are due to the administration of multiple tests.

Explanation of the results must be *post hoc*, since they were unanticipated, and requires validation. Three explanatory approaches were considered: that changes on the two tests represent different and independent regional brain dysfunctions; that dysfunction of a single brain region, anatomically defined, accounts for changes in both tests; and that a single change in brain physiology accounts for changes in both tests. The first, though supported by the absence of correlation between recovery-related changes in PA on the two tests, was rejected: each of the possible independent dysfunctions must differentiate between word and nonsense stimuli, altering one test but not the other. In addition, unless the number of such hypothetical functions and dysfunctions is to be increased, the same two functional alterations must be postulated to account for the changes in asymmetry seen in healthy subjects with concurrent visual tasks (Wexler & Halwes, 1985), and for the reciprocal day-to-day changes in asymmetry on these tests, noted in depressed patients during the initial phase of ECT (Wexler *et al*, unpublished).

The second possibility—that dysfunction of a single anatomically defined area led to opposite changes in asymmetry—seems improbable. According to existing models of perceptual asymmetry, change in function of all areas that contribute to asymmetry on both tests would affect both tests in the same way. It is possible, however, that efficiency of information processing in a particular area varies along an inverted U-shaped curve as a function of activation (or other factors) of that area, and that because of differences in the functional demands posed by processing words and nonsense, these two processes are at times on opposite sides of the maximum point of this curve. Changes in the function of such an area with disease, concurrent visual tasks, or ECT could then have opposite effects on asymmetry on the two tests. Dysfunction of a single anatomical area then remains a viable explanation, and one that might be amenable to further experimental validation.

The third approach invoked the possibility that a single physiological alteration might account for the opposite changes on the words and nonsense tests. I have developed (Wexler, 1986) a physiological model of brain function, based on Luria's notion of cerebral functional systems: specific behaviours or cognitive functions are not localised in specific brain regions, but are the result of the concerted action of a functional system. The specific anatomical components of these systems may vary, while the behavioural or cognitive output remains constant, and from this perspective, integrative and interactive processes within and among functional systems are central in normal brain function. Major alterations in mood and behaviour would be associated with changes in these processes.

The simultaneous and unacknowledged presentation of different stimuli to each ear in dichotic tests create unnatural functional demands: perceptual asymmetry is not an index of ordinary function. It probably does not make sense, therefore, to speak of the functional systems for processing the dichotic word and nonsense stimuli. The present data suggest, however, that in recovery from acute psychotic states the functional systems for processing auditory information as meaningful or as nonsense are altered in such a way as to have opposite effects on PA in the dichotic words and nonsense tests. A unitary explanatory hypothesis suggests that there is a change in the relationship between the functional systems, leading to opposite changes in PA.

The degree of PA is thought to reflect, among other things, facilitation of information flow from the right ear by stimulus-specific activation of left hemisphere attention centres (Kinsbourne, 1975). Assuming that the degree of such activation is proportional to the activity of the stimulating functional system, the present data suggest that: (1) the functional system for processing auditory information as meaningful, and that for processing auditory information as nonsense, are normally in a mutually inhibitory relationship, and (2) in some cases of acute psychosis, the balance of activity of the two systems is altered so that the functional system for processing auditory information as meaningful is more active and that for processing information as nonsense is less active. Decreased activity of the functional system for processing auditory nonsense during acute illness would lead to decreased activation of left-hemisphere attention centres and, consequently, less facilitation of the right-ear input pathway and a decreased right-ear advantage with presentation of nonsense stimuli. A similar decrease in activity of the functional system for processing auditory words with recovery would lead to the recovery-related decrease in asymmetry seen on that test.

The increase in errors on the word test, seen on initial testing, suggests that with a shift in the reciprocal balance between the word and nonsense systems toward the word system in acute illness, efficiency of the word system decreases.

Correlations between specific symptoms and laterality variables

Increase in PA on the nonsense test was significantly correlated with decrease in symptoms of psychotic thinking, but not with change in symptoms in energy level, or in motor or social activity. It is interesting that this was so in a group who were mainly psychotically depressed. The nature and extent of cognitive disturbance found in major depressive illness are variable, and these data suggest that PA on the nonsense test is associated with this important but variable component of the syndrome. Change in PA on the words test was not correlated with change in these symptoms, but instead tended to show an inverse correlation with change in social withdrawal, motor retardation, and lack of energy; those individuals with the greatest improvement in the symptoms showed less of the recovery–related decrease in PA that characterised the group as a whole. This is of interest because of the direction of the association, which suggests that a recovery and/or treatment-related change in brain function, as reflected in PA on the words test, may have a negative effect on certain symptoms. Identification of this process might aid in the improvement of treatment.

Errors on the word test when patients were ill were positively correlated with the severity of symptoms of psychotic thinking, and the degree of decrease in errors with recovery was correlated with the degree of improvement in these same symptoms. These associations are straightforward, and consistent with the recovery-related decrease in group mean errors. However, the association of errors on the word test with symptoms different from those associated with PA on that test eludes the explanation that errors on this test result from the same process that alters PA in it.

Asymmetry on the tones and dot tests

Asymmetry on these tests did not change with recovery for the group as a whole, and was not associated with particular symptom ratings. Some individuals did show changes on one or another of the two tests, and these may prove useful in defining clinically or physiologically meaningful sub-groups.

The absence of significant group-wide changes with recovery on either of these tests indicates some limits of the pathophysiological alterations revealed in the changes on the word and nonsense tests. Earlier writers suggested that global dysfunctions of one hemisphere or the other characterised the major psychiatric disorders. The interpretation here of opposite changes in PA on the word and nonsense tests is more specific, suggesting change in the functional relationship between two functional systems, each with important components in the left hemisphere, instead of a general left-hemisphere dysfunction. The absence of recovery-related changes in the dot and tone tests is consistent with such a limited hypothesis, but not with the earlier and more general one. The differences between controls and patients on these tests, when patients are recovered, do not fit the interpretation of recovery-related changes on the word and nonsense tests, however.

Conclusion

Four PA measures, with demonstrated reliability and validity, were used here to collect a large amount of data, which proved confusing, thus demonstrating the inadequacy of existing concepts and models in describing brain function and dysfunction. It has been postulated that normally, the functional systems for processing auditory words and nonsense are in a mutually inhibitory balance. Considerable confusion remains, however, indicating the primitive stage of the experimental and theoretical work. Though difficult, multi-dimensional physiological studies are essential if the organisational principles of the brain as an organ are to be discovered.

The most significant suggestion from the data is that normally, the functional systems for processing auditory words and nonsense respectively are in a mutually inhibitory balance. It is interesting to consider such a possibility from the perspectives of both normal and pathological development, since at first, during childhood, all is nonsense. It is also interesting to consider it in relation to those symptoms of psychosis which might be considered to reflect excessive assignment of significance—ideas of reference, delusions, and hallucinations.

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