THE EFFECT OF PREFRONTAL LEUCOTOMY ON THE PSYCHOGALVANIC RESPONSE.

By W. Ross Ashby, M.A., M.D., D.P.M., and
M. Bassett, Dip.Soc.Sc.
From Barnwood House, Gloucester, and the Burden Neurological Institute, Bristol.

[Received 3 February, 1950.]

Though it is now generally accepted that prefrontal leucotomy has an effect on the subject's behaviour, its mode of action and the intermediate stages of its effect are still obscure. Some evidence, which has been sufficiently reviewed elsewhere (Meyer and McLardy, 1949; Fleming, 1944), suggests that the operation acts by lessening emotional drive: the retrograde degeneration which usually occurs in the dorso-medial and anterior thalamic nuclei points to this. Clinically, however, the belief rests on little more than impressions. In order to obtain more objective evidence, we have used the psychogalvanic response, not because it measures emotional change with fidelity, but because it is one of the few objective tests available. Though its precise relation to emotional change is still not clear, that it does have some relation has been demonstrated repeatedly. We have therefore attempted to compare the sizes of the response before and after the operation.

We would have preferred to perform the test before and after operation on every subject; but as only six could be so tested, we have also examined twenty-one leucotomized patients, comparing them with an equal number of carefully selected controls. Almost every subject was examined at several sessions, and all were tested with a variety of stimuli. As we were interested chiefly in reactions of cortical origin, various "threats" were presented in symbolic form; but direct strong sensory stimulation was also given at each session, partly to reinforce the threats and partly to provide an estimate of the general reactivity at that session.

Apparatus and Method.

The subject's resistance was measured by a Wheatstone bridge, the circuit being arranged as in Fig. 1. By opening switch A, the resistance of the patient's branch could be increased by 500 ohms: the sensitivity of the galvanometer was always adjusted so that the change of 500 ohms caused a deflection of 25 divisions on the galvanometer's scale. The deflections have been recorded uniformly in these divisions: multiplied by 20 they will give the change in ohms. The galvanometer was highly sensitive, requiring only 0·02 micro-amps. per division. It was, however, sufficiently quick in movement to be able to follow with fidelity the comparatively slow changes of the psychogalvanic response.

https://doi.org/10.1192/bjp.96.403.458 Published online by Cambridge University Press

To avoid polarization, we used large electrodes and the whole surface of the subject's hands. Two jars containing 2 litres each were almost filled with saline (0·85 per cent NaCl), and a large sheet of zinc (area about 200 sq. cm., bent to form a cylinder) was placed in each. The subject's hands were immersed to the wrists in the saline, and the sheets of zinc connected to the bridge. In this way a large, uniform, and unvarying area of electrical contact was maintained. The electro-chemical potential between saline and zinc, being symmetrical, was balanced out. Since some workers (e.g. Richter, 1929; Forbes, 1936) obtained different responses from different areas of skin (e.g. dorsal and palmar surfaces of the hand) our method has the advantage of uniformity in sampling.

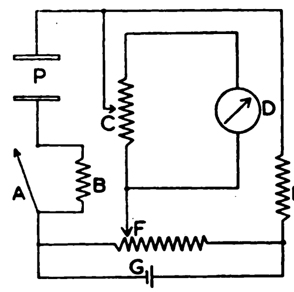

FIG. 1.—Circuit of the Wheatstone bridge used: P, position of subject; A, switch for calibration: usually closed, its opening adds resistance B to the subject's branch; B, 500 ohm resistor; C, potentiometer for adjusting the sensitivity of the mirror galvanometer D; E, 10,000 ohm resistor; F, variable resistor (200 ohms) for balancing the two branches; G, cell of 1·5 volts.

The resistance shown on the bridge is due partly to the subject and partly to the saline; but the effect of the latter is negligible. Sodium chloride at 0·85 per cent. has an equivalent conductivity of 90 (Kaye and Laby, 1942) and a molarity of 0·145; so the specific resistance of the solution is 77 ohms/cm^3. As the distance between hand and electrode is about 5 cm., and as the hand and electrode have each an area of about 200 sq. cm., and as there are two hands, the total resistance due to the solution will be approximately $77 \times 5 \times 2/200$, i.e. about 4 ohms. As the subject's resistance was never below 1,000 ohms, the resistance of the saline never exceeded a two-hundredth of the whole. It is therefore negligible compared with the other factors.

EFFECTS OF TEMPERATURE, HABITUATION, AND POLARIZATION.

The effects of the temperature in the handbath, of the decay in responsiveness commonly found to occur during a session, and of the polarization apt to occur during a session, were studied in a preliminary investigation. (It should be noticed that as habituation and polarization both tend to cause a lessening of the psychogalvanic response as the session progresses, their effects are confounded, and a distinction between them is not easily made. For our purpose, however, the distinction is not necessary: we accept that the response diminishes, for various reasons, during the session, and have so arranged the experiments that this change is allowed for in the subsequent comparisons.)

To find the effects of these factors, three subjects were given each of five stimuli—a pinch to the lobe of the ear, a bright light, the noise of a tin basin falling, the smell of 2 per cent. ammonia, and a light touch on the conjunctiva. These were administered in cyclic order when the hand-bath had each of four temperatures (10°, 20°, 30° and 40° C.).

As the response was obviously non-linear in its relation to time during the session, Ezekiel's graphic method (1930) was used for the analysis of the results. One independent variable (time) was taken, and a curve drawn showing the first regression, that of response on time. The residual deviations from this curve were then used as ordinates for the second regression, that of response on temperature. The residual deviations from this curve were then used to obtain a better approximation for the first regression, and so on. Each improvement in the regressions diminished the residual deviations: the process was continued until they were minimal. Examination of the data gave no evidence that the two regression curves were not independent. The

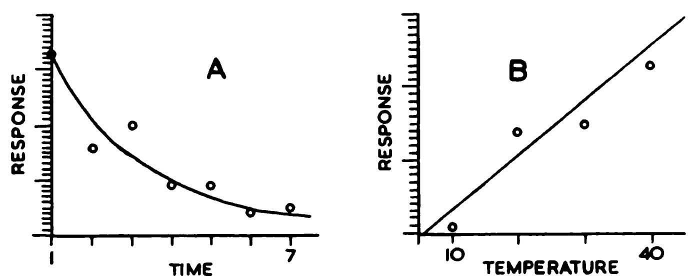

FIG. 2.—Changes in the psychogalvanic response: A, with time during one session; B, with temperature of the hand-bath. Each circle is the average of 7 to 10 observations. The responses are measured on an arbitrary scale.

effects of the two factors—time and temperature—were found to be as shown in Fig. 2. The response diminishes as the session proceeds, and increases as the temperature of the hand-bath is raised. These effects had to be eliminated.

The effect of temperature was eliminated by keeping the hand-bath always at 37° C. This temperature was chosen partly for the subject's comfort, but especially to obtain greater sensitivity; for, as can be seen in Fig. 2 (B), at the warmer temperature the response is larger. As the slope of the curve is not zero at 37° C., careful regulation of the temperature is essential, for any error appears unaltered in the final results.

The effect of time cannot be eliminated directly: it can only be equalized by taking care that all subjects are treated similarly. This precaution was taken, and should suffice to make any error negligibly small. It will be noticed that our final results are not subject to the full range of variation shown in Fig. 2 (A): each subject's score is the average over all tests given in each session, and no direct comparison is made between the individual tests given at different times within one session; consequently only differential effects will appear—and these are usually small. As the first-given stimulus tends to evoke a particularly large response, and as this excess cannot be reduced, we have used Fisher's principle (1935), equalizing the effect by presenting the stimuli in randomized order so that every stimulus has an equal chance of being given first. That the randomization should be adequate, we used the tables of Fisher and Yates (1938).

The Tests.

For the examination of our subjects we used eight stimuli. Four were real, direct, and strong: the smell of 2 per cent. ammonia; a pinch to the lobe of the ear by a spring clip which applied the same pressure on all applications; a brilliant illumination of the eyes by a "Photoflood" lamp; and a touch with a wisp of cotton wool on the conjunctiva. The variety of tests was used to reduce personal idiosyncrasies. These four stimuli almost always elicited a brisk psychogalvanic response. In addition the four stimuli were administered not actually but as a threat, i.e. in "symbolic" form; thus, the dish with the ammonia was brought near to the subject's nose but not uncovered, the lobe of the ear and conjunctiva were approached but not touched, and the lamp was exhibited but not switched on. Before each stimulus was given, the subject was told briefly what to expect, but no hint was given whether the stimulus would be real or threatened.

The Subjects.

The first group consisted of twenty-one patients who had undergone prefrontal leucotomy. Eleven were men and ten were women. Their average age was 46 years, and the average interval since operation 3·4 years. Eight men and two women were still resident in hospital: the others had recovered sufficiently to return home. At the time of operation, ten had been considered schizophrenic, six melancholic, and there were five others.

To act as controls, a second group was assembled; it was composed of the same number of psychotic patients selected to match the first group as closely as possible. There were thirteen men and eight women, of average age 47. Eight were schizophrenic, seven melancholic, and there were six others. (That this group was well matched to the other is supported by the fact that, since the completion of the experiment, prefrontal leucotomy has been recommended for six of them).

A third group was composed of six patients whom it was possible to examine both before and after operation. Though small in numbers, this group could act as its own control, and offered the advantage of a properly designed factorial experiment. It therefore provides information of peculiar value. Of the subjects, four were women, two men; three were melancholic, three schizophrenic; their ages lay between 19 and 74 years. In this group all tests were conducted within six months of the operation.

A factor of possible significance is the route of entry used: lateral or transorbital. Of the six patients in the last-mentioned group, four had been entered by the transorbital route. The other two, and the twenty-one in the first group, were entered by the lateral route.

The Experiment.

The events in one session have been described above. Each session yielded two scores: the sum of the four responses to the real stimuli, and the sum of the four responses to the threatened. Division by four gives the average response.

Each of the six patients was tested on 3 sessions before and 3 sessions after the operation: a total of 288 responses. The analysis of the results is given below.

The two groups of twenty-one patients could not, for reasons outside our control, be studied so systematically, and the orthogonality of the factors is imperfect. The defect, however, is only partial and, as will be seen, there is reason to believe that the relations between the factors are simple so that a slight lack of orthogonality is of little consequence. The defect is due chiefly to the fact that not all patients could be tested over the same number of sessions. But within each session the conditions and methods were uniform, and this uniformity was maintained over the whole study.

The leucotomized patients were studied at 57 sessions (456 psychogalvanic responses), and the controls at 73 sessions (584 responses). As the study of the six patients was completely orthogonal it has been kept separate. To some degree the two studies complement each other: a larger but less accurate study contrasts with one smaller but more precise.

The Effect of "Familiarity."

A minor effect, but one which had to be considered, was the tendency for each patient, as he became accustomed to the routine of the tests, to react less. The "habituation" described earlier showed only within each session; here we are discussing the change which tended to occur as session followed session. Not only is this change a source of variance, but, much more important, it would tend to be confounded with the effect of leucotomy. We shall refer to it as "familiarity."

Its size can be estimated from the two groups of twenty-one patients, for each patient would show, as session succeeded session, the effect of this factor alone. We have therefore fitted a straight-line regression curve to each of the four groups of results in the leucotomized and non-leucotomized groups subdivided into responses to real and to threatened stimuli. (There was no evidence that the regression differed significantly from the linear.) The effect was found to be small. In no group was the regression statistically significant, but all were of the expected sign (Table I).

Table I.—*Regression coefficients of psychogalvanic response on session number, in four groups.*

Group.		Number of tests.	Regression co-efficient.
Patients.	Stimuli.		
Non-leucotomized	Real	228	−0·679
,,	Threatened	228	−0·711
Leucotomized	Real	292	−1·235
,,	Threatened	292	−0·893

https://doi.org/10.1192/bjp.96.403.458 Published online by Cambridge University Press

The average of all four groups, however, differed significantly from zero ($P = 0{\cdot}01$). The effect of familiarity is therefore demonstrable in our results.

The average value of the fall was 0·88 divisions (i.e. 17·6 ohms) per session. This quantity has been added to all the scores discussed below. The correction, though worth while, is not large.

Experimental Results.

The presentation of our results is best commenced by the elimination of some factors which were found to have no significant effect on the patients' responses.

One such factor is the distinction in the leucotomized group between those patients who improved and those who did not. Of the twenty-one leucotomized patients, those who "improved" numbered eleven: three men and eight women. Their average age was 46 years, and the average interval since leucotomy three years. At the time of their examination, seven were in their normal employment: in business or in the home. (One subject was living at home at the time of examination, but has returned to hospital since.) The other three were leucotomized recently (average interval three months). Those who were "unimproved" numbered ten: eight men and two women. Their average age was 45 years, and the average interval since leucotomy four years. None had improved sufficiently to be discharged. The two groups were distinguished by a purely clinical criterion, the main question being whether they improved sufficiently to leave hospital. Though the mode of distinction is crude, our present knowledge can hardly suggest a better: the distinction is probably sufficient for practical purposes. The mean responses of the improved and of the unimproved, and the difference with its standard deviation, are shown in Table II.

Table II.—*Mean scores of psychogalvanic responses in the two groups "Improved" and "Not-Improved," and the standard deviation of their difference. Responses to real stimuli and to threatened are shown separately. (In units of* 20 *ohms).*

Type of stimulus.	Group.	Number of tests.	Mean score.	Difference.	S.D. (diff.).
Real	Improved	76	26·6	4·0	±5·4
,,	Not improved	152	22·6		
Threatened	Improved	76	14·7	0·4	±4·5
,,	Not improved	152	15·1		

The responses to real and to threatened stimuli are shown separately. Neither difference exceeds twice its standard deviation; so there is no evidence that the responses of the leucotomized patients are dependent on the degree of clinical improvement.

The 456 observations on the leucotomized patients can now be compared with the 584 on the controls. In the two groups the mean responses are 19·5 and 25·2 divisions respectively; the difference is 5·7 with standard deviation

2·4. The difference is 2·3 times its standard deviation, and P is 0·02. This difference (5·7) is derived from measurements over two groups: the real and the threatened stimuli. It is advisable to see whether these two groups agree in their estimates of this difference. Any disagreement would represent a statistical interaction between the two factors, "operational status" and "type of stimulus." Its presence is tested by finding the value of the linear function

$$w - x - y + z,$$

where the quantities are the mean responses in the groups

w,	leucotomized	patients,	real	stimuli.
x,	,,	,,	threatened	,,
y,	non-leucotomized	,,	real	,,
z,	,, ,,	,,	threatened	,,

and by comparing its value with its standard deviation. The function has the value −6·0, and its standard deviation is 4·8. As the effect does not exceed twice its standard deviation it must be judged insignificant. There is therefore no evidence that the two types of stimuli are affected differentially by the operation.

The conclusion is confirmed by the evidence presented in Table III, which shows the results of the patients who were examined at 3 sessions before operation and at 3 sessions after.

TABLE III.—*Psychogalvanic responses of patients each tested on three sessions before and on three sessions after prefrontal leucotomy. Each number is the sum of four individual tests. Each pair refers to one session, the upper number giving the response to real stimuli, the lower to threatened.* (*In units of* 20 *ohms*).

Patient.	Before operation.			After operation.		
1	52	92	73	28	39	13
	20	23	40	19	32	9
2	12	30	12	18	13	15
	0	34	6	8	7	8
3	9	4	19	16	32	37
	7	9	10	27	17	21
4	16	33	55	61	102	60
	5	26	35	22	57	36
5	17	43	93	49	81	70
	5	33	44	20	40	30
6	24	22	23	6	29	14
	20	64	42	4	15	7

In Table IV is given its analysis of variance.

TABLE IV.—*Analysis of variance of the observations in Table* III. *The capitals in the first column indicate two- and three-factor interactions.*

Variance.	D.F.	Sum sq.	Mean sq.	Var. ratio	P.	Sig.
Operation (A)	1	1·39	1·4	0·0	>0·2	O (1)
Type of stimulus (B)	1	3,612·50	3,612·5	41·2	<0·001	** (2)
AB	1	133·39	133·4	1·5	>0·2	O (3)
Patients (C)	5	10,432·44	2,086·5	23·8	<0·001	** (4)
CA	5	6,693·44	1,338·7	15·3	<0·001	** (5)
CB	5	3,137·00	627·4	7·2	<0·001	** (6)
CAB	5	2,041·11	408·2	4·7	<0·01	** (7)
Sessions (S)	24	9,720·33	405·0	4·6	<0·001	** (8)
SB	24	2,057·00	87·7	—	—	—
Total	71	37,828·60	—	—	—	—

** = significant at 1 per cent. level.
* = significant at 5 per cent. level.
O = not significant at 5 per cent. level.

We may first notice that the interaction between "operational status" and "type of stimulus" is insignificant (at (3) in the right-hand column of Table IV), confirming what was found in the previous groups.

Turning to Table III, we find suggestions that the patients are not equally affected by operation. The response of Patient 6, for instance, seems to be diminished after operation, while that of Patient 3 seems to be increased. The impression is confirmed by (5) in Table IV, which shows that the interaction between "patient" and "operational status" is significant with P less than 0·001. The changes in the patients' responses, following operation, are therefore not consistent, but show individual peculiarities.

These six patients show no general trend in the change induced by operation ((1) in Table IV), contrary to what was found in the two previous groups. The interpretation, however, seems clear. The fact, shown above, that patients react to the operation with individual peculiarity, some becoming more and some becoming less responsive, means that in any group the average result will depend chiefly on the particular sample of patients taken. With this major source of variability present the general average change becomes of less interest.

The results can also be analysed in a slightly different way. The experiment was arranged so that every stimulus given as a threat was also applied in real form at the same session. Inspection of the results in Table III shows that the two responses are correlated; so one of them can be used as an estimate of the patient's responsiveness at that session, and the effect of day-to-day variation in responsiveness can thus be eliminated from the results. This has been done by Fisher's method of the analysis of covariance. The results are given in Table V.

TABLE V.—*Analysis of covariance of response to threat, response to real stimuli being used as concomitant variable.*

Variance.	D.F.	Sums of squares and products.				D.F.	Mean sq.
		Threat.	Real.	Product.	Adjusted.		
Operation (A)	1	54	81	− 66	141·88	1	142
Patients (C)	5	1,825	11,745	+3,648	—	—	—
AC	5	2,414	6,321	+2,326	—	—	—
Sessions	24	4,349	7,428	+3,832	2,372·80	23	103
Total	35	8,641	25,575	+9,740	2,514·68	24	—

Variance ratio = 1·38 ; $P > 0{\cdot}2$.

The sums of squares and products between sessions were found by direct computation from each pair of degrees of freedom ; so that the equality of each total of four items with the total found over all 36 observations establishes the correctness of the arithmetical and algebraic processes. The variance ratio is 1·38, and P is more than 0·2. It follows that the effect of operation on the response to *threatened* stimuli, allowance being made for variations in the responsiveness at different sessions, is insignificant.

DISCUSSION.

The significance of these results will be better appreciated after a brief review of the anatomical basis of the psychogalvanic response and its possible relation to leucotomy.

The main structures activated in the psychogalvanic response are now known, though many details remain to be discovered. The fact that the response can be elicited by complex and symbolic stimuli shows that these structures can be reached from any part of the cerebral cortex. Langworthy and Richter (1930) found that in the cat the point of departure from the cerebral cortex lay in two particular areas : one lying in the premotor region (area 6) and the other lying in the anterior part of the temporal lobe. Stimulation of these areas caused a conspicuous fall in the electrical resistance of the skin, the effect being most marked contralaterally. By stimulating deeply, they followed the conducting fibres and found them to travel not by the pyramidal but by the fronto-pontine and temporo-pontine fasciculi. This work was confirmed by Schwartz (1937) who, having shown in the cat that total decortication abolished the psychogalvanic response, found by partial decortication that, however much cortex was removed, the response was retained if area 6 was retained, and that the ablation of area 6, however little else was removed, always abolished the response. When the ablation was unilateral, the response was lost on the contralateral, but preserved on the ipsilateral side. Wang and Lu (1930) confirmed Langworthy's results and found that a "galvanic" response of similar characteristics could be elicited by stimulation of the hypothalamus. As destruction of the hypothalamus did not abolish the response to cortical stimulation, they concluded that the two "centres" used separate extrapyramidal pathways.

Though the response is believed by Goadby and Goadby (1949) to be mediated through centres in the midbrain, little is known about these. Nor are the tracts of descent in the spinal cord known, though it has been shown (Bolton, Carmichael and Stirrup, 1936; Gilliat, 1948) that the impulses determining resistance and potential descend by the same tracts as those whose effects are recorded by the finger-plethysmograph, effects shown by Golla (1921) to have a latent period and form of curve identical with those of the psychogalvanic response. The impulses certainly traverse the sympathetic ganglia: both cervical and lumbar sympathectomy abolish almost completely the psychogalvanic response in the operated limb (Goadby and Goadby, 1949). The sympathetic chain, too, must carry some impulses, for the same workers found, in a patient with paraplegia, that a complete transverse lesion of the spinal cord at the eighth dorsal segment, proved by laminectomy, failed to cause any difference between the psychogalvanic responses in the upper unparalysed and in the lower completely paralysed limbs.

In the limbs themselves the impulses are conveyed by the peripheral nerves: perineural injection of procaine completely abolishes the response over the area of skin supplied by a nerve.

In the tissues the changes are complex and are probably not fully known. There is no doubt that changes in the activities of the sweat glands are of major importance (Darrow 1942; Carmichael, Honeyman, Kolb and Stewart, 1941), and it was shown by Golla in 1921 that most of the changes in resistance take place in the superficial layers of the epidermis. Goadby and Goadby (1949) have shown that the changes in potential and in resistance cannot be due to the same mechanism, for complete exsanguination, by an Esmarch's bandage, totally abolishes the change of resistance while leaving that of potential unrestrained.

The adequacy of our own method, measuring resistance, is supported by most workers, who find that the several ways of recording the peripheral changes tend to be equivalent.

From these facts it will be evident that only a provisional comparison can be made between those white-matter fibres which may be responsible for the psychogalvanic response and those fibres which may be cut in prefrontal leucotomy. Meyer and McLardy (1949) have emphasized the variability ot the anatomical positions of the cuts made, and this uncertainty must increase the difficulty of deduction. Such evidence as there is, however suggests that prefrontal leucotomy, whether done by the lateral or transorbital route, will seldom injure directly the fibres responsible for the psychogalvanic response: the fronto-pontine fibres will usually lie too low and the temporo-pontine too posteriorly. Though the human homologue of the cat's area 6 is uncertain, the cortical areas in man known to have autonomic function (the posterior orbital and the anterior cingular) are not likely to be damaged in leucotomy, except occasionally.

This being so, changes in the amplitude of the psychogalvanic response after leucotomy may reasonably be attributed to changes in the patient's "emotional responsiveness," by this being meant changes occurring in the other channels, e.g. thalamus and hypothalamus, through which the cortex can influence the peripheral mechanisms.

The interpretation of our results from this point of view is somewhat complex. The set of patients tested both before and after operation showed no uniform change, but did show that the patients varied among themselves, some increasing and some decreasing in responsiveness after operation. The group of forty-two patients, twenty-one operated and twenty-one controls, showed that on the average there was a small but significant fall in responsiveness (from 25·2 to 19·5 units). The difference between the result from the six patients and that from the forty-two cannot be accounted for with certainty. Most probably it has occurred because the effect of the leucotomy is small, one of the experiments just failing to show it and the other just succeeding. That it is partly irrelevant to the main effect of leucotomy is shown by the fact that when the leucotomized patients are divided into the "improved" and the "unimproved," corresponding, presumably, to those who do and those who do not show the main effect of leucotomy, the difference, instead of appearing more clearly, disappears. In fact, when real stimuli are used, the "improved" group actually responds more actively than the "unimproved" (Table II): a change in the opposite direction to that considered here.

Our general conclusion, then, must be that our results show that there is no major uniform change in the size of the psychogalvanic response after leucotomy. Especially should it be noticed that the response to threat, i.e. to a symbolic stimulus, shows no alteration.

Summary.

To test the effect of prefrontal leucotomy on emotional drive we have tested the effect of the operation on the psychogalvanic response.

A group of leucotomized patients was compared with a similar group of psychotics; and some patients were studied both before and after operation. At each session four stimuli were used, and each was presented once in real and once in symbolic form. Almost every patient was tested at several sessions.

The patients showed clear evidence of individual peculiarities in their change of responsiveness after operation; but there was little evidence that any uniform trend existed. Stimuli given in symbolic form retained their power of evoking the response.

These results do not support the suggestion that prefrontal leucotomy diminishes emotional drive.

Acknowledgment.

We should like to thank Professor F. L. Golla for his advice and interest throughout the investigation.

References.

Bolton, B., Carmichael, E. A., and Stirrup, G. J. (1936), *J. Physiol.*, **86**, 63
Carmichael, E. A., Honeyman, W. M., Kolb, L. C., and Stewart, W. K. (1941), *ibid.*, **99**, 329.
Darrow, C. W. (1943), *Physiol. Rev.*, **23**, 1.
Ezekiel, M. (1930), *Methods of correlation analysis*. New York.
Fisher, R. A. (1935), *The Design of Experiments*. London.
Idem and Yates, F. (1938), *Statistical Tables*. Edinburgh.
Fleming, G. W. T. H. (1944), *J. Ment. Sci.*, **90**, 486.
Forbes, T. W. (1936), *Am. J. Physiol.*, **117**, 187.
Freeman, W., and Watts, J. W. (1942), *Psychosurgery*. Baltimore.
Gilliat, R. W. (1948), *J. Physiol.*, **107**, 76.
Goadby, K. W., and Goadby, H. K. (1936), *ibid.*, **86**, 11 P.
Iidem (1949), *ibid.*, **109**, 177.
Golla, F. L. (1921), *Lancet*, **201**, 215.
Kaye, G. W. C., and Laby, T. H. (1942), *Physical and Chemical Constants*. London.
Langworthy, O. R., and Richter, C. P. (1930), *Brain*, **53**, 178.
Levin, P. M. (1936), *J. Comp. Neurol.*, **63**, 369.
Meyer, A., and McLardy, T. (1949), *J. Ment. Sci.*, **95**, 403.
Richter, C. P. (1929), *Johns Hopkins Hosp. Bull.*, **45**, 56.
Schwartz, H. G. (1937), *Arch. Neurol. Psychiat.*, **38**, 308.
Wang, G. H., and Lu, T. W. (1930), *Chi. J. Physiol.*, **4**, 303.

https://doi.org/10.1192/bjp.96.403.458 Published online by Cambridge University Press