AUTONOMIC CHANGES AFTER UNILATERAL LEUCOTOMY

BY

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Kennard (1944) has reviewed both the clinical and experimental evidence of "cortico-autonomic" interrelations. At that time she suggested that the frontal poles were autonomic centres distinct from the motor cortex but was able to adduce little evidence as to their exact role. Since Kennard's review Reitman (1945) and several subsequent authors have reported transient changes in autonomic regulatory functions following prefrontal leucotomy. Apart from the observations of Fairman and his co-workers (Fairman, Livingston, and Poppen, 1950), we are not aware of any previous studies to investigate whether unilateral autonomic changes can be demonstrated following unilateral leucotomy. In the present paper we report a series of such studies in which bilateral recordings of skin temperature and skin resistance have been made before and after unilateral operations on the frontal lobes. Differences in skin temperature between the two upper limbs were sought, both in the resting condition and after heating and cooling. Measurements of palmar skin resistance, an established method of studying sudomotor activity (McCleary, 1950), were made in the resting state, and the fall in skin resistance (psycho-galvanic response) following various stimuli recorded. Unilateral leucotomy was not in favour for long and our observations are confined to four cases.

Methods

In the absence of a constant temperature room, recordings were made at the temperature prevailing in the laboratory. The subjects sat lightly clad with their arms supported comfortably at heart level. They were shielded from draughts and throughout the examination period their arms were equally exposed. The temperature changes following heating and cooling were measured in the wards with the patients lying flat and shielded from draughts.

Temperature changes were measured with thermocouples and except for those following heating and cooling the readings were obtained from the pulp of the thumbs. Observations of resting skin temperature and skin resistance were made at the beginning and end of each test session, and those reported here were the final values recorded and were made after exposure to the laboratory temperature for at least half an hour.

Skin resistance was measured with an apparatus essentially the same as that described by Grant (1946), a graphic record of galvanometric changes being recorded on moving photographic paper. To obtain simultaneous responses the apparatus was duplicated. In order to ensure that any disparity between responses recorded from the two sides was not an artefact resulting from differences in the recording apparatus the analysis has been confined to observations which were controlled by alternating the two recording systems in a balanced manner with respect to the two hands. Various methods of stimulation were tried with the first two patients studied. We report here results which can be grouped either as responses to shocks or as responses to psychological stimuli. The psychological stimuli included intellectual tasks, impertinent questions, and warning light signals regularly preceding electrical shocks. The other two patients were examined by an identical procedure on each occasion except for the first recording with subject E. S. This procedure was adapted from one we have used to study pain perception before and after standard leucotomy. In the present investigation it consisted of a series of shocks, increasing regularly in strength, which were applied to the fifth fingers of each hand in balanced blocks, i.e., in the series . . . RLLR—LRRL. Each shock was preceded by a warning light and the time between the warning light and the presentation of the shock was 7 seconds. This allowed sufficient time for a psychogalvanic response to occur to the light and to be recorded before the arrival of the shock. This response to the light was not a time-conditioned response: it depended largely on its psychological significance as a warning signal and was greatly reduced or even abolished when the subject was told that no more shocks would follow.
Shock stimuli were given from a constant voltage Ediswan square wave stimulator.

Subjects
All four subjects were fully right handed. The clinical history and post-operative course of these subjects will be published elsewhere and only a bare outline is given below.

Case 1.—E. R. (hospital no. 13043), a woman aged 63, had severe post-herpetic pain in the left chest (D.8) of 15 months' duration. Medical treatment, deep x rays, and section of the dorsal roots D.7 to D.11 produced only transient effects. Left unilateral leucotomy in a coronal plane 3 cm. behind the external angle of the orbit was performed. Following operation there was a very temporary reduction in her affective responses to her pain.

Case 2.—H. W. (hospital no. 17797), a man aged 63, had severe right trigeminal neuritis of 10 years' duration. Medical treatment and alcoholic injections of the Gasserian ganglion on three occasions had failed to produce permanent relief. Full right prefrontal leucotomy carried out in a coronal plane 3 cm. behind the external angular process produced a marked alleviation of his symptoms. This persisted for three months with gradual relapse over the next three months.

Case 3.—E. S. (hospital no. 18957), a woman aged 53, had severe post-herpetic pain in the right side of the chest, D.5—D.6, of two years' duration. She had always suffered from migraine (right hemicrania). A full right leucotomy in a coronal plane was performed. Post-operatively there was a short period of apathy and a reduction in spontaneous complaints of her pain.

Case 4.—L. B. (hospital no. 29566), a woman aged 34, had disseminated sclerosis with pain in the left arm and face, central in type, and of 10 years' duration. Treatment with medicine and, on two occasions, by the alcoholic injection of the trigeminal nerve, had produced no relief. Right prefrontal leucotomy was carried out in a plane anterior to the lateral ventricle and sloping back slightly from the wing of the sphenoid. There was a temporary reduction in the frequency of the attacks of pain and in their subjective intensity.

Fig. 1 is a sample from a typical record. We have shown elsewhere (Elithorn, Piercy, and Crosskey, 1951) that unilateral shocks to the hand can produce an autonomic response which is bigger on the side stimulated than on the contralateral side. It follows that if, owing to differences in tissue resistance, the shocks to one limb were effectively less powerful, then there would be an apparent reduction in the mean response on that side. Inspection of the detailed data has enabled us to exclude this factor as an important one except on one occasion, which is discussed below. The psychogalvanic responses to the warning signal are of course free from bias from the side of the subsequent shocks, and where both types of response were recorded the lateral preponderance is the same for each, except on one occasion. On this occasion the difference between the means for the psychological responses was small and did not satisfy the test for significance. All comparisons of means between the two sides have been tested for their statistical significance. The variability of the psychogalvanic responses, even with apparently equal stimuli, is always large. This variability, however, has been almost excluded and our tests of significance made the more sensitive by using Student's t test for paired observations (Fisher, 1946). Since the variability of the means themselves is irrelevant, their standard deviations have not been included in the table.
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Subject E.R. 26 days after Left Unilateral Leucotomy

Right Thumb
Left Thumb

Subject H.W. 5 days after Right Unilateral Leucotomy

Right Index Finger
Left Index Finger

Results

Changes in Skin Temperature after Heating and Cooling.—Fig. 2 shows for two subjects the changes in skin temperature which occurred on the two hands when the trunk was heated and subsequently allowed to cool. Fig. 2a is drawn from recordings made with subject E. R. 26 days after a left unilateral leucotomy. It will be seen that the original resting levels in the cold state were identical, that both hands started to warm up at the same time, that the temperature increased at the same rate, and that there was no appreciable difference between the hands when the maximum dilatation was obtained. During the subsequent period of cooling the left thumb showed a slight delay, but the temperature difference is never greater than 1.5°C. Netsky and Starr (1948) state that temperature differences between two normal hands under resting conditions may reach 2°F. In the pre-operative control recording made with this patient the difference between the two hands was as great as 2°F. on at least one occasion. Fig. 2b shows the results of a similar test made with subject H. W. five days after a right unilateral leucotomy. Again the resting levels are identical and heating and cooling proceeds at the same rate.
The pre-operative control figures are not presented since no post-operative differences between the sides were observed. The only point noted was that post-operatively the response to heating and cooling appeared to be brisker: however, as the rates of heating and cooling were quite uncontrolled, this observation has little value.

Resting Skin Temperatures and Skin Resistance.— These showed no consistent differences between the sides. Table I gives the data for resting skin temperatures in a summarized form. It will be seen that there is a slight increase in the values recorded after the operation. The change itself does not reach a significant level of confidence and no attempt has been made to evaluate changes in environmental temperature. It affects each side equally.

Most of the figures for resting skin resistance are included in Table II. Only subject L. B. shows a marked post-operative discrepancy and that on one day only. This discrepancy is supported by the findings with the psychogalvanic responses and will be discussed below. A few additional readings of skin resistance in the resting state were obtained on days other than those on which responses to stimuli were recorded. These contribute little but do show that in subject E. R. the post-operative tendency for levels to be higher on the left was present before operation. They are not presented here.

Psychogalvanic Responses.— Table II gives the mean results obtained at each session with each of the four subjects.

Subject E. R.— Left-sided pain; left prefrontal leucotomy. Pre-operatively this patient was only examined with shocks as the stimulus. On both occasions the responses were larger on the right. Examined on the third post-operative day no change was detected but when re-examined on the seventeenth day the responses to shocks were bigger on the left. This finding exceeded the 5% level of confidence and was confirmed by the responses to psychological stimuli. Seven days later the observations were repeated and, although the number of observations was fewer, when the two types of stimuli were considered together the size of responses on the left significantly exceeded the size of those on the right. When the patient was followed up and examined four months post-operatively the change was still apparent, although not enough observations were made to establish its significance.

Subject H. W.— Right-sided pain; right-sided leucotomy. This patient showed considerable variation both before and after the operation which, though marked in its clinical results, failed to produce any clear-cut effect on the autonomic responses.

Subject E. S.— Right-sided pain; right-sided leucotomy. This patient was examined repeatedly both before and after operation. On three occasions pre-operatively it was shown that her responses on the right were between 20% and 30% smaller than those on the left. Following a right-sided prefrontal leucotomy this discrepancy was

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**Table I**

<table>
<thead>
<tr>
<th>Mean Skin Temperatures (°C)</th>
<th>Before Unilateral Leucotomy (n = 10)</th>
<th>After Unilateral Leucotomy (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipsilateral limb</td>
<td>31.3 (S.E. = 3.91)</td>
<td>32.9 (S.E. = 2.72)</td>
</tr>
<tr>
<td>Contralateral limb</td>
<td>31.4 (S.E. = 3.56)</td>
<td>32.9 (S.E. = 2.52)</td>
</tr>
</tbody>
</table>

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**Table II**

<table>
<thead>
<tr>
<th>No. of Days before and after Operation</th>
<th>Resting Skin Resistance Levels (ohms × 10³)</th>
<th>Psychogalvanic Responses (mean levels in ohms × 10⁶)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Patient E.R. (left-sided pain, left-sided leucotomy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-5</td>
<td>-3</td>
<td>-3</td>
</tr>
<tr>
<td>+3</td>
<td>97</td>
<td>87</td>
</tr>
<tr>
<td>+17</td>
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<td>66</td>
</tr>
<tr>
<td>+24</td>
<td>91</td>
<td>58</td>
</tr>
<tr>
<td>+122</td>
<td>97</td>
<td>105</td>
</tr>
<tr>
<td>Patient H.W. (right-sided pain, right-sided leucotomy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-7</td>
<td>-1</td>
<td>61</td>
</tr>
<tr>
<td>+11</td>
<td>85</td>
<td>109</td>
</tr>
<tr>
<td>+194</td>
<td>83</td>
<td>92</td>
</tr>
<tr>
<td>Patient E.S. (right-sided pain, right-sided leucotomy)</td>
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<td></td>
</tr>
<tr>
<td>-10</td>
<td>91</td>
<td>95</td>
</tr>
<tr>
<td>-6</td>
<td>106</td>
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<td>-3</td>
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<td>114</td>
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<td>+7</td>
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<td>+3†</td>
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<td>+25†</td>
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<td>120</td>
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<tr>
<td>+163†</td>
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<td>99</td>
</tr>
<tr>
<td>+499†</td>
<td>140</td>
<td>120</td>
</tr>
</tbody>
</table>

* Significant at the 5% level.
† Significant at the 1% level.
‡ Significant at the 0.1% level.

Those responses which are significantly greater than those on the opposite side are printed in italics. The actual level of confidence is also given.

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markedly exaggerated, the responses on the right being reduced to less than half the corresponding responses on the left. This phase of relative reduction of the responses on the right decreased and, when re-examined 15 months after operation, the responses on the right were bigger than those on the left. Though not in itself significant, the difference between the two sides is in the opposite direction from that found immediately post-operatively and is significantly different from it and from all the pre-operative observations.

Subject L. B.—Left-sided pain; right-sided prefrontal leucotomy.

Examined 10 days after the operation this patient showed a marked reduction of the responses on the left or contralateral side. This temporary change was accompanied by a corresponding difference between the two limbs in the resting level of the skin resistance. At the beginning of the test session the skin resistance was \(167 \times 10^4\) ohms on the right and \(112 \times 10^4\) ohms on the left. Over an hour later, with the right and left limbs equally exposed in a draught-free atmosphere, the figures were 163 and 92 respectively. This marked difference in skin resistance was reflected by a reduced effect of the shock on the right. As explained above, this would be likely to cause an apparent reduction of the responses on the right side. In fact, the responses to the shocks are bigger on the right, although much less so than is the case with responses to psychological stimuli. These responses would, of course, be unaffected by the differences in effective shock strength.

To summarize the results obtained with these four patients: one, H. W., showed no consistent effect. One, E. R., showed a persistent relative decrease in the contralateral limb (R). A similar but transient decrease in the contralateral limb (L) was seen in subject L. B. Subject E. S., however, who received the most detailed study, showed a relative increase in the contralateral limb (L). This persisted for at least a month post-operatively and was then gradually replaced by a relative over-activity of the ipsilateral side.

It is worth noting that each of the four subjects showed on at least one occasion pre-operatively a significant difference between the responses on the two sides. These differences are greater than would be expected from our own unpublished observations of bilateral responses in normal subjects. In each case where there is a significant difference between the responses these are smaller on the side of the body afflicted by pain. Korr (1949) has shown that areas of low skin resistance occur in areas segmentally related to painful lesions. Our figures do not show constant differences in resting skin resistance, but only one patient, L. B., had pain which was segmentally related to the recording electrodes (C.6—C.8). In this case the lesion was thought to be central.

Discussion

Reitman (1945) and many other workers have demonstrated changes in autonomic functions following bilateral prefrontal leucotomy. Taking advantage of this operation Livingston and his co-workers (Livingston, Chapman, Livingston, and Krantz, 1948) have shown that electrical stimulation of the orbital surface of the frontal lobes may cause marked changes in the blood pressure and in respiration. Unfortunately they were not able to look for different vasomotor responses on the two sides of the body. In a subsequent publication, moreover, Chapman, Livingston, and Livingston (1949) stated that their results might have been due to spread of the excitatory current to the temporal lobe. The majority of earlier experimental work on cortical autonomic control, most of which has been reviewed by Kennard (1944), has indicated that focal changes in vasomotor tone or sudomotor activity are associated with either stimulation of or damage to the sensorimotor cortex. Netsky and Starr (1948) have more recently discussed the literature and reported their own careful observations on 50 cases of focal head injury. They showed that removal of the post-central gyrus for traumatic epilepsy was followed by an increase in sweating on the contralateral side. Of the 50 cases, 22 showed differences between the two sides either in sweating or skin temperature. The lesions in almost all these cases were confined to the region of the sensorimotor cortex. Netsky and Starr conclude that their study indicates that the post-central gyrus is the posterior limit of the area with direct cortical representation of autonomic functions. The anterior limit beyond the pre-central gyrus is, they state, not known. However, nine of these authors' cases had damage which was limited to the frontal lobes. Of these nine cases six showed no lateral differences in autonomic function. One with bilateral damage and with a history of left hemiparesis showed increased sweating on the right and decreased skin temperature on the right. Another case with cortical damage in the inferior part of the left frontal lobe showed a contralateral increase in sweating, but in this patient too there was evidence of involvement of motor areas in that he had had an aphasia. The remaining patient showed decreased sweating on the contralateral side. There was no evidence of any motor or sensory deficit, though it is noted that the trauma involved the anterior longitudinal sinus. Thus of seven patients with lesions wholly anterior to the primary motor cortex only one showed a unilateral disturbance of resting autonomic function. These findings of Netsky and Starr confirm those of Lund (1944) who also studied a series of patients with
unilateral autonomic changes. Lund concluded that the cortical vasomotor centres lay within the motor and premotor areas and also in the parietal lobe. Fairman and his co-workers showed in three cases that following unilateral leucotomy the resting skin temperature in the first post-operative fortnight was less than two degrees lower on the side contralateral to the lesion.

Our own four subjects all had unilateral lesions involving the frontal lobes anterior to the motor areas. None showed any evidence of motor impairment. Although there was no clinically obvious alteration of autonomic function and only on one occasion evidence of changes in autonomic tone in the resting state on the side contralateral to the lesion, analysis showed that in three out of the four patients there was a definite change in the relative responsiveness on the contralateral side. (Two patients, E. R. and L. B., showed in the post-operative period a relative decrease on the contralateral side. The other patient, E. S., showed an increase on the contralateral side.) Guttman (1931) has maintained, and Netsky and Starr's results also suggest, that lesions of the cortex may in different subjects cause autonomic changes in the contralateral limb which are different in sign. The vast literature on the clinical effects of leucotomy shows that similar operations on the frontal lobes will relieve both (1) conditions characterized by anxiety and with over-activity and excitation of the autonomic system, and (2) conditions marked by profound depression or inhibition of both the intellectual and autonomic life. It is perhaps unreasonable therefore to regard the highest centres of nervous integration as either primarily inhibiting or primarily exciting. In fact there may be no anatomical distinction between mechanisms which reduce activity level and those which increase it. Damage to structures involved in such central mechanisms may cause secondary imbalance in lower centres. These disturbances may well be greater in the injured hemisphere and thus be reflected in a changed responsiveness in the autonomic responses of the contralateral limb.

**Summary**

Autonomic reflexes have been studied in four patients before and after unilateral leucotomy. The results provided no evidence of the presence of prefrontal cortical autonomic centres for the focal control of vascular or sweating responses. However, changes in responsiveness, different in sign in different subjects, support the suggestion that the frontal lobes exert both inhibitory and excitatory influence on centres which do have focal autonomic functions. Earlier experimental work and clinical observations suggest that such cortical autonomic control is centred around the sensorimotor areas.

Our thanks are due to the members of the hospital staff who allowed us to study their patients and in particular to Dr. E. A. Carmichael, whose encouragement and help made this study possible.

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