THE FUNCTIONAL RESPONSES OF THE SYMPATHETIC NERVOUS SYSTEM OF MAN FOLLOWING HEMI-DECORTICATION *

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THE relation of the cerebral cortex to the activity of the sympathetic nervous system is not yet fully clear. The clinical and experimental observations, which have recently been reviewed by Kennard (1937), have been conflicting, and there have been few quantitative determinations of the effects of cortical stimulation and ablation upon the functions of the human sympathetic nervous system.

Many indices of sympathetic function have been used in the past, peripheral vascular changes, the psychogalvanic response, sweating, pupillary changes, and visceral contraction being the most usual. The "galvanic skin reflex" is dependent on an intact sympathetic nervous system, and may be accurately measured. It has therefore been widely used as an index of sympathetic activity in studies of cortical function. In 1905 Bechterew stimulated the medial part of the anterior sigmoid gyrus in the cat and caused sweating of the pads. The response was greater on the contralateral side. Winkler (1908) obtained a symmetrically equal response to similar stimulation. In 1930 Langworthy and Richter found that faradic stimulation of cortical areas similar to those used by Bechterew lowered the skin resistance of a cat's pads. The response was bilateral, but was greater on the contralateral side. Schwartz (1937) continued the investigation by excising known areas of the cortex in cats, and observed the "psychogalvanic response" to various stimuli for three to six months afterwards. After unilateral removal of the area frontalis agranularis, peripheral pain and stimuli associated with fright caused no response on the contralateral side, but responses to sudden pressure on the limb remained symmetrically equal. Excision of cortex elsewhere did not modify the response in any way, so that Schwartz postulated two types of response—a "segmental galvanic reflex" independent of cortical control and a "psychogalvanic reflex" with a true cell station in the area frontalis agranularis.

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This implied a discrete cortical centre with sensory afferents and sympathetic efferents.

Stürup *et al.* (1935) investigated the effect of diverse cerebral lesions on the vasomotor response to peripheral stimulation in man. They concluded that the efferent pathway used by the response had not been involved in any of the lesions. They were therefore unable to advance any evidence in favour of cortical representation of the response. Marquis and Williams (1938) found that in man lesions of the sensory pathway below the thalamus modified the vasoconstrictor responses to peripheral sensory stimulation. The changes produced were related to the observed changes in sensation. Lesions of the thalamus, internal capsule, and cerebral cortex did not cause such alterations in the vasoconstrictor response. They therefore concluded that the reflex arc mediating the vasoconstrictor response to pain did not ascend above the hypothalamus, but they pointed out that the few cases of cerebral damage reported were not adequate, and did not exclude all areas of the cortex from participation in the vasomotor responses. Their observations suggested that the afferent pathway was the spino-thalamic tract and that its highest cell station was situated below the thalamus.

These observations show that there is an apparent difference between the results of similar experiments in animals and in man. The recent observations of Pinkston and Rioch (1938) on skin temperature following cortical ablation in monkeys contrast so strikingly with their earlier observations on dogs (Pinkston, Bard, and Rioch, 1934) that the authors postulate a species difference. As such wide differences as they have found can occur, it is obviously undesirable to apply to man information derived from animal experiments in this field. In order to determine if there is a cortical sympathetic centre in man, more extensive and exact cortical ablation would be required. Although the psychogalvanic and vasomotor responses to peripheral stimulation have so many common features, it is possible that they may use different pathways in the central nervous system. It would therefore be desirable to investigate them simultaneously in the same subject.

A girl who had had a complete hemidecortication two years previously was made available for study. Sympathetic activity, expressed as peripheral vasomotor responses and "galvanic skin reflexes" in response to various stimuli, were therefore investigated. It is the purpose of this paper to present the results obtained and to correlate them with previous observations. A report of the case used in these experiments has been presented by McKenzie (1938) and will be published in detail later. Only sufficient clinical data necessary to establish the state of the subject at the time of the experiment will therefore be presented. The subject, a girl of 20, had a severe head injury when 3 weeks old, followed 6 hours later by fits which appear to have been focal, beginning in the left face. She was subsequently found to have a left hemiplegia, which persisted throughout life. The fits continued, but changed in character, and when 5 years old she was having several *grand mal* seizures and "psychic variants" daily. There was no apparent mental deterioration. When 16 years old she came to the Toronto General Hospital and was found to have a left

hemiplegia, with a typical gait and posture. The paralysed extremities were smaller than those on the right and the skin of the hand was soft and smooth. There was fairly good movement of the large joints. She walked moderately well, but there was no voluntary movement of the hand or foot. There was absolute loss of cortical types of sensation in the left hand and foot, and a left homonymous hemianopia. Encephalography showed an extensive cerebral

Fig. 1.—The lateral aspect of the excised hemisphere. Measurements are in cm.

defect over the area of distribution of the right middle cerebral artery. On 22nd June, 1938, a complete right cerebral amputation through the internal capsule was performed by Dr. K. G. McKenzie. The operation report reads: "The whole of the right cerebral hemisphere was removed, with the exception of a very small amount of cortex representing the under surface of the frontal lobe adjacent to the anterior part of the sella, and a thin rim of temporal lobe adjacent to the optic thalamus." The extent of the hemidecortication is well seen in Figs. 1 and 2.

Following operation there was no change in the hemiplegic state, but the fits ceased completely. With the cessation of the fits, however, the girl's health improved, and when investigated her physical well-being and mental alertness were striking. She co-operated intelligently and understood the purpose of the investigations. There was a spastic left hemiplegia with characteristic posture and gait. Voluntary movement of the left hand and foot was impossible, but at the large joints movement was fairly good. Dr. E. H. Botterell, in an investigation to be published in detail later, found that the sensation to painful and thermal stimuli was normal throughout, while there was absolute loss of appreciation of light touch, joint movement, spatial

perception, and tactile discrimination in the affected hand and foot. All forms of sensation were normal on the opposite side of the body.

Fig. 2.—The mesial aspect of the excised hemisphere.

Method

The experimental procedure was identical with that which has been described before (Marquis and Williams, 1938). The patient, to whom the method had previously been described, sat comfortably at rest with the hands supported level with the heart, and with the eyes closed. The room was darkened and made as quiet as possible. Stimuli were applied under the same experimental conditions each day, and several rest periods were allowed to reduce fatigue of the patient to the stimuli. Various stimuli were used. A known intensity of pin-prick, applied with a modified Head algometer which has been described (Marquis and Williams, 1938), and melting ice in a flat-bottomed copper calorimeter were used as cutaneous stimuli. Sudden noise, apprehension, mental exertion, and deep inspiration were also used. These stimuli were applied in a predetermined random order to obviate anticipation. The cutaneous stimuli were applied with equal frequency to both sides.

Vasomotor Responses.—Small glass plethysmographs sealed with vaseline on both middle fingers were connected independently by pressure tubing through a closed-air system to sensitive tambours. Mirrors on the tambours reflected a beam of light on to moving bromide paper. Respiratory phases, time in seconds, and signals were also recorded. Vasodilatation, to ensure a constant background for the vasoconstrictor response to be measured, was obtained by immersing the legs in water at 40°–45° C. Time was allowed between stimuli for return to the basal dilated state.

Psychogalvanic Responses.—These responses were not obtained at the same time as the vasomotor responses, as they are greatly modified by the sweating which accompanies the rise in body temperature. Except that the subject sat at room temperature without immersion of limbs, the experimental conditions were identical. The recording apparatus consisted of an Einthoven string galvanometer (Cambridge Model). The shadow of the string was recorded on moving photographic paper. The electrodes used were small squares of zinc plate (3 × 3 cm.) to which leads had

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been soldered. These were applied to the dorsal and palmar surfaces of each hand after being moistened with zinc sulphate jelly. They were held in place by gauze pads and loose elastic bands. Care was taken not to obstruct the circulation or to cause discomfort. By means of a triple position selector switch the string could be quickly connected to either hand or to the control board for calibration. The tension of the string was adjusted till a potential of 1 millivolt caused a deflection of 10 millimetres on the photographic paper. Seconds and signals were recorded.

Results

Vasomotor Responses.—The subject at the commencement had the peripheral vessels in a constricted state, but on immersion of the feet in hot water, dilatation of the vessels and sweating took place on both sides of the body in a normal manner. It was not found possible to compare the vasodilator responses from the fingers of each hand to the rise in blood temperature, as the volume of the middle finger on the hemiplegic side was about 70 per cent. that of the normal. Thus a correspondingly smaller plethysmograph had to be used. With plethysmographs of equal volume, the average response to deep inspiration from the hemiplegic side was just 70 per cent. that of the normal, but with a smaller plethysmograph on the atrophic finger the recorded bilateral responses were similar in character and were approximately equal (Fig. 3). As the afferent

Fig. 3.—A record is shown of the volume of both middle fingers, decrease being downwards, with phases of respiration, time in seconds, and signals. The record reads from left to right. At the first signal the abnormal forearm was pricked, at the second signal ice was applied to the normal knee, and at the third signal the normal forearm was pricked.

pathway for the response to deep inspiration must be bilateral, it is probable that this disparity resulted from lack of vascular bed in the small immobile finger. The results obtained from stimulation of the skin with a known intensity of pin-prick and of cold are presented in the table on p. 318.

In this table the statistical significance of the difference between means was determined by Fisher's (1932) method for small samples. σ denotes the standard deviation of the individual samples from the mean, t the ratio of the difference to the estimated standard error of that difference, and P the probability of the observed difference arising by chance. When P is greater than 0.02, which indicates that the given difference might be expected to arise by chance less than twice in 100 random samples, the difference is not significant. It will be readily seen that none of the recorded differences are large enough to be outside the limits of chance. As has been shown (Marquis and Williams, 1938) 10 to 20 similar adequate stimuli were necessary in this procedure to furnish statistically significant results. A sufficient number of responses to pin-prick

TABLE 1.—THE VASOCONSTRICTOR RESPONSES TO MEASURED STIMULI OF PAIN AND COLD APPLIED TO THE NORMAL AND AFFECTED SIDE OF THE HEMI-DECORTICATE SUBJECT

EXPERIMENT	STIMULUS	STIMULATION OF NORMAL SIDE			STIMULATION OF ABNORMAL SIDE			DIFFERENCE (mm.)	<i>t</i>	P
		NUMBER	AVERAGE RESPONSE (mm.)	σ	NUMBER	AVERAGE RESPONSE (mm.)	σ			
1	Pin-prick	28	8.0	8.86	18	10.0	5.75	+2.0	0.93	0.7
2	Pin-prick	32	16.4	11.4	42	12.8	10.9	−3.6	1.23	0.2
1 and 2	Pin-prick	60	12.4	—	60	11.9	—	−0.5	—	—
1 and 2	Cold	14	16.8	10.2	14	19.3	11.6	+2.5	0.60	0.5

In this and the following tables the deflection is measured in millimeters; sigma (σ) is the standard deviation from the mean, *t* the ratio of the observed difference to the standard error of that difference, and P the probability of the observed difference arising by chance (see text)

were obtained to present each day's data separately. Neither day's results show a significant inequality. Grouping the two experiments reduces the experimental error and shows a high degree of equality. Similarly, responses to cold which were grouped to make the number adequate show no significant difference between the responses from both sides. The responses to noise, fright, and mental exertion did not show any obvious disparity, although their number was not large enough to be quantitated.

Psychogalvanic Responses.—Preliminary investigations of a normal subject showed that even under the stable experimental conditions employed the response was very variable, so that an average of several stimuli was needed to obtain accurate comparison of the responses from both sides of the body. In measuring the size of the response, the total amount of deflection of the image of the galvanometer string was determined, and the various groups of results averaged and subjected to the same statistical analysis as were the vasomotor responses (Fig. 4). The effects of stimulation of each side of the body, and the responses from each hand were averaged independently.

Fig. 4.—A record of the potential changes of the palm of the left hand in response to pin-prick of the right side of the neck, of the left knee and of the right knee, and lastly in response to a sudden noise. The record reads from left to right. Time is in seconds. Approximate time of stimulation is shown by a vertical line. 1 cm. deflection is equivalent to 0.1 millivolt, the narrow horizontal lines being 0.1 cm. apart.

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The results obtained from the normal control subject are contained in Table 2 and those from the hemidecorticate subject in Table 3.

TABLE 2.—COMPARISON AND STATISTICAL SURVEY OF GALVANIC SKIN RESPONSES TO STIMULATION WITH MEASURED PIN-PRICK ON BOTH SIDES OF THE BODY, AND OF THE RESPONSES OBTAINED FROM BOTH HANDS IN A NORMAL SUBJECT

PIN-PRICK ON RIGHT			PIN-PRICK ON LEFT			DIFFERENCE (mm.)	<i>t</i>	P
NUMBER	AVERAGE DEFLECTION (mm.)	σ	NUMBER	AVERAGE DEFLECTION (mm.)	σ			
12	7.1	6.47	12	6.0	5.68	-1.1	0.442	0.6
RESPONSE FROM RIGHT			RESPONSE FROM LEFT					
10	6.4	5.0	16	7.3	5.68	+0.9	0.45	0.6

TABLE 3.—RESULTS SIMILAR TO THOSE EXPRESSED IN TABLE 2, FROM THE HEMIDECORTICATE SUBJECT

PIN-PRICK ON NORMAL SIDE			PIN-PRICK ON ABNORMAL SIDE			DIFFERENCE (mm.)	<i>t</i>	P
NUMBER	AVERAGE DEFLECTION (mm.)	σ	NUMBER	AVERAGE DEFLECTION (mm.)	σ			
50	17.8	10.5	54	16.3	9.7	-1.5	0.789	0.4
RESPONSE FROM NORMAL SIDE			RESPONSE FROM ABNORMAL SIDE					
41	16.0	8.8	71	17.5	10.4	+1.5	0.81	0.4

It will readily be seen that in the normal subject the responses from stimulation on both sides of the body and the responses obtained from each palm do not show any significant difference. In the hemidecorticate subject there was a similar equality between the two sides of the body. The responses resulting from fright, apprehension, mental exertion, and deep inspiration, although too few to be averaged, did not show any apparent asymmetry, nor was there any asymmetry in their character or time relations.

Discussion

Marquis and Williams (1938) found that in five subjects with cerebral lesions causing sensory changes, the vasoconstrictor responses to sensory stimulation

were unaffected by the lesions. The sparing of the vasoconstrictor responses in these cases was most readily explained by the central arc for the vasoconstrictor response being complete below the thalamus. The possibility of a divergence of afferent sensory and afferent vasomotor fibres going to a specific centre could not, however, be excluded.

In this present case cortical removal had been as extensive and exact as in animal experiments, the only remnants of cortex left being adjacent to the anterior part of the sella and the lower part of the thalamus. It was therefore extremely unlikely that any ascending cortical afferent fibres had been spared. It is possible that the vasomotor afferent fibres were using an hypothetical cortical "centre" in the ipsilateral hemisphere, as there was clinical evidence of widespread cortical damage since infancy. The chronicity was evident from the extreme gliosis seen in the removed hemisphere. Its total weight was only 126 gm., suggesting long-standing and diffuse atrophy. Botterell (1938) has shown that in this subject pain and thermal sensations were normal throughout, while true cortical sensations—the appreciation of light touch, small joint movements, spatial perception, and tactile discrimination—were completely absent in the hand and foot of the hemiplegic side. There was marked diminution of tactile discrimination on the hemiplegic side of the trunk and in the affected limbs. There had thus been little recovery of the true cortical types of sensation and consequently little evidence that the sensory afferents had any representation in the ipsilateral hemisphere. Even were there a degree of recovery of the cortical afferent system, this would be reflected in some inequality of the vasomotor responses, if they utilized cerebral pathways. The absolute equality of the vascular responses and the absence of recovery of cortical sensation make such a compensating mechanism unlikely, but suggests that the reflex arc under discussion cannot have had cortical afferents.

No accurate measurements of vasomotor activity in man following hemidecortication have previously been made, but Zollinger (1935) did not notice any apparent difference in the skin temperature of a patient who had survived hemidecortication for only a few days.

The "galvanic skin reflex" has been used in this investigation solely as a measurable result of activity of the sympathetic nervous system. The afferents for the response to peripheral stimulation are the somatic afferents. As with the vasomotor response a disparity in the results of stimulation on the abnormal side compared with the normal would indicate involvement of the afferent pathway for the response, while an inequality of the responses from each side of the body would indicate interference with the efferent pathway or effector mechanisms. The equality of the responses obtained from stimulation of each side of the body can only be explained by completion of the afferent pathway at a level lower than the cerebrum or by bilateral representation of the response in the cerebral cortex. Schwartz's observations on the cat, referred to above, point to specific unilateral localization in the cortex of the cell stations involved, but this disparity may be due to a species difference. However, none of the evidence which has been advanced to support a discrete cortical sympathetic cell station in man has pointed to a bilateral representation of that centre. The

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alternative hypothesis, of generalized cortical projection to the sympathetic nervous system, would allow of hemidecortication without changes in the galvanic skin response of the contralateral side. This would explain the equality of the responses to bilaterally equal stimuli in the present case.

The same argument could be used for the efferent pathways. It has been pointed out that the skin of the affected hand was glossy and that the hand was atrophic. If this were to diminish the size of the responses, equality might be produced by overaction on the hemiplegic side, as suggested by Darrow (1932), who observed that the response was increased on the affected side in patients with cortical lesions who had no atrophy of the hemiplegic side. It is unlikely that the balance would be such as to cause the striking equality seen in Table 2, and furthermore the pattern of the responses and their time factors were also similar in the two hands. Thus the most plausible explanation of the bilateral equality of the afferent impulses and of the efferent responses would be that the pathway subserving the response did not reach the cerebrum.

It is evident that the cerebral cortex modifies sympathetic activity, for Doupe, Miller, and Keller (1939) found that the vasoconstrictor response to peripheral painful stimuli was diminished from areas which had been rendered hypalgesic by hypnotic suggestion. This diminution was only evident when the pain was sufficient to produce expressive signs of discomfort on stimulation of normal areas. They therefore thought that the emotional response to pain enhanced the vegetative response. As the appreciation of pain was unaffected in the present instance these observations do not contravert the conception of general cortical dominance over lower centres. On the other hand, no evidence can be obtained through the medium of the vasoconstrictor or galvanic skin responses of a localized cortical representation of the sympathetic nervous system, such as exists for sensation, voluntary movement, and the special senses in man.

Summary

The peripheral vasomotor reactions and the "psychogalvanic" responses have been investigated in a girl who had had a complete hemidecortication two years previously.

The equality of the responses from both sides of the body and from cutaneous stimulation of each side suggests that the reflex arcs used in these responses have no cortical cell station in man.

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REFERENCES

- Bechterew, W. (1905). *Arch. Physiol. Lpz.*, 297.
 Botterell, E. H. (1938). *Personal Communication*.
 Darrow, C. W. (1932). *Psychol. Bull.*, **29**, 674.
 Doupe, J., Miller, W. R., and Keller, W. K. (1939). *J. Neurol. Psychiat.* **2**, 97.
 Fisher, R. A. (1932). "Statistical Methods for Research Workers." 4th Edition, Edinburgh.
 Kennard, M. A. (1937). *Bumke's Handbuch*, **2**, 476.
 Langworthy, O. R., and Richter, C. P. (1930). *Brain*, **53**, 178.
 Marquis, D. G., and Williams, D. J. (1938). *Brain*, **61**, 203.
 McKenzie, K. G. (1938). *Proc. Amer. med. Assoc.*, Chicago.
 Pinkston, J. O., Bard, P., and Rioch, D. McK. (1934). *Amer. J. Physiol.*, **109**, 515.
 Pinkston, J. O., and Rioch, D. McK. (1938). *Ibid.*, **121**, 49.
 Schwartz, J. G. (1937). *Arch. Neurol. Psychiat.*, Chicago, **38**, 308.
 Stürup, G., Bolton, B., Williams, D. J., and Carmichael, E. A. (1935). *Brain*, **48**, 456.
 Winkler, F. (1908). *Arch. ges. Physiol.*, **125**, 584.
 Zollinger, R. (1935). *Arch. Neurol. Psychiat.*, Chicago, **34**, 1,055.