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Depressive Illness, Pulse Rate and Forearm Blood Flow

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Introduction

In depression alteration in mood is accompanied by pronounced physical and behavioural changes. Characteristically there is a decline in appetite, weight and libido, insomnia and a disturbance of diurnal rhythm. A slowing of thought and movement to the point of severe retardation or even stupor may occur. Anxiety is often present and in agitated depression is accompanied by restless psychomotor activity. As lesions in the hypothalamus may produce disturbances in appetite, weight, libido and sleep, it has been suggested that hypothalamic dysfunction may play a part in the aetiology of those depressions in which physical symptoms predominate (Pollitt, 1965).

Physiological studies on depressed patients also suggest hypothalamic disturbance. Depression is associated with an increase in plasma cortisol and a disturbance in the diurnal pattern of cortisol secretion (Board, Wadeson and Persky, 1957; Doig, Mummery, Wills and Elkes, 1966). Dexamethasone, which acts on the hypothalamic-pituitary axis, does not suppress high cortisol secretion in severely depressed patients, although it does suppress cortisol secretion in less severely ill patients and on recovery (Carroll, Martin and Davies, 1968). The plasma cortisol response to hypoglycaemia may be reduced in depression, again suggesting a hypothalamic-pituitary insensitivity in these subjects (Carroll, 1969).

Depressed patients show reduced salivary secretion which is particularly marked in association with retardation (Palmai, Blackwell, Maxwell and Morgenstern, 1967; Noble and Lader, 1971). Retarded depressives also show a reduction in the amount and variability of palmar sweat gland activity as assessed electrically (Lader and Wing, 1969). The secretion of sweat and saliva is mediated autonomically and hence is secondary to control by hypothalamic centres.

Specific vasodilator nerves are responsible for the increase in muscle blood flow which occurs during anxiety and the stress of mental arithmetic (Blair, Glover, Greenfield and Roddie, 1959; Barcroft, Brod Hesl, Hirsjärvi and Kitchen, 1960). There is also evidence that this vasodilation is secondary to hypothalamic control (Ganong, 1969). There are surprisingly few studies of the cardiovascular accompaniments of depressive illness, but raised pulse rate and muscle blood flow has been reported in agitated depression (Lader and Wing, 1969; Kelly and Walter, 1969).

Methods

The subjects were Maudsley Hospital in-patients whose primary diagnosis was depression and who were treated with ECT. They were examined to exclude intercurrent physical illness or brain damage and had normal blood films and chest X-rays. All drugs, apart from night sedation, were stopped for ten days before each assessment. All patients satisfying these criteria were accepted subject to the availability of the authors. Altogether 34 patients were tested prior to a course of ECT, and of these 31 were retested two weeks after their last ECT. The patients' ages ranged from 19 to 64 years. There were 12 men, mean age 44·3 years (± 13·6), and 22 women, mean age, 35·7 (± 11·4).

Forearm blood flow and pulse rate recordings

Blood flow was measured using a water-filled plethysmograph and the standard technique of intermittent venous occlusion (Barcroft and Swan, 1953; Kelly, 1967). During recordings a wrist cuff inflated to 200 mm. Hg. occluded the blood supply to the hand, and a cuff on the upper arm was inflated automatically to 70 mm. Hg. for 8 second periods at 30 second intervals. During venous occlusion the

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increase in forearm volume was registered by a Grass PT5A volumetric transducer and recorded by a Grass Model 7 polygraph. The apparatus was calibrated by injecting 4 ml. of water into the plethysmograph with the arm *in situ*.

Stimulation procedure

Recordings were taken for a ten-minute period with the subject at rest and then stopped for 2·5 minutes to allow a resumption of the blood supply to the hand. Further recordings were then taken for a 2·5 minute period during which the subject was required to perform mental arithmetic, and for 5 minutes subsequently. The total recording time was thus 17·5 minutes.

Patients were not warned beforehand about the arithmetical task. The task was related to the patient's mathematical skill and was intended to be difficult but not impossible. The usual task was the subtraction of serial 17s from 301. Patients were repeatedly requested to answer more quickly, and any errors were pointed out to them.

Experimental conditions

Blood flow recording was started between 9.30 a.m. and 10.30 a.m. in order to minimize the possible changes due to diurnal variation. The patient sat in a comfortable arm-chair with the left forearm supported and enclosed in the plethysmograph. The recording room was sound-protected and the temperature maintained at 20–22 °C. The leads from the patient led to a side room in which the polygraph was housed. Electromyographic and skin conductance data were recorded simultaneously, and the results will be presented elsewhere.

Clinical ratings

The patients were assessed on the Hamilton Rating Scale for Depression which provides a global rating of depression on a 0 to 50 scale, from scores on 17 groups of depressive symptoms. Hamilton (1960) describes the use of this scale and defines the 17 constituent items, which are listed in Table II. These assessments were made on the day before the physiological recordings and were based on an interview with the patient which lasted for approximately one hour and on information in the nurse's and psychiatrist's notes.

During the physiological recordings further psychometric ratings were also made. The patients rated themselves and were rated by an observer for anxiety by marking a 100 mm. line, the left hand end of which was labelled 'No Anxiety' and the right hand end 'Very Severe Anxiety'. Retardation was rated similarly. The distance in mms. of the marks from the left hand end of the lines afforded a measure of anxiety or retardation on a 0 to 100 scale.

Analysis of tracings

The forearm blood flow was calculated at minute intervals during rest and at 30 second intervals during mental arithmetic. The blood flow was computed from the recorded volume increase with time, arm volume, and a calibration constant. An estimate of pulse rate was obtained by counting pulse pressure notches in the plethysmograph tracing.

The pulse rate and forearm blood flow data were both positively skewed and were effectively normalized by a $\log_e$ transformation.

Results

After ECT the mean Hamilton Depression Score of the subjects decreased from 28·1 (± 5·5) to 16·0 (± 7·1). This improvement is highly significant ($F_{1,30} = 68·9$; $P < 0·001$).

The anxiety ratings made during the physiological recordings are displayed in Fig. 1. As might be expected, the stress of mental arithmetic produced a marked increase in

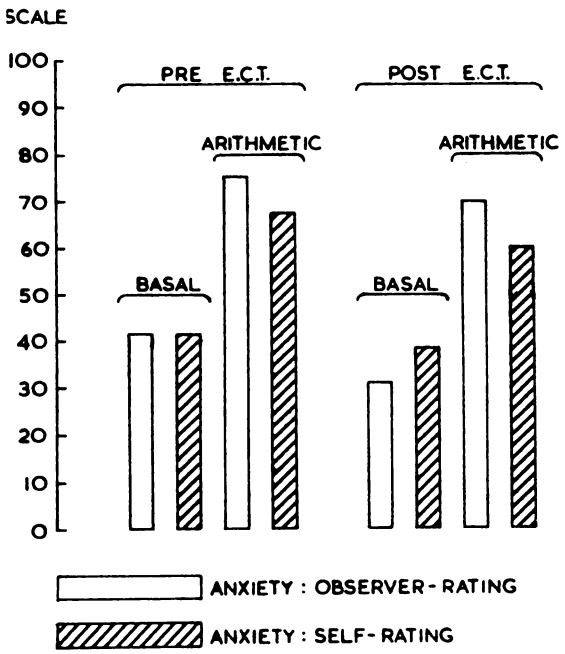

Fig. 1.
Mean anxiety levels: Pre and Post ECT.

anxiety. All the anxiety ratings were slightly lower after ECT, but the difference is only significant for the observer-ratings during stress ($F_{1,30} = 5{\cdot}6$; $P < 0{\cdot}05$).

Forearm blood flow

The mean results of the forearm blood flow readings are displayed in Fig. 2. Mean basal and mean post-stress flows are significantly higher after ECT (Table I). Mental arithmetic produced a substantial and significant increase in blood flow on both occasions (Pre ECT, $t = 9{\cdot}6$, $P < 0{\cdot}001$; Post ECT, $t = 7{\cdot}2$, $P < 0{\cdot}001$). Reactivity was not changed subsequent to ECT.

The number of ECT administered did not correlate with the change in basal forearm blood flow after ECT ($r = 0{\cdot}09$). This suggests that the increase in blood flow after ECT was not a direct effect of ECT administration.

Table II shows the correlations between forearm blood flow and the Hamilton Scale items on the pre-ECT occasion. These are generally of a low order, but some statistically

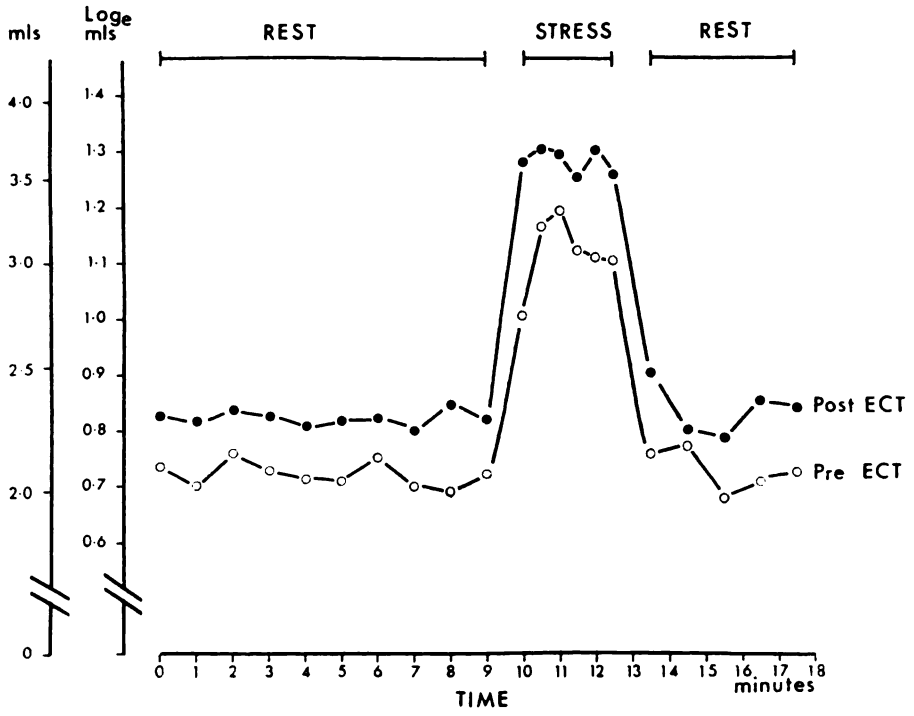

FIG. 2.

Mean forearm blood flow levels: Pre and Post ECT.

TABLE I

Forearm blood flow (log$_e$ ml./100 ml./min.): Pre and Post ECT

	Pre ECT		Post ECT		$F_{1,30}$	P
	Mean	S.D.	Mean	S.D.		
Basal	0·63	0·36	0·80	0·43	4·33	<0·05
Stress	1·12	0·46	1·27	0·45	2·51	N.S.
Post stress	0·62	0·38	0·80	0·39	5·43	<0·05

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TABLE II

Pre ECT correlations between forearm blood flow and Hamilton symptom scores

	Forearm blood flow		
	Basal	Stress	Reactivity
Depressed mood	·10	·03	−·09
Guilt feelings	−·14	−·14	−·04
Suicidal ideas	·10	−·13	−·31
Insomnia: initial	·10	·11	·05
Insomnia: middle	−·18	−·04	·16
Insomnia: late	−·12	−·27	−·25
Decline in work and interests	−·35*	−·23	·07
Retardation	−·30	−·49**	−·37*
Agitation	·25	·15	−·08
Anxiety: Psychic	·05	−·02	−·09
Anxiety: Somatic	·19	·13	−·04
Gastro-intestinal somatic symptoms	·04	−·17	−·31
General somatic symptoms	·00	−·25	−·38*
Genital symptoms (loss of libido)	−·02	−·04	−·04
Hypochondriasis	·14	·13	·03
Weight loss	−·24	−·30	−·15
Loss of insight	−·02	·03	·07
Total depressive score	·02	−·09	−·15

* $P < 0{\cdot}05$
** $P < 0{\cdot}01$

significant associations emerge. High scores for retardation are associated with low blood flow during stress and with diminished reactivity. 'Decline in work and interests' correlates with low basal flow and 'general somatic symptoms' with diminished reactivity.

Table III shows the correlations between forearm blood flow and the psychometric assessments of anxiety and retardation made during the physiological recordings. Before ECT the anxiety correlations are non-significant, but there is a significant inverse relationship between retardation and forearm blood flow reactivity. After ECT, anxiety (observer rating) correlates with high basal blood flow levels and diminished reactivity.

Pulse rate

Mean pulse rate data are illustrated in Fig. 3. The pre-ECT and post-ECT values are very similar, and there is no statistical difference between them. The stress of mental arithmetic was associated with a highly significant increase in pulse rate (Pre ECT, $t = 6{\cdot}8$, $P < 0{\cdot}001$; Post ECT, $t = 9{\cdot}8$, $P < 0{\cdot}001$).

Correlation coefficients between pulse rate and all the psychometric measures were calculated, but no consistent relationships were found.

TABLE III

Forearm blood flow and psychometric measures

A. Pre ECT

	Forearm blood flow		
	Basal	Stress	Reactivity
Anxiety: self-rating	·12	·05	−·07
Anxiety: obs.-rating	−·24	−·03	−·33
Retardation	−·27	−·31	−·37*

B. Post ECT

	Forearm blood flow		
	Basal	Stress	Reactivity
Anxiety: self-rating	·22	−·03	−·30
Anxiety: obs.-rating	·52**	·11	−·47**
Retardation	−·28	−·31	−·21

* $P < 0{\cdot}05$
** $P < 0{\cdot}01$

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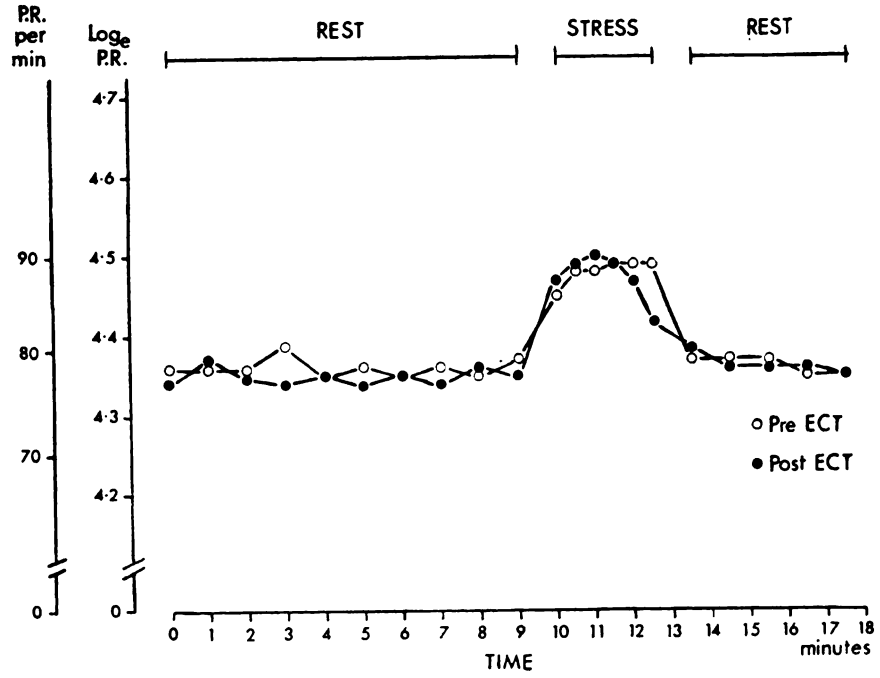

FIG. 3.
Mean pulse rate levels: Pre and Post ECT.

DISCUSSION

A correlation between basal forearm blood flow and anxiety was not apparent in the depressed state, but became demonstrable when the patients were retested subsequent to ECT. Pulse rate did not correlate significantly with anxiety on either occasion. Mental arithmetic was associated with marked increases in anxiety, forearm blood flow and pulse rate. Although the change in blood flow was proportionately much greater than the change in pulse rate the sensitivity of the two measures was similar as evidenced by the t values. As physiological correlates of subjective or overt anxiety, pulse rate and forearm blood flow are insufficiently precise for clinical use. However, these variables may be used as indices of *change in anxiety* in response to stress.

After ECT and improvement in depressive symptoms there was a significant increase in basal and post-stress blood flow, despite the fact that anxiety, which tends to elevate blood flow, was slightly lower after ECT. Again, before ECT low blood flow was associated with high scores on the ratings for 'retardation' and 'decline in work and interests'. Furthermore the mean pre-ECT blood flow levels, although apparently within the normal range, could be regarded as subnormal if the anxiety levels of the patients are taken into account. Depressive illness would therefore appear to have an inhibitory effect on muscle blood flow. Additional evidence for this conclusion may be adduced from the work of Kelly and Walter (1969). They suggested that depressive illness did not influence forearm blood flow, since non-agitated depressives had a mean blood flow of 2·1 (ml./100 ml. arm volume/minute), similar to that of normal subjects (2·2) but lower than that of both agitated depressives (3·2) and patients with anxiety state (4·4). However, their data show that the non-agitated depressives had an anxiety level (self-rating 3·8) close to that of the anxiety state group (4·1), although the *high* anxiety rating of these non-agitated depressives was not

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associated with an *elevated* blood flow. The agitated depressives had *higher* anxiety levels (5·0) and significantly *lower* blood flows than the anxiety state groups. Thus the blood flow levels of both the agitated and non-agitated depressives were substantially lower than their high anxiety levels would lead one to predict.

Hypothalamic control of vasodilator nerves is concerned in the increase in muscle blood flow normally associated with high anxiety (Blair *et al.*, 1959; Barcroft *et al.*, 1960; Ganong, 1969). It would thus seem likely that the inhibitory effect of depressive illness on blood flow is mediated via hypothalamic centres. This inhibition lessens the muscle vasodilatory accompaniments of anxiety.

The evidence that the diminution of muscle blood flow in depression is secondary to hypothalmic dysfunction is circumstantial. However, it is in line with disturbances of cortisol secretion, sweat gland activity and salivation in depressive illness, which have also been held to reflect a disturbance of hypothalamic control.

Summary

The forearm blood flow and pulse rate of 34 depressed psychiatric in-patients were recorded before and after a course of ECT. In the depressed state low blood flow correlated with 'retardation' and 'decline in work and interests'. Clinical improvement subsequent to ECT was accompanied by a significant increase in blood flow. It is suggested that depressive illness is associated with an inhibitory effect on muscle blood flow which may be mediated via hypothalamic control.

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