

A Clinical and Physiological Relationship between Anxiety and Depression

By DESMOND KELLY and C. J. S. WALTER

There has been a great deal of argument during the past 30 years about the symptomatic differences between anxiety and depressive states. Mapother (1926) thought that anxiety states should be regarded merely as one of the numerous sub-divisions of the manic-depressive illnesses, since they merged through a series of patients into agitated depression. Lewis (1966) too saw no sharp division between anxiety states and depression and classified agitated depression and anxiety states together as one sub-division of the affective disorders. Garmany (1956, 1958) and Mayer-Gross, Slater and Roth (1960), however, felt that anxiety states and depression were basically different forms of illness.

The arguments of the past 30 years have continued largely because of the lack of reliable objective measurements of anxiety and depression. Basal forearm blood flow has, however, recently been found to be a valid and reliable physiological index of anxiety (Kelly, 1965, 1966; Kelly, Walter and Sargant, 1966; Kelly and Walter, 1968). Fight or flight situations in animals lead to an increase in blood flow to muscle, which accounts for the majority of the tissue in the forearm. Basal forearm blood flow and other physiological measurements have, therefore, been explored in this paper to try to throw more experimental light on the relationship between anxiety and depression. A clinical classification of anxiety states and depression has been used and the different groups examined to see if there were psychological or physiological differences between the groups. Anxiety states were classified as acute, phobic, and chronic. Depression was categorized as agitated or non-agitated, depending on the degree of concomitant anxiety. Acute anxiety may occur in normal people in response to overwhelming stress. It is usually self-limiting

because the precipitating cause generally does not persist. Patients with phobic anxiety are normally relaxed but become anxious in specific, often circumscribed, circumstances or in anticipation of encountering these. The common situations which may produce panic attacks are public transport, restaurants, hair-dressers, cinemas, lifts, enclosed spaces, or on leaving one's house. Chronic anxiety states usually occur in anxiety-prone premorbid personalities and the illness is characterized by the presence of a high degree of free floating anxiety and by the long duration of symptoms. Classical depressive symptoms such as diurnal mood variation, self-reproach, loss of insight, feelings of hopelessness, nihilistic delusions, and suicidal thoughts are invariably absent. The clinical and physiological differences between chronic and phobic anxiety states have been considered before (Kelly and Walter, 1968), but the relationship between anxiety and depression was only briefly discussed.

Groups of normal controls, non-agitated depressions, agitated depressions, and chronic anxiety states were examined and contrasted in regard to forearm blood flow and other physiological and psychological measurements.

METHOD

Normal Controls

Sixty normal controls (32 female, 28 male), who had never had any psychiatric treatment and had a mean age of 38.8 years, were volunteers drawn from hospital porters and cleaners, people attending a welfare centre, surgical in-patients, medical students, and other ancillary medical staff.

Non-agitated Depressions

Fifty-six patients (38 female, 18 male) with a mean age of 42.7 years were selected. All

were unequivocally depressed clinically, many very severely so. Most of them were suffering from endogenous depression and many of them were obviously retarded. The majority were in hospital at the time of testing. Anxiety feelings were not a conspicuous feature of this group although they were present to a minor degree in many of the patients.

Agitated Depressions

There were 25 patients (17 female, 8 male) in this group, with a mean age of 47.2 years. Nearly all were suffering from endogenous depression and most of them were ill enough to be in-patients when tested. At the case conferences where these patients were discussed depression was considered to be the primary illness but they also showed a high degree of anxiety as well. Many complained of a feeling of internal tension which was often manifest as motor restlessness.

Chronic Anxiety States

Forty-five patients (26 female, 19 male), with a mean age of 39.4 years, were included in this group. All were suffering, in contrast, from chronic free floating generalized states of anxiety and were seldom, if ever, able to relax. A history of panic attacks often precipitated by quite trivial stimuli was common (58 per cent.). Only minor symptoms of depression were generally present, the depression being in part due to the length of incapacitating illness. The mean duration of symptoms was 9.8 years (range 2.5–25 years). It will be seen that only patients with severe long-standing illnesses were selected for this group to avoid any diagnostic doubts. Patients with purely phobic (situational) anxiety were not included.

Physiological and Psychometric Measurements

Measurements of forearm blood flow, heart rate, and anxiety self-rating were made under basal (resting) conditions, lasting 15 minutes, and during a period of experimentally-induced anxiety. This was produced by a 2½-minute period of harassing mental arithmetic. The method has been fully described elsewhere (Kelly, 1967). Professor Barcroft's water-filled venous occlusion plethysmographic technique

was used in these experiments (Barcroft and Swan, 1953).

The mean of the three lowest forearm blood flow recordings taken during the initial resting period of 15 minutes and the mean of the corresponding heart rates were calculated, and these means were designated as basal values. The peak forearm blood flow and heart rates during 2½ minutes of stressful mental arithmetic were likewise designated as stress values.

An anxiety self-rating scale was also used. Zero corresponded to complete relaxation and 10 to a life situation in which maximum anxiety had been experienced. The subjects were asked to give a numerical value to the subjective anxiety they had experienced during the resting period and during the stressful mental arithmetic. The Taylor scale of manifest anxiety (Taylor, 1953) and the Maudsley Personality Inventory, which measures neuroticism and extraversion (Eysenck, 1959), were also administered.

Except for night sedation patients discontinued all drugs for 24 hours prior to the physiological recordings. If large doses of drugs had been employed, or drugs had been used which are known to have a direct effect on forearm blood flow, they were discontinued for a longer period of time (Kelly, 1966).

RESULTS

Basal Forearm Blood Flow

The mean basal forearm blood flow of the patients suffering from *chronic anxiety* was 4.4 (ml./100 ml./min.), which was highly significantly greater than the corresponding value of the depressed patients and controls (Table I). The patients with *agitated depression* had a lower value of 3.2, suggesting that they were significantly less anxious than the patients with chronic anxiety states ($p < .001$). The agitated depressive group had, however, a significantly higher ($p < .001$) mean basal forearm blood flow than both the *non-agitated depressives* (2.1), and *normal controls* (2.2). This supports the clinical impression that patients with agitated depression are more anxious than depressives who do not appear agitated. It is important that no significant difference was found between the values of the non-agitated depressions and the controls.

TABLE I
Forearm Blood Flow, Heart Rate, and Anxiety Self-Rating

	N	Basal			Stress			Percentage Increase		
		Blood flow Mean S.D.	Heart rate Mean S.D.	Self-rating Mean S.D.	Blood flow Mean S.D.	Heart rate Mean S.D.	Self-rating Mean S.D.	Blood flow % flow	Heart rate % rate	Self-rating % rating
Chronic Anxiety Agitated	45	4.4 (1.3)	96.8 (11.5)	4.1 (2.1)	8.0 (3.2)	110.9 (14.1)	6.5 (1.9)	84	15	85
Depression Non-Agitated	25	3.2 (1.1)	91.6 (12.3)	5.0 (2.3)	5.1 (1.8)	99.6 (12.6)	6.6 (2.0)	68	9	60
Depression Controls	56 60	2.1 (0.7) 2.2 (1.0)	85.1 (14.5) 73.7 (11.6)	3.8 (2.3) 1.6 (1.3)	4.6 (3.0) 8.3 (4.5)	97.3 (16.2) 97.9 (16.8)	6.6 (2.0) 5.0 (2.1)	124 312	15 34	135 209

2-tailed "t" test significant differences between the diagnostic groups for "basal" values.

	Blood flow	Heart rate	Self-rating
Chronic anxiety v. Agitated depression..	p< .001	p< .001	p< .001
Non-agitated depression v. Agitated depression..	N.S.
Normal controls v. Agitated depression..	N.S.
Agitated depression v. Non-agitated depression..001
Normal controls v. Non-agitated depression..05
Non-agitated depression v. Normal controls..001

Basal Heart Rate

The patients with chronic anxiety states had higher mean basal heart rates (96.8) than the patients with agitated depression (91.6), but the difference was not significant (Table I). Both the patients with chronic anxiety and agitated depression had significantly higher values than those with non-agitated depression (85.1). This again indicates a higher level of anxiety in patients with agitated than non-agitated depression.

The controls had a mean basal heart rate (73.7) which was significantly lower ($p < .001$) than the patient groups, including the non-agitated depressives.

Basal Anxiety Self-rating

It was found that the mean basal anxiety self-ratings of the patients with chronic anxiety states, did not differ significantly from the agitated and non-agitated depressive groups. (Table I). The agitated depressives had significantly higher values than the non-agitated ($p < .05$), and the controls had highly significant lower values than all the patients ($p < .001$).

The Effects of Stress

Some interesting findings emerged. Thus the patients with the chronic anxiety states and the normal controls were found to have very similar mean stress forearm blood flow values (8.0 and 8.3), resulting from the period of experimentally induced anxiety (Table I). But the anxious patients were found to start from resting levels that were *twice as great* as the normal controls. The percentage increase in forearm blood flows was, therefore, correspondingly less for the anxious patients (84 per cent.) than normal controls (312 per cent.), though both reached similar eventual heights. The anxious patients were in effect halfway to experiencing maximum anxiety while trying to relax. This resulted in the further period of experimentally induced anxiety having a much smaller total effect.

The depressed patients on the other hand showed a markedly diminished autonomic response to the period of mental stress. The stress forearm blood flow value for the agitated depression was only 5.1 compared to 8.0 for

the chronic anxiety states, and for non-agitated depression it was only 4.6. Since the patients with agitated depression again started from a very much higher initial value the percentage increase in forearm blood flow was markedly less, only 68 per cent. compared with 124 per cent. for non-agitated depressions.

Despite the physiological differences resulting from the stressful mental arithmetic the mean stress anxiety self-ratings were similar in all three patient groups while the controls were somewhat lower.

Additional Psychometric Data

The mean score on the Taylor scale of manifest anxiety for patients with chronic anxiety was 35.7 and for the agitated depressives 33.6. These were not significantly different from one another (Table II). The neuroticism scores also showed no significant difference between chronic anxiety states (35.7), and agitated depression (33.9). These two measures also did not differentiate significantly between agitated and non-agitated depression though the basal forearm blood flow, heart rate, and anxiety self-ratings did. The controls however, had significantly lower Taylor and neuroticism scores ($p < .001$) than the patients and were more extraverted ($p < .001$) (Table II).

DISCUSSION

Important differences were found between groups of agitated and non-agitated depressed patients. Those with agitated depression had a higher mean basal forearm blood flow, heart rate, and anxiety self-rating. The results suggest that the clinical distinction used is a valid one. It would also appear to be useful clinically since the degree of concomitant anxiety may influence the selection of a particular antidepressant. Amitriptyline for instance has greater sedative properties than imipramine, so other considerations being equal it would be more appropriate for treating an agitated patient. If imipramine were to be used for such a patient it might be advisable to add a tranquillizer such as chlordiazepoxide to reduce the concomitant anxiety. Determining the degree of anxiety present in a depressed patient is often a difficult task, but

TABLE II
Age and Psychometric Data

	N	Age		Taylor Scale		Neuroticism		Extraversion	
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S. D.
Chronic Anxiety	45	39.4	(8.7)	35.7	(6.6)	35.7	(7.7)	16.5	(9.8)
Agitated Depression ..	25	47.2	(12.9)	33.6	(7.8)	33.9	(10.8)	15.9	(9.9)
Non-agitated Depression ..	56	42.7	(13.1)	30.9	(8.0)	30.7	(11.5)	18.2	(9.0)
Controls	60	38.8	(14.4)	14.0	(7.9)	19.7	(9.9)	25.9	(10.5)

2-tailed "t" test significant differences between the diagnostic groups for age and psychometric data.

	Age p<	Taylor p<	Neuroticism p<	Extraversion p<
Chronic anxiety v. Agitated depression ..	.01	N.S.	N.S.	N.S.
Non-agitated depression ..	N.S.	.005	.02	N.S.
Normal controls ..	N.S.	.001	.001	.001
Agitated depression v. Non-agitated depression ..	N.S.	N.S.	N.S.	N.S.
Normal controls ..	.01	.001	.001	.001
Non-agitated depression v. Normal controls	N.S.	.001	.001	.001

physiological measurements may make it easier if used in conjunction with all the clinical data.

The normal controls and patients with non-agitated depression had a very similar mean basal forearm blood flow. This parameter is, therefore, not a measurement of depression. Patients were seen who were extremely depressed, distraught, and weeping at the time of physiological testing, and yet had normal basal forearm blood flow values. Although these patients were clearly undergoing great suffering they were not experiencing clinical anxiety, nor did they show the physiological concomitants of this. Basal forearm blood flow measurements were not found to be elevated by depression or anguish *per se* but were elevated *only* if anxiety was present in addition. The severity of depression in agitated and non-agitated was similar clinically and yet only the agitated group had a high basal forearm blood flow.

The possibility that depression *per se* actually reduces the basal forearm blood flow has been considered. This seems unlikely because non-agitated depressives have mean values that are not significantly lower than those of normal controls or patients with, for instance, depersonalization, personality disorder, or hysteria (Kelly and Walter, 1968).

Delineating the relationship between anxiety and depression is made more difficult because of the frequent coexistence of the two conditions. The important point that arises, however, is whether chronic anxiety states and agitated depressions should be considered as separate entities. The clinical evidence suggests that they should be. Many of the anxious patients could pinpoint the onset of their symptoms to an acute attack of panic in their late teens or twenties, followed by gradual generalization of symptoms until anxiety became almost continuous. Others said they had been nervous all their lives. The anxious patients in this series were on average 8 years younger than the patients with agitated depression. There were also some physiological differences between the two groups. The anxious patients had a significantly higher mean basal forearm blood flow and showed a greater physiological response to the experimental stress.

There were, however, many points of similarity between the two groups. There was no significant differences between their Taylor, Neuroticism, and Extraversion scores or between their mean basal heart rates and anxiety self-ratings. Patients often find difficulty in expressing what they feel when they are depressed

and may use the word anxiety to describe the unpleasant quality of their illness. A better term for this extreme form of unhappiness is anguish. This important semantic difficulty might explain why the anxiety self-ratings did not differentiate between the chronic anxiety states and the depressed patients. Patients who were ill and sad tended to give high anxiety self-ratings to underline how bad they felt, without being able to differentiate anxiety from anguish.

Chronic anxiety states were found to have many differences when compared with phobic states (Kelly and Walter, 1968). A group of 32 phobic patients was significantly more extraverted, younger and had lower Neuroticism and Taylor scores, basal forearm blood flow and heart rates than a group of chronic anxiety states. Acute anxiety states are generally easy to diagnose and seldom give rise to confusion with the other two types.

In conclusion the physiological evidence lends tentative support to the simple classification of anxiety and depression used. The psychological measurements showed very good patient-control differences but fewer inter-group patient differences. Much work needs to be done though before the complicated interaction of anxiety and depression is fully understood.

SUMMARY

The relationship between anxiety and depression, has been the subject of much controversy. A simple clinical classification of anxiety and depressive states has been used and physiological and psychological measurements made to see if experimental data differed among the various groups. Anxiety states were classified as acute, phobic, and chronic. Depression was categorized as agitated and non-agitated, depending on the degree of concomitant anxiety.

There were significant differences between the agitated and non-agitated patients in

mean anxiety self-ratings, basal forearm blood flow and heart rate. The patients with chronic anxiety states had a mean basal forearm blood flow which was highly significantly greater than that of the patients with agitated depression. The physiological evidence presented here lends tentative support to the classification used. The psychological measurements showed very good patient-control differences but fewer inter-group patient differences.

ACKNOWLEDGMENTS

We are indebted to Dr. William Sargent who originally suggested examining this problem and to Professor Henry Barcroft, F.R.S., for allowing us to use his laboratory during the early part of the work. This project was carried out with the financial support of Sir Robert Sainsbury and the St. Thomas's Hospital Endowment Fund and a recent grant from Geigy (U.K.) Ltd.

REFERENCES

- BARCROFT, H., and SWAN, H. J. C. (1953). *Sympathetic Control of Human Blood Vessels*, London.
- EYSENCK, H. J. (1959). *Manual of the Maudsley Personality Inventory*, London.
- GARMANY, G. (1956). "Anxiety states." *Brit. med. J.*, *i*, 943-946.
- (1958). "Depressive states: their aetiology and treatment." *Ibid.*, *ii*, 341-344.
- KELLY, D. H. W. (1965). "Measurement of anxiety by forearm blood flow." M.D. Thesis. London University Library.
- (1966). "Measurement of anxiety by forearm blood flow." *Brit. J. Psychiat.*, *112*, 789-798.
- (1967). "The technique of forearm plethysmography for assessing anxiety." *J. psychosom. Res.*, *10*, 373-382.
- WALTER, C. J. S. (1968). "The relationship between clinical diagnosis and anxiety, assessed by forearm blood flow and other measurements." *Brit. J. Psychiat.*, *114*, 611-626.
- SARGANT, W. (1966). "Modified leucotomy assessed by forearm blood flow and other measurements." *Brit. J. Psychiat.*, *112*, 871-881.
- LEWIS, A. (1966). *Price's Textbook of the Practice of Medicine*, edited by R. Bodley Scott, London.
- MAPOTHER, E. (1926). "Discussion on manic-depressive psychosis." *Brit. med. J.*, *ii*, 872-876.
- MAYER-GROSS, W., SLATER, E., and ROTH, M. (1960). *Clinical Psychiatry*, London.
- TAYLOR, J. A. (1953). "A personality scale of manifest anxiety." *J. abnorm. soc. Psychol.*, *48*, 285-290.

Desmond Kelly, M.D., M.R.C.P., D.P.M., *Chief Assistant*
C. J. S. Walter, M.B., B.S., D.P.M., *Senior Registrar*

Department of Psychological Medicine, St. Thomas's Hospital, London, S.E. 1

(Received 19 March, 1968)