OBSERVATIONS ON THE RELATIONSHIP BETWEEN ANXIETY AND DEPRESSIVE SYMPTOMS DURING THE COURSE OF DEPRESSIVE ILLNESSES

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- 1 Roth *et al.* (1972) have proposed that within the affective disorders there are two distinct syndromes—anxiety and depression—differentiated by the relative predominance of these symptoms, the presence or absence of premorbid maladaptive traits, and the natural outcome of the disorder.
- 2 Goldberg (1982) on the other hand has suggested that there is a substantial overlap between the two syndromes, and the symptoms of anxiety and depression correlate highly with each other.
- 3 Patients tend to be treated with an anxiolytic or an antidepressant drug according to the predominance of anxiety or depressive symptoms.
- 4 There is conflicting evidence regarding the relative effectiveness of tricyclic antidepressants in psychotic (or endogenous) and neurotic (or reactive) depressive illness. Paykel (1972), however, found that the psychotic-neurotic dichotomy was not helpful in predicting outcome, whereas anxious depressives tended to respond poorly.
- 5 In three patients with affective illness, tested at regular intervals over the course of several weeks, anxiety and depressive symptoms fluctuated in a way which suggested that they were yoked to each other. A worsening indicated simultaneous deterioration of these symptoms. When they improved, this may have been due to the beneficial effects of the antidepressant drug administered. These findings suggest that antidepressants act, or fail to act, in a fundamental manner on the illness itself rather than on individual symptoms.

Introduction

This paper serves as an introduction to the main theme of the first session of the mianserin workshop. In it we shall try to identify a few of the difficult issues which for decades have been faced by clinicians working in the field of the affective disorders. Judging from the titles of the listed papers and the names of the distinguished speakers presenting them, we can anticipate that our discussions will be wide ranging. They will also focus more specifically on the relationship between anxiety and depression in the affective disorders, using these terms in at least two possible senses; the first denoting symptoms, the second denoting syndromes. In the workshop we shall consider the whole range of affective illnesses, from the severe to the minor forms, but in this paper we concentrate on the less severe forms of affective illness, the non-psychotic depressive disorders, in which the relationship between features of anxiety and depression raises important questions.

Review of the literature

The syndromes of anxiety states and minor depressive illnesses

The first question to be asked is whether there

exists a clear demarcation between anxiety states and minor depressive illnesses, or whether these two kinds of disorder are best considered as merging imperceptibly along a continuum of disturbed mood. Sir Martin Roth and his colleagues in Newcastle addressed themselves to this question in a series of articles in 1972 and 1982. Indeed in the first Newcastle study Roth cast his net so widely as to consider also the question of continuity or discontinuity between the neurotic depressions and the endogenous depressions (Roth *et al.*, 1972).

The first studies were conducted on a series of 154 patients with affective disorders admitted to psychiatric hospitals. They were allocated to a category of anxiety state or depressive illness according to the presence of the predominant affect, judged by clinical examination. Relying partly on clinical analyses and partly on the application of statistical techniques (principal component analysis), Roth and his colleagues observed that the two sets of symptoms were separable between depression on one side (with associated symptoms such as early morning waking and retardation) and anxiety on the other (associated, for example, with panic attacks or situational phobias). By applying another statistical technique (a discriminant function analysis, using a multiple regression programme), it was possible to identify those symptoms, other clinical features, and personality items which correlated more highly with

the original diagnoses (for example panic attacks with anxiety state; suicidal tendencies and retardation with depressive illness). Some 13 such items were thus judged to discriminate most precisely between the two disorders (Gurney *et al.*, 1972). When such items are weighted and composite scores calculated for each patient, the frequency distribution of these scores plotted along a single axis can provide an indication whether distinct categories of patients make up the original group studied (Moran, 1966). A bimodal distribution would indicate distinct categories. This was indeed the finding of Gurney *et al.* (1972), the two categories corresponding closely to the original diagnoses of anxiety state and depressive illness.

In the second Newcastle study (Roth & Mountjoy, 1982), a similar approach was used to investigate 117 patients, but this time endogenous depressions were excluded. Moreover, the analyses were confined to clinical symptoms without considering personality items. Clinical assessments were partly replaced by the use of rating scales which had the advantage of reducing selective bias when collecting the data.

This series of impressive studies led Roth and his colleagues to the following conclusions:

- 1) Within the group of patients with affective disorders there are two qualitatively distinct syndromes corresponding to anxiety and depression, and the patients diagnosed as anxiety states and neurotic depressive illnesses fall into two separate groups. The Hamilton Depression Scale was capable of differentiating the two clinical syndromes in 90% of cases of a mixed group of anxious and depressed patients (Roth & Mountjoy, 1982).
- 2) The presence of an anxiety syndrome reduces the likelihood that there is also a depressive syndrome.
- 3) The anxiety group contains a significantly larger number of patients with maladaptive and neurotic premorbid traits, and a higher neuroticism score on the Maudsley Personality Inventory. Depressed patients tend to be more stable, mature and independent (Roth *et al.*, 1972).
- 4) Features commonly associated with anxiety (e.g., derealization) tend to be correlated with a poor outcome, whereas features associated with depression tend to be followed by a good outcome (Kerr *et al.*, 1972).

The symptoms of anxiety and depression

Goldberg (1982) takes issue with the conclusions drawn by Roth and his colleagues: 'There is a

substantial overlap between the syndromes of anxiety state and depressive reaction, and the available evidence does not support a separatist model'. This view is based on a study in which the General Health Questionnaire (GHQ) was administered as a screening test to a large group of patients in general practice (Goldberg *et al.*, 1976). A principal component analysis was carried out on the responses. The first factor consisted of anxiety and depression and accounted for 21% of the variance. No solution could be found which produced anxiety items on one dimension and depressive items on the other. A subgroup of the patients was interviewed by a research psychiatrist who rated them for symptoms of anxiety and depression on the Interview Schedule of the General Practice Research Unit (Goldberg *et al.*, 1970), while remaining 'blind' to the GHQ results. These symptoms were found to be highly and significantly correlated with each other ($r = +0.63$) (Goldberg *et al.*, 1976). The emphasis in this research was more on the association of *symptoms* of anxiety and depression rather than on the unity or separation of the respective *syndromes*, but there is undoubtedly some overlap between the two issues. Goldberg's (1982) conclusion, nevertheless, is that the diagnosis of depressive reaction should be made in all cases with significant depressive symptom formation, irrespective of the severity of anxiety symptoms.

Relevance for treatment of separating anxiety states and depressive illnesses

The unity or separateness of anxiety states and neurotic depressive illness is a question of some theoretical interest, but it is more important to know whether the answer to this question will be of value in predicting the patients' response to treatment, and especially treatment with psychotropic drugs.

Downing & Rickels (1974) observed that general practitioners and psychiatrists vary their prescribing of psychotropic medication according to the predominance of anxiety or depressive symptoms. Some 270 outpatients were originally diagnosed as 'mixed anxiety-depression'. Their treating physician assessed the intensity of their symptoms, including anxiety and depression, before assigning them to treatment with an anxiolytic or an antidepressant drug. It is perhaps not surprising that the patients given an anxiolytic showed a predominance of anxiety over depression; those assigned to an antidepressant showed more depression than anxiety. More significant was the finding that, when the severity of anxiety and depressive symptoms

was rated by the patients on self-rating scales, the same trend held true. Thus clinicians tend to prescribe an anxiolytic when the main cluster of symptoms denotes anxiety, and an antidepressant when the main symptoms are depressive. This observation reflects the expectation that patients are more likely to benefit from a psychotropic drug credited with pharmacological actions which can be directed against the prevailing symptoms.

This expectation has received some confirmation. The traditional view is that tricyclic antidepressants are more effective in psychotic (or endogenous) than in neurotic (or reactive) depressions. Paykel (1972) has reviewed the evidence supporting this view, and he also mentions reports which are at variance with it. In his own study of 85 depressed women treated with amitriptyline, the psychotic-neurotic dichotomy was not helpful in predicting improvement. A multivariate cluster analysis led to a division of his patients into four groups: psychotic depressives, anxious depressives, hostile depressives and young depressives with personality disorders. This new typology was more helpful in identifying the patients who benefited from amitriptyline. The anxious depressives responded poorly, while the other three groups tended to respond well.

Interpretation of the clinical effects of psychotropic treatment

One of the issues which concerns this conference is how to assess the relative efficacy of psychotropic medication on anxiety and depressive symptoms which may co-exist in a patient or in a group of patients. The problem can be illustrated from the results of a double-blind trial of mianserin which was aimed primarily at assessing its antidepressant properties (Russell *et al.*, 1978). The efficacy of the drug on the depressive symptoms was demonstrated by a steeper fall in the Hamilton score for depression during the first three weeks in the group of patients given mianserin, than in control patients given diazepam (Figure 1). When the effect of mianserin on anxiety symptoms was measured (using the Zung Scale), it was found that they too were reduced during the corresponding period of time, a reduction equal to that achieved by diazepam (Figure 2). The problem is how to interpret the simultaneous diminution in the severity of anxiety and depressive symptoms. Is this the result of combined anxiolytic and antidepressant actions of mianserin? Or is it in the nature of the affective disorder that symptoms of anxiety and depression would tend to become altered simultaneously and in the same direction?

These questions were the subject of a preliminary enquiry which will now be reported.

Figure 1 Comparison of the mean Hamilton scores in the two treatment groups: ■ mianserin group; ● diazepam group. Drop-outs prevented further comparison between groups in the period indicated.

Figure 2 Comparison of the mean anxiety scores (Zung Scale) in the two treatment groups: ■ mianserin group; ● diazepam group. Drop-outs prevented further comparison between groups in the period indicated.

Study—fluctuations of anxiety and depressive symptoms during a depressive illness

The aim was to conduct single-case studies so as to follow fluctuations in the severity of anxiety and depressive symptoms during the course of an affective illness in individual patients.

Methods

Depending on the patient's response, each study lasted eight weeks or longer. So far three patients have been followed up while they received different forms of medication. In each patient, five self-rating tests were administered in random order at intervals of one to three weeks. They were:

- 1) The Wakefield Self-assessment Depression Inventory (Snaith *et al.*, 1971), omitting the two items concerned with panic attacks and anxiety feelings, so as to use this scale to assess mainly depressive symptoms.
- 2) The Beck Depression Inventory.
- 3) The Zung Self-rated Anxiety Scale.
- 4) A single test of General Anxiety (visual analogue scale).
- 5) An eight-item test of Anxiety Symptoms (visual analogue scales).

Results

Patient 1 This 28-year-old woman complained of long-standing general anxiety and tension in certain social situations. They included eating lunch with fellow employees and any form of contact with the opposite sex which went beyond kissing. When she anticipated a difficult social situation she would try to bolster up her confidence by drinking Martini and taking Valium tablets. Her depressive symptoms were more recent in onset, causing insomnia and loss of concentration, and they culminated in her taking an overdose of Valium. She was treated as an outpatient with doxepin (Sinequan) in increasing doses up to 125mg daily. Figure 3 shows a gradual and steady improvement over the course of the next 16 weeks. The reduction in depressive symptoms (measured by the Beck Inventory) closely paralleled that in anxiety symptoms (measured by the Zung Scale).

Patient 2 A 21-year-old man had, since early adolescence, been unable to approach girls in a normal way. Instead he had resorted to deviant sexual practices, including exposure of his genitals and smacking girls on the bottom. This behaviour led him to be apprehended by the police, one year after the death of his father. He was placed on

Figure 3 Patient 1: depressive symptoms (Beck Scale) and level of anxiety (Zung Scale) gradually diminished over the course of six weeks following treatment with doxepin.

probation. He became fearful of being sent to prison even though he had been able to control his abnormal sexual outlets. Over the course of the next few months he felt increasingly gloomy, was unable to work and entertained suicidal thoughts.

After admission to hospital he was treated with desipramine (150 mg daily), and appeared at first to respond favourably. When the question of discharge from hospital was raised he suffered a rapid relapse and he injured his hands while breaking windows. Figure 4 shows the initial improvement and the later increase in depressive symptoms (on the Wakefield and Beck Scales) and anxiety symptoms (on the Zung Scale). Again the two sets of symptoms followed each other very closely.

Figure 4 Patient 2: after an initial reduction in depressive symptoms (Wakefield and Beck) and level of anxiety (Zung Scale) there occurred a relapse during weeks 7 and 8.

Patient 3 A 45-year-old professional woman had for the past five years been taking a variety of antidepressant drugs for intermittent feelings of gloom and confusion. There had been two previous clear-cut depressive episodes which led her each time to stop work for periods of several weeks. There may also have been two transient episodes of elation with increased energy. Within a few months of achieving a promotion she began to feel tense and unable to cope with her work. Feelings of depression and depersonalization increased over the course of several months before she was admitted to hospital. She was treated with mianserin (up to 90 mg daily), and improved over the course of the next six weeks. Thereafter, however, feelings of tension and bodily symptoms recurred, followed by depersonalization and a full relapse of her depressed mood. During the remainder of her five-months stay in hospital, and in spite of changing the antidepressant medication to dothiepin, she showed wide fluctuations in mood from week to week. She was eventually discharged from hospital with many of her symptoms persisting and having decided to resign from her occupation. Figure 5 shows the weekly scoring of her depression and anxiety on the Beck Inventory and the Zung Scale, respectively. There is a striking correspondence in the peaks and troughs of these two sets of symptoms.

Relationship between the symptoms of anxiety and depression

In each patient correlations were sought between the symptoms of anxiety (measured on the Zung Scale and the two visual analogue scales) and symptoms of depression (Wakefield and Beck Scales), as they varied during the period of observation. The most valid method was that of calculating Spearman Rank correlation coefficients. The set of 10 possible correlation coefficients is shown in the form of a matrix in Tables 1, 2 and 3 for patients 1, 2 and 3, respectively. Very high correlation coefficients were obtained with nearly all the comparisons. In particular it may be noted that the coefficients between the Wakefield and Zung scores were 0.90, 0.85 and 0.77 for patients 1, 2 and 3, respectively, all highly significant statistically (product-moment correlation coefficients yielded substantially the same results). It may be concluded that in these patients, fluctuations in the course of their illness affected symptoms of anxiety and depression simultaneously, and as far as can be judged to a very similar degree.

Figure 5 Patient 3: the patient showed no sustained improvement after treatment with mianserin and dothiepin. Depressive symptoms (Beck) and anxiety symptoms (Zung) in parallel with each other.

Table 1 Matrix of correlation coefficients on patient 1

	Beck	Zung	Global Anxiety	Anxiety Symptoms
Wakefield	0.75 ^a	0.90 ^b	0.85 ^b	0.83 ^a
Beck		0.92 ^b	0.95 ^b	0.93 ^b
Zung			0.95 ^b	0.93 ^b
Global Anxiety				0.99 ^b
Spearman Rank correlation coefficients:				^a $P < 0.05$; ^b $P < 0.01$.

Table 3 Matrix of correlation coefficients on patient 3

	Beck	Zung	Global Anxiety	Anxiety Symptoms
Wakefield	0.72 ^b	0.77 ^b	0.62 ^b	0.77 ^b
Beck		0.69 ^b	0.46 ^a	0.50 ^a
Zung			0.436 ^a	0.74 ^b
Global Anxiety				0.77 ^b
Spearman Rank correlation coefficients:				^a $P < 0.05$; ^b $P < 0.01$.

Table 2 Matrix correlation coefficients on patient 2

	Beck	Zung	Global Anxiety	Anxiety Symptoms
Wakefield	0.82 ^b	0.85 ^b	0.76 ^a	0.75 ^a
Beck		0.48 (NS)	0.65 ^a	0.50 (NS)
Zung			0.69 ^a	0.78 ^a
Global Anxiety				0.62 ^a
Spearman Rank correlation coefficients:				^a $P < 0.05$; ^b $P < 0.01$.
NS not significant.				

Discussion and conclusions

The three patients studied all suffered from affective disorders in which anxiety symptoms were prominent. They could be classified as suffering from minor depressive illnesses (neurotic depressions), and all three patients showed some maladaptive traits before the onset of their illness. The longitudinal single-case studies demonstrated how the symptoms of anxiety and depression moved in parallel with each other, whether this was in the direction of drug-induced improvement, or that of spontaneous deterioration.

The brief review of the literature indicated that the emphasis of most research has been on seeking differences between patients in the relative prominence of anxiety or depressive features. The present study, admittedly at a preliminary stage, has concentrated on the fluctuations of these symptoms in individual patients. The striking finding is the way that anxiety and depressive symptoms are yoked to each other. This observation may influence us in the interpretation of different responses to psychotropic medication. In patients whose symptoms of anxiety and depression respond favourably (as in patient 1) it is tempting to deduce that the drug possesses both

anxiolytic and antidepressant properties. But in patients who failed to respond and continue to show both anxiety and depression, it should not be concluded that the drug lacks both anxiolytic and antidepressant properties. The evidence, as far as it goes, suggests that these drugs act (or fail to act) in a more general and fundamental manner on the illness itself, and not simply on one symptom or even on a set of related symptoms. Our search for more successful forms of treatment of the affective disorders should therefore be directed at drugs which are more effective in their action against the illness itself, rather than against symptoms treated in isolation.

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