

A unified hypothesis on depression and some observations from general practice

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FROM June 1964 to May 1968 all consultations, as they occurred in this West London single-handed practice, were recorded and classified in a morbidity register provided by the College of General Practitioners. Continuity of recording was broken only through unavoidable absences from the practice. A preliminary count of psychiatric conditions seen (1965), showed that these accounted for 13 per cent of all consultations, and that depression constituted about a quarter of this total.

With figures available for a four-year period, it was thought useful to abstract all cases of depressive illness, and to re-examine them in detail.

Data on survey sample

There are 1,450 patients in the practice. The total number of attendances recorded for all conditions over the four-year period was 16,892. Of these, depressive illness constituted 1,033, being 6.1 per cent of all consultations.

The number of patients presenting with depression for the first time was 321. Depression was diagnosed if symptoms had been present for one week or more. These patients were then classified into two broad categories, according to Pollitt's schema (1965).

Group I holds those with physiological or 'endogenous' depression, in whom physiological concomitants were significant. The latter include early waking, feeling worse in the mornings, changes in appetite and weight and slowing-down in thought and in movement. Clinical findings in this group may also include disturbance in autonomic function and in electrolyte balance. In this survey, for patients to be classified as in Group I, at least two of the following three arbitrary features had to be present: (a) sleep disturbance, (b) feeling worse in the morning and (c) slowing-down.

Group II contains all those patients in whom psychological aspects were dominant and definite environmental stress was present. Physiological concomitants were absent or considered to be insignificant. Their type of depression is sometimes labelled as 'atypical' or 'reactive'.

The number of attendances

The average number of attendances for all depressives was 3.2 per patient. Table I shows how the attendance rate in this varies according to sex and according to the type of depression. It will be seen that patients with 'physiological' depression (group I) had a significantly higher overall attendance rate than those of group II. This finding is entirely due to the more frequent attendances of group I patients represented in the extreme right-hand column. On the other hand, as the tables are constituted, the two contrasting groups show surprising similarity for this attendance factor.

Also, in both groups the female dominates over the male numerically, most markedly in group II.

TABLE I
ATTENDANCE RATES

	No. of patients	No. of attendances per patient					
		1		2		3 or more	
GROUP I		<i>percent</i>		<i>percent</i>		<i>percent</i>	
Male	72	24	33	21	29	27	38
Female	105	45	43	27	26	33	31
Totals	177	69	39	48	27	60	34
GROUP II							
Male	35	19	54	2	6	14	40
Female	109	53	48	21	19	35	33
Totals	144	72	50	23	16	49	34
		<i>Average attendance rate per patient</i>					
		<i>Group I</i>		<i>Group II</i>			
Males		3·7		2·1			
Females		3·9		2·6			

The age factor

Table II indicates a contrast in age distribution between groups I and II. A "baseline" is derived from the total registered practice population. The average percentage of 'over-44s' (total practice) for the years 1965-1968 inclusive was 25·1 per cent. Hence the representation of the older category is significantly above average in group I; the converse being the case in group II. Since it is recognized that the incidence of physiological depression rises with age, this particular result fits the observed facts.

Discussion

The manner in which these patients presented has not been separately recorded. In general, depression of mood was a frequent presenting symptom. Others attended because of tiredness, lack of energy, feeling run-down, or offered various somatic symptoms for elucidation. Some were ready to prescribe their own therapy: "Must be needing vitamins (a tonic), doctor" was a common self-assessment.

Treatment

Although the differences between groups I and II are undramatic for the parameters analysed, there still appears to be some profit of classifying depression into two separate groups. It offers a rule of thumb for the treatment of each new patient presenting with the illness.

TABLE II
AGE—SEX DISTRIBUTION

	Group I		Group II	
<i>44 years and under</i>	<i>percent</i>		<i>percent</i>	
Male	53		31	
Female	69		85	
	122	68·9	116	80·6
<i>Over 44 years</i>				
Male	19		4	
Female	36		24	
	55	31·1	28	19·4

Group I patients were invariably treated with one of the tricyclic drugs initially, usually amitriptyline, administered at bed-time. The starting dose was 25mg, increasing to 50mg after two to three days. In the majority of patients, this regimen proved therapeutically adequate. The maximum maintenance dose needed by any one patient in this series was 100mg at night and 25mg twice daily. If early waking was not a feature, nortriptyline or protriptyline was prescribed instead, the latter being given in divided doses throughout the day. In contrast, the treatment of group II patients was less-well demarcated. Out of a total of 144 in this group, monoamine oxidase inhibitor (MAOI) drugs were felt to be indicated in less than 30 patients. The remainder were all treated with modest doses of meprobamate, or a benzodiazepine drug, with or without a hypnotic. In a few instances, the definitive drug of choice for a patient of this group was a tricyclic drug, despite minimal initial physiological symptoms. The converse applied in a very few of the group I cases, who eventually responded to an MAOI preparation. All patients were prescribed two weeks' supply of drugs and asked to return for re-assessment in ten days, or earlier, if they wished.

If improvement was found to have occurred at a satisfactory rate, patients would be given a prescription for a month's supply of tablets. They would be instructed to continue therapy at the same level of dosage for that month. Then their progress would be reviewed again.

On the other hand, if results were not up to expectation, the whole evidence was re-considered, and treatment adjusted accordingly. At the subsequent interview, that is some five weeks after the start of treatment, the dosage would again be adjusted, or tailed-off, according to circumstances.

As shown in table I, a substantial proportion of depressives failed to attend again, even though clearly requested to do so. This is discussed below.

Attendance figures

Table I shows that, for group II, half the total number of patients scored only one attendance each. This finding is to be taken less as proof of effective therapy, and rather more as evidence of the self-limiting nature of the disease. Had MAOI drugs been used more generally in their treatment, these patients would have been exposed needlessly to a potentially hazardous drug.

Even more surprising is the observation that even in group I containing the physiologically depressed patients, as many as 66 per cent attended only once or twice. This confirms that even in this category depression is self-limiting.

In general, it was found that a pragmatic, empirical approach to the illness, as outlined above, has been satisfactory. It may have contributed to a low referral rate, estimated at less than five over the four year period, from a total of 321 patients.

There were five deaths while on anti-depressant treatment: one a woman, aged 67, who committed suicide after the period under review. The other four comprised one man, 59, who succumbed to bronchial carcinoma, and three women aged 56, 57 and 65, who died of coronary thrombosis, breast carcinoma and rheumatic heart disease respectively. There were three attempted suicides, two of whom were known to have a history of previous suicide attempts (one from group I; two from group II). Eight patients were known to have transferred to other doctors while under treatment. Of those who left the practice (including the four who died) eight were from group I and three from group II.

A certain negative feature of interest has been the rarity of manic disease during the period under review. Only one case of acute mania (not listed in the tables) presented. There were no cases of clear-cut manic-depressive illness.

Depression, is it divisible?

Whether the arbitrary separation of depressives into two groups, the physiological and the non-physiological is justified, remains debatable. It is of help in apportioning treatment, but this benefit hardly justifies a definitive taxonomical division. The above findings appear to give little support to such a dichotomy. With increasing knowledge it will probably be established that all depression is to a varying degree "physiological". The predominance of women in this series (214 out of 321 patients) suggests the importance of endocrine factors in matters of the mind.

Hypothesis

The existence of a suitable frame of reference, in the form of a model of the depressive mechanism, has been of value in the understanding of some of these problems. A past criticism, levelled against hypotheses of depression, has been their failure to lend themselves to experimental testing. This may not be held against the schema that links depression with a disturbance of time rhythm.

Briefly, it is postulated that inner time, or circadian rhythm, is controlled by a central biological clock within the brain-stem, which probably lies in close relationship to the hypothalamic structures concerned with important physiological functions, including the control of mood. This 'clock' has been shown to have its own inherent rhythm, independent of the 24-hour solar day time scale. In health, this inner rhythm stays suppressed by over-riding outer or solar time, at least in the hours of wakefulness. During sleep, this primitive inner rhythm may be allowed to find expression as the paradoxical or dream phase. When, on awaking, inner time happens to be out of step-with solar time, the latter promptly shows its normal dominance, and no ill-effects result.

When certain stresses arise, such as influenzal illness, surgical operation, childbirth, or the advent of the transitional seasons of autumn or spring, the imprint made by solar time appears to be less decisive than usual. Under these circumstances, the inner circadian rhythm has a chance to break through, and conflict between these two time scales ensues. It has been postulated (Heymann 1967) that as inner (or primitive) time is released, it may sweep along with it the equally primitive mood of stark realism, which we may call depression. In addition, the so-called hibernation trait, which represents the physical and mental slowing-down of some depressives, might also be released via the hypothalamus.

It is reasonable to interpret various aspects of the depressive reaction as disturbances of normal rhythm. For example, in physiological depression, the patient tends to feel at his worst in the mornings, and at his brightest in the evenings. The early waking in the small hours, a distressing symptom, may well be due to inappropriate triggering of the arousal mechanism by the inner clock, exerting its new authority.

Modern intercontinental jet travel offers a gratuitous example of an effect of disordered time, a subject recently reviewed in the *British Medical Journal* (1970). The air traveller, crossing the time zones to East or West at high velocity, suffers a temporary derangement of synchronisation between solar time and inner time. The symptoms this 'time zone fatigue' or 'jet lag' produces in many subjects can be likened to a mini-depression. This may show itself as mental sluggishness, irritability, depression or mood, or disturbance of sleep. On the biochemical side, there is in that condition a phase-shift away from the normal diurnal swing in water, electrolyte and cortisol secretions. This compares well with the biochemical events in certain depressed subjects. Since, in depression, the time discordance happens to be less violent, the clear-cut phase-shifts in electrolyte peaks and troughs present in the jet-commuter would not be expected in that illness. In other words, electrolyte and other biochemical shifts in depression are less predictable (Moody and Allsop 1969).

Although it is postulated that during depression the circadian or inner rhythm has

actually superceded solar time, the latter probably continues to maintain a measure of influence during the active hours of the day. This resulting uneasy equilibrium perhaps explains the variability in the diurnal swing of symptoms, as well as of the biochemical parameters.

Testing the hypothesis

The postulated conflict in time that offers various experimental openings to test this hypothesis.

1. *The direct approach*, which takes the form of an isolation study. In this, a suitable depressed subject would be monitored in a setting from which all outer time clues have been excluded. This would eliminate the postulated conflict between outer and inner time. If the hypothesis holds, then the patient would soon show clinical or biochemical improvement without any other treatment. This type of study has already been undertaken, using a depressed patient, though in search of different information (Jenner *et al.*, 1968).
2. *The indirect approach: prospective studies*. These would draw on the reservoir of young volunteers, by now numbering several hundreds, whose individual circadian rhythms have already been established in isolation experiments. These could be divided into two groups arbitrarily: one group would hold those, whose inner rhythm or time scale approximates that of the solar clock. The second group would be made up of the remainder, its subjects having circadian rhythms that differ appreciably from outer to solar time.

According to the hypothesis those of the first group, having a lesser risk of conflict between the two time scales, should also be less prone to develop depressive illness, than would be the members of the second category.

Another possible study would make use of 'pre-stressed' inter-continental air-comuters. The latter have their time-control system put in disarray repeatedly in their frequent projections through the time-zones. Again, these subjects may be more prone to develop depressive illness than would a control group.

If jet-travel time zone fatigue should prove to share a common pathology with depression, then it might even show a similar response to anti-depressant treatment. In the light of the rapid evolution of the Concorde supersonic air-liner, any effective method of protecting air-crew from time-zone stresses would be most welcome. Anti-depressant drugs, administered prophylactically, would be an elegant answer to an unsolved problem.

Summary

Some aspects of depression, as they appeared in one general practice, are analysed and discussed.

A working hypothesis is advanced to fit some of the observed facts of this illness. It is postulated, that depression originates from conflict between inner circadian rhythm and outer solar time. A parallel is drawn with time-zone fatigue of intercontinental jet-travellers.

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