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The Newcastle Chronic Depression Study

Patient Characteristics and Factors Associated with Chronicity

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Chronic depression is defined as "symptomatic non-recovery for a period of 2 or more years". Chronic primary major depressives ($n = 24$) were compared retrospectively with a control group of primary major depressives ($n = 20$) who had recovered from their illness episode within 2 years. The former had a significantly higher familial loading for affective disorder and showed an increased incidence of independent undesirable life events during the 6 months prior to and 2 years after the onset of their illness. Female chronic depressives also had a significantly greater number of previous illness episodes and a more frequent history of thyroid dysfunction. Personality as measured on the EPQ, psychiatric problems arising as secondary complications of the depressive illness, and developmental object loss did not differentiate chronic from non-chronic depressives.

The vast majority of depressed individuals suffer from illness episodes which either remit spontaneously or respond to one of the many well-established therapeutic interventions now available. There are, however, a significant minority whose illness exhibits chronicity despite all active attempts at treatment. In 1972, Robins & Guze reviewed 20 follow-up studies of affective disorders and concluded that a chronic course supervened in 1–28% of cases (average incidence 12–15%). This wide variation in the incidence of chronicity is probably attributable to the non-uniformity of diagnostic criteria for depression, the differing lengths of and intensity of follow-up, the assessment methods employed, the type of population studied, and the definition of chronicity used. The last factor is obviously a very important one: in this study, chronic depression has been defined on the basis of persistence of depressive symptoms for a specified period of time, as suggested by Cassano *et al* (1983):

> Chronicity refers to symptomatic non-recovery for a period of 2 or more years and may be a sequel to one or more episodes of depression from which the patient does not recover.

As yet there have been few systematic studies of the aetiology of chronic depression. Some researchers suggest that treatment-resistance underlies the evolution of chronicity (Freyhan, 1978; Perez de Francisco, 1979) while others have been more impressed by the premorbid personality of the sufferer, referring to the condition as depressive personality (Chodoff, 1972), characterological depression (Akiskal *et al*, 1978), or dysthymic disorder (American Psychiatric Association, 1980). The emphasis on maladaptive personality seems to have some validity in studies of out-patients with intermittent or chronic symptoms of a minor nature (Akiskal *et al*, 1981), but chronic major depression also exists and these individuals form a substantial minority of the "New Long Stay Patients" (McCreadie *et al*, 1983). Unfortunately, according to Weissman & Klerman (1977), the clinical stereotype depicting all chronic depressives as suffering from a character-based disorder still persists and often leads to inappropriate or inadequate treatment of the illness.

A prospective study by Akiskal *et al* (1981) of 137 out-patient probands followed up for a period of up to 6 years provides one of the most comprehensive reviews of the aetiology of chronicity. These cases were subclassified into unremitted primary major depressives, characterological depressives and chronic secondary depressives. Factors associated with chronicity in 38 patients in the primary depression group were – a positive family history of affective disorder, concurrent medical illness, multiple deaths within the family, significant illness in a spouse or family member, iatrogenic factors (such as inadequate or inappropriate psychotropic drug treatments or treatment with depressant anti-hypertensive drugs) and secondary 'sedativism' (such as excessive use of hypnotics or alcohol abuse). There were some methodological problems with this study: patients were grouped from the outset into clinical rather than statistical 'clusters', which is a rather crude technique with many drawbacks, and most of the patients described did not meet the full Feighner criteria (Feighner *et al*, 1972) for major depression throughout the period of follow-up. The exclusion

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of in-patients also increases the probability that individuals with less severe forms of depression were studied.

We present the results of an investigation into the factors associated with chronicity in a sample of 24 patients with primary major depression of 2 or more years' duration admitted consecutively to an in-patient psychiatric unit. Findings in this sample are compared with those in a control group of 20 patients with primary major depression admitted to the same unit over the same period of time who all recovered from their illness within 2 years. The main objectives of this study were to examine psychosocial factors associated with chronicity and to determine if it is possible to replicate some of the findings of Akiskal *et al* (1981) in a retrospective study of an in-patient population.

Method

Subjects

All subjects met the Research Diagnostic Criteria (RDC; Spitzer *et al*, 1978) for definite or probable major depression. Severity of depression was assessed using the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) and the Beck Depression Inventory (BDI; Beck *et al*, 1961). The Newcastle Diagnostic Index (NDI; Carney *et al*, 1965) was used to classify the patients into endogenous and neurotic subtypes.

The study population had been selected from a larger sample of patients referred to one of the authors (DE) by consultants from all over the northern region with a presumptive diagnosis of chronic depression. An initial out-patient assessment interview was performed and any patients whose depressive illness was of less than 2 years' duration, who had not received adequate trials of standard antidepressant treatments, or who were receiving any physical treatments known to cause depression were excluded from the study. Also excluded were individuals over the age of 65 years, those with a depressive disorder secondary to physical ill-health, and those with any evidence of organic brain disease.

The control group comprised 20 randomly selected patients suffering from primary major depression at the time of their admission to the in-patient unit. They met all the above inclusion criteria except that they recovered from their illness episode within 2 years.

Through a semi-structured interview with the patient and, when possible, with a close relative, and assessment of all previous case records, the following information was obtained and recorded on a specially devised data sheet.

Socio-demographic details. Age, sex, marital status, social class (Registrar General's classification), number of children and ages of children were noted.

Psychiatric history. The following were noted:

(a) length of current illness episode (calculated to the nearest month)
(b) previous psychiatric history –
  (i) age of onset of first illness episode – recorded as the age of the patient at the time of first contact with any psychiatric services;
  (ii) number of previous illness episodes – identified by applying RDC to the case-notes.

Family history of psychiatric disorder. Family history of psychiatric disorders in first-degree relatives was obtained using the RDC – Family History Version (Andreasen *et al*, 1977), and case-notes were examined when possible.

Life events. Life events occuring during the 6 months prior to and the 2 years after the onset of the current illness episode were recorded using a modification of the method described by Akiskal *et al* (1981). Paykel's (1979) questionnaire was used to document life events, and the independence of these events from the depressive illness was established using the method of Brown *et al* (1973). In view of the length of recall required in some cases, an attempt was then made to determine the exact timing of these events in relation to the onset of the illness episode. Only if the occurrence, independence and timing of such events could be substantiated were they included in our analysis.

Personality. The premorbid personality of the patient was assessed using the Eysenck Personality Questionnaire (EPQ; Eysenck & Eysenck, 1975). In order to avoid any distortions in this assessment due to the depressive illness, additional instructions were included (as suggested by Kendall & DiScipio (1968), so that the patients' scores referred to how they regarded themselves premorbidly rather than currently.

Secondary psychiatric complications of the depressive illness. These were only recognised if it could be established that the onset was after that of the current depressive episode and that the problem had not been a feature of any of the patient's previous psychiatric presentations.

Previous medical history. Previous medical history given by the patient was substantiated by examination of medical case-notes. Illnesses of a prolonged nature, marked severity, and those requiring long-term medication were noted.

Loss of parent. Loss of one or both parents and any prolonged periods of separation before the age of 11 years were recorded.

Statistical analysis

Results were analysed using the chi-squared test (with Yates's correction applied), Fisher's probability test, Student's *t* test and the Mann–Whitney *U* test.

Results

The socio-demographic details are shown in Table I. Overall there were no significant differences at the 5% level between

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TABLE I
Socio-demographic characteristics of chronic depressives

	Chronic depressives (n = 24)	*Control depressives (n = 20)*
Age (years)		
Range	28–62	23–64
Mean ± s.d.	49.9 ± 10.6	48.7 ± 13.3
Sex		
Male	9	7
Female	15	13
Marital status		
Married	18	11
Widowed	2	2
Divorced/separated	3	4
Single	1	3
Social class		
I + II	5	3
III	12	13
IV + V	7	4

the chronic depressives and the control group of recovered depressives. Both groups showed a preponderance of females and over half of the patients were married. No patient had three or more children under 14 years of age.

Forty-two patients met RDC for definite major depression and two patients (in the chronic group) met the criteria for probable major depression; four patients had a history of bipolar illness (Table II). The mean scores on the HRSD were not significantly different, but the mean BDI scores were ($P<0.05$), being higher overall in the chronic depressive (37.4) than in the controls (30.5). This difference appears to be the result of the significantly higher BDI scores of the female chronic depressives. There were no significant differences between the groups on their NDI scores.

The mean age at onset of the current illness episode was 45.8 years in the chronic group and 48.7 years in the control group. The length of the chronic illness was in the range 2–11.25 years (mean 3.2 years in males, 5.1 years in females). The mean length of the current illness episode in the patients who recovered from their depressive episode was 0.87 years. Age at onset of first-ever episode of psychiatric illness did not differ significantly, but female chronic depressives had significantly more illness episodes than any of the other groups of patients (see Table II).

There was a family history of affective disorder in first-degree relatives for 50% of the chronic depressives, compared with 15% of the control group, the difference being significant at the 3% level (Table III). On further examination, the main determinant of this difference appears to be the significantly higher incidence of unipolar depression in the families of the female chronic depressives. The incidence of bipolar illness in first-degree relatives was not significantly different; all patients with a bipolar illness had a family history of this. More chronic depressives than their controls had a multiple family history of affective illness (i.e. more than one first-degree relative affected).

Table IV summarises the data on independent, undesirable life events. Overall, the number of individuals reporting events during the 6 months before and the 2 years after the onset of the depressive episode was significantly higher ($P<0.05$) in the chronic depressives than in the depressives who recovered. In the 6 months prior to the onset of the illness, twice as many chronic depressives as control depressives experienced undesirable life events. Four patients in the chronic group and one in the control group reported independent life events only after the

TABLE II
RDC diagnosis, scores on HRSD, BDI and NDI, and number of previous episodes of affective illness in chronic depressives and control depressives

	Males		*Females*		*Total*	
	Chronic depressives (n = 9)	*Control depressives (n = 7)*	*Chronic depressives (n = 15)*	*Control depressives (n = 13)*	*Chronic depressives (n = 24)*	*Control depressives (n = 20)*
RDC major depressive disorder:						
Unipolar	7	6	14	13	21	19
Bipolar	2	1	1	—	3	1
HRSD: mean ± s.d.	21.8 ± 7.3	21.4 ± 5.3	23.3 ± 6.9	21.2 ± 3.6	22.5 ± 7.7	21.3 ± 4.3
BDI: mean ± s.d.	34.1 ± 11.6	31.6 ± 9.7	39.3 ± 9.5**	29.9 ± 5.2**	37.4 ± 10.6*	30.5 ± 7.2*
NDI:						
Endogenous (>6)	5	3	9	6	14	9
Neurotic (<6)	4	4	6	7	10	11
Number of previous episodes of affective disorder: mean ± s.d.	2.8 ± 2.9	2.4 ± 2.1	5.8 ± 4.1***	3.2 ± 2.1***	4.7 ± 3.9	2.9 ± 2.1

Two-tailed, paired *t*-test: *$P<0.02$ ($t=2.6$, d.f. = 42); **$P<0.01$ ($t=3.3$, d.f. = 26). Two-tailed, Mann–Whitney *U* test: ***$P<0.01$.

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TABLE III
Family history of psychiatric illness in first-degree relatives of chronic depressives and control depressives

	Males		*Females*		*Total*	
	Chronic depressives (n = 9)	*Control depressives (n = 7)*	*Chronic depressives (n = 15)*	*Control depressives (n = 13)*	*Chronic depressives (n = 24)*	*Control depressives (n = 20)*
Family history of affective disorder:	4	2	8***	1***	12**	3**
Unipolar	2	1	7*	1*	9	2
Bipolar	2	1	1	1	3	2
Multiple family history of affective disorder	2	1	4	1	6	2

Fisher's exact test: *$P<0.04$; **$P<0.03$; ***$P<0.02$.

TABLE IV
Number of individuals in the chronic depressive and control depressive groups reporting independent undesirable life events during the 6 months before and the 2 years after the onset of the current depressive episode

Type of life event	*Number of individuals*	
	Chronic depressives (n = 24)	*Control depressives (n = 20)*
Independent undesirable life events during 6 months before or 2 years after illness onset	16*	6*
Life events in 6 months prior to illness onset	12	5
Life events during 2 years after illness onset	4	1
Multiple life events	9	4

*χ^2 with Yates's correction = 4.27, d.f. = 1, $P<0.05$.

illness had begun. Multiple life events were recorded by 13 patients (nine chronic depressives and four recovered depressives).

Classification by area of activity showed that the recorded events fell into three categories: employment, health and family. Further analysis revealed that the most frequently recorded life events were the deaths of or serious illnesses in immediate relatives (ten chronic depressives; four control depressives). It is also notable that four of the males in the chronic group had been made redundant (due to factory closure, not due to illness).

No difference in personality, as assessed by the EPQ, were found between the chronic and control groups of depressives, although female chronics scored somewhat higher on the Neuroticism scale than their controls (mean score 14.7 compared with 11.4). Secondary psychiatric complications developed in four patients in the chronic depressive group and two patients in the control group. Alcohol abuse was the most frequent problem.

Although patients were euthyroid on entering the present study, four female chronic depressives had a past history of thyroid dysfunction. This difference between female chronic depressives and female control depressives was significant at the 1% level (Fisher's exact test). Loss of parent(s) in childhood and prolonged separations were no more common in the chronic depressives than in their controls.

Discussion

Before discussing the results of this investigation in detail, it is important to highlight some of the methodological problems encountered. The chronically depressed patients in this study were a select group of tertiary referrals to a consultant with an established interest in the biochemistry and psychopharmacology of affective disorders. This may have influenced the referral patterns of the consultants in the region and may throw into question how generalisable our findings are. In addition, the sample size is relatively small and, because the investigators were also involved in the treatment of these patients, the comparison between the chronic depressives and the recovered depressives in the control group was not blind. A further reservation relates to the nature of the data. An ideal investigation into the aetiology of chronicity would involve a prospective longitudinal follow-up study of depressed patients from the time of onset of the illness episode. In this study the patients were referred only after chronicity was established, and we then carried out a cross-sectional assessment of their longstanding illness. An attempt was also made to document life events occurring many years earlier and to establish the number of previous illness episodes. Such data is dependent to an uncertain extent on the recall of the individual and the quality of case-note recordings. In spite of these difficulties, our results show some important areas of agreement with those reported in the previously published literature.

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In the present study there was a preponderance of females in the chronic depressive group. Although this enhanced female-to-male ratio is similar to that found in depressive disorders in general, previous research (Winokur & Morrison, 1973) has shown that females are significantly more likely to develop chronicity than males. Chronic depression was also more frequent in unipolar rather than bipolar illness. This difference has been described previously (Lundquist, 1945; Morrison *et al*, 1973; Akiskal *et al*, 1981) and it has been postulated that depressive episodes in bipolar patients are interrupted by spontaneous shifts into hypomania or euthymia (Akiskal *et al*, 1981).

The importance of personality factors in the development of chronicity is problematical. The fact that most of the patients in this sample had suffered from previous episodes of depression which responded to standard therapeutic interventions suggests that personality is not of primary importance. The female patients in the chronic group did show a trend towards higher Neuroticism scores on the EPQ than females in the control group. Although this difference just failed to reach statistical significance, it concurs with the study of Weissman & Klerman (1977), who found that depressed women with pre-existing neurotic personality patterns were more at risk of developing a chronic illness. Their findings were not supported by Akiskal *et al* (1981). Only a prospective study can clarify the situation accurately, but we are impressed by the fact that while many of the patients received the label 'personality disorder' during the course of their chronic illness, this diagnosis was rarely recorded in their case-notes during their previous illness episodes. Kraines (1957) has suggested that the experience of depression can trigger the development of superimposed character pathology. The problems reported in these patients might represent a deterioration in personality functioning as a consequence of their prolonged illness rather than their premorbid adjustment.

Chronicity was significantly correlated with a positive history of affective disorder in first-degree relatives. The higher familial loading for affective disorder in chronic depressives compared with recovered depressives has been described previously (Akiskal *et al*, 1981; Akiskal, 1982), and also supports the view that chronicity has an affective rather than a characterological aetiology. Analysis of the family history data according to the sex of the patients was not documented in the previous studies. The finding of a significantly higher incidence of unipolar depression in the families of female chronic depressives may suggest that chronic depressions in males and females have differing aetiologies. This argument could be extended further, as female chronic patients also suffered significantly more episodes of depression prior to the onset of chronicity. The small number of patients investigated makes interpretation difficult, but future studies should try to confirm or refute this finding.

Paykel (1979) has argued that if life events are important in the precipitation of depression then they could also be expected to produce effects in situations other than the onset of the illness. We do not know of any studies which have looked at the role of independent undesirable life events in the maintainance of depressive episodes, but Paykel & Tanner (1976) have shown that relapse is significantly associated with further life events. The life events most frequently reported by the female chronic depressives were the loss of a first-degree relative and serious illness in an immediate member of the family. These events seemed to be particularly significant as they often robbed the patient of an important source of support at a critical moment (Cassano *et al*, 1983; Weissman & Akiskal, 1984) or, on occasion, left her with the burden of caring for a physically or functionally impaired relative. In male chronic depressives, redundancy was a frequent major life event, occurring in 57% of cases. Redundancy as an aetiological factor in chronicity has not been reported previously, although Melville *et al* (1985) have shown a higher incidence of depression in men made redundant when compared with men in regular employment. Our data support the view that these events can be regarded as important in maintaining the individual in the depressed state. Although not measured objectively, there was clinical evidence for marital and interpersonal difficulties in the chronically depressed patients. While it was not possible to determine whether such difficulties had a causative role or were consequences of the depression, it is likely that they played some role in the maintenance of the depressed state. It is seen as a deficiency in the current study that a more accurate assessment of these problems was not included.

The increased incidence of thyroid dysfunction in the female chronic depressives is an interesting observation. Examination of the previous treatment history does not suggest that it could all be attributed to lithium therapy or other drugs, and this finding merits further study, particularly in the light of Johnstone *et al*'s (1986) recent CAT scan study. Lastly, developmental object loss did not increase individual vulnerability to depression, a finding supported by previous studies of chronicity (Weissman *et al*, 1976; Akiskal *et al*, 1981).

It would seem that chronic primary major depressives comprise a very heterogeneous patient

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group and that many factors contribute to the causation of this form of illness. The role of precipitating and maintaining life events highlights the importance of psychological factors in the development of chronicity. In some individuals no such events were recorded, and the higher familial loading for affective disorder, the severity of the illness and the failure to respond to standard antidepressant regimes reminds us of the importance of biological factors in the evolution of 'treatment resistance'. Lehmann (1974) has argued that some forms of depression lie beyond our present pharmacological armamentarium and that new drug treatments are required. However, the secondary sequelae of chronic depression are many and the patient's family, social and work roles are significantly impaired. Akiskal *et al* (1981) suggest that a combined approach using pharmacotherapy and 'practical' psychotherapy can be beneficial. The combined treatment was tried because pharmacotherapy did not provide the patients with their previous coping skills, but many patients were too ill to actively engage in psychotherapy without receiving antidepressant medication (Weissman & Akiskal, 1984). Our treatment programme will be described in a future paper. In view of the prevalence, morbidity and mortality associated with chronic depression, we would suggest that systematic prospective studies of the causation and potential treatments of this disorder should be undertaken.

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