Brit. J. Psychiat. (1967), 113, 584–592

Body Water Variations in Manic-Depressive Psychosis

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Most of the water and electrolyte studies in mental illness have been carried out on patients suffering from periodic disorders and have been reviewed by Crammer (1962). Coppen and Shaw (1963) found increases in total body water and extracellular fluid and a decrease in residual sodium space on recovery from depression. Manic patients with a high vocal productivity were found by Anderson *et al.* (1964) to have a negative sodium balance, low plasma potassium levels and a positive potassium balance. Depressed patients with a low vocal productivity had a reduced rate of sodium loss and higher plasma potassium levels. Dawson *et al.* (1956) found extracellular expansion on spontaneous recovery from manic or depressive attacks. The purpose of the present study was to investigate variations in total body water and its distribution in manic-depressive psychosis. The investigation was complementary to a similar study of variations in body composition during recovery from depression reported by Hullin *et al.* (1967).

Patients and Methods

Four patients (1 male and 3 female) who had been admitted to the 6-bed Metabolic Research Unit at High Royds Hospital were studied for periods of 5–9 months. These patients were weighed daily and both the daily diet (containing 100 g. fat, 80 g. protein, 270 g. carbohydrate, 150 meq. of sodium, 90 meq. of potassium and 150 meq. of chloride) and the daily fluid intake (2 l. of water) were strictly controlled.

The behaviour and mood of each patient was assessed independently, using a rating scale, by the morning and afternoon nursing shifts. Each shift gave 0, 1, 2, or 3 points for each of seven manic and seven depressive behaviour traits, e.g. over- or under-activity, delusions of grandeur or of self-reproach. In this study, the daily total number of points as rated by the nursing staff (manic scoring as positive and depression as negative) has been used in the figures to indicate the mood of the patient. Normal behaviour and mood characteristics were also assessed on the rating scale but not scored. The results of weekly assessments of the patients by the panel of three consultant psychiatrists agreed well with those of the nursing staff. The weekly assessment was made independently by each psychiatrist by means of a common interview of the patient conducted by each on weekly rotation. A rating scale (Hamilton, 1960) modified to allow for rating of excitement was used. In addition to the variables suggested by Hamilton, the following were assessed on a five-point scale: elation, grandiosity, aggression, impairment of work and activities, over-activity and paranoid ideas and on a three-point scale: early and late insomnia, distractibility and impairment of insight. A fresh rating chart was used on each occasion to avoid halo effect. Statistical examination of the ratings, after some preliminary joint assessments, demonstrated an 86 per cent. concordance between the individual observers.

Total body water was determined at fortnightly intervals as described by Hullin *et al.* (1967). Extracellular space was determined at weekly intervals by the method described by Brown *et al.* (1963).

Results

A brief case history of each patient is given, together with the changes observed in body weight, total body water, extracellular water, "solid weight" (body weight less the weight of total body water) and intracellular : extracellular body water ratio (I.C.W./E.C.W. ratio).

Female patient, Miss M.C., aged 61, a typist, was originally admitted to hospital in 1948 suffering from depression. Since then she has been re-admitted frequently in a state of depression and on each occasion this has been followed by a state of mania. Her frequent admissions to hospital eventually resulted in premature retirement.

Fig. 1 shows the results obtained for patient M.C. who has demonstrated two complete mood cycles during the period of study, i.e. two depressed phases each followed by a period of mania. There was a tendency for the patient to increase in weight throughout the first cycle, particularly during recovery from depression. Weight changes were smaller in the second mood cycle but the weight loss which occurred prior to the onset of the second depressed phase was

reversed during recovery from the depression. Both swings from depression to mania were accompanied by increases in total body water and decreases in "solid weight"; during the change from mania to depression, the variations in body composition were in the opposite direction. The extracellular fluid volume tended to follow the same pattern of change as the total body water. The ratio of intracellular:extracellular water tended to decrease during both depressed phases, but a sharp increase occurred on each occasion when symptoms of depression were replaced by those of hypomania.

Female patient Miss M.W., aged 48, first became mentally ill at the age of 19. She was first admitted to High Royds Hospital suffering from a depressive illness in 1935. Since then there have been ten further admissions, and she has also been for a time a patient in a neighbouring hospital. On the majority of these occasions she has been admitted in a state of depression which has cleared up relatively quickly, but on three occasions she has been admitted in a state of hypomania. Since her present admission in August 1963, her mental state has varied between hypomania and depression, with very brief periods of normality in between. She is of below average intelligence and because of her illness has been able to have only short periods of employment as a domestic worker. Her condition appears to be that of a pure manic-depressive psychosis in a person of below-average intelligence.

Fig. 2 gives the results obtained for patient M.W. who showed three complete mood cycles during the investigation. Her body weight and total body water exhibit three minima and three maxima corresponding to the depressed phase and the latter stages of mania respectively. During the study there was an overall tendency for the amplitude of the manic phases as assessed by the rating scale to decrease. It is possible that treatment of the first two manic phases with lithium carbonate was significant in producing this effect, since the patient retained some of the administered lithium on each occasion. The cumulative retention of lithium was not excreted on discontinuance of the drug. The third depressed phase, during which no E.C.T. was administered, lasted more than twice as long as the two preceding depressed phases in which E.C.T. was administered. Corresponding with the overall tendency towards a decrease in manic rating, there was a similar tendency for the maximum values of total body water and body weight to decrease as the investigation proceeded. Since the changes in total body water were less than those in body weight, there was a net gain of "solid weight" in depression and a loss in mania.

The total body water changes in this patient do not parallel the changes in extracellular space, which tend to be high when the total body water volume is at a maximum, and also, paradoxically, when it is a minimum. There was a marked decrease in the I.C.W.:E.C.W. ratio on each of the three occasions during the investigation, when symptoms of hypomania disappeared, to be replaced after a very short normal period by depression. After each such fall, the ratio regained its previous value as the depression continued.

Female patient R.S., aged 48, was first admitted to High Royds Hospital in 1945, suffering from a hypomanic illness. She was discharged as recovered in 1946 but was readmitted in 1961, again in this hypomanic state. Whilst in hospital on this occasion, she relapsed into a state of depression from which she made a spontaneous recovery. She was in a hypomanic state when admitted for the third time in 1962. There was at this time a paranoid colouring to her illness and she expressed numerous delusional ideas about her husband. She was treated with E.C.T. and perphenazine and discharged as recovered two months after admission. Two further re-admissions in a state of depression occurred in 1962. This study commenced in August, 1963, when she was admitted yet again in a depressed state. After a period of treatment with amitryptyline, one E.C.T. was applied, and she became over-active and excited and expressed numerous delusional ideas particularly in regard to her husband. She was then treated with chlorpromazine, made a gradual recovery and was discharged in March 1964.

Patient R.S. had only one complete mood cycle during the study (Fig. 3). Despite rather complex weight changes the changes in total body water were similar to those observed in patients M.C. and M.W., i.e. there was an increase upon recovery from depression and a further increase just before the symptoms of mania disappeared. Following the latter increase, a rapid fall in body water occurred after the patient became mentally normal. The remarkably constant total body water demonstrated by this patient throughout mania was not observed in patients M.C. and M.W. The timing of the total body water determinations and the shorter manic phases of the latter

patients may be factors in this anomaly. Except when the total body water increased upon recovery from depression and in the final stages of mania, the "solid weight" of this patient showed a tendency to increase throughout the study. The I.C.W.:E.C.W. ratio was characterized by two sharp increases which occurred respectively at the beginning of the manic phase and at the return to normality. Apart from these changes, which were quickly reversed, no significant variations in the ratio were observed.

Male patient B.C., aged 54, was admitted to hospital in 1954, having attempted suicide by coal gas poisoning the previous day. On admission he was described as agitated, depressed and regarded as actively suicidal. He also showed marked hypochondriasis. There was no previous illness except deafness, and the family history was negative. Although the depression was said to have been related to his work as a weaver, there was evidence that he had always been prone to depressive mood swings. He was treated with E.C.T. without much effect and his mood continued to vary from cheerful, mild elation to a gloomy, hypochondriacal pre-occupation with tinnitus for which no adequate physical basis was found.

The pattern of mood swings in this patient is rather different from that in the previous three patients. B.C. had numerous, short, depressed phases and no manic phase during the period of study (Fig. 4). Immediately prior to the commencement of this investigation, he was very depressed. His short, depressed periods then began to decrease in severity as shown by the rating scores. He was rated without depressive symptoms from days 61–81 of the investigation, but subsequently the depressive episodes gradually increased in severity. If the general mood tendency of this patient is considered rather than individual short depressive phases, it can be observed that the total body water and body weight increase as the depressed phases become less severe and vice versa, with the "solid weight" changes occurring in the opposite direction. The extracellular space showed similar changes to the total body water. As the severity and frequency of short depressive episodes decreased at the beginning of the study, the I.C.W.:E.C.W. ratio showed a sharp, short-lived peak. When the frequency and severity of the depressions increased during the second half of the study, the ratio indicated a gradual but progressive decrease.

Discussion

Investigations of chronic patients with a long history of hospitalization have been much criticized. Invariably all the patients in the experimental group have received the same diet and lived in the same community for long periods, whereas the normal subjects in the control group have lived apart and received varied diets. As a result, observed differences between the experimental and control groups may be due to a number of extraneous factors, e.g. dietary deficiency, the presence of a similar pattern of intestinal flora or of the same sub-acute infection in the experimental group but not in the control group (Kety, 1959). Two types of patient, those attending out-patient clinics and those who have cyclical mood swings, provide better experimental material than the chronic institutionalized patient. Patients attending out-patient clinics or Day Hospitals come from varied backgrounds and therefore would not be expected to receive the same diet, possess the same intestinal flora or have the same sub-acute illnesses. There are, however, some disadvantages in studying this type of patient. Many depressed subjects eat very little, if at all, and may thus have a dietary deficiency. Sometimes it is advantageous to keep patients on a controlled diet during the period of study; this is, of course, impossible with out-patients. Another disadvantage is that patients attending Day Hospitals usually have less severe illnesses than those who are admitted to hospital and therefore any biochemical differences may be present to a lesser degree. Patients who show cyclical mood swings are ideal for biochemical studies. If admitted to hospital, these patients can be kept on a constant diet and fluid intake and the results of biochemical investigations in the abnormal phase(s) compared with those of the normal phase(s). Similarities of the intestinal flora and sub-acute infections are less important in these patients, since conclusions may be drawn by comparing observations made in the different phases of the cycle.

The two patients (M.C. and M.W.) who exhibited the classical features of manic-depressive psychosis showed similar cycles of change in body composition, namely, increases in body weight and total body water and a

decrease in "solid weight" during the transition from depression to normality. During the manic phases which followed the normal phases, these variables continued to alter in the same direction, so that in the later stages of mania the total body water and weight attained maximum values and the "solid weight" a minimum. These variations in body composition are essentially the same as those shown by a group of depressed patients during recovery from depression (Hullin *et al.*, 1967).

The return of normal mood associated with the disappearance of manic symptoms was characterized by an increase in "solid weight" and a decrease in total body water. Such changes also occurred in the group of depressed patients in the period more than six days after the last E.C.T. However, the total body water and body weight of patients M.C. and M.W., unlike the depressed group, continued to decrease in the post-manic normal phase, and depression returned.

The results obtained on patient B.C., who suffered from recurrent short episodes of depression, could be said to follow the same pattern if the overall mood tendency were considered rather than the individual discrete episodes. With lessening severity of depressive tendency, the weight and total body water increased and the "solid weight" decreased; these values changed in the reverse direction as the depressed moods became more severe.

Patient R.S. also showed similar changes in body composition during recovery from depression, but during her manic phase, which was much longer than those of M.C. and M.W., the total body water remained constant but the body weight increased. Disappearance of manic symptoms in this patient was associated with an initial increase and subsequent decrease of total body water and weight.

The extracellular space of patients M.C. and B.C. tended to vary in the same direction as the total body water. There seemed to be no such correlation with the other two patients (M.W. and R.S.). Consideration of the changes observed in I.C.W./E.C.W. ratio indicate that the ratio increases during the period when recovery from depression and onset of mania is occurring; the increase is due predominantly to an increase in the intracellular space. The commencement of depression, however, was characterized by a decrease in intracellular: extracellular water; both the intracellular and extracellular compartments tend to contract in this phase, but the greater decrease in the intracellular fluid volume (which is the numerator in the ratio) caused a reduction in the ratio. These results are in accord with those obtained in a group of depressed patients upon recovery from depression (Hullin *et al.*, 1967).

It would appear that the first body water change associated with the commencement of the recovery process is an expansion in the extracellular space without much change in the intracellular water, thus resulting in an initial decrease in the I.C.W./E.C.W. ratio. Little if any change in the mental state occurs at this time. The period of rapid improvement in mental state is associated with a significant increase in the ratio as a result of a marked increase in the volume of intracellular water. The results obtained with patient B.C. also conform to this pattern if the amplitude and frequency of short, depressive episodes is considered. The increase in ratio which occurred in patient R.S. with the disappearance of manic symptoms is somewhat atypical in that it is due mainly to a sharp decrease in extracellular space, not to any marked increase in intracellular space.

In this work, increases in total body water were usually accompanied by smaller increases in body weight and as a result the "solid weight" appeared to decrease. Any decrease in "solid weight" must be due to net catabolism. In general, increases in total body water were associated with recovery from depression, when increased physical activity usually occurred. Under these circumstances, net catabolism is not unlikely, despite a constant dietary intake of protein, fat, carbohydrate and minerals. Patient R.S. however, showed a decrease in "solid weight" after the end of mania, when physical activity was likely to decrease rather than increase.

Other authors (e.g. Crammer, 1959; Klein and Nunn, 1945) using balance studies have also demonstrated cycles of water retention in patients showing periodic mood changes. How-

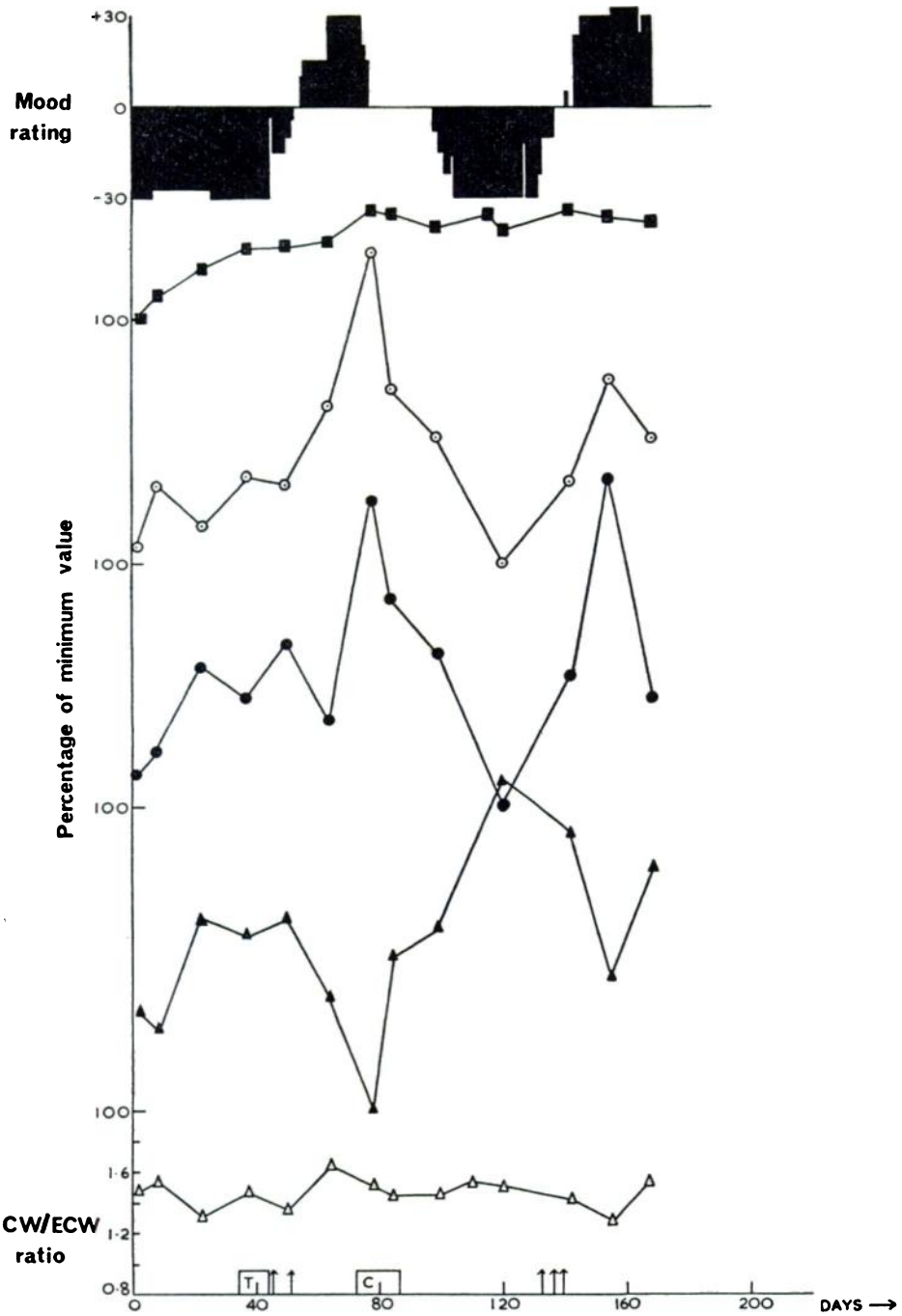

FIG. 1.—Changes in the body weight (■), total body water (O), extracellular space (●), "solid weight" (▲) and intracellular:extracellular body water ratio (△) of female patient M.C. The values of the first four variables are expressed as a percentage of the minimum value observed during the period of the investigation. The daily mood rating is also charted. The arrows indicate the occasions on which E.C.T. was administered. T and C indicate periods during which amitryptyline hydrochloride (25 mg./day) and chlorpromazine (50-100 mg. t.d.s.) respectively were administered.

The 100 per cent. value for each variable marked on the ordinate represents the 120 per cent. value of the variable charted immediately below it.

https://doi.org/10.1192/bjp.113.499.584 Published online by Cambridge University Press

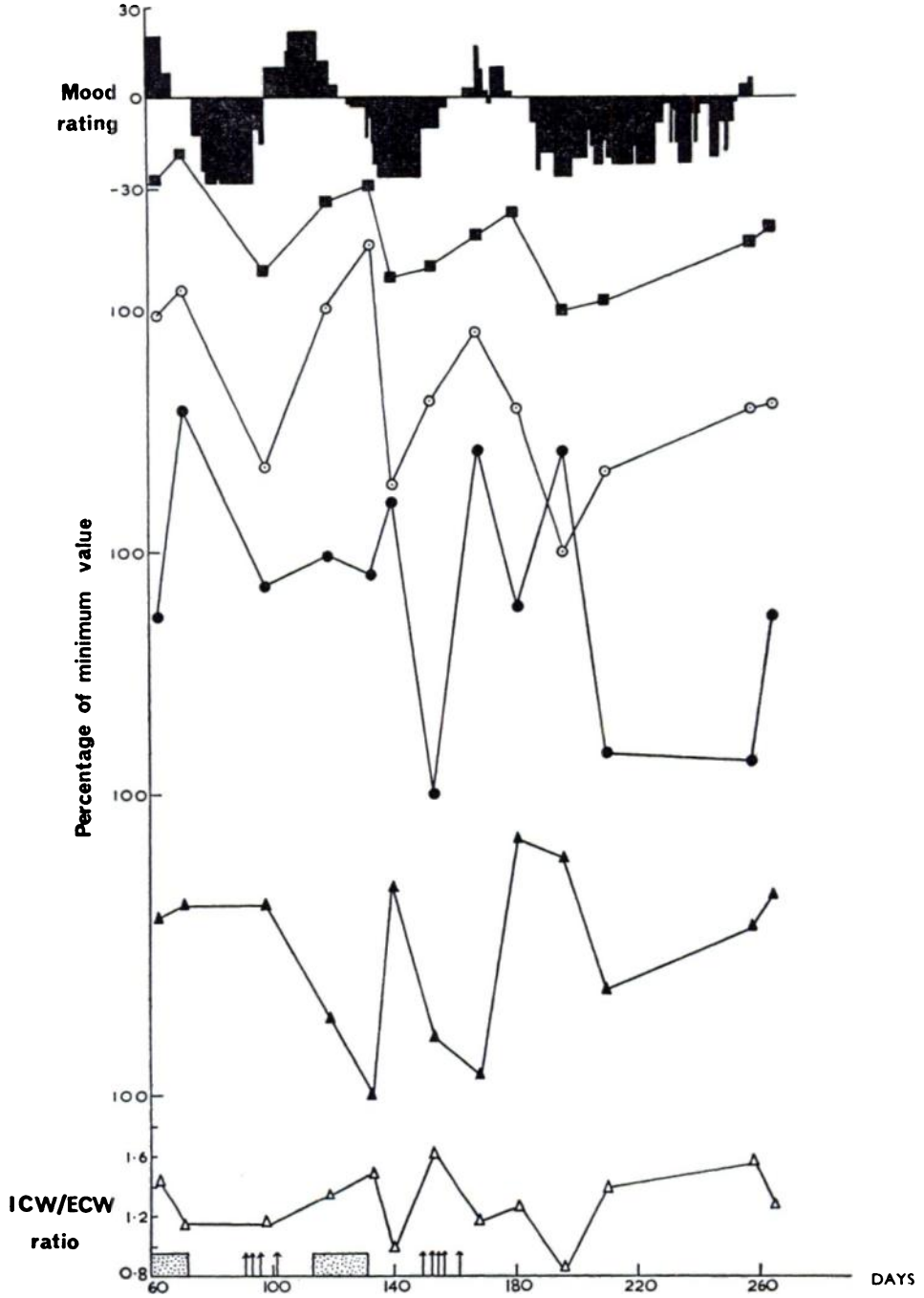

FIG. 2.—Changes in the body weight (■), total body water (○), extracellular space (●), "solid weight" (▲) and intracellular:extracellular body water ratio (△) of female patient M.W. The values of the first four variables are expressed as a percentage of the minimum value observed during the period of the investigation. The daily mood rating is also charted. The arrows indicate the occasions on which E.C.T. was administered. The spotted blocks show periods when lithium carbonate (500 mg. t.d.s.) was administered. The first determinations were made on day 63 of a complementary study.

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https://doi.org/10.1192/bjp.113.499.584 Published online by Cambridge University Press

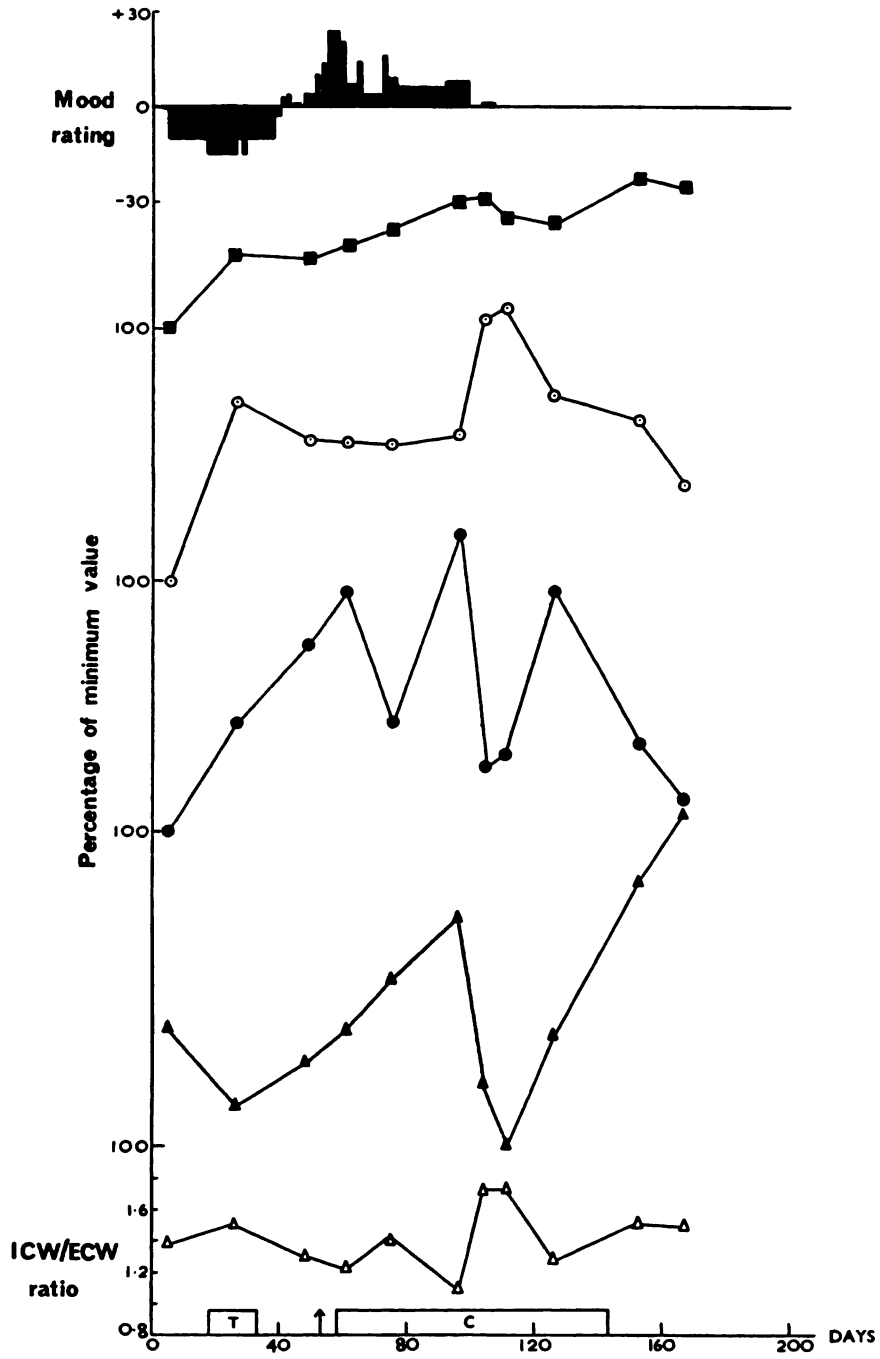

FIG. 3.—Changes in the body weight (■), total body water (O), extracellular space (●), "solid weight" (▲) and intracellular-extracellular body water ratio (△) of female patient R.S. The results, except for the ratio, are expressed as a percentage of the minimum value observed during the period of the investigation. The daily rating of the mental state of the patient is also given at the top of the figure. The arrow indicates one occasion on which E.C.T. was administered. T and C indicate periods during which amitryptyline hydrochloride (25 mg./day) and chlorpromazine (100 mg. t.d.s.) respectively were given to the patient.

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https://doi.org/10.1192/bjp.113.499.584 Published online by Cambridge University Press

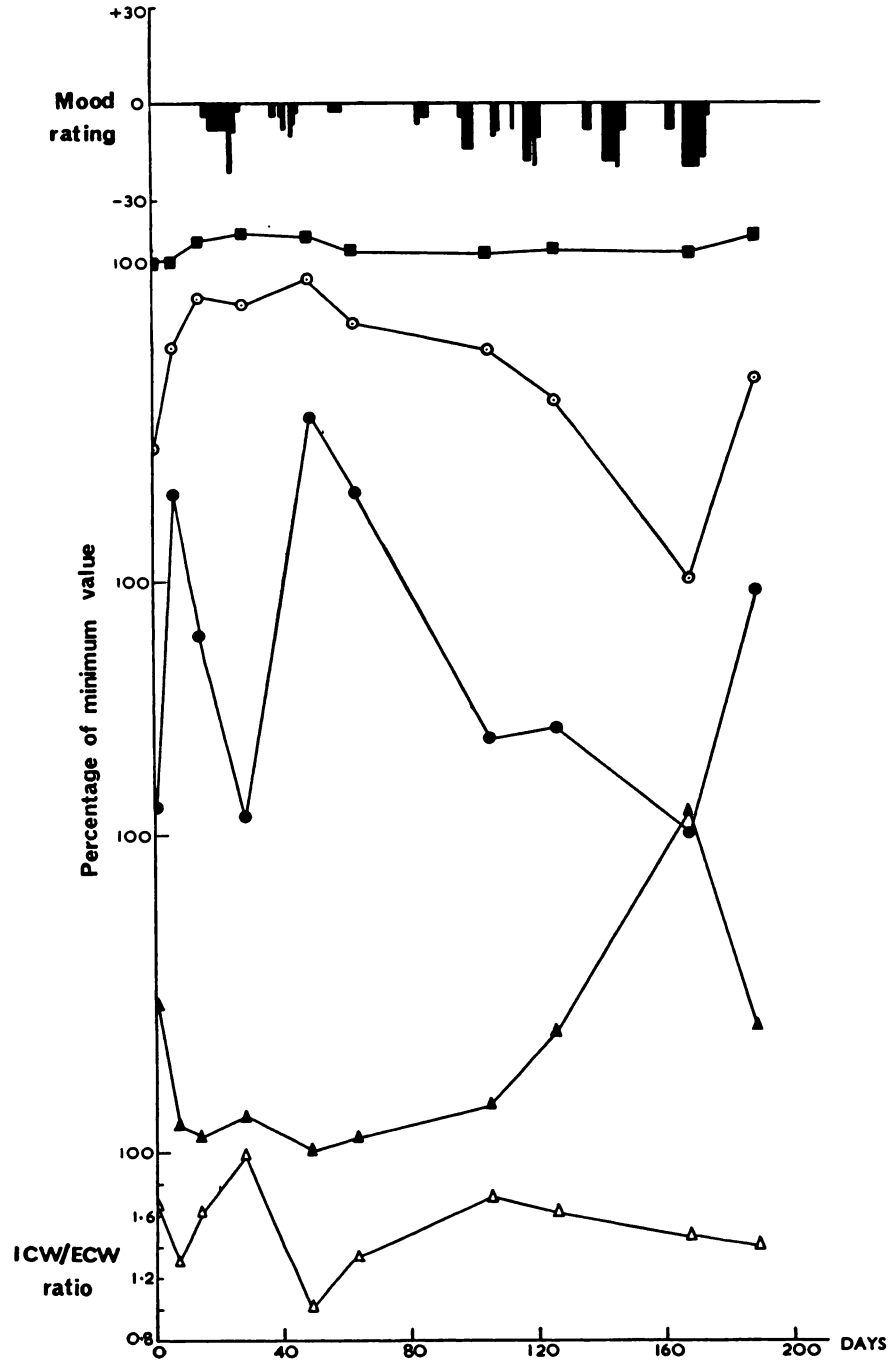

FIG. 4.—Changes in the body weight (■), total body water (O), extracellular space (●), "solid weight" (▲) and intracellular-extracellular body water ratio (△) of male patient B.C. The values, except for the ratio, are expressed as a percentage of the minimum value observed during the period of study. The daily rating of the mental state of the patient is also given.

The 100 per cent. value for each variable marked on the ordinate represents the 120 per cent. value of the variable charted immediately below it.

https://doi.org/10.1192/bjp.113.499.584 Published online by Cambridge University Press

ever, water retention has been reported at different phases of the mood cycle in different patients.

Total body water measurements have several advantages over balance studies for the investigation of water changes. It is never easy to control the fluid intake and ensure that complete urine samples are collected from mentally ill patients. Even if the patients are co-operative, mistakes can sometimes be made by the nursing staff. Also, the results of careful balance studies may not reflect the actual changes in total body water volume since more water may be lost through the skin and lungs during one phase of the cycle than another.

Summary

Patients suffering from manic-depressive psychosis showed cyclical changes in total body water, body weight and "solid weight" (body weight less the weight of the total body water) which corresponded to their mood cycles. The total body water and body weight were minimal and the "solid weight" maximal when depression was severe. The reverse was true in the latter stages of mania. Remission from depression was accompanied by similar changes in body composition as were reported earlier for a group of depressed patients during recovery.

Acknowledgments

It is a pleasure to express our gratitude to the High Royds Hospital Management Committee for the facilities which enabled this work to be carried out; to the nursing staff of the Metabolic Research Unit, especially Messrs. R. Stead, R. M. Parsons, R. Sanctuary and K. Walker; to Mr. J. Towers and the laboratory staff at High Royds Hospital; to Mrs. A. E. Neave, dietician; and to the patients who co-operated so readily.

Lastly, we would wish to thank the Smith, Kline and French Foundation for a grant to one of us (A.D.B.) and the Medical Research Council for a grant for technical assistance. The Ekco counter was purchased with a grant from the Mental Health Research Fund and the I.D.L. automatic counter with a grant from the Department of Scientific and Industrial Research.

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(*Received 23 May, 1966*)