BASAL AND SLEEPING METABOLIC RATES IN PSYCHIATRIC DISORDERS

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THE part played by the endocrine system in psychiatric illness is still controversial. Mental disorders may occur at the menopause or in the puerperium, accompany thyroid or pituitary dysfunctions, or appear in adrenocortical diseases. Castration in men and women may be followed by marked personality changes. But often there are little or no mental changes, and there is certainly no clear-cut mental accompaniment of specific endocrine diseases. It is probable that mental symptoms, when they do occur, are dependent upon the basic personality structure, not upon a particular diseased gland. It is also likely that glandular dysfunction in turn can be brought about by mental stress or disorder. In other words, the two systems function together and should not be artificially separated.

The activity of the thyroid gland is frequently questioned. Severe cases of myxoedema can easily be diagnosed but less obvious forms of hypothyroidism may be very difficult to identify, and often impossible if agitation is present. Similarly, patients with severe thyrotoxicosis present little difficulty in diagnosis, but milder cases may be impossible to distinguish from simple agitation. To add to the diagnostic difficulty it has been found that a proportion of patients with anxiety symptoms, particularly women, have diffusely enlarged thyroid glands and Brody (1949) has suggested, on the basis of blood iodine studies, that some of the symptoms of anxiety are produced by slight excess of thyroid. Fraser (1953) has remarked on the tendency of neurotic patients to have a relatively high uptake of radio-active iodine.

Thyroid activity may be measured by mean of various tests, but the simplest and probably the most reliable method at the present time is to estimate the basal metabolic rate (B.M.R.) of the patient. The basal state is defined as the amount of energy required just to maintain body processes when the person is at complete mental and physical rest, and is some twelve or more hours from the time of his last meal. A condition of complete mental and physical rest is essential, otherwise the test merely measures the metabolic rate of the person at that particular moment; the result will be misleading if regarded as the basal metabolic rate. In anxious patients, particularly those admitted to mental hospitals, complete mental rest is usually impossible to attain. Measurements of the B.M.R. of such patients in the past have been unreliable and often of little value either for diagnosis or for following the course of treatment. Consequently other methods, such as radioactive iodine uptake and excretion rates, and the level of protein-bound iodine in the serum, where facilities for such estimations exist, have come to be regarded as far more reliable than the B.M.R. However, it is important to realize, as Meckstroth (1952) has pointed

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out, that these different tests cannot be compared among themselves as they each measure a different aspect of thyroid metabolism. The B.M.R. measures the total body metabolism and therefore represents the end result of many oxidative processes, only one of which is due to thyroid hormone.

At St. Ebba's Hospital estimations of the B.M.R. with a Benedict-Roth machine have been carried out on all types of patient for the past twenty months. Initially the tests were done without sedating the patient.

Non-Sedated B.M.R.—Method and Results

The patient was given a trial run on the day preceding the test and told of the procedure and purpose of the test. No nourishment was given after 8 p.m. but short-acting hypnotics were allowed for the night. On rising at 7 a.m. the patient emptied his bladder and went to the "B.M.R. room" where he lay quietly in bed until 9 a.m. when the test was done. The temperature of the room was kept at 20°C.

During the test, whenever possible, the patient's consumption of oxygen over ten minutes was measured. But sometimes he became very agitated after a few minutes, his respirations increased in rate and amplitude, and the rate of oxygen consumption rose rapidly. Repetition of the test next day invariably produced the same response. When a patient complained of claustrophobia he usually found the procedure intolerable from the start. Psychotic patients sometimes refused to co-operate because of their delusions, or laughed and talked in the middle of the test, but in general were easier to manage than those with anxiety states.

The B.M.R. was calculated from the rate of oxygen consumption, in terms of calories per square metre of the patient's surface area per hour, and expressed as a percentage of the mean normal of the standards of Robertson and Reid (1952). These standards are some 10 per cent. lower than other standards, such as those of Boothby *et al.* The normal range for Robertson and Reid standards is generally taken as ± 14 per cent.

The results obtained in 189 consecutive estimations of the B.M.R. of unsedated psychiatric patients showed a very wide range:

64 were $+15$ per cent. or more
11 were -15 per cent. or more

40 per cent. were therefore outside the normal range of ± 14 per cent., 34 per cent. being above normal. Of this total, 4 patients only were clinically thyrotoxic, and 1 was clinically hypothyroid. These results may be compared with the work of Robertson and Reid who, in the course of determining their standards, found that 9 per cent. of their subjects (all presumably mentally healthy) gave initial readings 15 per cent. or more higher than those on the second day.

These results confirm the belief that the B.M.R., estimated under non-sedated conditions on anxious patients, is of little use as an index of thyroid activity. For the test to be of value it is necessary to produce basal conditions by artificial means, that is by inducing sleep. Possibly in a proportion of nervous patients, daily estimations of the B.M.R. such as Robertson and Reid carried out would eventually give a truly basal reading, but in practice this is far too time-consuming. This method was tried on several very tense patients with high B.M.R.s but as no appreciable drop occurred after six readings on each, it was abandoned.

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Bartels (1949), using thiopentone (Pentothal), found that there was a drop in the mean B.M.R. of 17 healthy people from +4 per cent. (+16 per cent. to −10 per cent.) to −9 per cent. (+9 per cent. to −26 per cent.), while little drop occurred in proven cases of hyperthyroidism. Rapport (1951) used pentobarbitone (Nembutal) and obtained an average fall from +13 per cent. to −2 per cent. in 74 euthyroid patients, while 74 hyperthyroid patients all remained above normal, showing an average fall from +46 per cent. to +33 per cent. More recently Fraser and Nordin (1955) have described their method of measuring the B.M.R. during sleep, and emphasized that this is the only satisfactory technique in nervous patients. It was therefore decided to measure the B.M.R. of patients under sleeping conditions, and see whether more reliable results could be obtained.

Method

Two methods of producing artificial sleep were tried:

Oral Method

Nembutal, gr. 3 was given by mouth hourly for three hours. This method was clumsy and unreliable compared with the intravenous method (described below). There was no means of controlling the depth of sleep. Some patients slept deeply after 3 gr., while others awoke during the test after 9 gr. 34 estimations by this method were made, but it has now been abandoned in favour of the intravenous technique. Tests were carried out in the non-sedated as well as the sleeping state, and the unreliability of the method is shown by the results:

Of 34 non-sedated patients 18 were +15 per cent. or more
Of 34 "sleeping" patients 9 were +15 per cent. or more
1 patient only was clinically thyrotoxic.

Intravenous Method

Nembutal was injected intravenously, 1 c.c. (50 mgm.) initially and then 0·5 c.c. per minute until sleep was produced. The average dose in adults was found to be 200–300 mgm. This took about ten minutes to give, and allowed initial agitation time to fade. The advantage of this method over oral sedation was that the operator could choose his own time and was able to produce light sleep easily and consistently. There was little or no risk of producing a dangerous level of anaesthesia provided the rate of injection was not increased. (It was important, however, to make sure that the patient really was asleep, otherwise false results were sometimes obtained.) Oxygen and Coramine were always at hand, but there was no occasion for their use.

The mouthpiece was inserted as soon as the patient was asleep. It was sometimes necessary to hold up the jaw, or lightly hold the lips around the mouthpiece, particularly with edentulous patients, but this procedure did not disturb the patient's sleep. A satisfactory record of oxygen consumption over 10 minutes was nearly always possible. The respiration rate generally dropped slightly but no more than normally occurs in sleep, but when too large a dose of Nembutal was inadvertently injected there sometimes occurred an increase in the rate. In such an event there was usually an over-large fall in the oxygen consumption. The pulse, when raised initially from anxiety, fell to within normal limits or otherwise remained unchanged. The patient tended to be

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drowsy for several hours, but this period could be shortened by giving 10 mgm. dexedrine on completion of the test. Occasionally, if food was taken before the drowsiness wore off, the patient felt sick and sometimes vomited.

Results

Eighty-one sleeping metabolic rates (S.M.R.) have so far been estimated. In all but two of the patients it was possible to determine the B.M.R. before inducing sleep.

In 79 non-sedated patients, 42 were +15 per cent. or more and 2 were −15 per cent. or less.

In 81 sleeping patients, 9 were +15 per cent. or more and 5 were −15 per cent. or less.

Four of these patients were clinically thyrotoxic; 1 patient was thought to have Cushing's Syndrome.

Discussion

In this small series 53 per cent. of non-sedated patients had a B.M.R. above normal. When the sleeping metabolic rates of these same patients were estimated only 11 per cent. were still above +14 per cent. The question that arises immediately is to what extent this sleeping state is equivalent to the basal state. Some authorities argue that barbiturates depress metabolism below the basal level. Certainly if so large an amount of barbiturate is given that surgical anaesthesia is induced then the metabolism will fall below basal level. But when nembutal is given intravenously and slowly as described above a state of light sleep can invariably be produced. The evidence accumulated during this investigation suggests that the sleeping metabolic rate under these conditions is, for practical purposes, similar to the basal metabolic rate. Thus, 35 patients had B.M.R.s within the normal limits of ±14 per cent., the mean being +5 per cent. (+14 per cent. to −7 per cent.). S.M.R.s were then estimated and the mean was found to be −1 per cent. These figures include, however, two patients who were hypersensitive to nembutal and one (later proven) hypothyroid patient whose agitation had lifted the B.M.R. to within the normal range. If these patients are omitted the mean S.M.R. is then +0·7 per cent. (+12 per cent. to −13 per cent.). When one considers that the B.M.R. may have been slightly raised anyway, the size of this fall, from +5 per cent. to +0·7 per cent., is small enough to suggest that the S.M.R. is synonymous with the B.M.R.

It was mentioned above that the B.M.R. represents the end result of many oxidative processes. Nervous factors obviously affect these processes and, as already shown, account for the high proportion of B.M.R.s above the normal range in non-sedated patients. The S.M.R. measures the metabolic rate in the absence of these nervous factors and it would therefore seem that the difference between the B.M.R. and S.M.R. should give a quantitative measure of the patient's tension.

Twenty-eight patients with clinical signs and symptoms of anxiety had a mean B.M.R. of +27·7 per cent. (+50 per cent. to +15 per cent.), falling during sleep to a mean of +4·7 per cent. (+22 per cent. to −12 per cent.). In eight of these patients the metabolic rate was estimated at varying intervals after induction of sleep. The results showed a progressive increase in the metabolic rate as the effect of nembutal wore off and twenty-four hours later the B.M.R. approached, and in one case exceeded the initial non-sedated level.

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	B.M.R. Non-sedated (Per cent.)	S.M.R. (I.V. Nembutal) (Per cent.)	3 Hours Later (Per cent.)	6 Hours Later (Per cent.)	24 Hours Later (Per cent.)
1 ..	+47	+14	+14	+19	+40
2 ..	+33	+22	+29	+29	+27
3 ..	+35	+9	+21	+21	+30
4 ..	+29	+16	+12	+19	+25
5 ..	+24	+7	+13	—	+21
6 ..	+38	−10	−8	+10	+32
7 ..	+39	−12	+21	+20	—
8 ..	+22	+1	+20	—	+26

These figures confirm the idea that the difference between the B.M.R. and the S.M.R. represents, in quantitative terms, the tension of each individual. This suggests that it may be possible to follow and measure a patient's progress under various forms of treatment.

Several patients have had their B.M.R. and S.M.R. repeated at monthly intervals in an attempt to confirm this possibility.

	B.M.R. %	S.M.R. %	Tension	
Mrs. A.				
January ..	+24	+9	15	Very tense on admission. Recovery
February ..	+8	+6	2	followed sedation and superficial psychotherapy.
Mrs. B.				
March ..	+26	+10	16	Very tense and depressed. Slow im-
April ..	+22	+7	15	provement until chlorpromazine was
May ..	+10	+8	2	given.
Mrs. C.				
June ..	+30	+3	27	Very tense. Failed to improve whilst
July ..	+30	−3	33	in hospital, in spite of various treat-
August ..	+24	+16	8	ments.
Mrs. D.				
August ..	+23	+13	10	Became increasingly tense whilst in
September	+47	+14	33	hospital and finally discharged her- self against advice.

In the cases of Mrs. A, B and D the tension corresponded well with the clinical progress. In Mrs. C's case there was a marked increase in the S.M.R. and it seemed likely that a vicious neuroendocrine circle had been set in motion.

Nine of the S.M.R. estimations of this series were +15 per cent. or more. Four of these were clinically thyrotoxic and one was an example of Cushing's Syndrome. The remainder showed severe anxiety symptoms. Each had a palpable smooth thyroid but none was clinically thyrotoxic and the radioactive iodine uptake and excretion rates were within the upper ranges of normal. None of these patients responded to sedation and psychotherapy. Two had rostral leucotomies and improved markedly (unfortunately the post-operative B.M.R. was not estimated), one was recommended for leucotomy but discharged herself, and the last was discharged to a general hospital for a hysterectomy (for uterine fibroids) and has not subsequently been traced. It seems therefore that a S.M.R. above the normal range, in the absence of thyrotoxicosis or other causes of increased metabolism, is of bad prognostic omen. A vicious circle seems to become set up in such patients which may need to be broken by leucotomy.

The four patients with thyrotoxicosis had S.M.R.s above normal, confirming the statement of Fraser and Nordin (1955) that the metabolic rates of hyperthyroid patients during sleep continue above the normal range. The actual values obtained were:

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	B.M.R. Per cent.	S.M.R. Per cent.
W.	+64	+44
X.	+29	+16
Y.	+36	+39
Z.	+36	+21

By contrast two women and three men had S.M.R.s below −14 per cent. Two of the men proved to be abnormally sensitive to nembutal and the low figures were almost certainly a reflection of this. The third man had a B.M.R. of −16 per cent. which fell to −23 per cent. during sleep. He was a schizophrenic and was later shown to be very insensitive to thyroxine. Very low B.M.R.s have quite frequently been described in apparently normal people (Booyens, 1957), and Knowland (1955) discusses a group of euthyroid people who have B.M.R.s 20–30 per cent. below average, unresponsive to thyroid extract. Of the two women, one was a severely agitated depression who refused to co-operate and whose B.M.R., when awake, would have been wholly unreliable. She was very thin and this may have lowered her basal metabolism. The other woman had had a thyroidectomy eighteen months previously and was showing marked anxiety symptoms on admission. The B.M.R. at this time was −6 per cent. and the S.M.R. −20 per cent. This last figure was thought to represent the actual index of her thyroid activity. The interesting point about this patient is that she was initially thought to have a recurrence of thyrotoxicosis.

Conclusion

1. Valid estimations of B.M.R. of psychiatric patients are possible, but it is essential to carry out such estimations under sleeping conditions if the patient is tense or agitated.

2. Sleep is best induced by giving nembutal intravenously. Oral nembutal is unsatisfactory for this purpose.

3. The sleeping state is synonymous with the basal state.

4. The difference between the basal metabolic rate and the sleeping metabolic rate is a quantitative measure of tension for each patient. This measure can provide an objective index of progress or deterioration under various treatments.

5. The sleeping metabolic rate of thyrotoxic patients remains above the normal range.

6. A sleeping metabolic rate that remains above the normal range, in the absence of thyrotoxicosis or other causes of increased metabolism, is of bad prognostic significance. Such patients may require leucotomy to relieve the tension.

7. The sleeping metabolic rate may reveal cases of hypothyroidism disguised by anxiety symptoms when awake.

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