British Journal of Psychiatry (1984), **145**, 645–648

Changes occurring in Appetite and Weight during Short-Term Antidepressant Treatment

BRIAN HARRIS, JOHN YOUNG and BILL HUGHES

Summary: Changes in appetite and weight were recorded in mild to moderately depressed out-patients during the course of clinical trials of various antidepressant drugs. After six weeks, differences due to treatment regimes were minimal. Patients who on becoming depressed experienced severe changes in appetite and weight in either direction, tended to return to normal. The significant associations of appetite and weight change during treatment were with weight, appetite, and carbohydrate preference at presentation, and also with the 'appetite history' and 'weight history'. The associations with the degree of depression were relatively minor.

The occurrence of weight and appetite change with depression and its treatment is long established, but of uncertain origin. Clinically, increase in appetite and weight is generally regarded as a favourable sign during treatment of patients presenting with more severe 'endogenous depression'. The converse may apply in those patients where depression is characterised by over-eating and weight gain. This has been recorded in individual cases, or in small groups (Bruch, 1974; Polivy & Herman 1976), but not in a population of depressives.

Long-term antidepressant drug treatment may be associated with marked weight gain and carbohydrate craving (Paykel, 1973). This effect must be partly due to pharmacological effects on the drive and satiety centres of the hypothalamus.

It has been suggested (Crisp, 1980) that the stimulant effect of tricyclic antidepressants on appetite may be an important part of their antidepressant action. This is a difficult hypothesis to test, since it is not easy to decide whether mood change precedes alteration in appetite or vice versa. Antidepressants may also affect appetite control in either direction; amphetamines, for example, are known to have a temporary mood-elevating effect, but suppress appetite. Similarly, newer antidepressants such as zimelidine, which act by 5 H.T. potentiation, have also been noted to have an anorectic action (Gottfries, 1981). It was therefore felt worthwhile to look at groups of patients taking antidepressant drugs who before treatment have opposite changes in appetite and weight. If the group who had increased appetite and increased weight on becoming depressed return to their normal appetite and weight with treatment, it is difficult to see how the action of tricyclic antidepressants could be explained by their action on appetite, at least in this particular group of patients.

Method

One hundred and sixty-eight mild to moderately depressed out-patients (Hamilton scores ranged from 12 to 50), were assessed for a period of six weeks, while completing antidepressant trials. All had satisfied Feighner's criteria for primary depressive illness (Feighner *et al*, 1972). The depression was rated using the Hamilton, MRC, and Beck scales and in addition, the presence of various symptoms was measured using the Middlesex Hospital Questionnaire (MHQ). Appetite was recorded in comparison to normal, and changes in appetite (in either direction) were rated on a seven-point linear scale. Particular interest in carbohydrate containing foodstuffs was rated as normal or increased on a three-point linear scale. Each patient was weighed at presentation and after six weeks of treatment.

Appetite history was defined as changes in appetite occurring with stress when the patient was quite well. It was measured on a linear scale with a mid-point of 'no change' and mild, moderate, and severe increase or decrease on either side. Severe changes represented eating twice as much as normal or half as much as normal respectively over the course of a day. Similarly, weight history was estimated linearly, with extreme steady weight at one end of the scale (weight change of less than 3 lbs in a year) and extreme unsteady weight at the other (weight change of 12 lbs or more in a year).

It should be noted that Hamilton and Beck scores were corrected throughout the study by extractions of that part of the score due to appetite and weight loss.

The patients were on one of seven antidepressant regimes in double-blind trials, viz oral medication in identical capsule form—amitriptyline, flupenthixol, phenelzine, isocarboxazid, trimipramine, trimipramine, and isocarboxazid in combination or trimipramine and phenelzine in combination (Young *et al*, 1976, 1979)

Results

Drug groups

Statistical analyses revealed no significant differences between patients in any drug group at presentation. After six weeks of treatment, there were minor differences between groups in terms of depression ratings. There was an overall tendency for patients to gain weight, appetite and carbohydrate preference. The group of patients taking isocarboxazid and trimipramine in combination experienced greater increase in preference for carbohydrate than the patients in all the other groups together ($P < 0.01$), and were characterised by greater increase in weight ($P < 0.01$).

Population as a whole

The incidence of various symptoms at presentation is shown in Table I.

TABLE I

Illustrating incidence of various 'endogenous' symptoms at presentation in the 168 patients

Symptom	*Percentage showing symptoms*
Appetite decrease	54%
Weight decrease	42%
Increased libido	5%
Decreased libido	85%
Early morning waking	35%
Morning worsening of mood	49%

Weight change, appetite change, and carbohydrate preference change at six weeks were strongly associated with presentation values for weight, appetite, and carbohydrate preference, and also with appetite history. These were all negative correlations. The minimal association with endogenous features such as early morning waking and morning worsening of mood is striking (Table II).

At six weeks, weight change, appetite change, and carbohydrate preference change were strongly associated with one another, but minimally with the changes in depression ratings (Hamilton) and other endogenous features.

Interestingly, appetite history and weight history were positively correlated ($P < 0.01$), i.e. patients who ate more when stressed had a history of variable weight.

The population was further divided into sub-groups who had presented initially with marked increase in appetite, moderate change, and marked decrease. Similar sub-groups for weight change were examined.

Appetite sub-groups

Thirty-one subjects were identified as having marked decrease in appetite and 20 as having a marked increase at presentation. Appetite had shown a roughly normal distribution at presentation, with a mean of 6.4, and these sub-groups were approximately one standard deviation or more beyond the mean.

Results were analysed in terms of paired t tests, showing the changes occurring in these appetite groups during six weeks' treatment. Unpaired t tests gave the differences between low and high appetite groups initially, at six weeks, and the differences between the changes occurring in the two groups (with direction of change taken into account).

These results are summarised in Table III. The general beneficial effect of the treatment is reflected in the Hamilton scores. At presentation, the low and high-appetite groups differed significantly in preference for carbohydrate, weight and appetite history ($P < 0.001$). The changes in score

TABLE II

Pearson correlation coefficients expressing the relationship between changes in weight, appetite, and carbohydrate preference at six weeks and initial scores

	Weight Change	*Significance*	*Appetite Change*	*Significance*	*Carbohydrate Preference Change*	*Significance*
Initial Scores						
Appetite	−0.35	0.001	−0.75	0.001	−0.30	0.001
Weight	−0.20	0.01	−0.23	0.001	−0.05	NS
Appetite history	−0.25	0.001	−0.44	0.001	−0.17	0.05
Carbohydrate preference	−0.14	0.05	−0.25	0.001	−0.49	0.001
Variable weight	−0.17	0.05	−0.02	NS	−0.06	NS
Hamilton	−0.05	NS	−0.02	NS	0.12	NS
Early morning waking	−0.04	NS	−0.06	NS	−0.07	NS
Morning worsening of mood	−0.03	NS	−0.02	NS	0.06	NS

https://doi.org/10.1192/bjp.145.6.645 Published online by Cambridge University Press

TABLE III

Data for Hamilton Ratings, Appetite, Carbohydrate Preference, Weight, Obsessional Symptoms (M.H.Q.) and Phobic Symptoms (M.H.Q.) for various groups at presentation and after 6 weeks treatment. Patients were weighed at presentation and after 6 weeks treatment. Weight is expressed as a percentage of normal weight

	Initial low appetite n = 31		*Initial high appetite n = 20*		*Low initial weight n = 28*		*High initial weight n = 27*	
Hamilton		s.d.		s.d.		s.d.		s.d.
Presentation	25.7	(5.1)	24.1	(5.8)	24.5	(4.7)	25.0	(5.8)
6 weeks	15.0	(9.3)	14.0	(7.0)	15.9	(9.6)	14.4	(8.6)
Appetite								
Presentation	3.1	(0.8)	10.5	(0.7)	5.1	(2.3)	7.9	(2.3)
6 weeks	7.7	(2.6)	7.1	(2.9)	7.1	(2.1)	7.2	(2.5)
Carbohydrate preference								
Presentation	0.3	(0.6)	1.6	(1.1)	0.3	(0.7)	0.7	(0.9)
6 weeks	1.2	(1.3)	1.3	(1.1)	0.9	(1.1)	1.1	(1.2)
Weight								
Presentation	97	(11)	106	(8)	89	(5)	117	(4)
6 weeks	101	(10)	106	(10)	92	(7)	117	(6)
Obsessional symptoms (M.H.Q.)								
Presentation	10.8	(3.4)	8.0	(3.2)	9.5	(3.7)	9.9	(3.4)
6 weeks	9.7	(3.5)	8.5	(3.4)	9.1	(4.0)	9.4	(2.8)
Phobic symptoms (M.H.Q.)								
Presentation	8.5	(3.9)	7.9	(3.4)	6.6	(3.8)	8.9	(3.4)
6 weeks	8.1	(4.5)	7.1	(3.7)	6.1	(4.1)	8.5	(4.2)

between 0 and 6 weeks for appetite, carbohydrate preference, and weight are very different in two extreme groups (they were in opposite directions). The change in weight is of interest, in that at six weeks the patients in the low-appetite group had increased in weight from 97% to 101% of their normal weight, while those in the high-appetite group had remained virtually unchanged at 106%. The significant difference in weight between the groups has now disappeared, but once again, the actual change in weight (which includes direction) is very significantly different ($P < 0.01$).

Weight sub-groups

Twenty eight subjects were identified as having an initial weight score of 94% or less of their normal weight, and 27 as having an initial weight of 110% of their normal weight or above (where normal weight is 100%). Weight at presentation had shown a roughly normal distribution, with a mean weight of 102%. These sub-groups were approximately one standard deviation or more beyond the mean. At presentation, the significant differences between the low- and high-weight groups were appetite (Table 3 $P < 0.001$), appetite history ($P < 0.05$), and phobic symptoms ($P < 0.05$—the high weight groups were more phobic).

At six weeks, the only difference between the groups is one of weight, the low-weight group having nevertheless gained significantly in weight, by 3% (Table III). This group also increased their appetite ($P < 0.01$) and preference for carbohydrate ($P < 0.05$), but the high-weight group has not changed significantly on these variables.

Discussion

Although the study was confined to mild to moderately depressed out-patients, changes in weight, appetite, and carbohydrate preference were strongly associated with their values at presentation, more than with the degree of depression, or with features of endogenous depression such as early morning waking and morning worsening of mood (Table II). This was true of the whole population and also for the sub-groups with high or low weight, and high or low appetite.

The reversal of appetite change is particularly interesting, since it challenges the concept of a simple pharmacological association between antidepressants and increase in appetite and carbohydrate craving. The

https://doi.org/10.1192/bjp.145.6.645 Published online by Cambridge University Press

appetite history appears to be involved, and patients whose appetite decreases as they get better, may simply be regaining control of food intake.

The importance of weight history is not so clear. However, a previous study had shown that those patients who gained weight on becoming depressed have a history of variable weight anyway—even when they are well (Harris *et al*, 1984). In this smaller group of 168 patients who completed the drug trials, after six weeks there is still an association of weight change occurring with treatment with variable weight history. (Table II).

Variable weight history is often an indication of latent obesity, and the increase in appetite and weight occurring in such patients with depression may be an exaggeration of the hyperphagic reactions which the obese and latent obese often show in response to stress (Meyer & Pudel, 1977). On the other hand, loss of weight and appetite with this depressive illness is associated with a steady weight history and hypophagic reactions to stress, the subsequent regain of appetite and weight having the same associations.

Appetite control is complex and depends upon many factors. Rodin (1978) has suggested that food intake is determined by the overall responsiveness of the individual, and this itself depends on many cues to feeding, as well as on the activity of the feeding centres in the hypothalamus. In addition, emotional factors are important, and it is well known that some individuals over-eat with anxiety or depression while others under-eat (Meyer & Pudel, 1977). Polivy & Herman (1976) have shown the importance of restraint in the control of normal eating and also as an important principle in controlling food intake in depressed individuals. Obese people and the latently obese tend to be restrained in their eating habits, and are preoccupied with diet, weight, and food. When such individuals become depressed or anxious, restraint is lost, and there is an increase in food intake, as happened in our group of patients who presented with increased food intake. This is reversed with recovery.

It is likely, therefore, that there are at least two major variables regulating the control of appetite and hence weight in this population of depressives. Firstly, loss of restraint with depression causes an increase in appetite and weight, which is then reversed on recovery. Secondly, depression itself, directly suppressing appetite with loss of weight, and reversal with treatment. These two factors are seen most clearly at work in the sub-groups high and low-appetite, and they are linked with appetite history and weight history (Tables II and III). The sub-groups represent extreme ends of the spectrum, but the principles are probably at work in the population as a whole, producing a variety of appetite responses.

This study suggests that before the long-term carbohydrate craving, increase in appetite, and increase in weight occur with antidepressant therapy, there is a simple reversal of the appetite and weight changes which occurred with depression. Further work is necessary to investigate the relationship between the long-term changes and such factors as appetite history and weight history, as well as with the pharmacological actions of various antidepressant drugs.

Acknowledgement

The authors would like to extend their thanks to Dr. Robert Newcombe (Medical Statistics, Welsh National School of Medicine), for his help with the statistics in this work.

References

Bruch, H. (1974) Eating Disorders: Obesity, Anorexia and the Person Within. New York: Basic Books.

Crisp, A. H. (1980) Sleep, activity, nutrition and mood. *British Journal of Psychiatry*, **137**, 1–7.

Feighner, J. P., Robins, E., Guze, S. B., Woodruff, R. A., Winokur, G. & Munoz, R. (1972) Diagnostic criteria for use in psychiatric research. *Archives of General Psychiatry*, **26**, 57–63.

Gottfries, C. G. (1981) Influence of depression and anti-depressants on weight. *Acta Psychiatrica Scandinavica Supplementia, 290, vol.* **63**, 353.

Harris, B., Young, J. & Hughes, B. (1984) Appetite and weight change in patients presenting with depressive illness. *Journal of Affective Disorders*, **6**, 331–339.

Meyer, J. E. & Pudel, V. E. (1977). Experimental feeding in man: A behavioural approach to obesity. *Psychosomatic Medicine*, **39**, 3, 153–157.

Paykel, E. S., Mueller, P. S. & de la Vergue, P. M. (1973) Amitriptyline, weight gain and carbohydrate craving: A side effect. *British Journal of Psychiatry*, **123**, 501–507.

Polivy, J. & Herman, C. P. (1976) Clinical depression and weight change: A complex relation. *Journal of Abnormal Psychology*, **85**, 3, 338–340.

Rodin, J. (1978) Has the distinction between internal versus external control of feeding outlived its usefulness? *Recent Advances in Obesity Research*, **2**, 75–85.

Young, J. P. R., Hughes, W. C. & Lader, M. H. (1976). A controlled comparison of flupenthixol and amitriptyline in depressed outpatients. *British Medical Journal*, **1**, 1116–1118.

Young, J. P. R., Lader, M. H. & Hughes, W. C. (1979). Controlled trial of trimipramine, mono-oxidase inhibitors, and combined treatment in depressed outpatients. *British Medical Journal*, **2**, 1315–1317.

*Brian Harris, BSc. MB. BS. MRCPsych. *Consultant Psychiatrist, Department of Psychological Medicine, University Hospital of Wales, Heath Park, Cardiff*

John Young, MD. MPhil. MRCP. *Consultant in Psychological Medicine St Thomas' Hospital, London*

Bill Hughes, MB. BS. MRCPsych. *Consultant Psychiatrist, David Rice Hospital, Norwich*

*Correspondence

(Received 12 December 1983; revised 16 April 1984)