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Suppression of Eating by Fenfluramine in Patients with Bulimia Nervosa

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Summary: Fifteen patients with bulimia nervosa received fenfluramine (60 mg po) or placebo under double-blind, randomly ordered conditions. Two hours later food was presented. Significantly less food was eaten after fenfluramine and the quantity eaten was inversely correlated with serum fenfluramine levels. Significantly fewer patients reported bulimic symptoms during the test after fenfluramine, but no significant effect was demonstrated after leaving the ward. Fenfluramine caused drowsiness but did not reduce hunger ratings. Similarly, eating failed to reduce hunger ratings normally in the patients. These findings suggest that in patients with bulimia nervosa, hunger is reported abnormally and eating is suppressed by fenfluramine. Bulimic symptoms were probably reduced by fenfluramine, which may prove to be a useful treatment for bulimia nervosa.

Bulimia nervosa is a serious condition in which the patient succumbs to intractable urges to overeat. During the resulting bulimic episodes, large amounts of easily ingested food, often of high calorific value, are rapidly consumed. These episodes are accompanied by mounting distress and, because of an underlying morbid fear of weight gain, they may be followed by self-induced vomiting, laxative abuse or other means of reducing the 'fattening' effects of the ingested food. Severely restrictive dieting frequently ensues and may be interrupted by another episode of bulimia. The episodes may occur several times in a day and lead to serious physical complications including dental erosion, hypokalaemia, and renal failure.

The term bulimia nervosa (Russell, 1979) has been used to identify a group of patients who suffer bulimic episodes, attempt to mitigate the effects of overeating by self-induced vomiting, laxative abuse or by other means, and who show a morbid concern with weight and body size. This concern is shared by patients with anorexia nervosa, and close links may be seen between the two conditions. Patients suffering from bulimia nervosa frequently give a history of previous true or 'cryptic' anorexia nervosa (Russell, 1979) while, conversely, bulimic episodes may complicate anorexia nervosa (Garfinkel *et al,* 1980). Episodes may also occur in patients with no history of anorexia nervosa (Stunkard, 1959; Fairburn, 1982) although dieting is prominent in these patients. There is, therefore, considerable overlap between patients currently suffering from anorexia nervosa, those with a past history of the disorder and those with no such history, in that they may all have bulimic episodes. The term 'bulimia nervosa' has been applied to bulimic patients with a past history of anorexia nervosa (Russell, 1979) and to patients with bulimic episodes irrespective of their past history (Fairburn, 1982). The term 'bulimia' has also been applied to the latter group of patients, (American Psychiatric Association, 1980) and has been extended to include patients currently suffering from anorexia nervosa, if they have bulimic episodes (Andersen, 1983), reflecting differing usage between various workers. In the present report, the term bulimia nervosa will be used to describe patients with bulimic episodes without severe weight loss but who in the past have fulfilled criteria for true or 'cryptic' anorexia nervosa.

The aetiology of bulimia nervosa remains obscure. Because of the shared psychopathology with anorexia nervosa and the occurrence of the latter in the histories of patients with bulimia nervosa, it may be viewed as a chronic complication of anorexia nervosa. Many patients, although of average weight, are attempting to maintain body weight at a level that is lower than the premorbid 'healthy' weight. Accordingly, it has been suggested that overeating in bulimia nervosa may represent, in part, a physiological response to the patient's attempts to maintain body weight at what is, for her, a sub-optimal level (Russell, 1979).

Attempts at treatment of this serious disorder have met with varying degrees of success. Admission to hospital under careful nursing supervision may prevent bulimic episodes, but relapse usually occurs on discharge. Behavioural methods of treatment have been used with apparent benefit (Fairburn, 1981), but their place in the long-term management of the disorder is not established.

The role of drug treatment is also uncertain. The anticonvulsant drug phenytoin was reported to reduce the incidence of bulimic episodes in eight

out of nineteen patients with the 'binge-eating syndrome' in a controlled trial (Wermuth *et al,* 1977) and in 9 out of 10 'compulsive eaters' with a variety of other diagnoses in an uncontrolled study (Green & Rau, 1974). The other pharmacological approach has been to use antidepressant medication. In an uncontrolled study of monoamine oxidase inhibitors (Walsh *et al,* 1982), improvement was reported in all six bulimic patients given the drugs, while two well controlled studies of antidepressant drugs each suggested different conclusions. Imipramine (Pope *et al,* 1983) was reported to improve eight out of nine patients with bulimia, compared to one out of ten given placebo. However, mianserin (Sabine *et al,* 1983) provided no clear benefit in a controlled double blind trial.

It has been shown recently (Ong *et al,* 1983) that intravenous methylamphetamine, in a double-blind placebo controlled experiment, significantly reduced the quantity eaten by eight patients with bulimia nervosa. Amphetamines have a number of different actions, including euphoria, suppression of appetite and increased alertness, and it is not clear which of these was responsible for the suppression of eating noted in the patients. Should a similar effect be produced by fenfluramine, which has appetite suppressant but no euphoriant or alerting action (Stunkard *et al,* 1973), then it might be deduced that suppression of appetite is the mechanism whereby both drugs inhibit eating in bulimia nervosa.

The finding that drug-induced suppression of hunger may modify the symptoms of bulimia nervosa is not all that readily predictable. Patients with bulimia nervosa often deny hunger, sometimes quite vehemently. They express their symptoms more in terms equivalent to a failure of satiety. However, the methylamphetamine study suggested that the use of drugs modifying appetite might prove beneficial in the treatment of bulimia nervosa. Amphetamines have serious unwanted effects such as dependence and psychosis (Connell, 1958) and could not be used in the treatment of these patients. Fenfluramine, however, has little or no potential for abuse (Connell, 1979) or drug-induced psychosis (Connell, 1975) and if it could be shown to prevent episodes of bulimia in an acute experiment, a chronic trial of the drug would be warranted. Fenfluramine has been shown to decrease food intake significantly over the two hours after oral administration of 60 mg although hunger ratings were not reliably suppressed at that dose (Kyriakides & Silverstone, 1979).

In the present study, the effects of fenfluramine on the consumption of food under controlled conditions, on self-rating scales of hunger, fullness and mood and on the incidence of subsequent bulimic episodes were studied.

Patients

Subjects were drawn from an outpatient clinic treating patients with eating disorders. All were female and satisfied criteria for both bulimia nervosa (Russell, 1979) and bulimia (American Psychiatric Association, 1979). From Table I, in which clinical data are summarised, it will be noted that 5 patients were maintaining a weight at least 10% below their premorbid weight, while four patients gave a history of having been more than 10% above standard weight. Eight of the patients

TABLE I

Principal clinical information

Patient Number	*Age*	*Duration of Bulimia (years)*	*Frequency of overeating*	*Frequency of vomiting*	*Laxative abuse*	*Past anorexia nervosa (1)*	*Current amenorrhoea*	*Current weight*	*Current wt as % of premorbid wt*	*Current wt as % of standard wt (2)*	*Hamilton Depression Rating*	*Eating Attitudes Test Score*
1	25	8	>weekly	>weekly	+	+	+	51	92	82	9	29
2	22	6	>daily	>daily	+	−	+	48	106	85	17	23
3	25	2	>daily	>daily	+	+	+	43	61*	86	18	56
4	20	2	>weekly	>weekly	+	−	−	57	100	101	8	39
5	18	4	>weekly	>weekly	+	−	−	58	107	98	22	42
6	36	3	>weekly	>weekly	−	−	−	55	101	94	12	41
7	28	8	>weekly	none	+	+	+	66	110	106	16	63
8	18	4	>daily	>daily	−	+	+	50	100	104	16	43
9	21	4	>weekly	>daily	+	−	−	51	89	94	24	72
10	26	6	>weekly	>weekly	+	−	−	57	81*	91	21	57
11	21	5	>weekly	none	−	+	−	73	137	117	20	46
12	29	6	>weekly	>weekly	+	+	−	54	77*	90	8	46
13	19	1	>daily	>daily	+	−	−	55	75*	91	20	78
14	31	9	>weekly	>monthly	+	+	−	49	102	84	22	70
15	29	5	>daily	>daily	+	+	−	66	98	91	22	84
Means	25	4.7						55.5	95.7	94.3	17	55.9

(1) + Definite past anorexia nervosa − Weight loss ± amenorrhoea in past but not meeting criteria for anorexia nervosa

(2) Corrected for height, sex and build. (Documenta Geigy 1959).

*Past history of being at least 10% over standard weight

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had in the past fulfilled diagnostic criteria for anorexia nervosa (Russell, 1977) while the rest had a history of weight loss with or without menstrual symptoms, but had not satisfied full diagnostic criteria for anorexia nervosa.

Most of the patients showed fairly severe psychological disturbances in addition to the bulimic symptoms. This is reflected in scores on the Hamilton Depression Rating Scale (Hamilton, 1960) and the Eating Attitudes Test (Garner and Garfinkel, 1979) which are given in Table I. Two typical case histories are presented.

Patient 2 is a 22 year old music student whose weight had been 45kg since puberty. At the age of 17 she lost 3kg after a febrile illness, began to feel fat, and experienced guilt after eating. Her attempts to diet were interrupted by bulimic episodes during which she would consume over 10,000 Calories in bread, cakes and sweets, induce vomiting, and take 20–30 laxative tablets. On a number of occasions she was not satisfied that all the food had been disposed of, and she swallowed a large number of aspirin tablets, presented herself at a casualty department and obtained a stomach washout. In the past, she has stolen compulsively and she is amenorrhoeic. A sister has had anorexia nervosa in the past and her mother is obese. When first seen she was having 4 or 5 bulimic episodes daily and was unable to pursue her music studies.

Patient 11 is a 21 year-old *au pair* girl, who developed anorexia nervosa at the age of 16. She lost weight from 54 to 42kg and her periods ceased. At the time, important examinations were imminent and her mother was divorcing her father who suffered from alcoholism and manic depressive psychosis. Because of reading difficulties, the patient had always felt inferior to her successful sister. She has been and remains, over-dependent on her mother. After one year of low weight, she began to have bulimic episodes interspersed with periods of complete starvation lasting up to three days. Her weight has fluctuated between 45 and 73kg. She has been severely depressed and has made two suicide attempts.

Method

Testing was begun in a single room on a research ward at 9.30 am after an overnight fast. At 10.00 am, fenfluramine hydrochloride 60mg (Servier Laboratories Ltd) or placebo was administered orally under double blind and randomly ordered conditions. The two preparations were administered in two tests, separated by an interval of about one week, enabling a comparison between placebo and fenfluramine to be made. The patient was informed that she was to receive one of two preparations which may or may not influence her eating. Two hours after taking the tablets, when the anorectic action of fenfluramine would be expected to be maximal (Silverstone & Fincham, 1979), a blood sample was taken for serum fenfluramine estimation and the patient was left alone for thirty minutes with a liberal supply of food chosen by her in advance. She had been asked to choose the specific food that she was most likely to eat during a bulimic episode. On presentation of the food, the patient was asked to eat some of what was given and to continue to eat as much as she wished within the 30 minutes. The food was weighed before and after the test and the calorific value of the food consumed was calculated by reference to tables (Documenta Geigy 1959). During this part of the test, the quantity of food eaten was determined with fair accuracy. However, laboratory conditions differ markedly from the settings in which bulimic episodes in these patients usually occur. Accordingly, the patient was allowed to leave the ward at 12.30 pm and asked to record, on a standard sheet, for the next five days, bulimic episodes and other food consumed as well as any adverse effects possibly attributable to the medication. In this way, a record of the occurrence of bulimic episodes under natural conditions was obtained.

For the purposes of the study, a bulimic episode was said to have occurred when the patient reported consumption of a large amount of food, rapidly, within a discrete period of time. In addition, the patient's subjective assessment of whether the episode constituted a 'binge' or not was used. For different patients, a variety of elements appeared to be important in making this assessment including 'a feeling of loss of control', depressive and self-deprecating thoughts, and the later occurrence of self-induced vomiting, purging or fasting. Although unavoidable, reliance on this subjective evaluation clearly introduces a possible source of error. When the diary sheet was returned, it was discussed in detail with the patient, and it was ascertained that the bulimic episodes recorded fulfilled the above criteria. The eating that had occurred during the test on the ward was also discussed and characterised.

From the time the patient took the tablets until leaving the ward, 100mm visual analogue scales were completed every 30 minutes. These were labelled as follows:

Alert–Drowsy
Not at all hungry–Extremely hungry
Extremely sad–Not at all sad
Not at all full–Extremely full
Extremely tense–Not at all tense
No urge to eat–Extreme urge to eat
Extremely fat–Not at all fat.

In order to allow a comparison to be made between the patients' analogue scale results and those that would be expected from a normal group, a limited experiment was performed using controls. Subjects drawn from the hospital staff, who denied any history of eating disorder were matched with the patients for sex and for age (± 20%) and weight (± 12%) and were tested after an overnight fast under the same conditions as the patients. They were given only placebo, but were told that they were receiving tablets that may or may not affect their

TABLE II

Calories consumed, bulimic symptoms and drug levels

Patient number	*Food eaten*	*Calories consumed*			*Description of test meal*		*Symptoms after test (time)*		*Fenfluramine level ng/ml*	*Test order*		*Complaints of Side effects*	
		PLA	*FEN*	*CON*	*PLA*	*FEN*	*PLA*	*FEN*		*PLA*	*FEN*	*PLA*	*FEN*
1	Cake	792	256	528	DB	—	—	—	44	2	1	—	+
2	Cottage cheese	798	32	198	DB	—	—	—	NA	2	1	—	+
3	Cake	976	60	434	DB V	—	—	—	22	1	2	—	—
4	Cake	292	140	292	—	—	V (1pm)	—	61	1	2	—	+
5	Cake	115	115	115	—	—	—	—	61	1	2	+	+
6	Bread, butter	435	448	430	—	—	BV (2pm)	—	18	2	1	—	+
7	Chocolate	289	149	298	—	—	—	B (1pm)	57	1	2	—	+
8	Bread, ham	440	557	440	—	—	BV (5pm)	—	21	2	1	—	+
9	Chocolate	298	75	298	—	—	BV (4pm)	—	22	2	1	—	+
10	Toast, butter	548	443	283	—	—	—	—	15	1	2	+	—
11	Cheese cake	879	340	289	DB	—	—	—	52	1	2	—	—
12	Biscuits	134	67	134	—	—	—	—	58	1	2	—	—
13	Chocolate	90	90	90	—	—	—	—	48	1	2	—	+
14	Cake	642	321	214	NB	—	—	—	NA	1	2	—	—
15	Cake	642	428	642	NB	—	—	—	38	2	1	—	+
Means		492	234	312					39.8				

Bulimic symptoms reported

DB Definite binge NB Near binge B Binge V Vomiting PLA placebo FEN Fenfluramine

CON Control subjects (Placebo)

eating. They completed the analogue scales every 30 minutes and after two hours, a sample of blood was taken and the subjects were presented with the same amount of the same food that had been consumed after placebo by the patients with whom they had been paired. They were asked to consume some of the food and to eat as much as they wished within 30 minutes.

Statistical comparisons were made as follows: Calories consumed at 2 hours were compared, using analyses of variance, to determine the effects of drug treatment and of order of presentation of the tablets and, to compare patients with controls. Correlations were derived by calculation of Pearson's r.

The number of patients who characterised the meal two hours after fenfluramine as a bulimic episode was compared with the number after placebo, using McNemar's Chi-squared test for non-independent samples (Hays 1973).

The McNemar test was also used to compare the incidence of bulimia, vomiting and laxative abuse in the first 20 hours after the tablets, this period representing the half-life of oral fenfluramine (Campbell 1971) and in the third 20 hours, when little or no pharmacological action would be expected.

The visual analogue scale results were compared, using an analysis of variance with repeated measures. The groups were drug, placebo (patient) and placebo (control), and the repeated measure was timed at 0, 30, 60, 90, 120 and 150 minutes, the last time being post-prandial.

In all analyses, differences were regarded as significant if $P < 0.05$.

Results

Eating at two hours: The number of calories consumed by patients having received fenfluramine was significantly smaller than their consumption after placebo. ($F(1,26) = 8.46$, $P < 0.01$). In the same two-way analysis of variance, there was no significant effect of order of presentation of drug or placebo. ($F(1,26) = 1.73$, $P > 0.1$).

In a one-way analysis of variance including the control group, there was a significant treatment effect ($F(2,42) = 5.69$, $P < 0.01$). Planned comparison t-tests of differences in mean calories consumed suggest that not only did patients eat more after placebo than after fenfluramine, but patients having had placebo ate significantly more than controls who received placebo and were presented with identical quantities of food ($t > 2.29$, $P < 0.05$).

After fenfluramine, there was a negative correlation between plasma drug level at 2 hours and calories eaten. (Pearson's $r = -0.50$).

Four of the patients (patients 1, 2 3 and 11) characterised their eating after placebo as a 'definite binge' and one of these (patient 3) induced vomiting on the ward. Two additional patients (14 and 15) reported that the meal had some qualities of a bulimic episode in that it was, for them, excessive consumption of a 'forbidden' food, but both felt that the quantity eaten did not satisfy their criteria for a 'binge'. They did classify them as 'near binges' and have been designated as such in Table II. One of these two patients, who ate 6 small chocolate rolls commented "I wanted to eat all 18, but knowing you would be back I was too much of a lady". One patient (4) induced vomiting immediately after

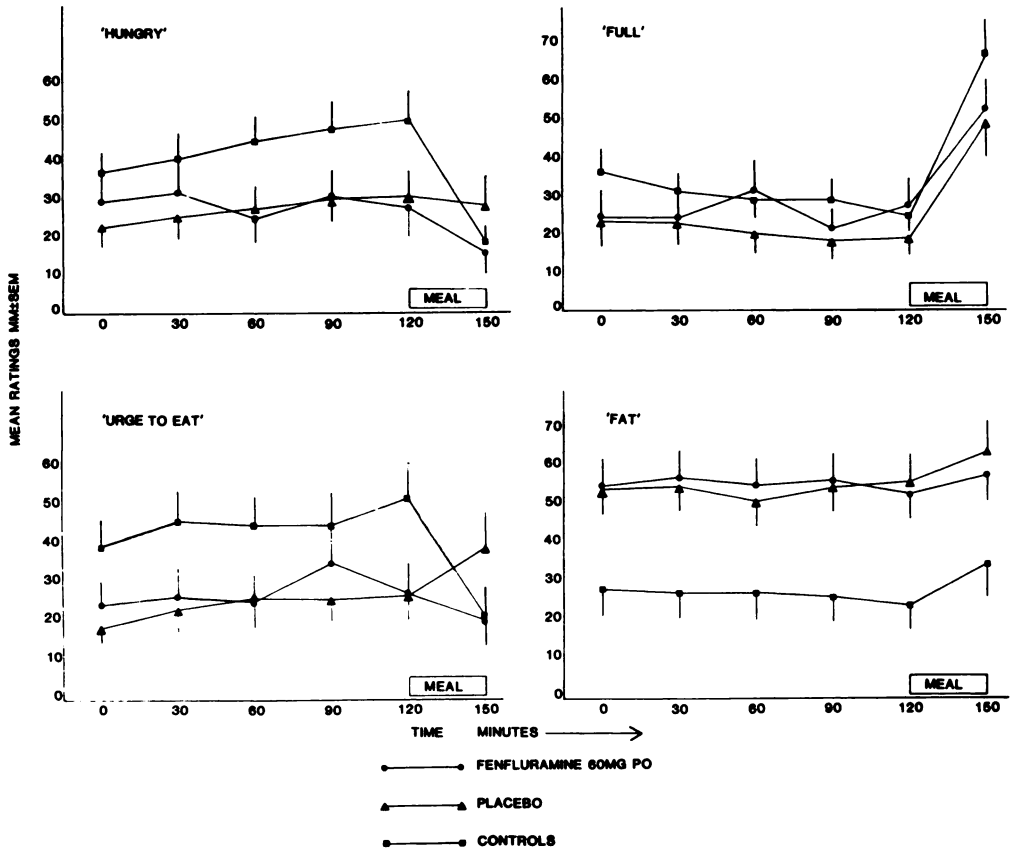

FIG. 1 Visual analogue scale results in patients (Fenfluramine and Placebo) and controls

leaving the ward while three more (6, 8 and 9) suffered bulimic episodes within four and a half hours of leaving the ward. In contrast, after fenfluramine, no patient complained that eating on the ward constituted a 'binge' or a 'near binge' and none admitted to inducing vomiting after the test. One patient (7) had a bulimic episode immediately after leaving the ward, having received fenfluramine. In summary, there was a significant decrease in the number of patients showing bulimic symptoms ('binges', 'near binges' and vomiting) on the ward after fenfluramine (McNemar Chi-squared = 4.17, df = 1, $P < 0.05$). The incidence of bulimic symptoms arising shortly after leaving the ward and experienced by the patient as closely linked to the meal taken during the test was also lower after fenfluramine, although the difference was not significant when this period is considered in isolation.

Eating in the four days following the test:

Bulimic episodes: There was no significant difference between the number of patients reporting bulimic episodes or episodes of vomiting or laxative abuse in the 20-hour period after placebo (7 patients) and fenfluramine (2 patients). Episodes occurring during the ward test were not counted in this comparison.

Other meals: Ten of the fifteen diaries gave sufficiently detailed information to allow some analysis of eating patterns, apart from bulimic episodes. There was no significant difference in the number of meals taken in the 24 hours after leaving the ward between drug and placebo. In view of the tendency of patients with bulimia nervosa to restrict carbohydrate intake, and the possibility that fenfluramine might result in an increase of this tendency, meals were classified according to their carbohydrate content (more or less than two slices of bread or equivalent). No significant difference between drug and placebo in the incidence of either type of meal emerged.

Side-effects

Ten patients complained of side-effects, either before or after leaving the ward, compared to two after placebo. (McNemar Chi-squared = 4.08, df = 1, $P < 0.05$). The most common effects reported after active drug were drowsiness, headache, and unsteadiness, while two patients reported euphoria. The effects were mild to moderate in severity, lasted a mean of 21.8 hours, and did not appear to be related to the plasma drug level. After placebo, one patient described headache and

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drowsiness and the other reported euphoria, and two control subjects described moderate loss of appetite for 48 hours.

Visual Analogue Scale Results

Analyses of variance with repeated measures provided tests of significance of effects of treatment (drug, placebo, control), time (0, 30, 60, 90, 120 and 150 min) and interaction between the two.

Patients rated themselves as increasingly drowsy throughout the test after fenfluramine compared to placebo, maximal at 120 minutes, reflected in a significant effect of treatment ($F(1,28) = 8.28$, $P < 0.01$) and time ($F(4,112) = 22.22$, $P < 0.01$). Hunger ratings showed no significant effect of treatment but a significant effect of time ($F(5,210) = 5.379$, $P < 0.01$) and a significant interaction ($F(10,210) = 2.20$, $P < 0.05$). Inspection of cell means shows that the effect of time is derived fom a reduction in hunger ratings which occurred after eating. However, the interaction effect reflects a difference in the reduction between groups.

Mean hunger ratings in controls fell 32.2mm (Planned comparison t-test: $t = 5.32$, $P < 0.002$), patients receiving placebo showed a mean fall of 1.7mm after food ($P > .25$) while after fenfluramine a mean fall of 11.7mm occurred ($t = 1.93$, $0.05 < P < 0.1$). These results suggest first that the patients were rating themselves on a hunger scale differently from controls, and secondly that fenfluramine tended to restore the normal fall in hunger ratings after food. The scale 'urge to eat' showed a pattern in controls very similar to the 'hungry' scale, with a mean fall of 31.6mm after eating. (Planned comparison $t = 4.91$, $P < 0.001$). Patients, having received placebo increased their ratings of 'urge to eat' by a mean of 11.8mm ($t = 1.83$, $0.05 < P < 0.1$) and after fenfluramine ratings fell by a mean of 7.1mm ($P > 0.25$). These varied responses are reflected in a significant interaction effect in the analysis of variance ($F(10,210) = 3.54$, $P < 0.01$).

Post-prandial ratings after placebo were compared with ratings after fenfluramine, using paired t-tests. 'Urge to eat' was significantly lower after the active preparation ($t = 2.56$, $P < 0.05$) and hunger ratings were lower after fenfluramine, compared to placebo ($t = 1.73$, $0.05 < P < 0.1$). In contrast, ratings of fullness showed a uniform increase after the meal under all three conditions, reflected in a significant effect of time ($F(5,210) = 24.45$, $P < 0.01$) but no difference between groups and no interaction.

In order to test whether the differences observed between the groups could be attributed to the different quantities of food eaten under the three conditions, correlation coefficients were determined between calories eaten and ratings of hunger, urge to eat, and fullness. The only correlation approaching significance was between the controls' post-prandial (150m) hunger ratings and calories consumed ($r = -0.45$, $P < 0.1$), indicating that the proportion of the variance in the ratings contributed by the differences in caloric intake was small. The foregoing results are summarised in Figure 1.

Results of the other scales reflect additional aspects of the patients' mental state. The scale 'fat' showed a significant treatment effect ($F(2,42) = 6.18$, $P < 0.01$) and a significant effect of time ($F(5,210) = 5.14$, $P < 0.01$). The patients rated themselves twice as 'fat' as controls, and subjects under all conditions increased their ratings after eating (Figure 1).

Patients rated themselves higher than controls on the scales 'sad' (mean ratings: patients 37mm, controls 12.6mm, $F(2,42) = 9.73$, $P < 0.01$) and 'tense' (means 31.6mm, 15.2mm, $F(2,42) = 4.9$, $P < 0.05$) and there was no effect of time and no interaction.

Discussion

In fifteen patients with bulimia nervosa, fenfluramine reduced the quantity of food consumed under laboratory conditions. This reduction in eating is consistent with previous reports of the drug's action in normal volunteers (Kyriakides & Silverstone, 1979) and suggests that, in terms of calories consumed, bulimic patients respond to fenfluramine in a manner comparable to normal subjects. The negative correlation between calories consumed and plasma fenfluramine supports a direct pharmacological effect upon eating behaviour.

Secondly, there appeared to be a significant reduction in abnormal eating during the test, reflected in a difference in the number of patients who described the experience as a 'binge' or a 'near binge'. It is clear that the definition of abnormal eating relies substantially on the subjective report of the patient, for which no standardised assessment is currently available. Characterisation of eating episodes was performed, using clinical assessment, taking into account the patient's description of the eating and accompanying affective changes. However, this measure is clearly subject to error.

Fenfluramine failed to produce a significant suppression of bulimic symptoms after leaving the hospital. Five patients suffered episodes of bulimia or vomiting shortly after leaving the ward and in all but one instance, these patients had received placebo. However, taking the immediate post-test period or the first 20 hours after the drug, no significant effect has been demonstrated. At least two factors may contribute to this. Firstly, the additional support of a hospital environment may be required for the drug to be effective and, secondly, plasma fenfluramine levels may, after several hours, have fallen below a therapeutic range.

The mechanism of action of the drug in suppressing eating in bulimic patients has not been clarified. In the previous study of Ong *et al* (1983), methylamphetamine resulted in enhanced alertness and euphoria and suppression of hunger. However, the

predominant effect of fenfluramine was drowsiness, euphoria was noted in only two patients, and while hunger ratings were reduced post-prandially, this effect failed to reach statistical significance. The effect that the two drugs share, and therefore the most likely mechanism whereby they suppressed eating, is a specific reduction in eating behaviour. The failure of fenfluramine, at the dose used, to suppress ratings of hunger significantly has been noted previously in normal subjects (Kyriakides & Silverstone, 1979), while other findings presented here, namely reduction of food intake and a variety of side-effects, are consistent with the known properties of the drug (Kyriakides & Silverstone, 1979, Silverstone *et al*, 1975). Moreover, the mean duration of side-effects in our patients, 21.8 hours, is consistent with the estimated plasma half-life of fenfluramine after a single administration, which is 20.3 hours (Campbell 1971).

Drowsiness ratings were significantly greater after fenfluramine. However, the suppression of eating seems unlikely to be due to this efect. It is conceivable that the presence of side-effects allowed patients to realise that they had received the active preparation, and thereby compromised the blind nature of the experiment. This possibility was not explored.

The apparent suppression of bulimic episodes seen after flenfluramine can be understood in a number of ways. Patients with bulimia nervosa frequently report that a bulimic episode will invariably follow the consumption of a certain threshold quantity of a high-calorie food. Fenfluramine may therefore act by suppressing food intake so that the threshold is not exceeded, and thereby prevent the triggering of a bulimic episode. Secondly, the action of the drug in suppressing bulimia may suggest that there exists, in patients with bulimia nervosa, a disorder of the neural control of eating behaviour which can be modified by drugs. Thirdly, the abnormal increase in 'urge to eat', seen after the meal in the bulimic patients, was partially reversed by the drug which may therefore act to facilitate mechanisms underlying satiety and thereby suppress bulimia.

The failure of hunger ratings to be suppressed by eating in patients with bulimia nervosa is a phenomenon that has not previously been described. Garfinkel (1974) found that patients with anorexia nervosa were less likely to report gastric fullness after a standard meal, compared to controls, while Robinson *et al* (1983) found patients with bulimia to have lower hunger and higher fullness ratings both before and after a standard meal, compared to controls. However, inspection of the data presented in the latter study suggests that their control subjects reported significantly reduced hunger and increased fullness following the meal, while the bulimics showed no changes in mean hunger ratings, but did significantly increase ratings of fullness. These are similar to the present findings and suggest an abnormality in the way patients with bulimia experience or report hunger which merits further study.

Apart from contributing to our understanding of the symptoms of bulimia nervosa, the study of the actions of appetite suppressant drugs may also lead to a useful treatment for this condition, which often resists therapeutic efforts. The present study provides evidence suggesting that fenfluramine influences bulimic symptoms, at least in a ward environment, and points to the need for a controlled trial of the drug given to out-patients over a period of several weeks. Such a study should be designed to monitor not only therapeutic effects of the drug in suppressing bulimic episodes, but also the possible adverse effects on dietary intake and mood.

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