

A DOUBLE-BLIND CLINICAL TRIAL TO TEST THE EFFECTIVENESS OF NORTRIPTYLINE IN CONTROLLING HOSTILITY IN THE MENTALLY SUBNORMAL HOSPITALIZED PATIENT

S. H. C. THOMSON, M.A.⁽¹⁾ and A. A. VALENTINE, M.B., CH.B., D.P.M.⁽²⁾

In the hospitals for the mentally subnormal, hostility is one of the main disrupting influences in the struggle for peaceful co-existence. However, in a recent paper, Bennett (1) claims that the drug Nortriptyline, which is mainly used as an anti-depressant, can control hostility—and he quotes the figure of a 69% positive response in this connection. In his own words: "The unusual finding was the decrease or alleviation in hostility beyond the usual decrease in irritability with other anti-depressants. Not only was this effect seen in hostility mixed with depression, but in hostility less obviously depression-related." Thus it was decided to give Nortriptyline a clinical trial, to see whether or not it would control hostile behaviour in the mentally subnormal hospitalised patient.

Although the manufacturers of Nortriptyline claimed that it embodied "anti-hostility activity," no definition of the term "hostility" was given, neither had any objective measurement of this trait been used in estimating the effects of the drug. This, in fact, is one particular point on which Nortriptyline was criticised in the Drug and Therapeutics Bulletin, November 15th, 1963—namely, that there was a need for objectivity in assessing mental illness and the change in mental illness. On this ground too, the use of such unscientific terms as "better," "equal," or "worse," with no objective measure is deplored.

As no scale exists for the measurement of such observed hostility, one was constructed. In a paper by Culbertson et al⁽²⁾ "hostility" is shown as serving quite different functions for different mentally subnormal individuals, and a former paper by Angelino & Shedd⁽³⁾ shows that mentally subnormal people tend to express hostility in much the same way as do normals, and although they could be assumed to utilise hostility in much the same way as normals, Culbertson also suggests that the personality characteristic of hostility is, in fact, multi-dimensional and that a population of individuals would be non-homogeneous in regard to this characteristic. They suggest that the measurement of hostility might be more accurate if individuals were classified in terms of the predominant function which hostility serves for them rather than in terms of the degree to which they exhibit hostile behaviour. However, this study was based on responses to items of a questionnaire, and the relationship between these responses and the actual behaviour of the subjects was not studied. In this trial it was the behavioural manifestations which were to be controlled and as no further exploration seemed to have been carried out on the above hypothesis, it was these aspects of hostility most in evidence and which prove most troublesome to the nursing staff that were utilised in the construction of the present scale. But it must be borne in mind that, as Culbertson et al⁽²⁾ have shown, individuals who appear to be equally hostile in much the same way in overt behaviour may in actuality perceive hostility very

(1) Assistant Psychologist, Leicester Area Psychological Service.

(2) Medical Superintendent, Glenfrith Hospital, Leicester.

differently and make use of it to satisfy quite different needs. This may prove helpful in future investigations.

As a basis for the construction of the rating scale, the multi-dimensional aspect was used in that two aspects of hostility, i.e. active hostility or outgoing aggressive behaviour and passive hostility or stubbornness, were utilised. Also, as there was evidence that mentally subnormals express hostility in similar ways to normals, several items from questionnaires standardised on normals were used. The main sources were four scales from the M.M.P.I. and after several questions had been chosen and altered to terms of a rating scale, several original questions which were directly applicable to the behaviour of subnormals were added.

The four scales used were:—

- (1) Schultz's "Hostility Control" scale.
- (2) Cook and Medley's "Hostility."
- (3) Schultz's "Overt Hostility."
- (4) Siegel's "Judged Manifest Hostility."

Scales 2 and 4 showed a considerable overlap of questions but in any scale, those not suitable for conversion to a rating scale applicable to subnormals were omitted. These selected and converted questions, and the original ones related to directly observable behaviour, and any which allowed of personal bias or projection were eliminated. Both aspects of hostility were included in the questions. The final questionnaire contained 44 questions, 42 of which were scored, and 2 of which were later used as a check for the validity of the scale. The majority of the questions were answerable in 3 ways, and the rest in 2 ways, thus allowing for "improvement" scores if the drug was successful. Each of the 3-choice items were scored according to the criterion—

Most hostile choice 5 points
Medium hostile choice .. 3 points
Least hostile choice 1 point

The 2-choice items were scored—Hostile choice 5 points
Non-hostile choice 1 point

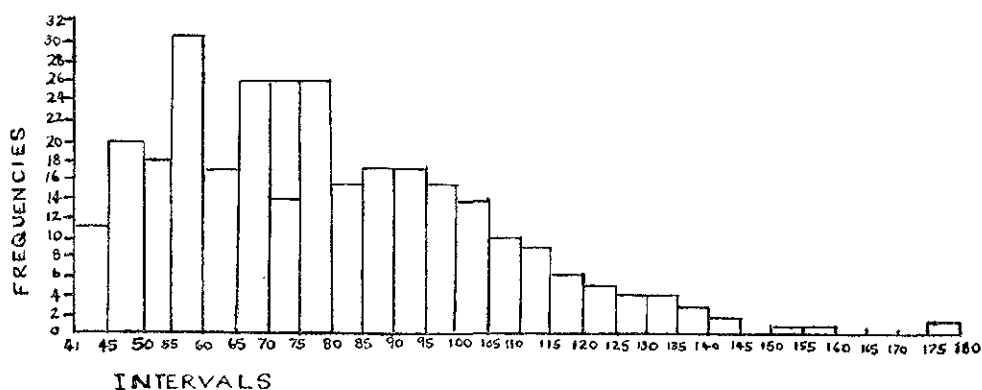
These were nearly all "all or none" items answerable by direct "Yes" or "No." The one question with 4-choice items was scored 5, 4, 3, and 1. Irrespective of whether the ratee's hostility was mainly active or passive, the most hostile choice in each item was given the highest score. This was found to increase the scatter of scores.

Several questions were really not applicable to many of the severely subnormal patients, who, for example, cannot speak, do not work, or are handicapped in some physical manner. However, as an absolute measure was required in these cases the patient was credited with the lowest scoring available for the particular item. Thus the possible range of scores was from 42 to 210—the lowest score indicating the very mild personality and the highest score indicative of the most hostile. For rating scale see APPENDIX.

The rating scale was then given to the Charge Nurses and Sisters on each Villa in the hospital and 294 patients were rated. After scoring each of them the actual range of scores was found to be 42 to 180. Tabulation showed that scores of hostility on this scale were not normally distributed in this population.

This may be due to the bias in that only hospitalised subnormal patients were rated, or it may be that if the submissive end of the scale had been explored more fully, the "hostility-submissiveness" dimension would have been more likely to approach a normal distribution.

TABLE I — DISTRIBUTION OF "HOSTILITY" SCORES IN S.N. POPULATION



Validity of Scale

Each final score was set against the criteria of the two check questions, and was put into the following categories:—

- Those rated as very aggressive and very stubborn — very hostile
- Those rated as mildly aggressive and mildly stubborn — mildly hostile
- Those rated as not aggressive and not stubborn — not hostile

The scores were then adjusted to nullify any overlap. Those scores which did not fit in exactly with the criterion were assigned to the categories as follows:—

- (a) Any rated as "very" either "aggressive" or "stubborn"—irrespective of the other rating, were assigned to the very hostile category and according to their scoring in the appropriate box.
- (b) Those then remaining were assigned to the category (Very Hostile, Mildly Hostile, etc.) of the higher rating of the check questions, and placed in the appropriate scoring range. A final table was then drawn up:—

TABLE II

Scores	Very Hostile	Mildly Hostile	Non-Hostile	Totals
180-107	42	5	0	47
106-72	32	87	4	123
71-42	5	52	67	124
Total	79	144	71	294=N

The Contingency Coefficient was then found to be 0.55, which is equivalent to a $X^2=126.64$, which is significant beyond the .001 level. Thus this scale can be said to be very valid.

Reliability of Scale

The reliability of the scale was done by the Split-Half technique and the reliability of the whole scale was computed using the Spearman-Brown Prophecy formula. The scale was split by calculating the scores of the odd-numbered items and of the even-numbered items. After rating the scores it was found to be equal to .85 and the reliability coefficient of the whole scale was .92, with a P.E. of .0102. This high positive reliability coefficient and the very low P.E. show this rating scale to be very reliable. Although no item is repeated, this high reliability coefficient may be due to the fact that there are similar questions or questions for similar areas in both halves of the scale. The scale is also fairly long, which increases the reliability.

Selection of Patients

When selecting the patients for the trial, all those who had been found to be psychometrically untestable were omitted, thus the I.Q. range was from 30 upwards to 90. Those on a "hostel" basis were also excluded, as they have relatively no supervision, have fairly responsible jobs in the hospital community, and have had no medication for several years. Because of possible effects from certain conditions or certain other drugs, those with diabetes, spasticity, Parkinsonism, Huntington's Chorea, hydrocephaly, microcephaly, and hyperthyroidism were also excluded. From the very hostile group were then chosen the 31 most hostile patients. From the mildly hostile group were chosen those in the range of scores from 80 to 98, i.e. the "mid-range" of mild hostility, thus eliminating in the mildly hostile group those tending to severe hostility or non-hostility. This then provided 2 separate experimental groups.

Those patients who were on medication already were kept on it, and the Nortriptyline thus served as a second drug. This was because of the practical difficulties which may have occurred in nursing the patients, and further because former trials of Nortriptyline on mentally subnormals had found the drug to be more effective when used in conjunction with phenothiazines. Four patients refused the drug and could not be persuaded to take it at all:— 3 of these came from the very hostile group and 1 from the mildly hostile group—further confirmation of their very hostile behaviour. The final number of patients completing the trial was 72—31 from the very hostile group and 41 from the mildly hostile group.

Method of Trial

The patients were divided randomly into two groups and a double-blind trial was carried out for 6 weeks. During the initial 3 weeks, half the patients were given Nortriptyline and the other half were given a placebo, which had been specially prepared to look in every way like the Nortriptyline tablet itself. Over the final 3 weeks the groups were reversed and those receiving Nortriptyline initially were then given the placebo and vice versa. Only the pharmacist knew which patients were on which tablet.

The dosage was Nortriptyline tabs. 25 mgs. t.d.s. and although several patients reported side effects such as dryness of the mouth and dizziness none of these effects was severe enough to warrant discontinuation of the drug.

After the first 3 weeks, the patients were re-rated on the original scale—on which was an additional question which was thought may give further information on the effects of Nortriptyline. At the end of the following 3 weeks—the patients

were rated for the third time. In spite of steps taken to try to ensure uniformity of raters, this was not always possible on account of illness and movement of staff: but whenever possible each patient was rated 3 times by the same rater.

Results

Each patient was used as his own control in this experiment, and in order to utilise information regarding relative magnitude as well as direction of differences between scores from rating after administration of the drug and after administration of the placebo, the statistic used was T—calculated by the Wilcoxon matched pairs signed-ranks test.

Tabulation of Results

TABLE III

	T	P	
Very & Mildly Hostile Group	-.96	.1685	Not significant.
Very Hostile Group	-1.04	.1492	Not significant.
Mildly Hostile Group	-2.35	.0094	Significant at .01 level for placebo.

From Table III the only significant result is in the mildly hostile group where T is significant at .01 level, but for the placebo and not the drug. The reason for this, however, proved very difficult to trace as there were no significant differences either in age or I.Q. between those in the mildly hostile group, who responded to the placebo, and those who responded to Nortriptyline. There are tendencies for the other groups to be subject to a placebo effect, but this does not reach significant proportions.

There is a significant difference in age, however, between 6 patients in the mildly hostile group, to each of whom had been assigned comments showing their behaviour to have been adversely affected by Nortriptyline. Mean age for these patients was 17.5 years: S.D.=4.9 against a mean age of 37.7 for the rest of the mildly hostile group. It would seem then that the younger the patient in the mildly hostile group, the more likely he is to become more hostile on the drug. The sample is very small, however, and this finding should not be generalised. These patients may be similar in some way to those described by Bennett⁽¹⁾ in whom the "hostility became directed outward" and they therefore became more amenable to psychotherapy. As the mean I.Q. for this sub-group is only 38 it is not very likely that such a reaction would be beneficial to these patients.

The Mann-Whitney U Test was used to test for any significance of difference in both age and I.Q. between those who improved on the drug and those who did not in both the very hostile and mildly hostile groups. U was also calculated to test for significance of difference between those who improved on Nortriptyline in very hostile group and those improving in mildly hostile group:— similarly for those improving on placebo in the two groups. None of these findings reached the level of significance, but there was a tendency in the mildly hostile group for the older ones to improve on the drug.

The following 2 × 2 table was drawn up to test any significance between those who were already on drugs + Nortriptyline, and those who were not on drugs but responded to the placebo—for both groups.

TABLE IV

	Improved on Nortriptyline	Improved on Placebo	
With other drugs	10	17	27
Without other drugs	22	19	41
	32	36	68

$X^2=1.8$ was not significant—thus it may be concluded that in the control of hostility Nortriptyline's effect is not enhanced if the patient is taking other drugs—whether phenothiazines or barbiturates—simultaneously.

Conclusion

It was found from the present trial, that Nortriptyline is not effective in controlling hostility in the mentally subnormal hospitalised patient. In fact, in several of the younger ones who were classed as mildly hostile, their hostility appeared to be more in evidence while having Nortriptyline. Although Bennett⁽¹⁾ finds this to be a therapeutically desirable effect, this would not seem to be the case with the patients on this trial, because their intellectual levels are so low (mean I.Q.=38) that psychotherapy would have little or no effect on their behaviour. Generally it was found that there was a tendency for the patients to respond to the placebo and that even the actual Nortriptyline had a similar placebo effect. There were no other findings of significance.

Summary

A double-blind clinical trial was set up to test whether or not Nortriptyline was effective in controlling hostility in the mentally subnormal hospitalised patient. The patients most suitable for the trial were selected after they had been rated on a scale, specially constructed for measuring hostility. Nortriptyline was not found to be effective in controlling this aspect of behaviour and, in fact, some of the younger subjects rated as mildly hostile became more hostile while taking the drug. It did not even prove effective in those patients who were taking phenothiazines or barbiturates simultaneously.

Acknowledgements

We would like to thank Dista Products Ltd. for supplying us with Nortriptyline in order to carry out this trial, Mr. S. Taylor, F.P.S., for his help in coding and distributing the drug and all nursing staff of Glenfrith Hospital for their co-operation in nursing and rating the patients during the trial.

References

- (1) Bennett, Ivan F. "The Constellation of Depression: its treatment with Nortriptyline. II: Clinical Evaluation of Nortriptyline." *J. Ment. and Nerv. Disease.* 1962, 135, 59-68.
- (2) Culbertson, E., Guthrie, G. M., Butler, A. J. and Forlow, L. "Patterns of Hostility among the Retarded." *Amer. J. Ment. Defic.* 1961, 66, 421-427.
- (3) Angelino, H., and Shedd, C.L. "A Study of the Reactions of 'Frustration' of a Group of Mentally Retarded Children as measured by the Rosenzweig Picture-Frustration study." *Psychol. Newsletr., N.Y.U.,* 1956, 8, 49-54.

APPENDIX

Rating Scale

This is a shortened form of the original rating scale on which was rated almost the entire hospital population. To test the effectiveness of the drug, which several of the patients are now having, it is essential to rerate each of the patients on the trial on this scale. The procedure is the same as before viz:— Go through the questionnaire, rating the patient according to the criteria given by drawing a line under the one alternative which you think best describes the patient's behaviour over the past 3 weeks (i.e. the length of time s/he has been on the drug).

e.g.: If the patient has smashed things occasionally over the past 3 weeks, the answer to Question 13 would look like this: 1. Often. 2. Sometimes. 3. Never.

Patient's Name Villa

- | | |
|--|---|
| 1. When someone speaks sharply to the patient does (s)he automatically answer back ? | 1. Frequently. 2. Sometimes. 3. Never. |
| 2. Does patient get mad easily and then get over it soon ? | 1. Yes. 2. No. |
| 3. Is the patient a | 1. Very poor mixer ? 2. Poor mixer ?
3. One who mixes fairly well ? |
| 4. Does patient ignore requests or commands from the ward staff ? | 1. Frequently. 2. Sometimes. 3. Never. |
| 5. Is the patient | 1. Very impatient ? 2. Slightly impatient ?
3. Not impatient at all ? |
| 6. Can the patient be described as hot-headed ? | 1. Yes. 2. No. |
| 7. Has patient absconded at least once during past 3 weeks ? | 1. Yes. 2. No. |
| 8. Does patient hide his/her tablets instead of swallowing them ? | 1. Frequently. 2. Sometimes. 3. Never. |
| 9. Is patient's swearing | 1. Very frequent ? 2. Rather frequent ?
3. Normal ? 4. Very infrequent ? |
| 10. Does patient consistently break rules ? | 1. Yes. 2. No. |
| 11. Does patient pick fist fights with other patients ? | 1. Frequently. 2. Sometimes.
3. Seldom or Never. |
| 12. Does patient wait for someone to speak to him/her before (s)he speaks to them ? | 1. Always. 2. Sometimes.
3. Seldom/Never. |
| 13. Does patient smash things ? | 1. Often. 2. Sometimes. 3. Never. |
| 14. Is patient's ward behaviour consistently bad ? | 1. Yes. 2. No. |
| 15. Is patient cross and grouchy ? | 1. Frequently. 2. Sometimes. 3. Never. |
| 16. Does the patient "natter" ? | 1. Frequently. 2. Sometimes. 3. Never. |
| 17. Has the patient been in trouble with the law within the past 3 weeks ? | 1. Yes. 2. No. |
| 18. Is patient destructive with bedding and/or upholstery ? | 1. Frequently. 2. Sometimes. 3. Never. |
| 19. Is patient rude to other patients ? | 1. Frequently. 2. Sometimes. 3. Never. |

20. Does patient tear his/her clothes or tear off "accessories" such as buttons ? 1. Frequently. 2. Sometimes. 3. Never.
21. Does patient physically attack other patients ? 1. Frequently. 2. Sometimes. 3. Never.
22. Does patient consistently avoid more than one other person on ward ? 1. Yes. 2. No.
23. Is (s)he inclined to be impatient when interrupted from a job of work ? 1. Frequently. 2. Sometimes. 3. Seldom/Never.
24. Has patient injured herself/himself for no apparent purpose (excluding accidents) within the past 3 weeks ? 1. Yes. 2. No.
25. Does (s)he poke fun at other patients ? 1. Frequently. 2. Sometimes. 3. Seldom/Never.
26. Is patient 1. Very easily angered ?
2. Easily angered ?
3. Not very easily angered ?
27. Is (s)he reluctant to enter into conversation with staff ? 1. Frequently. 2. Sometimes. 3. Seldom/Never.
28. Does patient quarrel with other patients ? 1. Frequently. 2. Sometimes. 3. Never.
29. Does patient offer resistance to tablets or any form of treatment ? 1. Frequently. 2. Sometimes. 3. Never.
30. Has patient sexually assaulted anyone within the past 3 weeks ? 1. Yes. 2. No.
31. Does patient "act out" either by himself/herself or with others any aggressive scenes (s)he has watched on T.V. or seen or read in pictures or stories of in papers or books ? 1. Often. 2. Sometimes. 3. Never.
32. Is the patient physically rough with people ? 1. Frequently. 2. Sometimes. 3. Never.
33. Is (s)he rude to ward staff ? 1. Frequently. 2. Sometimes. 3. Seldom/Never.
34. Does patient do the opposite of what (s)he is requested or told to do ? 1. Frequently. 2. Occasionally. 3. Never.
35. Does patient physically attack ward staff ? 1. Habitually. 2. Occasionally. 3. Never.
36. Does patient have periods when (s)he is mute ? 1. Yes. 2. No.
37. Does patient tell lies ? 1. Frequently. 2. Sometimes. 3. Seldom/Never.
38. Is (s)he prone to temper tantrums ? 1. Frequently. 2. Sometimes. 3. Never.
39. Does patient quarrel with staff ? 1. Frequently. 2. Sometimes. 3. Seldom/Never.
40. Is patient 1. Very easily annoyed ?
2. Easily annoyed ?
3. Not easily annoyed ?
41. Does patient do harmful or shocking things ? 1. Frequently. 2. Sometimes. 3. Never.

42. Does patient injure other people ?

1. Frequently. 2. Sometimes. 3. Never.

43. Would you say the drug had affected the patient's behaviour in any way, other than in those ways already mentioned in questions 1—42.

1. Yes. 2. No.
(If the answer is "Yes" describe the change(s) of behaviour noticed in the space below.)

Signature of Rater