

## THE EFFECT OF CHLORPROMAZINE ON VERBAL AGGRESSION.

By

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In the ten years which have elapsed since the end of the war, many interesting compounds have been synthesized in France from the aromatic base phenthiazine. They exhibit pharmacodynamic antagonisms of a specific kind to such tissue hormones as adrenaline, histamine, and acetylcholine, and they modify CNS activity in a highly specific way. After protracted trials in almost every field of medicine and surgery, many of these compounds have been soundly established as safe useful remedies in a variety of common clinical conditions, and many of them are well known to us in the U. K. and frequently prescribed under their specific trade name.

Exactly five years ago, the therapeutic potentialities of this group were further extended by the synthesis of a new compound which, in terms of broad spectrum usefulness has completely overshadowed the reputation of its parent and siblings. Produced to the formula: 3-chloro-10-(3'-dimethylaminopropyl)-phenthiazine hydrochloride, it entered the French Codex under the name chlorpromazine, and has since received extensive use on the continent. Available in the U. K. under the trade name "Largactil", its many uses, successes, side-reactions and contra-indications are already wellknown, and the published literature appertaining to its clinical and experimental employment runs into many hundreds of papers, and need not be cited here. It possesses an intrinsic analgesic activity which differs from that of the other drugs of this class, in that it appears to produce an indifference rather than an insensitivity to pain, and additionally it possesses a vagolytic and spasmolytic activity for which the term "neuroplegic" has been coined.

Although its particular pharmacology has led it into a variety of medical channels, it has been the centre of widespread interest in psychiatry, and although much of the enthusiasm which greeted its first appearance has abated, it has now established itself in the treatment of mild stress disorders encountered in general practice. O'Neill (1955) estimates that about one quarter of the patients going to their doctor in an urban practice, and about one fifth of those in a country practice, are suffering from some disorder of bodily function or structure associated with emotional tension. Chlorpromazine has a number of important actions on those emotional functions connected with tension, in particular, that of aggression. There is

plenty of evidence to support the fact that this drug does reduce clinically observed overt aggression and some of the more recent work has been described by Charaton (1954), Denber (1954), Friedgood (1955), Trethowan and Scott (1955), Vaughan (1955), Bonafede (1955) and Bair and Herold (1955). In order to shed some light upon the way in which aggression is reduced, a test of verbalised aggression was given to patients undergoing chlorpromazine therapy and the results analysed. A comparison was then made between these results and those obtained from a clinically similar control group of patients for whom chlorpromazine had been contra-indicated for one reason or another (based on the table of contra-indications kindly supplied by Messrs. May and Baker, Ltd.).

### Sample

The sample consisted of 50 patients diagnosed as psycho-neurotic and for whom chlorpromazine therapy had been recommended, together with 50 other patients reasonably well matched for age, sex, and diagnosis, who formed the control group.

The distribution of these characteristics between the two groups was analysed statistically by means of the six by two contingency table, the resulting value of chi square showing that differences were attributable to chance rather than selection.

The dose prescribed for the experimental group was 75 mgms. t.d.s. orally in each case, and this was decided by the psychiatrist in charge before it was known that any particular patient would be included in the experiment. That is, the selection of the sample was subordinated to the therapeutic needs of the patient, and for this reason, the experimental sample proved to be less than 20% of the original sample under consideration for this research.

### Method

Each patient received a psychological assessment before the commencement of therapy, and then six weeks later when the chlorpromazine medication was terminated. The assessment was by means of the Rosenzweig Picture Frustration Test, designed by Rosenzweig (1954) to provide a somewhat subjective but statistical analysis of an individual's reactions to frustrating situations likely to be encountered in real life. The test consists of 24 sketches illustrating commonplace but highly frustrating situations, the figures being vague enough to permit a degree of projection to take place. The frustrating figure makes some remark (by means of the inevitable cartoonist's balloon) which throws blame upon the frustrated figure: or which serves to accentuate the frustration, and thus stimulates him to make a verbal response. The subject is invited to write in the blank balloon emerging from the frustrated figure's mouth an appropriate response which he, as the person involved,

would ordinarily make. The test sheets were scored in a conventional manner in conformity with the Rosenzweig notation (1947), using the revised norms, (Rosenzweig, 1949); in addition, each patient received a 'verbal aggression' score, one point being allotted for each unequivocal aggressive response, with a maximum of 24, (one per picture). Holzberg et al (1955) have shown that the reporting of aggression in a projective situation is a valid indication of aggressive tension, so that we may consider the aggression score as a quantitative assessment of aggressive tension existing within the individual. This score correlates highly with the sum of the scores of intro-punitive and extropunitive frustration obtained by means of the Rosenzweig scoring system.

### Results

In the following tables are shown (a) the differences in scores between the experimental and control groups before therapy, (b) the differences in scores after therapy, and (c) the differences in the scores of the experimental group only, as obtained before and after therapy.

**Table I**

Scores of Neurotic Patients before therapy			
Score	Experimental	Control	Difference
Intro-punitive	6.9	7.1	N. S.*
Extropunitive	9.8	9.3	N. S.
Aggression	14.9	12.6	N. S.

**Table II**

Scores of Neurotic Patients after therapy			
Score	Experimental	Control	Difference
Intro-punitive	10.7	8.9	N. S.
Extropunitive	3.5	9.9	0.1†
Aggression	12.9	17.2	0.5

\*N. S.—Not Significant

†P. Value.

**Table III**

Changes in Scores of Neurotic Patients after receiving chlorpromazine therapy			
Score	Before therapy	after	Difference
Intro-punitive	6.9	10.7	0.5
Extropunitive	9.8	3.5	0.1
Aggression	14.9	12.9	N. S.

## Discussion

The results tabulated above show a distinct, though not necessarily causal, relationship between the responses of patients on this test and chlorpromazine medication. Contrary to expectation, the score of verbal aggression, which is taken here to indicate aggressive tension existing within the individual has not decreased by a statistically significant amount during the six weeks' therapeutic period. In fact, there has been an increase in the aggression scores of the control group, and it is this that has provided a statistically significant difference between the two groups being studied. Examination of table II shows that there has been a counterbalanced swing in scores, with a marked decrease in extropunitive frustration and an increase in intro-punitive frustration. In so far as these scores can be validly related to the psychological variables whose name they bear, the interpretation of these findings is that during the therapeutic period the aggressiveness of the patient has been internalised. If this is true, it means that chlorpromazine has not reduced aggression, but has changed its valence from object to subject, the clinical manifestation being represented as a change from overt to covert aggressivity. The change in the intro-extro punitive balance confirms the suggestion of Holzberg (op cit.) that the psychiatrically more passive individuals tend to show high aggressive tension in terms of differential learning scores. Holzberg and his co-workers have repeatedly found that the more passive individuals are charged with greater aggressive tension than individuals who show more overt aggression within normal limits. Such former individuals are classified by Holzberg as "under-reporters" of aggression, the under-reporting of such individuals is unlikely to affect the scoring in the present experiment since the tasks are quite different. In Holzberg's experiment, the subjects were handling an ambiguous situation whereas in the present instance the situation was quite clearly defined; the projection, in so far as it occurred at all, took place in a fully structured situation, similar to the condition which obtains between cinema audience and screen picture. This relation between verbalised aggression to a structured and semi-structured stimulus carries an implication of importance in clinical work; it suggests that the clinician interested in finding out how his patient handles his personal aggression can obtain useful information in two separate and distinct situations—one being structured and fully-defined, the other semi or unstructured and permitting considerable projection, as in the Thematic Apperception Test. There seems to be no reason why the appropriate situation-setting stimulus should be confined to the visual field, although data at present are confined to this sensory modality.

A cautionary word must be introduced at this point concerning the test-retest-reliability of the Rosenzweig Picture Frustration Test when applied to clinical samples. Although there are no adequate norms available relating to British clinical populations, the writer has noticed that considerable

variation exists in the scores obtained from any one patient in a consecutive series of administration. The effect of such variation if existing in the present sample used here would be to reduce the significance of the results by an unpredictable amount. Some attempt has been made to assess the intra-individual S. D. for the patients concerned, during a follow-up period, but because of discharges and transfers it proved impossible to obtain complete data, and modification of the statistics was therefore unwarranted.

As far as the pharmacological aspects of the drug's apparent reduction of overt aggression is concerned, there is little that can be said at present. The physiological concomitants of aggression are not clearly enough defined at present to permit us to discuss possible mechanisms by which these results could be brought about. We can expect that the anti-adrenaline factor of chlorpromazine may play a part as also will the particular characteristics which assist its sedative and depressant effects. Some light on this problem may also be shed by the work of Sigwald and Boutier (1953) who have shown that this drug has the property of inhibiting in the rat, conditioned reflexes which had previously been established. This study on the rat gives some indication of the way in which this compound may act, supported by clinical findings by these and other investigators. These findings suggest that chlorpromazine establishes some blockade between stimuli (both internal) and external) and their conscious perception. Laborit (*op cit.*) describes its action as a chemical blockade between cortex and diencephalon, and explains that it is this blockade which effects the inhibitory properties of the drug. It is because of this that its pain-relieving effects are situated, to some extent at least, in the higher integrative levels, and this makes clear its action in what has been termed "functional" or "temporary" leucotomy. Can the results of the present study be interpreted in the light of this pharmaco-neurological mechanism? In the writer's opinion they can. One possible explanation that can be offered is that in producing this chemical blockade between diencephalon and cortex, neural influences on motor activity which arise from the so-called emotional centres of the hypothalamus are minimised. This would be seen as a reduction in overt behaviour, which indeed proves to be the case. On the other hand, the blockade still permits the use of cortico-cortical association fibres; if we accept that the 'super-ego' functions involved in guilt feelings and self-condemnation arise, or at least have concomitant neurological activity, in the frontal lobes, it is reasonable to suppose that intropunitive feelings would be unaffected by such a blockade. There is a large body of evidence which supports such a supposition derived from the many reported cases of leucotomy in which the guilt feelings which have formed a prominent and often the predominant—feature of the disabling mental condition have been relieved by psycho-surgery in which these particular areas have been partially or wholly isolated. The picture is by no means as simple as this explanation would suggest, however, for some of the

physiological effects in the cortex produced by chlorpromazine show a binomial curve of effect with dosage. Cortical chronaxie, for example, is first increased with chlorpromazine medication, and then gradually becomes reduced with higher dosages. This finding has been interpreted as representing a sensitivity difference between cortex and the mesencephalic chronaxie regulatory centres—that is, that a selective action exists in the basal centres. Surveying the literature on the neurological effects of this drug, particularly the extensive work which has been completed in the French animal laboratories, one comes to the conclusion that the mechanisms involved are much too well integrated into total nervous functioning to permit ready isolation of effect. However, the clinical cases that have been reported in the last pentade support the hypothesis of this differential blockade between affectivity and super-ego functions. Delay et al (1952) describe a number of case-histories in which these functions are prominent in the symptomatology. The patients concerned are described as “being over-conscientious”, “having doubts about ability at work”, “pre-occupied with questions of conduct” and so on, which existed in a setting of depression or diffuse anxiety. After medication, the patients became euphoric, their depression lifted, and their anxiety disappeared. Important from the present point of view, however, is the fact that their *ruminations often returned, but without any affective loading!* Clinicians with experience of leucotomised obsessional and phobic patients will readily recognise this situation, and will understand how chlorpromazine gained the appellation of “functional leucotomy”.

#### SUMMARY

The Rosenzweig Picture Frustration Test was administered to 50 psychoneurotics before and after a course of chlorpromazine therapy, and to a matched group of 50 psychoneurotic patients receiving conservative treatment only. The degree of verbal aggression, and intropunitive and extropunitive frustration was assessed and compared. No statistically significant difference was found between the two groups before the therapeutic period, but afterwards the experimental group showed a decrease in extropunitive responses and an increase in intropunitive responses. Caution in the acceptance of this data is suggested, and an interpretation is offered based on the hypothesis of a chemical block between cortex and diencephalon. Such a block should permit the continuance of frontal lobe functions but should minimise the affective loading by reducing corticofugal signals proceeding from the hypothalamus. Clinical findings in which overt aggressive behaviour and the emotion connected with psychoneurotic ruminations etc., are reduced by chlorpromazine support this explanation, although the difficulty in devising a simple physiological model is stressed. Clinical behaviour is seen to approximate very closely to the hypothetical psychological substrate suggested by the findings of this study.

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