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Effects of Chlorpromazine and Trifluoperazine on the Activity of Chronic Schizophrenics

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There is a widespread belief among clinicians that trifluoperazine (Tr) is more effective than chlorpromazine (Ch) in activating retarded schizophrenic patients. We examined the effect of these two drugs on the motor activity of three groups of inactive patients: A, very inactive; B, moderately inactive and C, mildly inactive. All these patients were under 60, with at least 10 years duration of illness. We excluded those with subnormality or physical illness and those who had a leucotomy. They were all sufficiently inactive to fall below the mid-point on the Venables scale (Venables, 1957), so that an increase in activity constituted an improvement. The same supervisors and raters were used throughout and attempts were made to maintain the work environment as constant as possible. The raters did not have access to their earlier scores.

Motor performance was measured: (1) by assessing quantity and quality of work at a factory type of task; (2) by use of the Venables activity-withdrawal scale (Venables, 1957 *J. ment. Sci.*, 103, 197), before the experiment and at the end of each phase. The patients worked in three groups of 12, with the same supervisor throughout: initial placebo period of six months, 10 patients placebo (Pl), 2 Ch; phase 1, six weeks, 6 Ch 6 Tr; phase 2, six weeks, 12 Pl; phase 3, six weeks, 6 Tr 6 Ch.

Before the initial placebo period, the level of treatment with Ch or Tr considered optimal, ranged from 200 mgm. to 600 mgm. Ch and from 20 mgm. to 60 mgm. Tr per day. During the experiment these 'optimal' dosages were used. Drugs and placebo were identical in appearance. The patients were not told when changes in medication were being made.

Results

Performance at the factory task has been analysed in terms of (a) the weighted mean task error, that is, the ratio of the total error per minute to the total number of pieces produced, giving a general measure of performance; (b) the total quantity produced in unit time, giving a measure of the speed of work; (c) the mean error giving a measure of the accuracy of work. The effect of drugs was examined by analysis of covariance within groups. Statistical data can be made available on request to the authors.

(a) *Weighted mean task error.* Significant differences between drugs were found in two instances, half of groups B and C (the more active groups) but the direction differed in the two groups, the drug which was given first was significantly better than the other ($p < 0.01$ and $p < 0.025$). This order effect was evident in the other halves of these two groups, but it did not reach significant levels there. With groups treated as wholes, non-significant changes with time were observed in C and B. Group A behaved differently: there was no difference between drugs, and performance rose progressively throughout the experiment. It was significantly better ($p < 0.05$) at the end than at the beginning. Their performance showed no tendency to fall off after 18 weeks, but the greatest increment occurred during the intervening placebo phase (phase 2).

(b) *Quantity produced in unit time.* This was examined by analysis of covariance within groups. There was no significant difference between drugs. The most inactive group (A) showed a pattern similar to that seen with the weighted mean task error. The other two groups, while starting the experiment at a much higher level of performance than group A, finished it with virtually the same means that they started with and showed less change during the intervening placebo phase.

(c) *The mean task error.* Differences between drugs were examined for group C only. No significant difference was found. Group C as a whole did show a significant ($p > 0.01$) improvement in quality of work during phase 1. This improvement was maintained during the placebo phase and then lost again during phase 3. Group B showed a similar initial improvement which was not maintained during the placebo period or later. No changes reached significant levels. Group A behaved differently, showing an initial deterioration and thereafter steadily improved both during the intervening placebo phase and during phase 3 ($p < 0.05$).

The Venables Scale. This is a measure of general motor behaviour. It showed no significant difference between drugs within the groups or between crossover periods, when examined by analysis of variance and by the Friedman test. A small increase in score (an improvement) occurred during phase 1 on

both drugs. While the increment was small (weighted average of 26·62 rising to 27·30) it was highly significant ($p < 0·01$). During the Pl phase (phase 2) relapse as indicated by a fall in score means was seen with those treated during phase 1 with Ch but not with those treated with Tr. During phase 3 the scores remained virtually constant, with the result that comparison between the scores at the end of phases 1 and 3 showed a significant ($p < 0·05$) fall in performance, although the numerical difference (weighted average of 27·3 to 26·63) was small. The difference between drugs was least apparent with the most active group.

When pre-treatment and treatment scores were compared a significant difference ($p < 0·01$) was found, scores being higher, i.e. better, on drugs, although the increment in mean score (26·2 to 27·3 per session) was again small. Similar findings were obtained when the two factors, motor and social, on this scale were examined differentially. All correlations between these factors were positive, but they became closer as the experiment progressed (details available on request).

Conclusions

Taking even this restricted group of patients, the aim of establishing clear cut differences between the drugs has not been achieved. The most clear cut finding was that no statistically significant difference was found between the ability of the two drugs, chlorpromazine and trifluoperazine, to improve motor activity in underactive schizophrenic patients. There were however, a number of observations which may be of interest. For the more active patients an overall measure of performance at the factory task showed an inconstant and non-significant initial improvement with both active drugs with maximum effect at the end of six weeks. Thereafter performance deteriorated, and when active drugs were reintroduced this deterioration was not reversed. The less active behaved differently. At the factory task they improved progressively throughout the experiment, but the greatest increment in their performance occurred during the Pl phase.

No group's speed of work was changed differentially by the two drugs. The least active group A increased their speed of work more during the six weeks Pl phase than at any other time; Group B showed similar improvement during the Pl phase, but did not improve further when drugs were reintroduced; Group C showed virtually no change in speed of work during the three phases of the experiment.

When on drugs there was a small but highly statistically significant improvement over pre-drug scores on the Venables scale, indicating that the two drugs were effective. No significant difference between drugs was found, and after the first six weeks of treatment the maximum response was reached, with some worsening thereafter.

There is a strong suggestion that the worsening in behaviour during the intervening placebo phase seen on the Venables scale occurs only in those previously treated with chlorpromazine. To this extent, therefore, trifluoperazine is to be preferred as a treatment. On this scale, as with the factory task, gains in behaviour obtained during the first six weeks of treatment were not repeated during the latter part of the cross-over.

Strenuous attempts were made to maintain the environment constant for all groups, so that it is unlikely that chance environmental stimulation could be the sole explanation for these changes. A more likely explanation seems to be that, for the very inactive, once new patterns of behaviour have been initiated with the aid of drugs further improvement may occur without continuous medication. For the more active, however, starting drugs may also produce a temporary improvement, but the improvement is inconstant, it does not last as long and may be lost even when drugs are continued. Intermittent medication is evidently effective for inactive patients and may be advantageous. The more active seem to be improved to a much smaller extent by these drugs.

The correlation, steadily increasing with treatment, between the two factors of the Venables scale suggests that both drugs have a beneficial effect on another puzzling aspect of the chronic schizophrenic: the differences between tests within individuals which they show on most measures of behaviour. This is an area of performance of importance therapeutically, but one which hitherto has been neglected in drug studies. We found no evidence to suggest that intermittent medication would have an adverse effect on this aspect of behaviour.

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