WHAT DIFFERENTIATES A DIFFERENTIAL PSYCHOPHARMACOLOGY?

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ABSTRACT

The methodological implications of a differential psychopharmacology are discussed. It is shown that the technique of stratifying subjects with personality scores depends on one basic assumption: the personality score is not affected by the other experimental factors. Two experiments are reported in which pre- and posttest (after the experiment) scores were measured. The pre-post-differences showed themselves to be affected by the medication. It is argued that in psychopharmacological experimentation an additional step must be included. All non-treatment factors must be examined for their stability in the course of the experiment. If they are stable, usual evaluation may take place. If changes are attributable to the treatment, personality scores must be regarded as dependent variables. They have to be evaluated together with the other observables with a multivariate model. Additionally, a procedure like this yields as "experimental differential psychology" a self-reliant contribution to the problems of differential psychology.

KEYWORDS

Differential psychopharmacology; differential psychology; drug-personality interaction; methodology of differential psychopharmacology; personality traits; neuroticism.

I. THE PATTERN OF EXPERIMENTATION IN PSYCHOPHARMACOLOGY

The general pattern of experimenting in psychopharmacology is given by the expression

$$R = f\ (D,S)$$

where R = reaction, D = drug and S = situation. The effect in R is interpreted as a consequence of the factors D and S, given by independent definition in physical (e.g. db white noise) and chemical (e.g. 5 mg from a benzo-diazepine) terms. The differential approach in psychopharmacology (as introduced by Eysenck, in Germany by Lienert and Janke) is comparable with the evolution from behaviorism to neo-behaviorism. A "cognitive" element named personality is inserted in

the formular above:

$$R = f\ (D,S,P)$$

with P = personality. This pattern is also instructive for the way in which experiments are conducted. Since D,S, and P as factors can be varied independently, experiments in psychopharmacology are regularly *multifactorial*. Our further considerations will emphasize above all the consequences of this model for the experimental design.

In psychopharmacology a large number of results extended the influence of the two independent factors personality and situation. First these factors were thought to be only modifying the drug response, but more and more a constitutive function was noted.

In a systematic overview, Janke and Debus demonstrated (Debus and Janke, 1978; Janke and others,1979) the essential effects of situation and personality on drug response. Following these authors, the present state of an individual is influenced by the drug, by the situation and by long-term characteristics, more generally by personality. The present state is modified by these factors, resulting in a primary drug response, covert to the experimenter. This primary response is the equivalent to the neo-behavioristic internal response, which in interaction with the possibilities to react in the experimental situation yields the overt, observable response named here "secondary drug response".

The advantage of such a model is obvious: most of the experimental results can be ordered. But it is obvious too that the high generality hides some problems:

- There is no attempt to make understandable the interaction between personality and situation.

The personality factor is an experimental tool to control the'psychological situation' of the subjects, ending in a reduction of variance. The experimenter states the hypothesis that the organismic factor is a generalized reaction to situations of which the experimental situation is part. The personality factor yields groups of subjects with comparable reactions (given the validity of the trait for the actual state). Introduction of a personality variable is in fact a declaration by the experimenter that the same situation describable in objective terms is psychologically not the same for all subjects. We have had an extended discussion in personality theory about the model of person-situation interaction. The controversy is still going on, recently with Eysenck & Eysenck's (1980) rejection of the arguments from Mischel (1968). But without respect to the ending of this discussion one fact still remains: the results of personality research do not allow to speak of situation and personality as independent factors. In the experimental procedure the factors personality and situation may be varied independently. Extraversion and a noise condition are independent in an experimental and statistical view. But psychologically they are highly dependent: a zero correlation between personality and situation would render personality theory superfluous.

- There is no attempt to make understandable the interaction between drug and situation.

Do subjects treated with a tranquillizing drug experience a situation in the same way as subjects with placebo? Since the work of Lewin it is accepted that situation is the 'state of the actual field' which

must be defined in psychological terms. Objective descriptions may only be an approximation to the description of the psychological situation.

-There is also no attempt to make understandable the interaction between personality and drug.
Are the reactions to drugs different for subjects with different personality scores without changing the personality? Or: Does the drug change the long-term characteristic (personality trait) itself or the portion of short-term characteristics (state) in the personality concept? Anew these factors are independent: each drug condition may be applied to each personality condition in stochastic manner. Thus, the conditions for the internal validity of the experiment sensu Campbell and Stanley, (1963) is guaranteed. But the problems are essentially the same as in the case of situational variables.

II. A PRAGMATIC VIEW ON PERSONALITY VARIABLES

As this discussion shows, the role of the personality variables is constitutive and may be discussed in highly theoretical terms. But we also can look at them from a pragmatic view point. There was a practical need to introduce such modifying variables because drug effects have been often too small. It is a usual tool in experimentation to reduce intra-group variance by stratifying the subjects.

Let us start with a single-situation experiment with drug as the only treatment factor. V(T) is the effect variance due to the drug, V(E) the error variance. By introducing an organismic factor (Edwards, 1968) like personality, V(E) is split into V(E) = V(P) + V(PxT) + V(E*) where V(P) is variance due to personality, V(PxT) is the interaction between drug and personality and V(E*) is the new (smaller) error variance. If the sum V(P) + V(PxT) is small or, equivalently, V(E) is of comparable size as V(E*) there would be no need for organismic factors. A 'differential psychopharmacology' would not have been created. This research is essentially based on the interaction term V(PxT) with V(T) small or zero.

If an effect in V(P) is observed without an effect on V(PxT), then the experimenter has chosen an organismic factor which is correlated with the dependent variable (observable) or, in another view, we have defined two or more subpopulations. The conditions to detect treatment effects are better now - some variance in the observable is assigned to organismic differences independent from drug action.

In single-situation experiments significant effects on V(P) and/or V(PxT) may be considered as an internal validation of the organismic factor personality. If an anxiolytic drug is given to a sample of subjects stratified to anxiety and the dependent variable is 'experienced anxiety' we should expect an effect on the organismic factor, whether as main or interaction term. If not, the validity of the organismic trait for the actual state in the experimental situation is questionnable. A 'hidden effect' of the personality factor has to be seen in the technique of many experimenters to improve drug effects only in subpopulations (subjects with high neuroticism, high anxiety and so on). This technique may be effective in some cases but has a great disadvantage: the validity of the personality variable is only based on plausability, but is not proved explicitly in the experimental situation. If variation of the organismic factor is seen as 'treatment

by the nature', the definition of subpopulations is comparable to drug studies without reference drugs or without placebo. It is impossible to explain treatment effects as general or as differential only, because V(T) and V(PxT) are confounded.

In the second case V(PxT) is significant. If additionally V(P) becomes significant, the organismic factor has led to a differential experience of the experimental situation which is modified by the drug (e.g., subjects with high anxiety show a greater decrease in experienced anxiety than subjects with low anxiety). On the other side, when V(P) is not significant, the organismic factor is drug-specific, not situation-specific. Figure 1 shows the possible results.

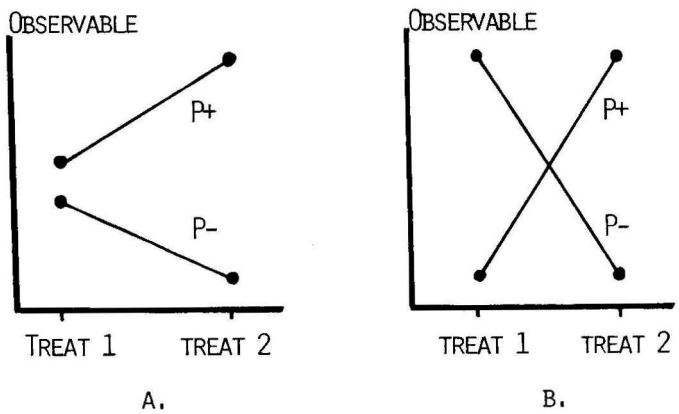

Fig. 1. Types of interactions between personality variables and drug treatment.

In case A (left side of Fig. 1) the personality factor differentiates between the persons without respect to treatment (main effect). The personality factor describes the differential experience of the experimental situation. Drug modifies this experience. In case B (right side of Fig. 1) the experimental situation is the same for the two subpopulations given by the organismic factor (no main effect personality) which itself shows as situation-indifferent. But reaction to the drug treatment is clearly dependent on personality.

So, introducing an organismic factor in psychopharmacological experiments we have to decide whether this factor is determining

a. the experience of the situation (a case only interesting in differential psychology),
b. the experience of the drug or
c. the reaction to situation a n d drug.

Case B as a double disordinal interaction (see Bredenkamp, 1980) would be highly desirable. The reaction to drug would be determined by characters of subjects which are independent from situation. Perhaps examples may be found in 'physiological traits' - psychology has not been able to produce situation-free parameters up to now. Even the purest 'personalist' would not declare that situation should be neglected.

So at the moment one should expect only effects of personality on situation and drug simultaneously. The overview about the effects of the organismic factors 'extraversion' and 'action-orientation' given by Janke and others (1979) reveals in fact that with few exceptions only interactions of our type A are occuring in psychopharmacological research. This indicates that organismic factors change situation as well as drug response.

Interpretation of those interactions is difficult and dependent on the psychophysiological model of the researcher. But before arguing with theoretical terms, a reconsideration of the methodological implications which are underlying the experimental procedure has to take place.

III. THE TECHNIQUE OF STRATIFYING

As mentioned stratifying is a tool to reduce error variance. Usually in statistical textbooks only one desiderat is stated: the stratum variable must be independent from the observable. That is why in experimental practice the stratum variable is measured previous to the experimental action. The independence of the stratum variable is only a question of measurement, not one of the association between stratum variable and observable. If in a teaching experiment comparing two methods of learning, intelligence is introduced as stratum variable, results in performance are highly dependent on this factor (the observable is correlated with the stratum variable). Only error variance is reduced.

But independence in measurement of both variables is only a necessary, but not sufficient condition in designs with stratum variables. The logic of factorial designs (usually evaluated with ANOVA) demands that effects of factors are orthogonal for all cells in two and higher orders. In nonpsychological experiments this demand is usually out of question. Suppose a pharmacologist is interested in the interaction of a certain drug with alcohol. He designs an experiment with two levels of dosages of drug and alcohol. By injecting the drugs in animals he can be sure that at every level of drug every dosage of alcohol is the same. Or: if the observable in this experiment would be 'dosage of alcohol' only a main effect alcohol has to be expected, no other effect is possible. Every main effect of this observable on other factors, every interaction with other factors would render the results uninterpretable, because treatment is no longer guaranteed to be successful.

The desiderat of independence seems trivial in experimenting with treatment factors, though becomes critical in designs with stratifying factors. Eysenck's model of the effects of stimulant action (excitation - introversion) and depressant action (inhibition - extraversion) may be a very dangerous one if you read it in the reverse direction. Then it may be possible that drugs change personality or: personality becomes drug specific. But if the personality factor (thought as independent factor) changes itself during the experimental action, the effects are no longer interpretable. Following these considerations, a precondition for interpretation is the stability of the organismic factor in the course of the experiment. But we have great empirical evidence that personality variables are affected by drugs.

IV. EMPIRICAL EXAMPLES

In an experiment from Kohnen & Krüger (1981) N=72 healthy young subjects (36 males and females) were divided by random in 3 groups receiving placebo, 2.5 and 5.0 mg of the benzodiazepine lopirazepam. In the course of the experiment (2 hours after the oral application of the drug) they had to solve arithmetic tasks sitting in a circle with 6 members and being called up by the experimenter one by one. They had to stand up and to calculate for 1 minute. This call-up situation was shown to be highly stressing to the subjects (see Kohnen and Lienert, 1980). Days before the experiment subjects got the FPI (Fahrenberg and others, 1973) as a personality test which among other scales also measures neuroticism. Scores were thought to stratify subjects. After the experiment (4 hours after application and 1 hour after the stressing experiences in the group) subjects got the parallel form of the test. The difference between the pretest and posttest score of neuroticism (N2 - N1) was calculated and introduced in the ANOVA as observable with drug treatment as independent factor.

Following our considerations above drug effects in connection with personality factors can only be interpreted if drug does not change personality in the course of the experiment. Thus we expected that the null hypothesis of no difference in the pre-post values is not to be rejected.

With $F = 3.12$ (df 2,69) in the unifactorial ANOVA HO has a probability smaller than 5%. Changes in neuroticism scores are attributable to drug levels. This effect is not due to the initial values (the pretest scores). In the respective ANOVAs we got

a. for the pretest score an F-value of 2.62 (df 2,69),
b. for the posttest score an $F = 0.60$ (df 2,69).

Both F-values are not significant, a result which supports trait theorists. Also the retest correlations are sufficient: for the placebo group $r(tt) = .25$, for 2.5 mg $r(tt) = .86$ and for 5.0 mg $r(tt) = .84$ with $n = 24$ in each group. With exception of the placebo group coefficients are of expected size. Only the calculation of the difference N2-N1 disturbs the picture. In Fig. 2 A (upper left) the changes N2-N1 are plotted against medication separated for the subjects with high and low neuroticism pretest score.

The differentiation according to the pretest score (N+,N-) shows that shift in the neuroticism score is,except to the placebo/N- group, generally: the posttest scores are the more stable the higher the dosage. An interpretation may be that highly threatening situations (as the call up situation is) lead to a repression of anxiety which is extremely shown by high neurotics in the placebo condition, not by the subjects with low neuroticism. If the anxiolytic action of the drug is the liberation of anxiety (as Lader, 1978, suggests) the tranquillizing agent enables the subjects to 'handle' the situation in its challenging aspects. The result can be a stabilization of reported neuroticism.

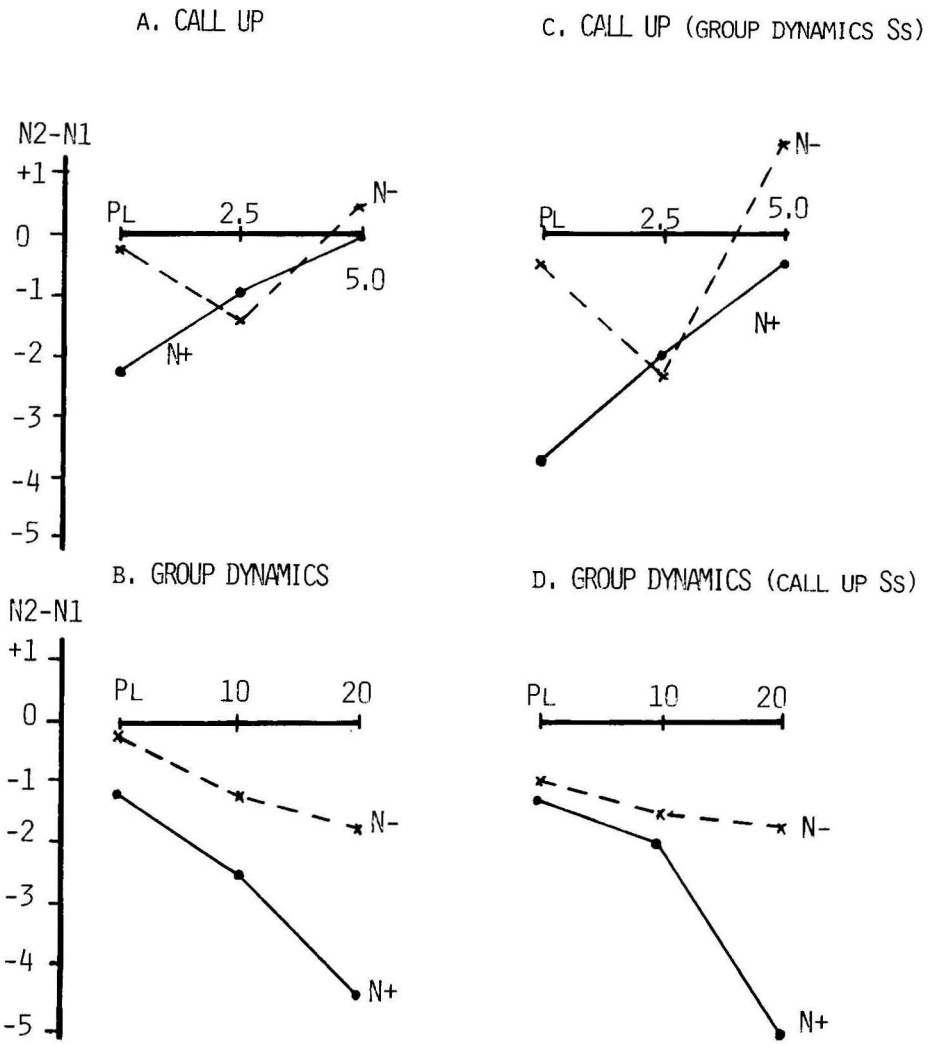

Fig. 2. Pre-posttest-differences of neuroticism dependent from medication in two experiments.

This psychopharmacological interpretation is not substantial for our considerations - other models are possible. Essential is the fact that the stratifying factor personality itself changes in the course of the experiment dependent from the treatment factor. In the language of differential psychology this result indicates a greater part of state aspects in the neuroticism score. The methodological implications will be discussed below after we have reported another experiment with comparable results.

In an experimental analog to a group-psychotherapy situation Krüger and Kohnen (1981) realized a wide variety of social situations. The program tried to generate very different situations in groups of 6 persons (3 male, 3 female) as discussions between two or more, but also exercises with touching the others. Phases of medication and self-reflection are also integrated following the lines of the Gestalt-therapy from Perls (1976). In total a more relaxed situation was created with some stressful events (like touching). As tranquillizing agent the benzodiazepine prazepam in the dosages of 10 and 20 mg was used together with placebo. Four groups of subjects (total N = 24) got previous to the experiment the FPI (yielding the pretest neuroticism score). Four hours after medication and 1 hour after the group dynamics subjects were measured with the parallel scale (posttest score). The results are shown in Fig. 2 B (left below) separated for subjects with high (N+) and low (N-) neuroticism pretest score.

In total the posttest score is lower than the pretest score for all groups. The results are inverse to those reported above: the higher the dosage the lower the posttest score. The retest-coefficients are for the placebo group .55, for the 10 mg group .41 and for the 20 mg group .10 (n = 8). The interpretation of the drug effect would be comparable to those given above. The therapeutic effect of group dynamics is greater in the verum groups which, as in the experiment above,are better able to 'handle' the situation, here in its relaxing aspects.

The effect is with F = 1.89 (df 2,21) not significant (p = 17.5%) in the ANOVA. Essentially for our purposes is another fact. N = 15 subjects of this experiment are the same as in the call up experiment reported above. The two experiments were separated by two months. Now we can ask whether the inverse effects of the two total groups (N = 72 and N = 24) are replicated in the subgroup (N = 15) involved in both experiments. Results are shown in Fig. 2 C (right above) and Fig. 2 D (left below). As may be seen the course of the total group is fully replicated by the subgroup. The same persons show in one situation an increasing, in the other situation a decreasing course of difference scores.

V. DISCUSSION

The retest-correlations showed that a constant character was measured. The changes in scores attributable to the situation and medication indicate that self-description varies if the psychological situation is changed. The psychological situation is influenced by the characters of the situation (threatening call up, more relaxing group dynamics) as well as by the drug. This result gives great hope that psychopharmacology may be used as an 'experimental differential psychology'. But these results also show a great problem for the methodology of a 'differential psychopharmacology'.

The organismic factor neuroticism was thought to be independent in a statistical manner since it was measured before the experiment. Results show that treatment changes this score. The psychological interpretation is simple: neuroticism has to be seen as a combination of a trait and a state variable. The trait-aspect is measured in the high retest-correlation, the state-aspect in the treatment effect. It is another question to think that treatment has changed the trait. Subjects were healthy young people, treatment was a single application - a greater change in the trait cannot be expected. This problem is more one of differential psychology but has no consequence in our discussion of the methodological implications of a stratum variable affected by medication.

Statistically these results indicate that the formal model of ANOVA is violated. Effects of the factors themselves have to be the same for every group in the experimental design. If we have had as observable 'mg tranquillizer in blood' and ANOVA would have shown that the mgs are different for subjects with high and low neuroticism, nobody would interprete the effects on all observables introduced, arguing that medication conditions were different. The same consideration for neuroticism yields difficulties in the interpretation.

What consequences should be drawn? In a substantial sense our results render the concept of neuroticism not questionnable. They emphasize only the necessity for a reconsideration about what portions of this concept are to be seen as trait and state. To what extent is neuroticism a measure of the actual state of the organism? What is rendered questionnable is the method of evaluating experimental designs including stratifying variables by the model of the 'uni-observable' ANOVA (to use a distinction of Lienert & Krauth, 1974) with the stratum variable as factor. If stratum variables can be shown as affected by treatment factors the logic of ANOVA is violated. Interpretation of main and interaction effects is no longer conclusive.

On the other hand, those stratifying variables could be shown as highly effective in psychopharmacology. There are only two ways out of the problematic methodological situation:

1. If stratum variables are affected by treatment they are in fact observables. If dependence of pharmacological effects from those variables is given, a multivariate ('multi-observable') evaluation has to take place. Drug effects are not to be proved with the model of two factors and one observable (factors drug x personality affect observable) but with the model of one factor and two observables (factor drug affects the observables personality x observable). Thus differential psychopharmacology becomes necessarily multivariate.

2. Controlling stratum variables has to be done not by introducing them as factors in the ANOVA but by defining two ore more subpopulations with the stratum. Subjects with high or low neuroticism are no longer viewed as coming from the same population. Doing so, in the ANOVA no common variance can be defined for stratified groups. The way out is to evaluate the drug effects separately for the subpopulations. The two-factorial design recurs to two one-dimensional designs. This procedure is suggested as the most conclusive by Lienert (1981).

Basic requirement for both ways is information about the effect of treatment on the stratum variable. This information can only be gotten with additional experiments. All independent variables in an experiment which not can be randomized (non-treatment factors) have to be

remeasured in the course of the experiment. The first analysis has to prove whether the difference between pre- and posttest score has an effect on the treatment-factor or not. Only in the latter case, can statistical analysis be made as usual.

An effect occuring, evaluation becomes complicated: the stratum variable has to be considered as a covariate. It has to be decided whether (a) the pretest stratum score, (b) the posttest score, (c) the difference pre-post, or (d) the sum pre + post is the adequate measure to be introduced in the (now) multivariate evaluation.

A procedure like this has to wait for the end of the experiment before knowing what has been the independent factors in the experiment. This is unsatisfying for psychology (and in a strong sense not allowed by the statistical model). Therefore we want to argue for a multivariate model which enables the experimenter to plan experiment and evaluation of data fully in advance. Since it is not clear up to now how great the portions of situation, of state, of trait are in our personality concepts we should be conservative in evaluating those effects by considering them as observables. This is no disadvantage for differential psychology: a deeper knowledge about the effect of treatment on personality scores is in fact experimental differential psychology. Thus differential psychopharmacology with personality as a dependent variable yields a self-reliant contribution to differential psychology (Krüger, 1981).

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