

## **Tranquillizer Effects in an Experimental Analog of Verbal Examinations**

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**Abstract.** In an experimental analog of verbal examinations, the call-up situation, the effects of two dosages of a tranquillizing agent (lopirazepam) are compared to placebo treatment. 72 male and female, healthy, young volunteers have been randomly assigned to 12 groups of 6 subjects each. Pulse frequency and performance were registered. The results indicated differential drug effects which were interpreted according to the hypotheses of 'differential effects of social stressors'. If a situation was highly challenging for a subject, the application of a tranquillizer in an adequately high dosage enabled him to perform well in spite of or because of strong increases in pulse frequency.

### **Real-Life Examination Conditions in Experimental Laboratories**

From clinical observations, it is obvious that individuals themselves demand psychotropic drugs, especially in view of highly challenging situations. For adolescents, such situations are very often examinations. The subjects expect that sedating drugs, for example prevent or reduce high activation usually experienced during examinations and, most important, improve performance. Can a psychotropic agent really produce such miraculous effects?

While an unknown number of individuals indeed deal with psychopharmaca by consuming a lower or higher dosage only once at a time (on

the day of examination), empirical results in this field are very scarce. *Krishnan* [1975], comparing 40 mg oxprenolol and 2 mg diazepam during real examinations, found higher self-confidence but rather bad performance in the tranquillizer group. In experimental studies, also very small in number, settings such as public speaking [*Droppleman and McNair*, 1971; *Karst and Most*, 1973] are assumed to be an experimental analog to real-life conditions. However, drug effects in these situations are highly inconsistent.

In a preliminary study [*Kohnen and Lienert*, 1980, 1981], the 'call-up' situation promised to reproduce examination stress in the laboratory and to allow the measurement of drug effects, too. In the call-up situation, subjects had to rise in front of a group of co-examinees and perform tasks given by an experimenter. In this way, the experimental call-up is similar to the well-known call-up of pupils by a teacher. Getting called-up yielded high physiological activation: the pulse rate increased about 50–80% with peaks at about 160 beats/min. The effects of a tranquillizing agent were compared with naive expectations: the performance was better under drug conditions than under placebo conditions.

The reason why the experimental call-up situation worked as a high stress-inducing situation in all or most subjects, was the social embedding of the call-up. The social character of this experimental set makes it realistic [*Kohnen and Krüger*, 1981]. Without this social context, being called-up has only slight activational effects [*Kohnen and Lienert*, 1981].

In the following an experimental study is reported, within which a modified version of the call-up situation is used to evaluate the effects of two dosages of a tranquillizing agent of the benzodiazepine-type (lopirazepam). Lopirazepam is a new compound of the pyridodiazepines: 3-hydroxy-5-(*o*-chlorphenyl)-7-chlor-1,2-dihydro-<sup>3</sup>H-pyrido-(3,2)-1,4-diazepin-2-on, produced by Chemiewerk Homburg/GB Pharma Degussa, D-6000 Frankfurt/Main.

## The Experimental Call-Up Study

### *Procedure*

Realizing some modifications, the following procedure was chosen. In a fixed order each member of a group of subjects was called up by an experimenter. The subject rose and tried to solve addition tasks of two-digit numbers (e.g.  $37 + 79 = ?$ ) by mental arithmetics, which were given to the subject by the experimenter. After the subject had given the solution, being right or wrong, the next task followed and so on. The instruction was to

work as fast and well as possible. The waiting subjects were instructed to observe performance and behavior of the calculating subject critically. After 1 min, the subject sat down and the next subject rose. In all three trials took place, i.e. each subject was called three times.

The experimental setting allows answers to the following questions. (a) What is the effect of being called up? The answer to this question should include an evaluation of the preceding and following minutes and the adaptation process during the three call-ups. (b) Does the tranquillizing agent modify the physiological reactions of the subjects to the call-up? (c) Does the tranquillizing agent influence the performance of the subjects?

#### *Design and Sample*

The call-up situation was realized in a  $3 \times 2$  factorial design. As a treatment variable a drug factor with three modalities was introduced, consisting of two dosages of lopirazepam, a small one of 2.5 mg and a higher one of 5.0 mg, and placebo. As a stratification factor, the sex of the subjects was controlled. The stratification based on the hypotheses that the call-up situation by proving performance may have sex-differential effects on the subjects' motivation [Aletky and Carlin, 1971].

A sample of 72 volunteer, healthy male and female students, 20–28 years of age, was randomly subdivided into 12 experimental groups of 6 subjects each, each group containing a member of the  $3 \times 2 = 6$  experimental cells.

#### *Apparatus*

To evaluate the drug effects in the call-up situation, pulse frequency and performance in simple arithmetic tasks were measured.

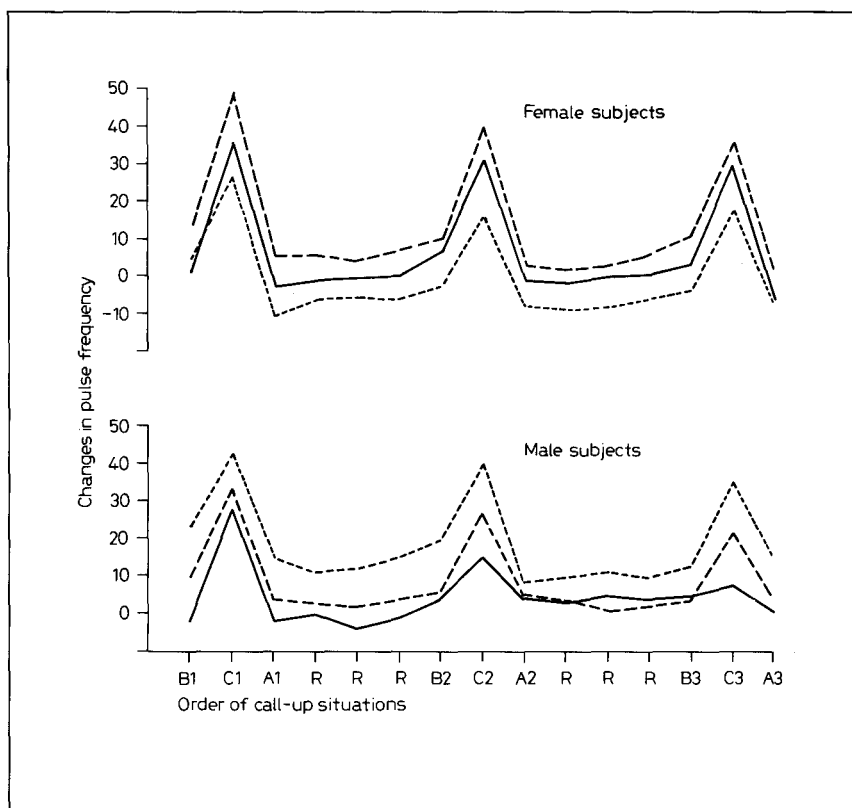
As a physiological indicator of activation [Bartenwerfer, 1963], pulse frequencies were registered during the complete testing procedure. Simultaneously and continuously, ECG was derived and transmitted by a telemetric apparatus (Monitel, Messerschmitt/Boelkow/Blohm, Munich, FRG). To eliminate interindividual somatic differences, all experimental pulse rates are referred to a resting pulse, which was measured before application of the drugs.

To evaluate performance of the subjects in the call-up situation, the solutions of the mental calculations were noticed. The number of right solutions are taken as an indicator of successful or vain examination performance.

The experiment itself started by equipping the subjects for continuous pulse frequency measurement. Before application of the drugs, the resting pulse was registered. The double-blind application of the drug was followed by a 2-hour resting interval. The call-up procedure lasted 25 min.

## **Results**

First of all, the question whether the call-up situation actually has high activating characteristics, expected according to the *Kohnen and Lienert* [1980, 1981] study, has to be answered. Depending on these effects, the action of the tranquillizing agent should be discussed.



**Fig. 1.** Changes in pulse frequencies (differences between call-up-situation-pulse minus resting-pulse) in male and female subjects under different drug treatments during the call-up procedure. B = Before call-up; C = call-up; A = after call-up, R = resting interval; 1, 2, 3 = order of call-ups. ..... = 2.5 mg; --- = 5.0 mg; — = placebo.

#### *Drug Effects on the Subject's Experience of the Call-Up Situation*

In figure 1, the course of pulse frequency in the three call-up situations is shown. For comparing purposes, the subjects are ordered according to corresponding time points. Though losing four time points in this way, all the important information is included.

From the first view on the pulse curves, the three call-ups can be identified and differentiated from the waiting situations. The difference between a call-up and the mean values of the waiting minutes amounts to about

20–40 pulsations. Individually, the pulse frequency increased up to 60 pulsations. The difference between the call-ups and the waiting minutes is statistically significant, calculated by an ANOVA with a single situational repeated-measurement factor (14 levels). These pulse frequency increases indicate an extremely high activational effect of the call-up.

Remarkably, the course characteristics of the pulse curves is not changed under drug conditions. The drug influenced only the level, according to which the subjects were reacting in the call-up situation. Statistically, these drug effects are symbolized in a significant drug  $\times$  sex interaction. The statistical significance is constituted especially by the effect of the 2.5-mg dosage. As can be seen from figure 1, the female subjects of the 2.5-mg group reacted only with small increases in pulse rates (the respective curve is the lowest one); male subjects, however, reacted all in all with a high increase in pulse frequency (the 2.5-mg curve is the highest one). Neither under placebo nor under 5 mg loriprazepam did any remarkable overall difference between men and women appear.

These physiological reactions to the call-up support the hypotheses that this situation represents a high activating experimental setting. From these results, the internal validity [*Campbell and Stanley, 1973*] of the call-up as an experimental analog of verbal examinations is no longer only a content one, but has also strong empirical evidence.

#### *Drug Effects on Performance in the Call-Up Situation*

The crucial question evoked by the dosage-dependent modifications of the subject's physiological reactions to the call-up situation is the following: Does the drug influence the subject's performance? And if so, what relationship exists between the dosage-dependent physiological reactions to the call-up situation and changes in performance?

Different multifactorial ANOVAs indicated that the answer to these questions must be based on rather complex relationships between drug treatment, sex, pulse frequency and performance, leading to difficulties in interpretations.

A more simple statistical procedure than the ANOVA for proving complex coherences between several variables is the 'Configuration Frequency Analysis' (CFA), suggested by *Krauth and Lienert [1973]* and *Lienert [1978]*. To apply this method, all the data had to be transformed into categorical ones. Therefore, pulse frequency and right solutions in performance tasks were dichotomized at their median into supra- and supermedian level data. So, a 4-factorial complete 'Interaction Structure Analy-

**Table I.** Triple ISA association between drug treatment, increase of pulse frequency and performance

	Placebo		2.5 mg		5.0 mg	
	L-	L+	L-	L+	L-	L+
P-	4	8	5	5	7	3
P+	10	2	6	8	4	10
$\varphi =$	-0.501		-0.073		+0.410	

+ = Supermedian; - = supramedian.

sis' (ISA), a modification of the CFA [Lienert, 1978, 835ff.] with one treatment factor (medication), one stratification factor (sex) and two dependent variables (pulse frequency and performance) was calculated. Regarding only configurations including the treatment factor, totally seven configurations had to be evaluated. Adjusting the significance level as to the number of tests [Krauth and Lienert, 1973], for  $\alpha = 0.05\%$  the new significance barrier is  $0.05\%/7 = 0.00714\%$ .

Only one CFA configuration, including the performance variable, reached the adjusted  $\alpha$  level: the configuration medication – pulse frequency – performance. This triple interaction is symbolized in table I.

Under (1) placebo, there is an interaction between pulse frequency and performance of the following kind: subjects reacting with a low pulse rate increase very often gave the right solutions; bad performance is seldom. On the contrary, subjects reacting with a high pulse rate increase more often showed bad performance, only in a few cases good performance. Expressed in a correlation coefficient,  $\varphi = -0.507$  indicates a statistically significant negative correlation between pulse frequency and performance under placebo ( $u = 2.484$ ). (2) 2.5 mg lopirazepam yielded no connection between pulse rate and performance ( $\varphi = -0.071$ ). (3) 5 mg lopirazepam, however, changes the relationship, observed under placebo. Now, subjects with a high pulse rate increase showed good performance, subjects with a low increase, on the other hand, were bad in the solution of mental arithmetic tasks. The statistically significant correlation between pulse frequency and performance is positive,  $\varphi = +0.410$  ( $u = 2.008$ ).

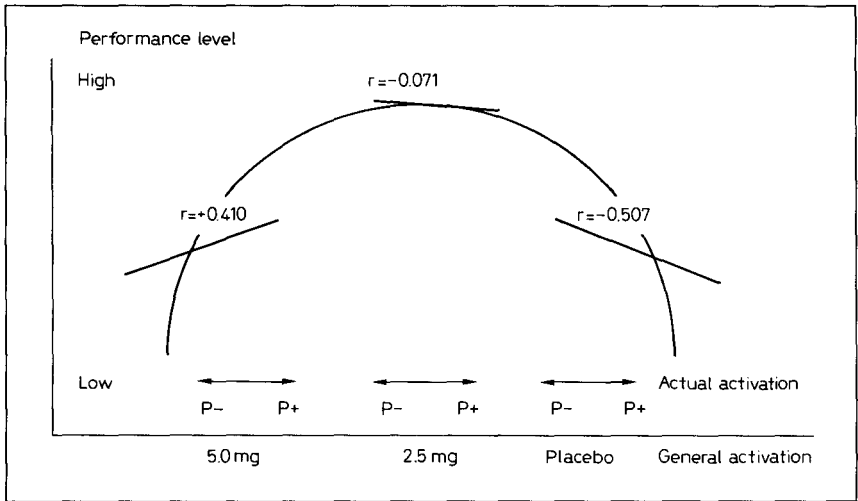
## Discussion

The call-up situation can be regarded as a suitable experimental set for reproducing high-stress characteristics within a psychological laboratory, as has already been shown by *Kohnen and Lienert* [1980]. Not only do the results of the variables measured in this study confirm this statement, but also observations on the behavior of the subjects, scalings of psychic variables, and self-reported experiences, which will be reported in a separate paper. Taking all the information together, there are many reasons to assume that the call-up situation is actually an experimentally valid analog of verbal examinations with rather high activational demands.

From our point of view, the drug  $\times$  sex interaction in pulse frequency increase under the three drug treatment levels expresses a general principle: though the call-up situation evokes changes to higher activational states in all subjects, the burdens of the situation or, using the stress concept of *Lazarus* [1967], the psychic deformation seem not to be the same for all subjects. Using the results of further experimental studies in social stressors, the authors have suggested 'differential effects of stressors' on individuals or groups of individuals [*Kohnen and Krüger*, 1981]. Performance situations, for example, seem to be highly challenging for males and less challenging for females. Depending on the stressor-induced activational state, different dosages of tranquillizing agents will produce different effects which have to be evaluated according to the demands or the challenge of a situation for the subject.

The evaluation of performance changes supports these hypotheses of differential stressor effects. The negative correlation between pulse frequency and performance under the placebo condition can be interpreted in the following way: if the stressor is highly challenging for a subject, he will be too highly activated (the increase of pulse frequency is too strong), bad performance is the most probable result. If, however, the situation is not so challenging and pulse frequency does not increase very much, the activation level is favorable for good performance. The positive correlation between both variables under 5 mg lopirazepam can be interpreted accordingly. If we assume a general deactivating effect of the drug: if the stressor is highly challenging, the increase of pulse frequency leads to an optimal activation level for good performance. If, on the other side, the stressor is not challenging, the subject is not activated enough, rather bad performance is a probable result.

This interpretation implies two activational concepts. General activa-



**Fig. 2.** Hypothetical model of drug action. P+ = High increase of pulse frequency; P- = low increase of pulse frequency.

tion is influenced by the drug: the higher the dosage of the drug, the lower the general activational state. The situation effect produces differences in an actual activational state: if the situation is highly challenging, the actual activation is high, if the situation is less challenging, the actual activational state is lower. According to the Yerkes-Dodson law (1917), the activational state influences the level of performance to be good or poor. The reported correlations are shown in figure 2.

The effects of the 2.5-mg dosage are difficult to integrate in this model. It must be assumed that the sex-different activational reactions (see beginning of Results) hide the relationship between the activational state and performance. However, it can also be possible that the effects of this condition are somewhat like an intermediate state between the placebo effects and the 5-mg dosage effects.

The model of differential effects of stressors is up to now, only a heuristic one. It assumes that there is no situation challenging or even threatening people generally. Sex and other variables modify the characteristics of a situation. In the ears of practitioners and clinicians, it sounds rather trivial. Nevertheless, the principle of differential stressor effects is neglected in the scientific study of tranquillizing drugs. Though constitutive in papers of



several authors [e.g., *Eysenck*, 1981] and demanded by others [e.g., *Debus and Janke*, 1978], there is a lack of systematic investigation. It can be assumed that many of the results, which are inconsistent as to the effects of tranquillizing drugs in the psychological laboratory [*Janke et al.*, 1979], actually agree, if ordered according to the challenge produced by different experimental settings.

To answer the initial question, whether a tranquillizer can produce desired and expected miraculous effects in examinations, we first have to make some considerations about the reactions of a subject, which are desirable in stressful situations like the call-up. Examinations (e.g. the call-up) are threatening situations, individually experienced at least since school entrance. To react adequately in such situations, a subject must be vigilant, i.e. in a high but not too highly activated state, and, at the same time, has to keep a clear head. This state is not present in a lot of placebo-treated subjects but is induced by the tranquillizer, if an optimal dosage of the drug is chosen. Thus, the drug is not preventing an increase of physiological activation, which seems to be conditioned to fearful situations like examinations. However, the drug enables the subjects to a good performance in spite of high physiological activation. If they are treated with placebo, high activation is correlated with bad performance.

However, it should be noted that the interpretations above are not based on statistical main effects, i.e. not all the drug-treated subjects show the reported drug effects. There are only reaction types, being more frequent in certain conditions than to be expected at random. Therefore, the tranquillizing drug does not enable good performance in general but only in those subjects who experience situations like examinations as highly challenging. For these people, lopirazepam in fact has the quality of a crutch the examinee can lean on.

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