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Electrophysiological parameters in anxiety and failure: Evaluation of doxepin and hydroxyzine

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This double-blind investigation compared the effects of doxepin, hydroxyzine HCl, and placebo on muscle action potentials (MAPs) and skin conductance (GSR) parameters as functions of experiencing either success or failure in concept-identification performance of 30 psychiatric anxiety patients. Results showed the following: (1) increase in MAPs with failure, (2) reduction of MAPs by both medications, (3) a greater number of spontaneous GSRs in the success condition compared with the failure condition, and (4) a significant negative relationship between MAPs and GSRs.

Cognitive deficit has been demonstrated by introducing antecedent failure (insoluble problem) to normal (Pishkin, 1965; Pishkin & Shurley, 1968) as well as psychiatric (Pishkin, Fishkin, Shurley, Lawrence, & Lovallo, 1978; Pishkin, Shurley, & Wolfgang, 1967) populations. This type of deficit is especially evident in the high-anxiety normal population with antecedent failure when compared to the low-anxiety group (Meites, Pishkin, & Bourne, 1981). The experience of cognitive failure has been shown to produce a state of stress that is also reflected by psychophysiological parameters (Pishkin, Fishkin, & Shurley, 1979). Moreover, experimentally manipulated motivation and drive-level factors interact with the success/failure dimension to further inhibit cognitive performance (Pishkin, Wolfgang, & Bradshaw, 1963).

Both doxepin (Krakowski, 1968) and hydroxyzine HCl (Pishkin et al., 1967) reduce anxiety with minimal lessening of cognitive abilities (Pishkin et al., 1978). There is evidence that hydroxyzine is also effective in relief of anxiety and tension states in adults as well as children (Feinberg, Pruzansky, Feinberg, & Fisherman, 1958; Nathan & Andelman, 1957; Sanchez-Ibanez, 1957). Hughes and Kopmann (1960) demonstrated that hydroxyzine was effective in reducing conditioned avoidance behavior without lessening discriminative capacity of rats. Doxepin is a tricyclic compound with chemical resemblance to amitriptyline, from which it differs by the presence of an oxygen atom in the central ring. Doxepin also differs from the other tricyclic amines in that it possesses both antianxiety and antidepressant properties (Goldberg & Finnerty, 1972). Doxepin is effective in treating patients with a variety of disorders, including alcoholism, allergy management, severe emotional disturbances associated with physical illness, sleep disturbances, and treatment of anxiety neuroses (Ayd, 1969; Karacan, Blackburn, Thornby, Okawa, Salis, & Williams, 1975). Accordingly, this study was designed to evaluate the comparative effects of doxepin and hydroxyzine upon cognitive stress (success/failure paradigm) that increases arousal levels as manifested by electrodermal (GSR) and electromyographic (EMG) activities of anxiety patients.

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METHOD

Subjects

The subjects were 30 volunteer, newly admitted, first psychiatric admission patients at the Veterans Administration Medical Center, Oklahoma City, Oklahoma. All subjects had a primary diagnosis of anxiety disorder. The selection criteria were as follows: (1) Patients with CNS pathology or a history of either acute or chronic brain syndrome as specified in earlier work (Pishkin & Burn, 1971) were excluded; (2) all patients had been free of psychotropic medication for at least 15 days before the beginning of the study; (3) each patient had a complete medical and psychiatric examination, a thorough physical examination, and a mental status and clinical examination by the admitting psychiatrist prior to diagnosis and admission to the project; (4) subjects ranged in age from 25 to 50 years (mean = 37.61 years); and (5) all participants signed an informed consent form (VA-10-1086).

Twenty of the patients were given either doxepin or hydroxyzine, the remaining 10 (control) patients were given placebo (lactose) during the investigation. The medication was administered in identical capsules and contained either 20 mg of doxepin or 50 mg of hydroxyzine. The dosage administered was one capsule 3 times/day for 2 weeks. At the end of the 15-day period, the subjects performed on a concept-identification (CI) task. The stimuli were geometric patterns projected on a screen in front of the subject. The subject's task was to categorize the patterns in accordance with a relevant dimension by pressing one of the two response keys. The feedback was automatically pro-

vided by amber lights above the keys. A more detailed description of the CI task and apparatus was provided in an earlier report (Pishkin & Wolfgang, 1964). The CI problems were designed to elicit an expectation on the part of the subject of either success or failure. In the success condition, subjects received correct feedback on all trials; in the failure condition, they received 50% misinformation (Pishkin, 1960), making it impossible to reach solutions. This misinformation condition has been shown to evoke an experience of failure and to reliably inhibit performance on subsequent cognitive tasks (Pishkin, 1965).

Procedure

The GSRs and EMGs were recorded concurrently with CI performance. The GSRs were recorded as DC resistance changes and converted to conductance measure. The active electrode was a .625 x 1.0 in. silver plate electrolytically coated with AgCl anodized in 1-M NaCl (3 mA for 5 min). The EMGs were taken from the forehead utilizing frontalis placement specified by Davis (1952). The muscle action potentials (MAPs) were taken six times at the end of each 5-min interval, representing a 120-msec segment; the greatest amplitude within each segment was utilized in analysis of the data. The conductance change was computed in accordance with Edelberg's (1967) method: $\Delta C = \Delta R/R^2$.

The ΔR is resistance change, and R^2 is the basal resistance squared at the onset of the response. The spontaneous GSR measures consisted of the number of GSRs within six of the 5-min segments. Only the GSRs that were equal to or greater than .001 of basal resistance were counted as spontaneous GSRs in the analysis of the data. The subjects performed for 30 min on either success or failure CI task measures. A more detailed description of the psychophysiological procedures was reported earlier (Pishkin & Shurley, 1968).

Design

This was a 2 by 3 factorial design with two CI problems (success or failure) and three drug conditions (doxepin, hydroxyzine HCl, or placebo). Since the two-choice CI task was a relatively simple problem (three irrelevant dimensions), no difference in performance between the drug groups was expected in the success set condition (Pishkin et al., 1967), and, obviously, with 50% misinformation feedback, no learning could occur in the failure condition.

RESULTS AND DISSCUSSION

As anticipated, by design, there was no difference in CI performances between the drug groups in either the success or the failure condition (Fs < 1.0). All subjects in the success condition solved the problem within the first 21 min, and the failure subjects performed at the chance level, matching 50% misinformation feedback throughout the 30-min period. Two independent analyses of variance were performed on the EMG and the GSR data.

Significantly greater degree of MAP was found in the failure conditions across the three drug groups as compared to the success condition [$F(1,24) = 8.14$, $p < .01$]. The main effect of drugs on MAP was also significant [$F(1,24) = 6.07$, $p < .05$], revealing the greatest amount of muscle tension in the placebo group and the least tension in the hydroxyzine condition. It is noteworthy that the placebo group produced the highest level of MAP (mean = 29.03), doxepin the middle level (mean = 20.41), and hydroxyzine the lowest (mean = 11.52). The EMG data are displayed in Figure 1.

The spontaneous GSR data revealed that only the main effect of success/failure was reliable [$F(1,24) = 7.32$, $p < .01$]. There was no main effect of drugs; neither was the interaction of Drug by Success/Failure significant (See Figure 2).

An overall significant negative correlation was found between spontaneous GSRs and MAPs ($r = -.61$, $p < .01$), suggesting that the two measures tap different types of autonomic activation (i.e., more MAP is associated with failure than success, whereas increase in GSR activities reflects a state of experiencing success). This interpretation is consistent with earlier findings for which it was proposed that MAP concomitant with CI is an indicator of autonomic, internal disturbance associated with inability to process information, whereas spontaneous GSRs reflect successful intake of information (Pishkin & Shurley, 1968). Apparently, this trend is significantly accentuated in anxiety patients, as demonstrated in this experiment.

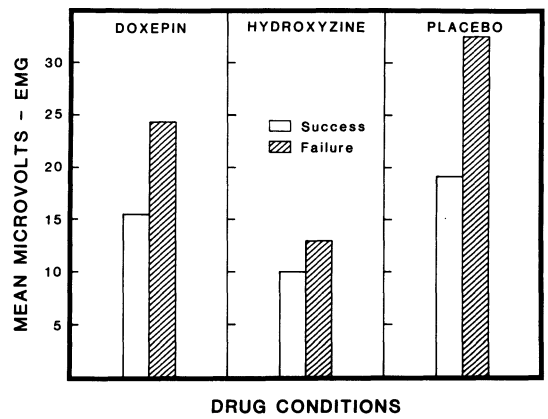

Figure 1. Muscle action potential activity as a function of success/failure manipulation and the three drug conditions.

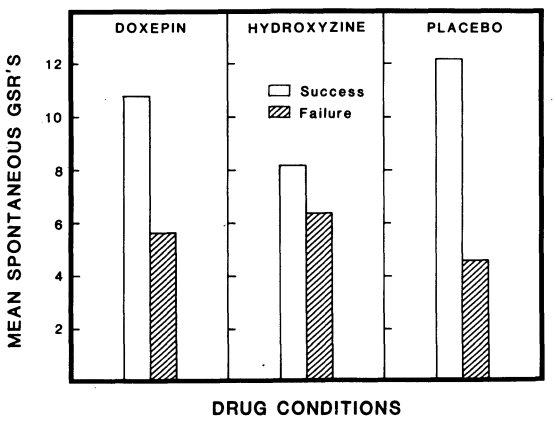

Figure 2. Spontaneous changes in skin conductance as functions of success/failure manipulation and the three drug conditions.

It is noteworthy that hydroxyzine and, to a lesser degree, doxepin suppressed the muscle tension that was produced by the stress of experiencing failure when compared to the placebo. Moreover, it was demonstrated that CI failure is reliably related to an increase in muscle tension of clinically anxious subjects. If our speculation that spontaneous GSRs represent successful information intake is valid, then it may be concluded that the medications used in this study should have no detectable influence on cognitive performance. Most important, this study confirms an earlier finding with normal college subjects, in which high-anxiety subjects, as determined by the Taylor (1956) Manifest Anxiety Scale, performed better on the CI task following a success condition than they did following a failure condition (Meites et al., 1981). The success and failure conditions in the present experiment and the cited experiment were identical.

On the whole, a reliable relationship was shown between success/failure manipulation and the two electrophysiological parameters utilized. Furthermore, hydroxyzine reduced failure-induced muscle tension of the anxiety reaction patients. Future research is needed to explore how nonanxious subjects, under the cognitive stress of failure, would respond autonomically when medicated by the two frequently prescribed drugs that were utilized in the present study.

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