Drug Conditioning and Drug Effects on Cardiovascular Conditional Functions

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It is true that the nervous system is earthly, whereas behavior seems to be evanescent, but the interesting things are evanescent, and one must deal with them as they pass.—B.F. Skinner (Evans, 1969, p. 17)

The modern application of some old and general laws of conditional behavior to physiologic and pharmacologic problems is a novel phenomenon in American science. The general laws of conditional behavior were first explored and postulated by Pavlov (1928) and Thorndike (1911) some fifty years ago. Pavlov established that the fundamental process of conditioning was psychic in nature and that it depended on two major variables: a conditional stimulus and a reinforcement. More recently, with the discovery of the stimulus properties of drugs, the area of conditioning and behavioral science acquired additional dimensions in terms of both experimental and clinical applications. The present report concerns the use of drugs and classical Pavlovian conditioning procedures in the study of cardiovascular function.

To mention the fact that drugs have behavioral or reinforcing effects often sets the classical pharmacologists thinking in terms of neurotic or psychotic clinical behaviors. By behavioral effects, however, we mean much more, including the psychologic, psychophyslogic, or neurologic control of basic behavioral functions. Processes that are behavioral are not necessarily organic or unconditional. They may also be conditional, resulting from the pairing of environmental stimuli. The experimental data we have accumu-

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lated in this latter area over the past ten years may suggest possible applications for treatment and possible implications for the genesis of such pathologic states as essential hypertension and heart disease. Hopefully, therefore, we may be at the threshold of a new era in therapeutics, with the application of behavioral techniques for the treatment of disease.

MODIFICATION OF THE CARDIOVASCULAR SYSTEM

The problem of modifying the physiologic state of the cardiovascular system with drugs is very old. For example, the treatment of congestive heart failure with the leaves of common foxglove (digitalis) was discovered by trial and error many years ago. For centuries the effects of drugs on pathologic conditions of vital systems have dealt with the unconditional effects of drugs on such systems. We are only beginning to use drugs to examine the conditional modification of these systems.

The conditioning of drug effects on cardiovascular functions involves two general paradigms: (1) the actual conditioning of “specific” drug effects, namely, “specific” pharmacologic conditioning (“specific” in this sense is used here to state the nature of the response but not its mediation, origin, and complexity), and (2) the primary and secondary effects of drugs on cardiovascular conditioning. In the first paradigm a conditional stimulus (CS) usually precedes the injection of a drug known to produce specific unconditional effects, such as alterations in the electrocardiogram or changes in heart rate or blood pressure. After several repetitions of the CS and the drug reinforcement (unconditional stimulus or US), the CS is presented alone or followed by the injection of a neutral substance that does not produce pharmacologic effects. If conditioning has been established, the CS alone will produce changes similar or identical to the ones produced by the drug reinforcement. In the second paradigm, conditioning is established with a known agent such as cutaneous electrical stimulation to the skin or food, and the effects of drugs on this already established cardiac conditional reflex are determined. This method has been used in the past to determine the effects of certain tranquilizers on autonomic activity, but recently it has also been used to explore the physiologic mediation of these learned reflexes.

Early accounts of investigations concerning specific conditioning of the electrocardiogram were first reported by Bykov (1957). According to Bykov, the actions of morphine, nitroglycerin, strophanthin, epinephrine, and acetylcholine have been conditioned by various Russian investigators working in Pavlov’s laboratories. The conditioning of the effects of morphine on the electrocardiogram was accomplished by Delov. After 30 repetitions of an