“Accidental Conditioning” with Chronic Methamphetamine Intoxication: Implications for a Theory of Drug Habituation*

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Abstract. Methedrine was chronically administered twice a day to a group of cats over a period of eleven days. The stereotyped behavior elicited after injection became increasingly constricted over the eleven days. After Day 1 when the cats were placed in the observation cages just prior to injection, the stereotyped behavior would most often be initiated even before the injection, indicating a conditioning process. The behavior induced, as well as the parameters of reward, appears to fit well the accidental contingencies conditioning paradigm.

Key-Words: Amphetamine — Psychopharmacology — Conditioning and Drug Abuse.

Introduction

Both experimental and clinical evidence with a wide variety of drugs indicates that there is a conditioned effect from repeated drug intoxication. Wikler (1961) has emphasized the “conditioned” aspect of drug seeking and related behavior in addicts. This behavior (in the addict lingo called “hustling”) is the preoccupation of addicts not merely when under pressure from withdrawal pangs, but is noted even in the thoughts and conversations in the hospital after complete withdrawal. Deneau et al. (1964) have demonstrated that animal self-administration of drugs includes both compounds that induce physiological dependence as well as those that do not. In the parlance of the conditioning laboratory, self-administration would be an instance of operant conditioning with the drug serving as a reinforcer. Pickens not only demonstrated self-administration of d-amphetamine in rats (Pickens and Harris, 1968) but also reported that when injected by the experimenter, there was a conditioned increase in behavioral activity when subsequently injected with saline (Pickens and Crowder, 1967).

The present series of experiments was not designed to elicit conditioning but many individual observations indicated there was a

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conditioned effect following repeated injections of Methamphetamine in cats. Fortunately the behavioral data was either recorded on T.V. tape or transcribed in detail, thus allowing for a re-examination of the conditioned effect.

Method

Forty-five cats weighing $2^{1/2} - 4$ kg were chronically administered Methamphetamine over a period of eleven days. Starting with 15 mg/kg per day, the dosage was gradually increased 2 mg/kg/day to 35 mg/kg. Methamphetamine was injected i.p. twice daily at 8:00 A.M. and 4:00 P.M., allowing 16 h between days for recovery and sleep. On T.V. recording days, the first dose was not given until 11:00 A.M., thus the observed period was 19 h after the last injection.

Observation on nine cats were recorded on an Ampex 660-B, two-inch videotape recorder for later analysis. Recordings were made on Days 1, 3, 11, 12, and 15 after the beginning of treatment. Each of these days except 12 and 15 was divided into 3 min recordings taken in a pre-injection control and at 10, 20, 30, and 90 min after the first injection of the day. Behavior in 36 cats was observed and recorded on charts, but not recorded on T.V. tape.

Results

Profuse, viscous salivation is noted within 20 min of a large dose of Methamphetamine (over 7.5 mg/kg) in approximately 70% of the cats injected (Fig. 1, L). Salivation usually continues for at least 20–25 min (Ellinwood and Escalante, 1970a and b). In six cats after 3–4 days of Methamphetamine injection, profuse salivation was noted prior to injection and appeared triggered by stimuli associated with injection. In two of these cats, salivation appeared when the cat was handled just prior to injection. Both cats had been scratched on the back previously to calm them before Methamphetamine injection (handling in this manner was stopped in later cats). Subsequently when scratched on the back, they salivated profusely within 15 sec. This response extinguished quite slowly; salivation to scratching was elicited eight times in a two-week period after the last injection of Methamphetamine. One of these cats saved for long term studies still salivated $1^{1/2}$ months later, but not at 4 months. One year later, after only two subsequent injections, this cat again salivated when handled. Four other cats were repeatedly noted to salivate shortly after the experimenter entered their home cage room (i.e. they reacted only to the presence of the experimenter). Pupil dilation prior to injection was observed in other cats, but this response was thought to be too non-specific to be directly related to the Meth-