The Effects of Chlorpromazine on the Decay and Consolidation of Short-Term Memory Traces in Mice

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Summary. F₁ hybrids of two highly inbred strains of mice were trained in a one-trial passive avoidance learning situation. Chlorpromazine, in doses of 0.5, 2.0 and 3.5 mg/kg, was administered at one of four injections times, 10 min before and 0.5, 2 and 10 min after learning. Pre-learning drug administration completely blocked acquisition of a learned avoidance response. Post-learning drug effects were more complex, involving reduced expression of avoidance learning but less rapid extinction of the learned response. The results were related to effects of the drug on short-term memory trace decay and consolidation.

Key Words: Chlorpromazine — Short-Term Memory — Memory Decay — Memory Consolidation — Passive Avoidance.

Introduction

The impairment by chlorpromazine of the acquisition of avoidance responses has been extensively documented (Herz, 1960; Dews and Morse, 1961). The effect has been noted in learning established under conditions of positive as well as negative reinforcement (e.g., Hanson et al., 1964; Ray and Bivens, 1966, 1967) in a wide variety of experimental test situations and in different species of experimental animals. Less is known, however, regarding the effects of the drug upon the retention of the learned responses, i.e., upon memory processes, although several workers (e.g., Courvoisier et al., 1953; Ambrus et al., 1957) have demonstrated a chlorpromazine-induced blocking of an already acquired conditioned avoidance response. Since drug administration preceded testing in such studies, rather than following immediately upon the learning process, the implication is that the drug's action involved impairing response elicitation rather than influencing a memory mechanism. Nevertheless, since chlorpromazine acts, in part, as a central nervous system depressant, it might be expected to impair the process of consolidation of short-term memory traces. Several workers have demonstrated this effect for various other depressant drugs (Leukel, 1957; Essman and Jarvik, 1960; Abt et al., 1961; Pearlman et al., 1961; Doty and Doty, 1964; Garg and Holland,
1968). On the other hand, Steinberg (1959) and Summerfield and Steinberg (1959) have shown that a depressant drug, nitrous oxide, administered shortly after a learning experience, may actually enhance retention. These investigators have suggested that the drug may act to prevent the establishment of subsequent memory traces and hence to reduce intertrace interference.

Chlorpromazine is particularly interesting to investigate in this connection in view of its suggested action in attenuating or blocking input to the midbrain reticular formation from ascending sensory pathways (Bradley and Key, 1958, 1959). In thereby reducing the cortical arousing action of sensory input arising immediately subsequent to the learning experience, chlorpromazine might be expected to reduce post-learning interference and hence act in the manner proposed by Summerfield and Steinberg for nitrous oxide. Roberts (1965) has in fact commented on an apparent, but non-significant, enhancement of retention following post-learning chlorpromazine administration, and the present investigations were undertaken in an attempt to provide definitive information on the effects of chlorpromazine upon retention mechanisms.

Several considerations were important in determining the nature of the test situation employed and the behavioural measures examined. As Cooper and Krass (1963) have pointed out, in any behavioural test situation involving repeated acquisition trials, drug injections which follow one acquisition trial necessarily precede the next, and it may not be possible entirely to distinguish post-learning from pre-learning effects of the drug. Accordingly, a one-trial learning situation was employed in the present experiments. The learned response was one of avoidance, the training conditions being so arranged as to permit only incomplete learning to occur in saline-treated control subjects. This was to ensure that there remained a margin for improvement in the drug-treated experimental subjects. The non-significance of the apparent drug-induced enhancement of retention in Robert's experiment may have resulted from the high level of learning demonstrated by his saline-treated controls.

Roberts (1965) and Roberts et al. (1965) used, as a measure of the level of avoidance learning, the total time which a rat spent in an area where it had previously received an electric shock. This measure, however, may be regarded as a function of two distinct components, the first being the degree of avoidance learning present at the beginning of the test session, and the second the rate at which this learning extinguishes. Thus, a high level of learning followed by rapid extinction would be expected to give similar results to a low level of learning resistant to extinction. In the experiments reported here three behavioural measures were analysed...