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## AMINEPTINE AND RESPONSE TIMING IN THE RAT

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The operant Fixed Interval (FI), Differential Reinforcement of Low rate (DRL) and duration discrimination schedules were used to assess the effect of the antidepressant drug amineptine on internal clock mechanisms. Subjects were groups of 10 adult male albino rats (Wistar). Injections (I.P.) were made in each case after stabilization of performance, 20 minutes before the beginning of the daily session. Experiment 1 tested single doses of 1, 5, 10 and 20 mg/kg on response rate variables and response timing in FI and DRL. Experiment 2 explored the effects of the chronic injection of a dose of 10 mg/kg on FI, DRL and duration discrimination behavior. Experiment 3 was aimed at testing the effect of a chronically injected low dose of the drug (1 mg/kg) in FI and DRL. Taken together, results from experiment 1 show a dose-dependent effect of the drug on response rate and response timing : response rates increased significantly, whereas response timing was significantly impaired. However, the lowest dose of the drug (1 mg/kg) induced a non-significant trend towards a decrease in response rates and an improvement of the temporal regulation of behavior. Experiment 2 replicated findings from experiment 1. Furthermore, the accuracy of temporal discrimination between auditory stimuli lasting respectively for 2 and 8 seconds was not affected by the chronically injected dose of 10 mg/kg. Experiment 3 partially replicated findings from Experiment 1. Nevertheless, as in experiment 1, trends did not reach statistical significance.

Results collected over the successive experiments show that amineptine at doses of 5, 10 and 20 mg/kg exerts an aspecific stimulation on operant responding in FI and DRL, without specifically altering internal clock mechanisms (duration discrimination). Impairment of response timing in FI and DRL is most probably a by-product of increased motor activity. Results also indicate that the 10 mg/kg dose does not induce behavioral tolerance, sensitization or dependance as assessed from operant responding (other behaviors were not recorded). The absence of significant effects of the 1 mg/kg injections precludes the use of this dose of the drug as a cognitive enhancer, within the limits of the type of task described here. Finally, results suggest that improvements in temporal "awareness" or "anticipation" observed in depressed patients treated with the drug might not be bound to a specific effect of the drug on timing mechanisms, but rather result from its overall aspecific stimulating effects.