

The Effects of Caffeine on Activity Rhythms in Rats

BACKGROUND AND SIGNIFICANCE

Caffeine is a psychoactive stimulant found in many popular beverages, such as coffee, tea and colas. It is also a component of several therapeutic drugs (Barone and Roberts, 1996). In humans, low and intermediate doses of caffeine produce increased alertness and positive inotropic effects on the myocardium, while high doses cause adverse anxiogenic effects, tachycardia and ventricular arrhythmia (Kaplan et al., 1997; Mosqueda-Garcia et al., 1993). Similar stimulant effects are seen in rats. Studies suggest that the mechanism of action involves enhanced dopaminergic activity by competitive antagonism of adenosine receptors that are co-localized and functionally interactant with dopamine receptors.

Most investigations into the effects of caffeine have looked at the time period immediately following drug administration. The effects of caffeine on circadian rhythmicity are unexplored but are of great importance, because such effects, if present, could introduce bias into chronopharmacological studies of psychoactive or cardiovascular drugs.

RESEARCH OBJECTIVES

The goal of this study is to measure the chronopharmacological effects of caffeine on rats with respect to the time of day that the drug is administered. Particular parameters of interest are heart rate, locomotor activity and body temperature. Rats injected with saline will serve as controls for procedural stressors such as injection and handling.

DATA COLLECTION

The subjects, eight Wistar AF adult male rats, will be housed individually under controlled environmental conditions (50% relative humidity, temperature 24 ± 1 °C, LD 12:12). Surgically implanted radiotelemetry devices (inserted under ketamine hydrochloride anesthesia, 100 mg/kg) will be used to obtain continuous readings of H (beats/min), T (°C) and A (counts) via a Dataquest III® remote recording and analysis system. After a period of recovery from implantation surgery, data will be collected across three 7-day periods. During P1, baseline values of H, T and A will be obtained. During P2, four rats will receive a daily dose of caffeine subcutaneously (25 mg/kg) at 0900h while four rats will serve as saline controls. P3 will consist of the final post-treatment (recovery) span.

DATA ANALYSIS AND INTERPRETATION

A Fourier transform power spectrum analysis will be applied to 30-min average daily intervals to identify the dominant period of the three rhythms of P1, P2 and P3. Single cosinor analysis will then be applied to raw telemetered data of H, T and A from

P1, P2 and P3 to detect whether or not circadian periodicities are significant. MESOR (Midline Estimating Statistic of Rhythm), amplitude and acrophase values will be estimated using the linear method of least squares (Morgan and Minors, 1995). The data will then be evaluated for statistical significance with ANOVA, with observation span (P1, P2, P3) and treatment (caffeine or saline) as factors.

It is expected that caffeine administration will have general stimulatory effects on locomotor activity and heart rate. The results will also indicate whether repeated caffeine administration perturbs the circadian periodicity of circulatory physiology, body temperature and locomotor activity. In the event of such perturbations, the analysis will also characterize them as phase-advance or phase-delay effects. If present, such perturbations of rhythmicity would indicate an effect of caffeine on the SCN circadian pacemaker, perhaps mediated through melatonin secretion. This would be consistent with a growing body of work showing that caffeine acts as an adenosine antagonist, leading to a decrease in pineal melatonin production (Babey et al., 1994).

REFERENCES

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