Publication

Comparison of methods for the assessment of locomotor activity in rodent safety pharmacology studies.

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Abstract

INTRODUCTION:
General neurobehavioral assays, like a modified Irwin test or a functional observational battery, are necessary for central nervous system (CNS) safety pharmacology testing near the end of the target validation (early discovery) stage of preclinical drug development. However, at earlier stages, when a greater number of test compounds must be screened for potential CNS side effects, locomotor activity assessment may be a better tool for the comparison of compounds.

METHODS:
Spontaneous locomotor activity counts obtained from two automated test systems - an infrared beam-based activity meter (Actimeter) and the mechanical vibration-based LABORAS - were compared in rats dosed with chlorpromazine (2-8mg/kg) or caffeine (3-24mg/kg), p.o. A modified Irwin test was also performed to visually observe the neurobehavioral effects.

RESULTS:
In all three assays, dose-dependent sedation- and excitation-related effects were observed with chlorpromazine and caffeine, respectively. The two automated activity-detection systems exhibited similar sensitivities in determining changes in locomotor activity, but with the LABORAS being more sensitive than the Actimeter in detecting caffeine-induced increases in vertical activity (rearing behavior).

DISCUSSION:
Infrared beam-based activity detection systems and LABORAS provide relatively-comparable quantitative data regarding locomotor activity. Practical considerations, such as relative cost versus degree of versatility, should be considered when deciding which system to use for the screening of test compounds during the earliest stages of preclinical drug development.