# Scopolamine-induced changes in activity measured in a home cage observation system

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## Background

The internal body clock (suprachiasmatic nucleus of the basal hypothalamus) regulates the circadian rhythms which controls sleep/awake cycles, locomotor activity and feeding/drinking behaviour in both humans and animals [1]. Various drug treatments and neurotransmitters can interfere with these rhythms [2] and consequently drug-induced effects obtained in memory experiments may be due to the direct action of the drug on circadian biological rhythms. Moreover, the effects of the drug may depend on the administration time during the 24 hr cycle.

Scopolamine, a competitive $M_1$ muscarinic cholinergic receptor antagonist, is known to induce cognitive deficits [3], as well as effects on locomotor activity [4, 5] and alteration of sleep stages [6].

## Aim

The present study aimed to investigate the effects of sub-chronic administration of scopolamine on locomotor activity and circadian rhythms of freely moving mice using the PhenoTyper system (Noldus)

## Methods

C57BL6/j male mice were habituated for two days to the PhenoTyper cage to bring the activity to basal levels. Mice were maintained on a 12:12 hr light/dark cycle (light off at 7pm). On days 3-6 mice were intraperitoneally injected for four consecutive days with either saline or scopolamine (0.5 mg/kg) 1-2 hr prior the beginning of the dark phase and returned into the PhenoTyper cage. Locomotor activity was continuously recorded (24 hr/day) with the tracking software Ethovision (Noldus), and data were analysed using time intervals of 1 hr. Further analysis of activity in light and dark phases and 3 hr post-injection was performed. Data were analysed with repeated measures Two-way ANOVA, with treatment and time point as independent variables followed by Bonferroni post-hoc test with no correction for large number of possible comparison. Thereafter data recorded during the first 3 hr post injection were averaged for each day of treatment. The null hypothesis "does scopolamine has a lower activity compared to controls" was defined and Student t-tests were used to compare the two treatment groups at each day. For all comparisons, a 95% confidence level ($p<0.05$) was set for the differences to be considered as significant.

## Results

The PhenoTyper detected circadian rhythm of mice as changes in locomotor activity (see Figure 1a), with no drug-induced effects in scopolamine-treated subjects, which showed similar circadian rhythms of activity to controls ($p>0.05$). However, further analysis revealed that scopolamine induced a significant reduction in overall locomotor activity during the first three hours post-injection, this effect was only evident following the first two days of treatment with effects no further observed following subsequent administration (see Figure 1b).

## Conclusions

The PhenoTyper measured circadian rhythms and locomotor activity of the mice. Scopolamine did not affect such rhythms; however, it decreased the activity during the light/dark change event (or crepuscule), during which an increase in activity is normally expected. Moreover, the decrease of locomotor activity was time-dependent with effects only observed following initial treatment, suggesting a possible tolerance to the effect of scopolamine. Scopolamine is known to increase locomotor activity [4, 5], yet the results presented in this study, suggest that such effect may depend on the time of the light-dark cycle at which the drug is administered. In conclusion, the present data indicate the versatility of the PhenoTyper as a device to investigate not only drug-induced changes in locomotor activity, and cycle-dependent effects, but also the possible establishment of behavioural tolerance to such effects of the drugs.

### References

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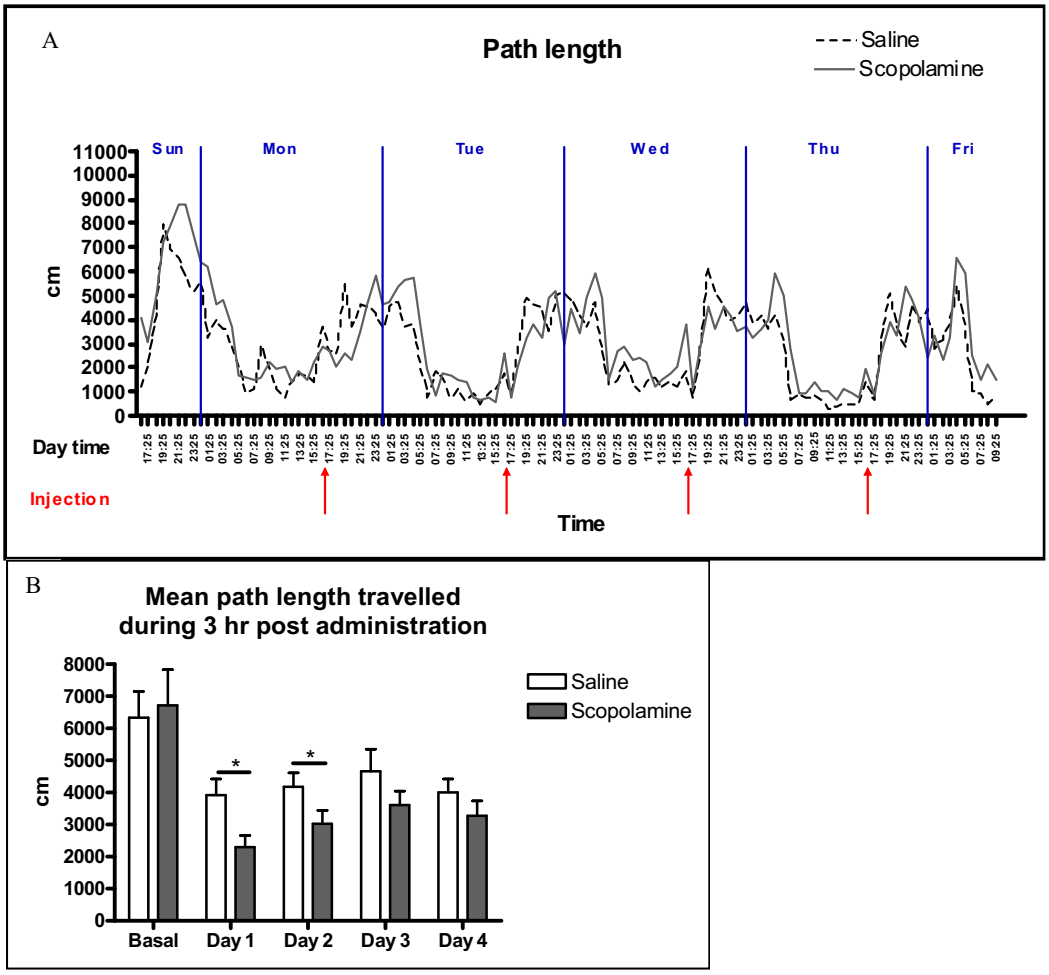


***Figure 1.*** *Circadian rhythm recorded over four consecutive days in saline- and scopolamine-treated mice as changes in locomotor activity (a). Scopolamine did not change the normal circadian locomotor activity, but it decreased activity for 3 hr post-administration during the first two days of administration only (b). Asterisks represent significant difference at $p<0.05$.*