Introduction: Traditional core battery CNS safety pharmacology assessment relies on the FOB/Irwin, a subjective behavioural screen including a panel of rodent-specific parameters that are difficult to translate to human outcomes. Home cage monitoring systems objectively measure continuous rodent behavior, day and night, over multiple days. The welfare benefits of the approach, which allows group housing and non-invasive monitoring, are established. However, the value of these data in CNS safety assessment compared to those obtained from the FOB/Irwin remains largely untested.

The aim of this collaborative work was to assess the potential of rodent home cage monitoring, using a few key parameters (locomotor activity, rearing and body temperature), to better predict risk over traditional FOB/Irwin remains largely unexplained.

Methods: For each test condition, six male Han:Wistar rats (sourced from Charles River UK Limited, Margate) were implanted with temperature sensitive RFID transponders (BioMark USA) and housed 3 per cage. Cages were placed inside the home cage monitoring system and tested for 10 days to provide an initial 4 days baseline measurement followed by the dose/treatment day and then followed by a further 5 days post-dose. In addition to the dose procedure, a blood sample was taken within 24 hrs. Both events are indicated on the plots. On post-dose day 3, the cages were changed.

For each animal, 3 days of pre-dose data are averaged to form a 24 hr baseline profile. The continuous profiles (24 hr or 5 days) show the behavioural profile from the previous 24 hrs to 5 days. These data are highlighted by a yellow overlay. The bar graphs focus on specific time windows for reference. The bar graphs focus on specific time windows for reference. The bar graphs focus on specific time windows for reference.

Activity – dosing day (dark phase)
Rearing – dosing day (dark phase)
Activity – dosing day (post blood sample)
Activity – five days post dose (dark phase)
Temperature – 9h post dose
Activity – five days post dose (dark phase)
Rearing – last 9h dosing day (dark phase)
Activity – one hour post dose
Activity – five days post dose (dark phase)

Conclusions: All three test compounds clearly affected behavioral activity and in some cases at concentrations that observed in previous Irwin tests. The continuous behavioural profile obtained from home cage monitoring graphically demonstrates the natural behavioral variability in animals over time and clearly highlights a sampling risk in using snapshot observations at arbitrary times. Effects that were not originally detected in FOB/Irwin tests may well be due to the sampling effect, which is particularly acute during the dark phase (which is generally not observed). In addition to the continuous non-evolved behavioral profiles, we show that routine interventions, such as blood sampling and cage changes, can be used to evoke behavioral responses with measurable effects reported for two of the test compounds. In summary, continuous collection of a few key parameters using home cage monitoring represents an animal welfare refinement and could be used to improve sensitivity in repeat dose toxicity studies alongside clinical observations or in place of FOB/Irwin.