Basal and exploratory activity of mice: individual testing versus automated monitoring in a social home cage context

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Summary

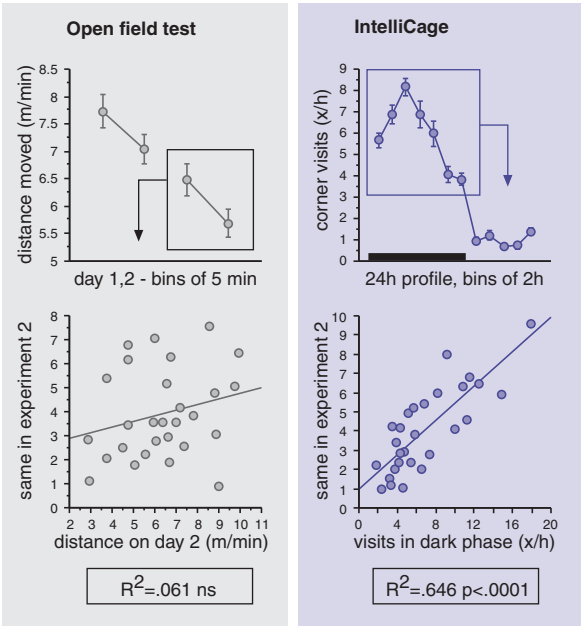
Basal and exploratory activity of mice are traditionally assessed in test batteries in which animals are tested individually. This approach is labor intensive and inefficient given the large number of genetically modified mouse lines that need to be phenotyped. In addition it yields unreliable results due to the lack of standardization and the stress induced by social isolation of the animals, frequent handling, and exposure to changing testing environments. TraffiCage and the operant learning environment IntelliCage are newly developed fully automated and standardized testing devices that permit to investigate transponder tagged mice directly in their home cage and in a social context.

In order to evaluate the suitability of TraffiCage and IntelliCage to assess basal and exploratory activity of mice, we have tested three mouse strains (C57BL6, DBA/2, B6129F1) and a mutant line underexpressing the subunit NR1 of the NMDA receptor first in TraffiCage and IntelliCage and then individually in an established test battery (open field, light/dark box, O-maze, emergence test, object exploration). In order to compare the reproducibility of results, a genetically heterogeneous population (C57BL/6 x 129Sv F2) was tested twice with an interval of 4 months in IntelliCage and in the open field test.

Results and Conclusions
TraffiCage and IntelliCage readily discriminated the mouse strains as well as mutants and controls of the NR1 line based on measures of spontaneous activity. Differences correlated well between TraffiCage and IntelliCage, but were only partial predictors of results in subsequent individual tests, indicating that new protocols in the environment of TraffiCage and IntelliCage need separate validation. Repeated analysis of the F2 population revealed much improved reproducibility of activity measurements obtained in IntelliCage compared to individual testing in the open field.

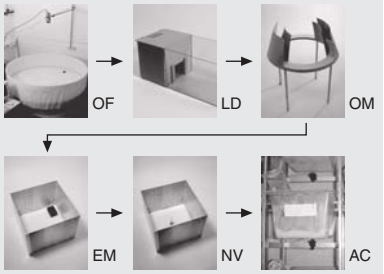
Methods. Animals all female ca. 9 weeks at onset of testing. B6 (C57BL/6JOla), D2 (DBA/2JOla,) F1 (B6129SvF1/Ola) from Harlan Netherlands. NR1neo (Mohn et al. Cell 98:427, 1999) and WT littermates from heterozygous crossings at Institute of Anatomy (background F1 C57BL/6J x 129S6/SvEvTac), breeders gift from University of North Carolina. F2 (B6129SvF2) from Jackson Laboratory. Behavioral tests: OF (Open field) diameter 1.5 m, 2 days x 10 min. LD (light-dark box) 1x5 min, 500 lux. NM (elevated O-maze) 1x10 min, diameter 46 cm. EM (emergence test) 1x30 min, 50x50 cm followed by NV (novel object test) 30 min habituation, 30 min with object. OF-NV recorded using Noldus EthoVision 3.0. AC (ActiviScope) cage rack with passive IR sensors. TraffiCage and IntelliCage (modules default and nosepoke adaptation) by NewBehavior Inc. (www.newbehavior.com).

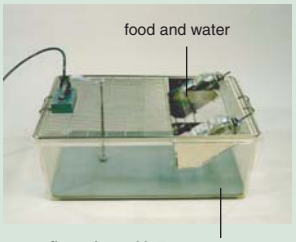
IntelliCage improves reliability

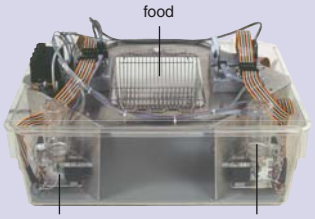


30 female B6129F2 mice were observed for 6 days in IntelliCage, then on 2 days in the open field test. This was repeated several months later. Test - retest reliability was much better for IntelliCage than for the open field test.

IntelliCage and TraffiCage discriminate strains and mutants based on spontaneous activity

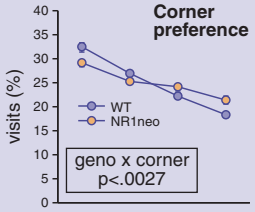


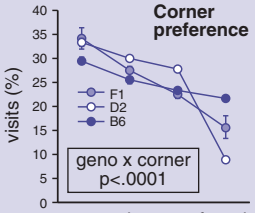


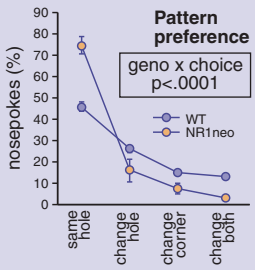


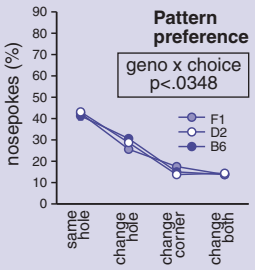

nosepoke at one of two water acces doors in a corner

parameter	standard test battery	TraffiCage	IntelliCage
activity in novel environment	D2<B6=F1 (OF, LD) D2>B6=F1 (OM,NV,EM)	B6>D2=F1	B6=D2>F1
	NR1neo=WT (OF,LD,EM) NR1neo>WT (OM,NV)	NR1neo<WT	NR1neo<WT
basal activity	D2=B6<F1 (AC)	B6=D2=F1	B6>D2=F1
	NR1neo<WT (AC)	NR1neo=WT	NR1neo<WT
anxiety-related measures	D2>F1>B6 (OF,LD,EM) D2=F1>B6 (OM) D2<F1<B6 (NV)	F1=D2>B6	F1>D2=B6
	NR1neo>WT (OF) NR1neo=WT (LD,EM) NR1neo<WT (OM,NV)	NR1neo<WT* NR1neo>WT**	NR1neo>WT
	time/activity near wall (OF,EM) time in dark (LD) time in closed sector, less head dips (OM) object avoidance (NV)	*time under cover **object avoidance	latency to 1st visit and 1st nosepoke









10 D2, 10 129B6F1 and 10 B6 mice were observed for 6 days in TraffiCage and IntelliCage, tested in a battery of exploration tests, and monitored for 14 days in ActiviScope. 14 NR1neo mice and 14 controls did the same program. 5 NR1neo were excluded from IntelliCage because they refused to drink.

Corner preferences and nose poking patterns in IntelliCage discriminate strains and are affected by the mutation. NR1neo mice showed a strongly increased tendency to perform repeated nosepokes at the same door.