Supplementary materials

Materials and methods

Detailed description of the 5-CSRTT paradigm

The test procedure was conducted in a five-hole box system (TSE, Germany). Animals were trained for two different setup of 5-CSRTT. In the usual "light on" version, rats had to nose-poke into that hole where the light was turned on. In the "light off" paradigm, all holes were lit and the stimulus was turning off the light in one of the holes. Half of the animals were trained for the "on", half of the animals were trained for the "off" version in each strain.

The boxes were equipped with 5 nose-poke modules on the back wall and with a magazine at the front wall. After 5 sec inter-trial interval, in one randomly selected nose-poke module a 1 sec long stimulus was presented. The animal made a correct response if nose-poked into this hole during the stimulus presentation or within 5 sec afterwards (limited hold). Correct responses were rewarded with a pellet delivered into the magazine. Nose-poke into the magazine initiated the next trial. The animal made an incorrect response if nose-poked into one of the holes where the stimulus was not presented. An omission response was recorded when the rat did not make any nose-poke up to the end of the limited hold. Incorrect responses were followed by 5 sec time-out punishment, when the house light was turned off ("light on" version) or on ("light off" version). After the time out, the house light was set back and the rat could start the next trial by nose-poking into the magazine. The animal made a premature response, if nose-poked into any of the holes during the inter-trial interval. These responses were also punished with time-out. Length of a daily test session was 20 min. Ratio of correct responses was regarded as a measure of attention, while number of premature responses was regarded as a measure of impulsivity (Robbins, 2002).

Rats were trained for the task in stages with gradually increasing difficulty. Animals could step to the next training stage, if they collected at least 40 rewards during a training session. In the first stage they were trained to use the magazine, in the next stage they were trained to use the nose-poke module. In the following stages limited hold and stimulus duration was gradually decreased. In the last stage, beside premature and incorrect errors, omissions were also punished. The "on version" had 10 training stages, while the "off version" had 12. In the "off version" in the 3rd stage only 3 holes were active and only incorrect responses were punished. From the 4th stage training scheme was similar to that of the "on version", except the number of the active holes (Supplementary Table 1). In the last stage all the five holes were activated.

Supplementary Table 1. Training stages of the 5-CSRTT.

”on” version					“off” version				
Training stage	Open holes	Time out for	Stimulus duration (s)	Limited hold (s)	Training stage	Open holes	Time out for	Stimulus duration (s)	Limited hold (s)
1	none	nose-poke to magazine rewarded			1	none	nose-poke to magazine rewarded		
2	3rd	p	30	15	2	3rd	p	30	15
					3	1st, 3rd, 5th	i	30	15
3	all	i, p	30	15	4	1st, 3rd, 5th	i, p	30	15
4	all	i, p	30	5	5	1st, 3rd, 5th	i, p	30	5
5	all	i, p	15	5	6	1st, 3rd, 5th	i, p	15	5
6	all	i, p	8	5	7	1st, 3rd, 5th	i, p	8	5
7	all	i, p	4	5	8	1st, 3rd, 5th	i, p	4	5
8	all	i, p	2	5	9	1st, 3rd, 5th	i, p	2	5
9	all	i, p	1	5	10	1st, 3rd, 5th	i, p	1	5
10	all	i, p, o	1	5	11	1st, 3rd, 5th	i, p, o	1	5
					12	all	i, p, o	1	5

i = incorrect, p = premature, o = omission

When rats completed the training, task difficulty was increased in two sessions. In one, stimulus duration was decreased to 250 ms. Reducing the duration of the stimulus increases the attentional load of the task (Robbins, 2002). In the other, inter-trial interval was increased to 8 s. Increasing inter-trial interval induces impulsive responses (Robbins, 2002). Our results showed that the "off" version was a little bit more difficult than the „on" version: it took two days more for the animals to acquire the task, but afterwards the two groups showed similar performance even in the above mentioned two challenge conditions (Gyertyán et al., 2016).

Description of the stages in ASST

Long-Evans rats were trained in the following sequence: the first stage was simple discrimination, in which only stimuli of the relevant dimension (odor or floor texture) were present; compound discrimination (CD), where stimuli of the irrelevant dimension were introduced alongside the same exemplars of the relevant dimension; intradimensional shift (IDS), where new exemplars of both dimensions were introduced but the same dimension remained rewarded, reversal-1 (IDR) when the stimulus set remained the same but the reward contingency was reversed in the relevant dimension, extradimensional shift (EDS), in which new exemplars of both dimensions were introduced but the earlier relevant dimension became irrelevant and the earlier irrelevant one became relevant and finally reversal again of the stimuli in the relevant dimension (EDR). After the EDR stage, we introduced a second EDS: either back to the original relevant stimulus set (EDSback) or to a new stimulus dimension (color). Those individuals which completed this stage, too were then challenged with subsequent EDS trials to any of the three stimulus set (multiple EDS). LH rats started the training with CD, moreover, animals faced two irrelevant dimensions out of three right at the beginning: odor was the relevant cue and doormat and color were irrelevant cues. After the acquisition of CD, half of the animals advanced to a reversal task, the other half entered IDS trials. Then those animals which had received a reversal task went into IDS, and those who had completed the set-shift received reversal trials. This was followed by an EDS phase in case of both groups. Afterwards, we ramified the route again: half of the animals received a reversal stage (EDR) followed by a second extradimensional set-shift (EDS2) to the third stimulus set (color) while the other half did it in reverse order. Finally, the most proficient

animals were tested in extradimensional shift trials without substitution (EDSwos) where the cues themselves remained unchanged

According to their achieved stages a performance level score was assigned to each animal depending on how many cognitive functions it could use: 0-random choice; 1- discrimination only; 2 – IDS or reversal; 3 – IDS and reversal; 4 – EDS; 5 – EDSback (LE) or EDS2 (LE, LH); 6 multiple EDS (LE) or EDSwos (LH).

Handling of missing data

One source of missing data were those cases, when a rat was not able to complete the training or stopped working in the paradigm after the completion of the training (i.e. variables measuring performance in a task could not be recorded). These data were substituted by the worst value observed in the variable plus the twofold standard deviation (worst+2SD). Following this procedure, the missing values of those animals which did not participate in the task were substituted. The proxy value was the mean of the variable calculated including "worst+2SD" values. Missing data calculation was separately performed for the strains.

In the 5-CSRTT, one LE rat was able to complete the training, but stopped working in the paradigm. Therefore, its change in correct and premature responses were replaced with "worst+2SD".

In the ASST, 11 LE and 7 LH rats were not able to complete the compound discrimination stage. In case of these animals time required for completing compound discrimination was replaced with "worst+2SD".

In the COOP test, two LH animals from different cages died before the training. Their cage-mates were also omitted from the training, because the three types of pairs could not be formed within the same cage. Data of the omitted LH rats were replaced with the mean of the strain. One LE animal died before the training, its data were replaced with the mean of the strain. Similarly, missing data of two animals displaying aggressive behavior against their pair were replaced with the mean. Furthermore, two LE rats could not complete the training, their values were substituted with "worst+2SD".

One LE rat died before the episodic memory test, its missing data were substituted with the strain mean.

In the NOR test, discrimination indices were not calculated in case of 8 LH rats, because they were excluded as their exploration time did not reach 10 s on the acquisition or on the retention trial. There data were replaced with the mean of the strain.

Results

Raw variables

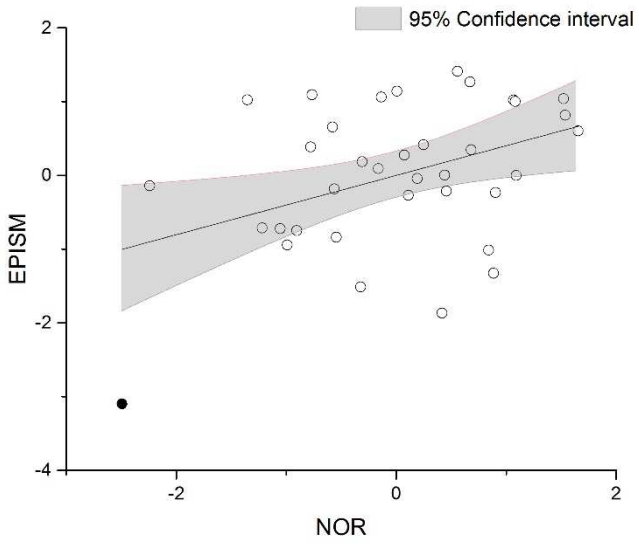
LH \ LE	5Ch_Lev@50	5Ch_Td50	5Ch_Td100	5Ch_pinc	5Ch_cdec	5Ch_rew	A_TdCD	A_Stage	Co_Lev@50	Co_Td50	Co_Td100	Co_rew	Co_SuccTr	ot	te	ld	Expl_T1	Expl_T2	NOR	M_day1	M_day2	M_day3	E_first_tr1	E_first_tr2	E_last_tr1	E_last_tr2
5Ch_Lev@50		-0,87	-0,47	-0,26	-0,01	0,41	-0,10	-0,01	-0,18	0,14	0,09	-0,14	-0,09	-0,04	0,05	-0,09	-0,15	-0,20	0,10	-0,23	-0,08	-0,35	-0,15	-0,02	-0,36	-0,16
5Ch_Td50	-0,40		0,58	0,31	0,05	-0,41	0,22	-0,07	0,05	-0,05	-0,03	0,26	0,22	0,11	0,04	0,28	0,05	0,17	-0,18	0,04	-0,12	0,41	0,17	0,10	0,24	0,19
5Ch_Td100	-0,42	0,99		0,10	0,01	-0,35	0,19	-0,03	0,11	-0,08	-0,12	0,29	0,25	0,30	0,30	0,23	-0,17	0,00	-0,12	-0,07	0,06	0,17	0,08	0,25	0,15	0,22
5Ch_pinc	-0,09	0,00	0,01		0,21	-0,10	0,00	-0,14	-0,24	0,23	0,26	0,05	0,05	0,15	-0,01	-0,08	-0,03	-0,16	-0,01	-0,16	-0,07	0,12	0,17	-0,02	0,15	0,00
5Ch_cdec	0,22	-0,13	-0,13	-0,21		0,19	0,08	-0,17	-0,16	0,09	0,06	-0,08	-0,08	0,20	0,19	-0,02	-0,15	-0,23	0,07	-0,13	0,08	0,03	0,17	0,08	-0,25	-0,13
5Ch_rew	0,41	-0,13	-0,19	-0,09	0,52		0,04	-0,20	0,01	-0,07	-0,15	0,18	0,20	0,18	0,25	-0,05	0,29	-0,20	0,17	-0,25	0,04	-0,05	-0,08	-0,10	-0,24	-0,15
A_TdCD	0,08	0,04	0,03	0,09	0,26	0,07		-0,83	-0,16	0,42	0,16	0,09	0,09	-0,13	0,00	0,11	0,12	-0,31	-0,23	-0,02	-0,20	-0,16	0,19	0,15	0,18	-0,01
A_Stage	-0,06	-0,01	0,00	0,05	-0,16	-0,03	-0,86		0,12	-0,35	-0,10	-0,20	-0,21	0,18	0,02	-0,07	-0,09	0,33	0,15	0,03	0,00	0,10	-0,19	-0,23	-0,23	-0,01
Co_Lev@50	0,01	0,18	0,17	0,08	-0,12	-0,10	-0,25	0,27		-0,88	-0,84	0,43	0,38	-0,02	-0,05	0,02	-0,05	0,25	-0,04	0,04	0,10	-0,14	-0,17	0,00	0,00	-0,07
Co_Td50	0,05	-0,15	-0,17	-0,13	0,10	0,10	0,16	-0,19	-0,84		0,84	-0,34	-0,32	0,04	0,06	-0,04	0,06	-0,24	-0,06	0,00	-0,16	-0,04	0,09	-0,08	-0,03	0,01
Co_Td100	0,18	-0,18	-0,19	0,11	0,04	0,15	0,11	-0,16	-0,64	0,53		-0,55	-0,55	-0,07	-0,03	-0,07	0,01	-0,20	0,01	-0,01	-0,19	-0,01	0,08	-0,07	-0,13	-0,01
Co_rew	-0,06	-0,05	0,00	-0,05	0,15	-0,20	0,07	0,09	0,14	-0,21	-0,33		0,99	0,49	0,27	0,08	0,00	0,05	0,02	-0,11	0,09	0,12	-0,10	-0,04	-0,02	0,06
Co_SuccTr	-0,09	-0,09	-0,03	-0,02	0,09	-0,24	-0,02	0,16	0,12	-0,17	-0,31	0,98		0,46	0,25	0,10	0,00	0,03	0,02	-0,11	0,10	0,14	-0,08	-0,02	0,02	0,06
ot	-0,25	-0,09	-0,05	0,16	0,01	-0,22	-0,04	0,13	-0,08	0,05	-0,15	0,13	0,14		0,51	0,03	0,00	0,10	0,27	-0,21	-0,10	0,07	-0,29	-0,30	-0,26	0,14
te	-0,03	0,05	0,05	0,09	-0,04	-0,12	0,14	-0,17	-0,16	0,29	0,10	-0,41	-0,39	-0,04		0,04	-0,12	-0,17	0,23	-0,26	-0,13	-0,03	-0,19	-0,23	-0,21	-0,11
ld	-0,30	0,06	0,08	-0,09	-0,09	-0,39	-0,09	0,01	0,23	-0,22	-0,18	0,13	0,14	0,02	0,07		-0,18	0,10	-0,33	0,13	-0,12	-0,13	0,09	0,26	-0,17	0,24
Expl_T1	-0,27	0,16	0,16	0,27	-0,08	0,05	-0,01	-0,04	0,14	-0,14	-0,29	-0,01	-0,02	0,09	0,10	-0,15		0,40	0,03	0,02	-0,06	-0,18	-0,18	-0,20	0,06	-0,18
Expl_T2	-0,06	0,03	0,05	-0,03	-0,04	0,01	0,09	-0,26	0,07	0,01	-0,13	0,20	0,18	-0,29	0,06	0,19	0,44		-0,09	0,16	-0,09	-0,06	-0,29	-0,20	0,12	0,20
NOR	-0,04	-0,17	-0,13	0,37	-0,14	-0,08	-0,21	0,21	-0,06	-0,04	0,34	0,12	0,15	0,18	-0,23	-0,04	-0,21	-0,06		-0,33	0,09	0,22	-0,21	-0,42	-0,10	-0,35
M_day1	0,02	0,09	0,09	0,01	-0,02	-0,02	-0,01	-0,10	0,17	-0,20	-0,07	0,02	0,03	-0,06	-0,11	-0,09	0,27	0,11	-0,22		0,57	-0,02	0,14	0,16	0,27	0,28
M_day2	0,01	-0,20	-0,18	-0,14	0,10	0,03	-0,18	-0,02	0,00	-0,12	0,16	-0,21	-0,21	0,00	-0,03	-0,08	0,24	0,05	0,03	0,51		0,11	0,12	0,12	0,25	0,24
M_day3	0,18	-0,24	-0,23	0,03	0,01	-0,05	-0,15	0,05	0,08	0,00	-0,01	-0,25	-0,23	0,21	0,11	0,33	-0,09	-0,01	-0,16	0,29	0,33		0,00	0,04	0,18	0,06
E_first_tr1	0,07	-0,05	-0,03	0,31	0,25	0,10	0,36	-0,18	-0,05	-0,07	0,09	-0,12	-0,17	0,06	-0,17	0,02	-0,16	-0,24	0,03	-0,21	-0,11	-0,12		0,71	0,18	0,01
E_first_tr2	-0,25	-0,01	-0,02	0,01	0,01	-0,09	-0,07	0,17	-0,06	0,10	0,02	-0,36	-0,34	0,16	0,24	0,22	0,06	-0,13	-0,02	0,09	0,23	0,16	0,20		0,09	0,22
E_last_tr1	-0,29	0,01	0,05	-0,21	0,14	-0,07	-0,15	0,26	-0,01	-0,08	-0,23	0,32	0,33	0,19	0,06	0,03	-0,02	-0,22	-0,23	-0,05	-0,13	-0,12	-0,18	0,04		0,43
E_last_tr2	0,09	-0,22	-0,17	0,00	0,16	0,02	0,01	0,02	0,01	-0,13	-0,22	0,07	0,03	0,02	0,04	0,19	-0,04	0,03	-0,23	0,17	-0,06	0,32	0,08	-0,03	0,40	

Supplementary Fig. 1. Results of the correlation analysis on raw data. The upper and lower panel shows correlation coefficients for LE and LH respectively. Significant correlations are marked with red. Correlations within the same test are marked with gray background. For the variable codes see Table 1.

Composite variables

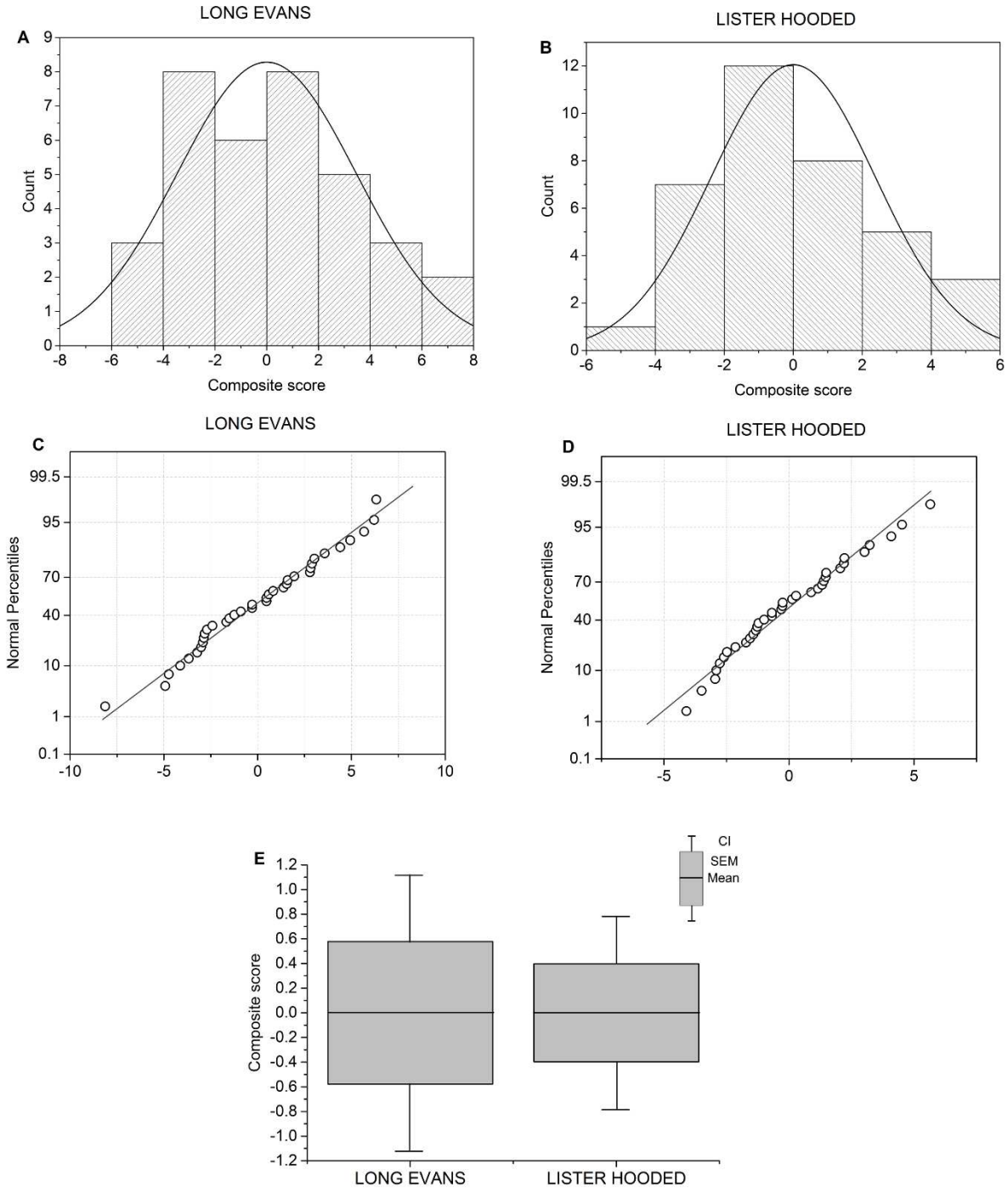
LH\LE	EXPL	NOR	5CSRTT	ASST	COOP	MWM	EPISM
EXPL		0.04	-0.12	0.16	0.08	0.19	0.25
NOR	-0.15		0.18	0.22	0.00	0.01	**0.40**
5CSRTT	-0.30	-0.09		0.04	0.00	0.17	0.31
ASST	-0.09	0.22	-0.07		0.24	-0.12	0.16
COOP	0.13	-0.13	-0.21	0.26		0.08	0.00
MWM	0.15	0.15	-0.12	-0.06	-0.08		0.33
EPISM	0.06	0.20	-0.05	-0.02	-0.06	0.03	

Supplementary Fig. 2. Result of correlation analysis on composite variables. The upper and lower panel shows correlation coefficients for LE and LH respectively. Significant correlations are marked with red.



Supplementary Fig. 3. Correlation between the composite variables of episodic memory and NOR in LH rats ($r = 0.40$, $p < 0.05$). Gray band indicate 95% confidence interval. Data point marked with filled circle indicate the outlier value. By removing the outlier the value of the correlation coefficient dropped back to 0.23 and significance of the correlation was lost.

Composite scores



Supplementary Fig. 4. Descriptive statistics of the composite variables in the two rat strains: histograms (panel A and B), normal probability plots (panel C and D) for LE and LH respectively and comparison of composite scores of the two strains (panel E).