

	<u>analysis</u>	<u>significance</u>	<u>factor</u>		<u>analysis</u>	<u>significance</u>	<u>factor</u>
Plasma concentrations				Home cage activity			
(nicotine [$\mu\text{g}\cdot\text{l}^{-1}$])	multivariate	$F_{(3,12)}=0.71, p=0.415$	sex·genotype	(time active [%])	repeated measures	$F_{(3,39)}=0.63, p=0.641^*$	treatment·time·sex·genotype
	multivariate	$F_{(1,12)}=1.69, p=0.621$	genotype		repeated measures	$F_{(3,39)}=0.55, p=0.801^*$	time·treatment
	multivariate	$F_{(1,12)}=0.74, p=0.406$	sex		repeated measures	$F_{(3,39)}=0.58, p=0.676^*$	time·genotype
(cotinine [$\mu\text{g}\cdot\text{l}^{-1}$])	multivariate	$F_{(3,12)}=0.49, p=0.499$	sex·genotype		repeated measures	$F_{(3,39)}=0.60, p=0.660^*$	time·sex
	multivariate	$F_{(1,12)}=0.26, p=0.218$	genotype		repeated measures	$F_{(3,39)}=3.65, p=0.013^*$	time
	multivariate	$F_{(1,12)}=0.30, p=0.593$	sex				
Caloric intake				Working memory			
<u>7-13 days food restriction</u>				<u>forced alternation training</u>			
(food consumption [$\text{g}\cdot\text{d}^{-1}$])	univariate	$F_{(7,9)}=0.17, p=0.686$	treatment·sex·genotype	(time reward collected [s])	repeated measures	$F_{(3,169)}=0.94, p=0.474^*$	treatment·time·sex·genotype
	univariate	$F_{(1,9)}=0.16, p=0.310$	treatment		repeated measures	$F_{(3,169)}=0.74, p=0.551^*$	time·genotype·sex
	univariate	$F_{(1,9)}=0.25, p=0.631$	genotype		repeated measures	$F_{(3,169)}=0.65, p=0.716^*$	time·treatment·sex
	univariate	$F_{(1,9)}=0.22, p=0.651$	sex		repeated measures	$F_{(3,169)}=0.70, p=0.670^*$	time·treatment
<u>free access to food</u>				<u>paired-trial alternation test</u>			
(animal weight [g] at day 6)	multivariate	$F_{(7,71)}=0.07, p=0.797$	treatment·sex·genotype	(% correct alternations)	univariate	$F_{(2,44)}=3.84, p=0.029$	treatment·sex·genotype
	multivariate	$F_{(1,71)}=0.77, p=0.384$	treatment		univariate	$F_{(2,44)}=6.63, p=0.003$	treatment·genotype
	multivariate	$F_{(1,71)}=0.20, p=0.657$	genotype		univariate	$F_{(2,44)}=1.70, p=0.936$	treatment
	multivariate	$F_{(1,71)}=75.61, p<0.001$	sex		univariate	$F_{(1,44)}=0.14, p=0.708$	genotype
(animal weight [g] at day 14)	multivariate	$F_{(7,71)}=0.12, p=0.730$	treatment·sex·genotype		univariate	$F_{(1,44)}=6.63, p=0.199$	sex
	multivariate	$F_{(1,71)}=0.83, p=0.366$	treatment	- <i>split by treatment</i>	univariate	$F_{(1,17)}=8.72, p=0.009$	genotype
	multivariate	$F_{(1,71)}=0.19, p=0.663$	genotype	saline	univariate	$F_{(1,18)}=4.89, p=0.040$	genotype
	multivariate	$F_{(1,71)}=93.34, p<0.001$	sex	nicotine [24 mg·kg ⁻¹ ·d ⁻¹]			
Two bottle choice preference				- <i>split by genotype</i>			
(nicotine cons. [$\mu\text{g}\cdot\text{g}^{-1}$ BW])	repeated measures	$F_{(1,42)}=0.77, p=0.439^*$	sex·time·genotype	WT	univariate	$F_{(2,25)}=3.16, p=0.060$	treatment
	repeated measures	$F_{(1,42)}=2.28, p=0.125^*$	time·genotype	-- <i>post hoc</i>			
	repeated measures	$F_{(1,42)}=1.83, p=0.179^*$	sex·time	saline vs nicotine (24 mg)	Bonferoni	$p=0.033$	treatment
	repeated measures	$F_{(1,42)}=37.53, p<0.001^*$	time	TG	univariate	$F_{(2,22)}=4.56, p=0.022$	treatment
(nicotine preference [%])	repeated measures	$F_{(5,135)}=1.23, p=0.297^*$	sex·time·genotype	-- <i>post hoc</i>			
	repeated measures	$F_{(5,135)}=0.48, p=0.795^*$	time·genotype	saline vs nicotine (24 mg)	Bonferoni	$p=0.021$	treatment
	repeated measures	$F_{(5,135)}=2.01, p=0.081^*$	sex·time				
	repeated measures	$F_{(5,135)}=0.83, p=0.539^*$	time				

	<u>analysis</u>	<u>significance</u>	<u>factor</u>		<u>analysis</u>	<u>significance</u>	<u>factor</u>
PPI				(% inhibition at +15 dB)	multivariate	$F_{(7,71)}=5.133, p=0.027$	treatment·sex·genotype
<u>day 6</u>				- <i>split by sex</i>			
(% inhibition at +5 dB)	multivariate	$F_{(7,71)}=6.41, p=0.014$	treatment·sex·genotype	males	multivariate	$F_{(3,36)}=0.46, p=0.503$	treatment·genotype
- <i>split by sex</i>				females	multivariate	$F_{(3,35)}=6.55, p=0.015$	treatment·genotype
males	multivariate	$F_{(3,36)}=1.96, p=0.170$	treatment·genotype	-- <i>split by genotype</i>			
females	multivariate	$F_{(3,35)}=7.11, p=0.012$	treatment·genotype	WT	multivariate	$F_{(1,18)}=1.90, p=0.185$	treatment
-- <i>split by genotype</i>				TG	multivariate	$F_{(1,17)}=4.86, p=0.041$	treatment
WT	multivariate	$F_{(1,18)}=1.99, p=0.176$	treatment				
TG	multivariate	$F_{(1,17)}=5.54, p=0.031$	treatment	Social recognition			
(% inhibition at +10 dB)	multivariate	$F_{(7,71)}=3.07, p=0.084$	treatment·sex·genotype	<u>social interaction (1st exp.)</u>			
- <i>split by sex</i>				(interaction time [s])	univariate	$F_{(7,71)}=0.53, p=0.467$	treatment·sex·genotype
males	multivariate	$F_{(3,36)}=0.81, p=0.814$	treatment·genotype		univariate	$F_{(7,71)}=0.01, p=0.971$	treatment·sex
females	multivariate	$F_{(3,35)}=3.51, p=0.070$	treatment·genotype		univariate	$F_{(7,71)}=0.04, p=0.845$	sex·genotype
-- <i>split by genotype</i>					univariate	$F_{(1,71)}=1.43, p=0.236$	treatment
WT	multivariate	$F_{(1,18)}=5.54, p=0.379$	treatment		univariate	$F_{(1,71)}=0.24, p=0.630$	genotype
TG	multivariate	$F_{(1,17)}=4.32, p=0.053$	treatment		univariate	$F_{(1,71)}=5.60, p=0.021$	sex
(% inhibition at +15 dB)	multivariate	$F_{(7,71)}=8.43, p=0.006$	treatment·sex·genotype	<u>2h intertrial</u>			
- <i>split by sex</i>				(interaction time [s])	univariate	$F_{(15,60)}=0.32, p=0.575$	treatment·object·genotype·sex
males	multivariate	$F_{(3,36)}=0.81, p=0.373$	treatment·genotype		univariate	$F_{(15,60)}=4.54, p=0.037$	treatment·object·genotype
females	multivariate	$F_{(3,35)}=6.47, p=0.013$	treatment·genotype		univariate	$F_{(1,60)}=0.19, p=0.669$	treatment
-- <i>split by genotype</i>					univariate	$F_{(1,60)}=0.05, p=0.818$	genotype
WT	multivariate	$F_{(1,18)}=2.55, p=0.128$	treatment		univariate	$F_{(1,60)}=6.60, p=0.013$	object
TG	multivariate	$F_{(1,17)}=9.63, p=0.006$	treatment		univariate	$F_{(1,60)}=0.31, p=0.578$	sex
<u>day 14</u>				- <i>split by genotype</i>			
(% inhibition at +5 dB)	multivariate	$F_{(7,71)}=6.51, p=0.013$	treatment·sex·genotype	WT	univariate	$F_{(3,36)}=6.53, p=0.015$	object
- <i>split by sex</i>				-- <i>split by treatment</i>			
males	multivariate	$F_{(3,36)}=1.07, p=0.309$	treatment·genotype	saline	univariate	$F_{(1,18)}=7.00, p=0.016$	object
females	multivariate	$F_{(3,35)}=7.04, p=0.012$	treatment·genotype	nicotine	univariate	$F_{(1,18)}=0.99, p=0.340$	object
-- <i>split by genotype</i>				TG	univariate	$F_{(3,32)}=3.12, p=0.087$	treatment·object
WT	multivariate	$F_{(1,18)}=2.78, p=0.113$	treatment	-- <i>split by treatment</i>			
TG	multivariate	$F_{(1,17)}=4.54, p=0.048$	treatment	saline	univariate	$F_{(1,16)}=0.06, p=0.810$	object
(% inhibition at +10 dB)	multivariate	$F_{(7,71)}=11.01, p=0.001$	treatment·sex·genotype	nicotine	univariate	$F_{(1,16)}=4.83, p=0.043$	object
- <i>split by sex</i>				<u>4h intertrial</u>			
males	multivariate	$F_{(3,36)}=0.27, p=0.604$	treatment·genotype	(interaction time [s])	univariate	$F_{(15,64)}=5.17, p=0.026$	treatment·object·genotype·sex
females	multivariate	$F_{(3,35)}=14.41, p=0.001$	treatment·genotype		univariate	$F_{(15,64)}=5.61, p=0.021$	treatment·object·genotype
-- <i>split by genotype</i>					univariate	$F_{(1,64)}=0.13, p=0.720$	treatment
WT	multivariate	$F_{(1,18)}=6.03, p=0.024$	treatment		univariate	$F_{(1,64)}=0.53, p=0.469$	genotype
TG	multivariate	$F_{(1,17)}=9.17, p=0.008$	treatment				

	<u>analysis</u>	<u>significance</u>	<u>factor</u>		<u>analysis</u>	<u>significance</u>	<u>factor</u>
				Morris watermaze			
				<u>escape training</u>			
- <i>split by genotype</i>				(distance moved [m])	repeated measures	$F_{(4,146)}=0.69, p=0.617^*$	sex·treatment·time·genotype
WT	univariate	$F_{(1,64)}=0.01, p=0.996$	object		repeated measures	$F_{(4,146)}=2.36, p=0.048^*$	treatment·time·genotype
-- <i>split by treatment</i>	univariate	$F_{(1,64)}=3.80, p=0.056$	sex		repeated measures	$F_{(4,146)}=5.72, p<0.001^*$	treatment·time
saline	univariate	$F_{(3,36)}=4.17, p=0.049$	treatment·object		repeated measures	$F_{(4,146)}=1.67, p=0.153^*$	genotype·time
nicotine	univariate	$F_{(1,18)}=2.67, p=0.120$	object		repeated measures	$F_{(4,146)}=1.80, p=0.123^*$	sex·time
TG	univariate	$F_{(1,18)}=1.55, p=0.230$	object		repeated measures	$F_{(4,146)}=66.22, p<0.001^*$	time
-- <i>split by treatment</i>	univariate	$F_{(3,36)}=4.28, p=0.046$	treatment·object	- <i>split by treatment</i>	repeated measures	$F_{(6,108)}=2.40, p=0.033$	genotype·time
saline	univariate	$F_{(1,18)}=0.84, p=0.371$	object	saline	repeated measures	$F_{(3,66)}=0.85, p=0.492^*$	genotype·time
nicotine	univariate	$F_{(1,18)}=4.77, p=0.042$	object	nicotine	repeated measures		
Novelty preference				- <i>split by genotype</i>	repeated measures	$F_{(6,108)}=5.22, p<0.001$	treatment·time
(interaction time [s])	univariate	$F_{(1,14)} = 4.48, p=0.053$	sex·genotype	WT	repeated measures	$F_{(3,67)}=2.57, p=0.048^*$	treatment·time
	univariate	$F_{(1,14)} = 1.19, p=0.293$	genotype	TG	repeated measures		
	univariate	$F_{(1,14)} = 0.03, p=0.858$	sex	(velocity [cm/s])	repeated measures	$F_{(4,145)}=0.34, p=0.874^*$	sex·treatment·time·genotype
(nose contact time [s])	univariate	$F_{(1,14)} = 5.76, p=0.031$	sex·genotype		repeated measures	$F_{(4,145)}=3.93, p=0.003^*$	treatment·time
	univariate	$F_{(1,14)} = 0.13, p=0.720$	genotype		repeated measures	$F_{(4,145)}=1.50, p=0.200^*$	genotype·time
	univariate	$F_{(1,14)} = 0.08, p=0.781$	sex		repeated measures	$F_{(4,145)}=2.23, p=0.061^*$	sex·time
					repeated measures	$F_{(4,145)}=41.21, p<0.001^*$	time
Operant conditioning				- <i>split by treatment</i>	repeated measures	$F_{(6,108)}=1.02, p=0.418$	genotype·time
(day 10 reward [N])	Kruskal Wallis	$p<0.001$	4 groups	saline	repeated measures	$F_{(3,68)}=1.03, p=0.397$	genotype·time
- <i>post hoc</i>				nicotine	repeated measures		
WT saline vs WT nicotine	Dunnett-T3	$p<0.001$	2 groups	<u>memory test</u>			
TG saline vs WT nicotine	Dunnett-T3	$p=0.004$	2 groups	(distance moved [m])	univariate	$F_{(7,72)}=0.75, p=0.389$	treatment·quadrant·genotype
TG nicotine vs WT nicotine	Dunnett-T3	$p=0.097$	2 groups		univariate	$F_{(7,72)}=2.87, p=0.095$	quadrant·genotype
TG nicotine vs WT saline	Dunnett-T3	$p=0.322$	2 groups		univariate	$F_{(1,72)}=0.01, p=0.929$	treatment
TG nicotine vs TG saline	Dunnett-T3	$p=0.761$	2 groups		univariate	$F_{(1,72)}=6.11, p=0.016$	genotype
(day 10 total nosepokes [N])	Kruskal Wallis	$p=0.001$	4 groups		univariate	$F_{(1,72)}=15.42, p<0.001$	quadrant
- <i>post hoc</i>				- <i>split by genotype</i>			
WT saline vs WT nicotine	Dunnett-T3	$p=0.001$	2 groups	WT	univariate	$F_{(1,36)}=24.67, p<0.001$	quadrant
TG saline vs WT nicotine	Dunnett-T3	$p=0.012$	2 groups	-- <i>split by treatment</i>			
TG nicotine vs WT nicotine	Dunnett-T3	$p=0.156$	2 groups	saline	univariate	$F_{(1,18)}=0.48, p=0.002$	quadrant
TG nicotine vs WT saline	Dunnett-T3	$p=0.550$	2 groups	nicotine	univariate	$F_{(1,18)}=0.92, p=0.003$	quadrant
TG nicotine vs TG saline	Dunnett-T3	$p=0.746$	2 groups				
(day 1 total nosepokes [N])	Kruskal Wallis	$p=0.190$	4 groups				

	<u>analysis</u>	<u>significance</u>	<u>factor</u>		<u>analysis</u>	<u>significance</u>	<u>factor</u>
TG				<u>α7 binding</u>			
saline	univariate	F _(1,18) =1.32, p=0.048	quadrant	(¹²⁵ I) α-bungarotoxin	multivariate	F _(17,478) =0.64, p=0.861	treatment-genotype-region
nicotine	univariate	F _(1,18) =0.06, p=0.924	quadrant	[fmol·mg tissue equivalent-1])	multivariate	F _(1,478) =0.53, p=0.466	treatment-genotype
- <i>split by quadrant</i>					multivariate	F _(17,478) =1.18, p=0.279	genotype-region
error	univariate	F _(1,36) =0.39, p=0.538	genotype		multivariate	F _(17,478) =0.46, p=0.970	treatment-region
target	univariate	F _(1,36) =7.14, p=0.011	genotype		multivariate	F _(17,478) =112.08, p<0.001	region
-- <i>split by treatment</i>					multivariate	F _(1,478) =33.30, p<0.001	genotype
saline	univariate	F _(1,19) =1.98, p=0.177	genotype		multivariate	F _(1,478) =0.47, p=0.492	treatment
nicotine	univariate	F _(1,19) =5.66, p=0.029	genotype	- <i>split by region</i>			
Autoradiography				cingulate cortex	multivariate	F _(1,28) =5.66, p=0.024	genotype
<u>α4β2* binding</u>					multivariate	F _(1,28) =4.42, p=0.044	treatment-genotype
(cytisine-sens.[¹²⁵ I]epibatidine	multivariate	F _(27,719) =0.74, p=0.824	treatment-genotype-region	-- <i>post hoc</i>			
[fmol·mg tissue equivalent-1])	multivariate	F _(1,719) =0.03, p=0.853	treatment-genotype	TG saline vs WT saline	Duncan's	p=0.006	2 groups
	multivariate	F _(27,719) =0.37, p=0.999	genotype-region	TG nicotine vs WT nicotine	Duncan's	p=0.847	2 groups
	multivariate	F _(31,828) =1.47, p=0.030	treatment-region	basomedial amygdala	multivariate	F _(1,22) =6.87, p=0.015	genotype-treatment
	multivariate	F _(27,719) =198.14, p<0.001	region	-- <i>post hoc</i>			
	multivariate	F _(1,719) =75.51, p<0.001	treatment	TG saline vs WT saline	Duncan's	p=0.025	2 groups
	multivariate	F _(1,719) =1.40, p=0.237	genotype	TG nicotine vs WT nicotine	Duncan's	p=0.276	2 groups
- <i>split by region</i>				ventral medial			
caudate putamen	multivariate	F _(1,26) =6.34, p=0.018	treatment	hypothalamus	multivariate	F _(1,25) =8.34, p=0.007	treatment-genotype
preoptic area	multivariate	F _(1,25) =4.50, p=0.043	treatment	-- <i>post hoc</i>			
lateral dorsal thalamic nuclei	multivariate	F _(1,26) =6.14, p=0.020	treatment	TG nicotine vs WT nicotine	Duncan's	p=0.026	2 groups
olfactory tubercles	multivariate	F _(1,25) =9.68, p=0.005	treatment	TG saline vs WT saline	Duncan's	p=0.141	2 groups
retrosplenial cortex	multivariate	F _(1,27) =12.42, p=0.002	treatment	dentate gyrus	multivariate	F _(1,28) =5.08, p=0.032	treatment-genotype
hypothalamus	multivariate	F _(1,24) =16.00, p<0.001	treatment	-- <i>post hoc</i>			
medial septum	multivariate	F _(1,23) =36.28, p<0.001	treatment	TG nicotine vs WT nicotine	Duncan's	p=0.049	2 groups
vertical diagonal band	multivariate	F _(1,22) =37.49, p<0.001	treatment	TG saline vs WT saline	Duncan's	p=0.268	2 groups
hippocampus	multivariate	F _(1,27) =13.77, p<0.001	treatment	dorsal endopiriform	multivariate	F _(1,30) =5.73, p=0.023	genotype
frontal association	multivariate	F _(1,28) =39.31, p<0.001	treatment	ventral medial geniculate	multivariate	F _(1,24) =4.46, p=0.045	genotype
prelimbic cortex	multivariate	F _(1,28) =59.27, p<0.001	treatment	CA1	multivariate	F _(1,25) =4.30, p=0.048	genotype
primary motor cortex	multivariate	F _(1,28) =66.40, p<0.001	treatment				
secondary motor cortex	multivariate	F _(1,28) =71.04, p<0.001	treatment				
cingulate cortex	multivariate	F _(1,28) =21.73, p<0.001	treatment				
somatosensory cortex	multivariate	F _(1,28) =47.26, p<0.001	treatment				
piriform cortex	multivariate	F _(1,28) =29.58, p<0.001	treatment				
visual cortex	multivariate	F _(1,28) =25.00, p<0.001	treatment				
auditory cortex	multivariate	F _(1,21) =55.50, p<0.001	treatment				
interpeduncular nucleus	multivariate	F _(1,27) =5.20, p=0.031	genotype				

* Greenhouse-Geisser corrected, as data are not spheric