FUNCTIONAL POLYMORPHISMS IN DOPAMINERGIC GENES MODULATE NEUROBEHAVIORAL AND NEUROPHYSIOLOGICAL CONSEQUENCES OF SLEEP DEPRIVATION

Supplementary information

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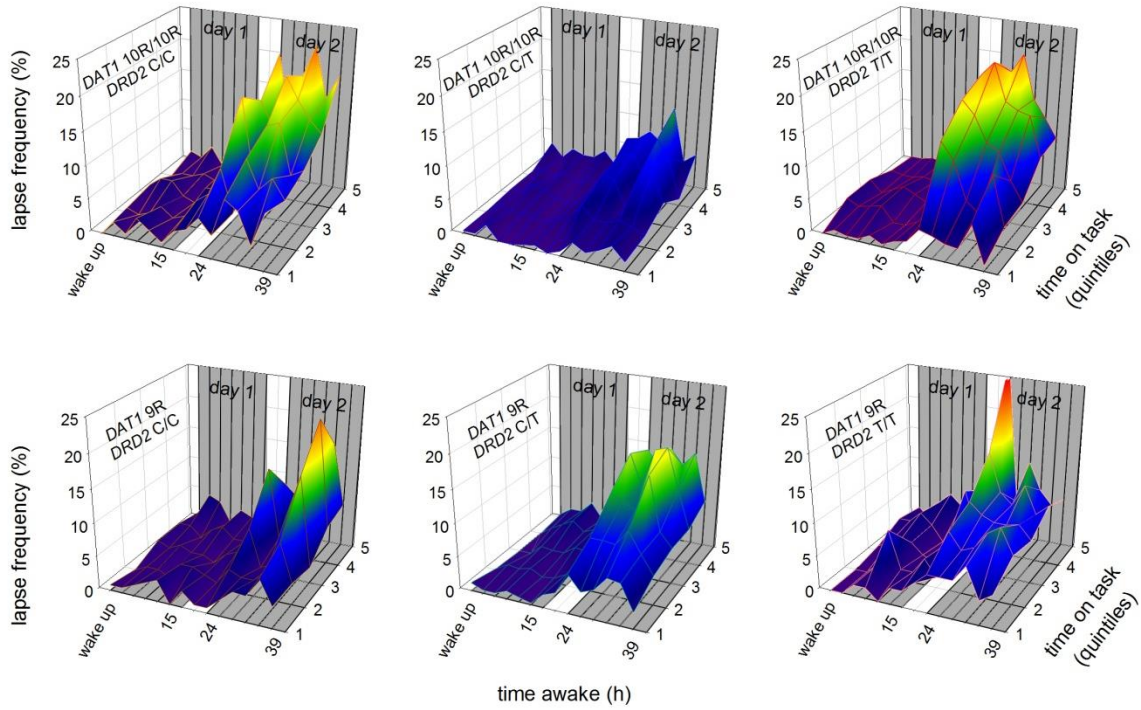[4] *Institute of Medical Molecular Genetics, University of Zürich, Schlieren, Switzerland*
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Abbreviated title: *Dopaminergic polymorphisms and human sleep loss*
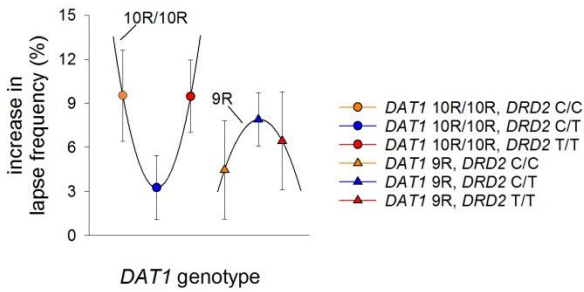
Supplementary figure 1.

A

B

Illustration of the PVT lapse frequency data included in statistical models. **A:** PVT attention lapses (y-axis) as a function of time-on-task (z-axis) and time awake (x-axis). Warmer colors refers to higher lapse frequency. B: The relative increase in PVT lapse frequency from baseline to the sleep deprived day split by the six *DAT1-DRD2* genotypes plotted on a U-shaped curve. The figure resembles the reported increase in subjective sleepiness (Fig. 2C).

Supplementary table 1. Results of all genotype independent ANOVAs.

		F-value	P-value
PVT lapses	Session	$F_{5,544} = 9.41$	1.31E^{-08}
	ToT	$F_{4,520} = 34.92$	7.68E^{-26}
	Day	$F_{1,1183} = 536.60$	3.44E^{-98}
	Session x ToT	$F_{20,279} = 0.70$	0.83
	Session x Day	$F_{5,544} = 9.87$	4.82E^{-09}
	ToT x Day	$F_{4,520} = 24.19$	2.26E^{-18}
	Session x ToT x Day	$F_{20,279} = 1.16$	0.29
PVT standard deviation	Session	$F_{5,734} = 6.89$	2.70E^{-06}
	ToT	$F_{4,845} = 2.31$	5.61E^{-02}
	Day	$F_{1,2122} = 259.21$	4.10E^{-55}
	Session x ToT	$F_{20,390} = 0.81$	0.71
	Session x Day	$F_{5,734} = 2.50$	2.96E^{-02}
	ToT x Day	$F_{4,845} = 0.87$	0.48
	Session x ToT x Day	$F_{20,390} = 1.12$	0.33
Subjective sleepiness	Session	$F_{5,567} = 17.73$	2.44E^{-16}
	Day	$F_{1,218} = 920.00$	3.58E^{-80}
	Session x Day	$F_{5,555} = 3.41$	4.85E^{-03}
Waking EEG – Delta band 1 - 4.5 Hz	Session	$F_{5,619} = 7.02$	2.17E^{-06}
	Day	$F_{1,213} = 108.81$	7.67E^{-21}
	Session x Day	$F_{5,573} = 4.99$	1.75E^{-04}
Waking EEG – Theta band 5 – 7.5 Hz	Session	$F_{5,626} = 8.26$	1.44E^{-07}
	Day	$F_{1,193} = 233.57$	4.56E^{-35}
	Session x Day	$F_{5,566} = 9.14$	2.22E^{-08}
Waking EEG – Alpha band 8 – 11.5 Hz	Session	$F_{5,649} = 9.33$	1.36E^{-08}
	Day	$F_{1,169} = 1.81$	0.18
	Session x Day	$F_{5,569} = 5.87$	2.69E^{-05}
Waking EEG – Theta/Alpha ratio	Session	$F_{5,636} = 2.14$	5.88E^{-02}
	Day	$F_{1,164} = 177.14$	6.81E^{-28}
	Session x Day	$F_{5,556} = 1.71$	0.13
Waking EEG – low Beta band 12-19.5 Hz	Session	$F_{5,598} = 13.65$	1.24E^{-12}
	Day	$F_{1,207} = 24.62$	1.45E^{-06}
	Session x Day	$F_{5,556} = 20.72$	5.27E^{-19}
Waking EEG – high Beta band 20-30 Hz	Session	$F_{5,590} = 3.46$	4.34E^{-03}
	Day	$F_{1,182} = 5.66$	1.84E^{-02}
	Session x Day	$F_{5,537} = 6.77$	3.91E^{-06}

Subscript F values represent numerator and denominator degrees of freedom, respectively. Red values are below the standard 5% alpha criteria.

Supplementary table 2. Overview and results of all genotype related ANOVAs performed.

		DAT1			DRD2			DAT1-DRD2		
		F-value	p-value	q-value	F-value	p-value	q-value	F-value	p-value	q-value
PVT lapses	Genotype	$F_{1,134}=1.00$	0.32	0.57	$F_{2,135}=2.20$	0.14	0.24	$F_{5,128}=4.75$	$5.14E^{-4}$	$1.82E^{-3}$
	Session	$F_{5,533}=9.32$	$1.61E^{-08}$	$1.06E^{-07}$	$F_{5,508}=7.61$	$6.64E^{-07}$	$3.74E^{-06}$	$F_{5,509}=6.59$	$5.84E^{-6}$	$2.61E^{-5}$
	ToT	$F_{4,509}=34.44$	$1.86E^{-25}$	$2.75E^{-24}$	$F_{4,503}=30.79$	$6.01E^{-23}$	$8.38E^{-22}$	$F_{4,451}=25.95$	$2.22E^{-19}$	$2.75E^{-18}$
	Day	$F_{1,1154}=530.44$	$7.17E^{-97}$	$1.70E^{-94}$	$F_{1,1141}=502.83$	$1.46E^{-92}$	$1.73E^{-90}$	$F_{1,1024}=432.91$	$1.82E^{-80}$	$1.44E^{-78}$
	Genotype x Session	$F_{5,533}=0.48$	0.79	0.91	$F_{10,510}=2.10$	$2.32E^{-02}$	$6.10E^{-02}$	$F_{25,531}=1.85$	$7.54E^{-3}$	$2.29E^{-2}$
	Genotype x ToT	$F_{4,509}=0.23$	0.92	0.98	$F_{8,500}=0.65$	0.73	0.91	$F_{20,452}=0.76$	0.76	0.91
	Genotype x Day	$F_{1,1154}=0.57$	0.45	0.71	$F_{2,1135}=4.82$	$8.23E^{-03}$	$2.44E^{-02}$	$F_{1,1023}=12.01$	$2.55E^{-11}$	$1.95E^{-10}$
	Session x ToT	$F_{20,271}=0.69$	0.84	0.94	$F_{20,265}=0.77$	0.75	0.91	$F_{20,254}=0.76$	0.76	0.91
	Session x Day	$F_{5,533}=9.76$	$6.17E^{-09}$	$4.30E^{-08}$	$F_{5,508}=7.60$	$6.79E^{-07}$	$3.74E^{-06}$	$F_{5,509}=6.27$	$1.17E^{-5}$	$5.03E^{-5}$
	ToT x Day	$F_{4,509}=23.84$	$4.31E^{-18}$	$4.44E^{-17}$	$F_{4,503}=23.60$	$6.66E^{-18}$	$6.58E^{-17}$	$F_{4,451}=19.04$	$1.75E^{-14}$	$1.49E^{-13}$
	Genotype x ToT x Day	$F_{4,509}=0.42$	0.80	0.91	$F_{8,500}=0.59$	0.79	0.91	$F_{20,452}=0.87$	0.63	0.86
	Genotype x Session x Day	$F_{5,533}=0.32$	0.90	0.97	$F_{10,510}=2.06$	$2.59E^{-02}$	$6.74E^{-02}$	$F_{25,531}=1.85$	$7.75E^{-3}$	$2.33E^{-2}$
	Genotype x Session x ToT	$F_{20,271}=0.32$	1.00	1.00	$F_{40,267}=0.38$	1.00	1.00	$F_{100,271}=0.36$	1.00	1.00
	Session x ToT x Day	$F_{20,271}=1.14$	0.31	0.56	$F_{20,265}=1.06$	0.40	0.66	$F_{20,254}=0.90$	0.59	0.81
	Quadrupled interaction	$F_{20,271}=0.35$	1.00	1.00	$F_{40,267}=0.41$	0.99	1.00	$F_{100,271}=0.39$	1.00	1.00
PVT Standard deviation	Genotype	$F_{1,63}=0.64$	0.43	0.69	$F_{2,62}=0.08$	0.92	0.98	$F_{5,59}=0.50$	0.78	0.91
	Session	$F_{5,713}=6.90$	$2.68E^{-06}$	$1.32E^{-05}$	$F_{5,727}=8.17$	$1.62E^{-07}$	$9.86E^{-07}$	$F_{5,649}=7.03$	$2.05E^{-06}$	$1.06E^{-05}$
	ToT	$F_{4,826}=2.27$	$6.00E^{-02}$	0.14	$F_{4,851}=2.24$	$6.29E^{-02}$	0.14	$F_{4,770}=2.31$	$5.61E^{-02}$	0.13
	Day	$F_{1,2080}=258.25$	$7.21E^{-55}$	$2.44E^{-53}$	$F_{1,2122}=233.64$	$4.05E^{-50}$	$1.20E^{-48}$	$F_{1,1971}=219.79$	$3.20E^{-47}$	$8.41E^{-46}$
	Genotype x Session	$F_{5,713}=2.16$	$5.68E^{-02}$	0.14	$F_{10,724}=1.77$	$6.29E^{-02}$	0.14	$F_{25,669}=1.72$	$1.69E^{-02}$	$4.70E^{-2}$
	Genotype x ToT	$F_{4,826}=0.95$	0.44	0.70	$F_{8,845}=0.18$	0.99	1.00	$F_{20,769}=0.55$	0.94	0.99
	Genotype x Day	$F_{1,2080}=0.37$	0.54	0.78	$F_{2,2106}=0.74$	0.48	0.74	$F_{5,1965}=0.77$	0.57	0.80
	Session x ToT	$F_{20,397}=0.81$	0.71	0.90	$F_{20,379}=0.83$	0.68	0.88	$F_{20,441}=0.76$	0.76	0.91
	Session x Day	$F_{5,713}=2.47$	$3.14E^{-02}$	$7.99E^{-02}$	$F_{5,727}=1.96$	$8.30E^{-02}$	0.19	$F_{5,649}=2.15$	$5.78E^{-02}$	0.14
	ToT x Day	$F_{4,826}=0.86$	0.49	0.74	$F_{4,851}=0.73$	0.58	0.80	$F_{4,770}=0.53$	0.72	0.90
	Genotype x ToT x Day	$F_{4,826}=1.96$	$9.85E^{-02}$	0.22	$F_{8,845}=1.43$	0.18	0.37	$F_{20,769}=1.18$	0.27	0.49
	Genotype x Session x Day	$F_{5,713}=2.87$	$1.41E^{-02}$	$3.99E^{-02}$	$F_{10,724}=1.61$	$9.88E^{-02}$	0.22	$F_{25,669}=1.91$	$5.15E^{-03}$	$1.61E^{-2}$
	Genotype x Session x ToT	$F_{20,397}=0.70$	0.83	0.94	$F_{40,387}=1.00$	0.47	0.73	$F_{100,436}=1.07$	0.32	0.57
	Session x ToT x Day	$F_{20,397}=1.11$	0.33	0.58	$F_{20,379}=1.23$	0.22	0.44	$F_{20,414}=1.22$	0.23	0.44
	Quadrupled interaction	$F_{20,397}=0.580$	0.93	0.98	$F_{40,387}=1.17$	0.23	0.44	$F_{100,436}=0.94$	0.65	0.86
Subjective sleepiness	Genotype	$F_{1,80}=0.59$	0.45	0.70	$F_{2,78}=0.73$	0.49	0.74	$F_{5,74}=1.45$	0.22	0.42
	Session	$F_{5,553}=17.24$	$7.24E^{-16}$	$6.60E^{-15}$	$F_{5,439}=5.22$	$4.08E^{-04}$	$1.46E^{-03}$	$F_{5,507}=15.75$	$1.99E^{-14}$	$1.63E^{-13}$

		F	p	p	F	p	p	F	p	p
	Day	$F_{1,213} = 884.54$	$9.42E^{-78}$	$5.58E^{-76}$	$F_{1,161} = 587.12$	$1.66E^{-55}$	$6.55E^{-54}$	$F_{1,201} = 756.34$	$5.35E^{-70}$	$2.54E^{-68}$
	Genotype x Session	$F_{5,553} = 0.32$	0.90	0.97	$F_{10,439} = 0.63$	0.75	0.91	$F_{25,508} = 0.58$	0.95	1.00
	Genotype x Day	$F_{1,213} = 0.47$	0.49	0.74	$F_{2,161} = 0.63$	0.88	0.97	$F_{5,201} = 3.51$	$4.59E^{-03}$	$1.45E^{-02}$
	Session x Day	$F_{5,541} = 3.29$	$6.12E^{-03}$	$1.88E^{-02}$	$F_{5,453} = 3.04$	$1.71E^{-02}$	$4.72E^{-02}$	$F_{5,502} = 2.52$	$2.87E^{-02}$	$7.39E^{-02}$
	Genotype x Session x Day	$F_{5,541} = 0.16$	0.98	1.00	$F_{10,454} = 0.44$	0.90	0.97	$F_{25,502} = 0.48$	0.99	1.00
Waking EEG Delta band 1 – 4.5 Hz	Genotype	$F_{1,79} = 0.60$	0.44	0.70	$F_{2,77} = 1.24$	0.30	0.54	$F_{5,74} = 0.64$	0.67	0.88
	Day	$F_{1,209} = 108.42$	$1.01E^{-20}$	$1.33E^{-19}$	$F_{1,201} = 98.40$	$3.88E^{-19}$	$4.38E^{-18}$	$F_{1,193} = 100.88$	$2.32E^{-19}$	$2.75E^{-18}$
	Session	$F_{5,612} = 7.08$	$1.90E^{-06}$	$1.00E^{-05}$	$F_{5,592} = 6.03$	$1.85E^{-05}$	$7.54E^{-05}$	$F_{5,568} = 6.08$	$1.68E^{-05}$	$6.98E^{-05}$
	Genotype x Day	$F_{1,209} = 0.13$	0.72	0.90	$F_{2,202} = 0.34$	0.71	0.90	$F_{5,193} = 0.85$	0.52	0.75
	Genotype x Session	$F_{5,612} = 1.00$	0.42	0.69	$F_{10,593} = 1.09$	0.37	0.63	$F_{25,573} = 0.97$	0.50	0.75
	Session x Day	$F_{5,565} = 5.03$	$1.61E^{-04}$	$6.06E^{-04}$	$F_{5,547} = 4.21$	$9.23E^{-04}$	$3.17E^{-03}$	$F_{5,525} = 4.47$	$5.31E^{-04}$	$1.85E^{-03}$
	Genotype x Session x Day	$F_{5,565} = 1.45$	0.21	0.41	$F_{10,547} = 0.54$	0.86	0.96	$F_{25,539} = 0.80$	0.75	0.91
Waking EEG Theta band 5 – 7.5 Hz	Genotype	$F_{1,79} = 0.04$	0.85	0.95	$F_{2,77} = 2.24$	0.11	0.24	$F_{5,74} = 1.20$	0.32	0.57
	Day	$F_{1,191} = 233.03$	$6.26E^{-35}$	$1.48E^{-33}$	$F_{1,185} = 211.86$	$1.69E^{-32}$	$3.33E^{-31}$	$F_{1,180} = 221.20$	$3.95E^{-33}$	$8.51E^{-32}$
	Session	$F_{5,619} = 8.26$	$1.46E^{-07}$	$9.08E^{-07}$	$F_{5,601} = 6.51$	$6.54E^{-06}$	$2.87E^{-05}$	$F_{5,575} = 6.08$	$1.67E^{-05}$	$6.98E^{-05}$
	Genotype x Day	$F_{1,191} = 0.18$	0.68	0.88	$F_{2,186} = 1.13$	0.33	0.57	$F_{5,180} = 1.96$	$8.68E^{-02}$	0.19
	Genotype x Session	$F_{5,619} = 0.33$	0.90	0.97	$F_{10,602} = 0.88$	0.56	0.80	$F_{25,577} = 0.88$	0.64	0.86
	Session x Day	$F_{5,559} = 9.17$	$2.15E^{-08}$	$1.38E^{-07}$	$F_{5,543} = 6.89$	$3.01E^{-06}$	$1.49E^{-05}$	$F_{5,521} = 6.77$	$3.95E^{-06}$	$1.87E^{-05}$
	Genotype x Session x Day	$F_{5,559} = 0.91$	0.47	0.73	$F_{10,544} = 1.35$	0.20	0.40	$F_{25,523} = 1.09$	0.35	0.60
Waking EEG Alpha band 8 – 11.5 Hz	Genotype	$F_{1,79} = 0.00$	0.97	1.00	$F_{2,77} = 1.05$	0.36	0.61	$F_{5,74} = 0.79$	0.56	0.80
	Day	$F_{1,171} = 2.06$	0.15	0.32	$F_{1,163} = 5.45$	$2.08E^{-02}$	$5.53E^{-02}$	$F_{1,162} = 4.42$	$3.71E^{-02}$	$9.26E^{-02}$
	Session	$F_{5,638} = 9.39$	$1.19E^{-08}$	$8.09E^{-08}$	$F_{5,622} = 7.96$	$2.78E^{-07}$	$1.65E^{-06}$	$F_{5,594} = 7.86$	$3.52E^{-07}$	$2.03E^{-06}$
	Genotype x Day	$F_{1,171} = 10.65$	$1.33E^{-03}$	$4.49E^{-03}$	$F_{2,164} = 3.01$	$5.20E^{-02}$	0.13	$F_{5,162} = 3.97$	$2.02E^{-03}$	$6.75E^{-03}$
	Genotype x Session	$F_{5,638} = 0.62$	0.69	0.89	$F_{10,622} = 0.66$	0.77	0.91	$F_{25,601} = 0.76$	0.79	0.91
	Session x Day	$F_{5,561} = 5.97$	$2.15E^{-05}$	$8.62E^{-05}$	$F_{5,546} = 5.40$	$7.33E^{-05}$	$2.85E^{-04}$	$F_{5,524} = 4.88$	$2.26E^{-04}$	$8.37E^{-04}$
	Genotype x Session x Day	$F_{5,561} = 0.59$	0.71	0.90	$F_{10,546} = 0.76$	0.67	0.88	$F_{25,528} = 0.75$	0.81	0.92
Waking EEG Theta/Alpha ratio	Genotype	$F_{1,79} = 0.02$	0.89	0.97	$F_{2,77} = 0.54$	0.59	0.81	$F_{5,74} = 0.78$	0.57	0.80
	Day	$F_{1,166} = 187.57$	$4.47E^{-29}$	$7.06E^{-28}$	$F_{1,160} = 196.91$	$1.10E^{-29}$	$1.85E^{-28}$	$F_{1,158} = 202.13$	$4.62E^{-30}$	$8.42E^{-29}$
	Session	$F_{5,629} = 2.19$	$5.36E^{-02}$	0.13	$F_{5,608} = 1.85$	0.10	0.22	$F_{5,580} = 1.79$	0.11	0.24
	Genotype x Day	$F_{1,166} = 8.58$	$3.88E^{-03}$	$1.26E^{-02}$	$F_{2,160} = 6.14$	$2.69E^{-03}$	$8.85E^{-03}$	$F_{5,158} = 5.03$	$2.62E^{-04}$	$9.55E^{-04}$
	Genotype x Session	$F_{5,626} = 0.74$	0.59	0.81	$F_{10,609} = 1.97$	$3.45E^{-02}$	$8.70E^{-02}$	$F_{25,584} = 1.17$	0.26	0.48
	Session x Day	$F_{5,549} = 1.72$	0.13	0.27	$F_{5,533} = 2.26$	$4.76E^{-02}$	0.12	$F_{5,512} = 1.79$	0.11	0.24
	Genotype x Session x Day	$F_{5,549} = 0.45$	0.81	0.92	$F_{10,533} = 1.34$	0.21	0.41	$F_{5,515} = 1.07$	0.38	0.64
Waking EEG Low Beta 12 – 19.5 Hz	Genotype	$F_{1,79} = 0.43$	0.51	0.75	$F_{2,77} = 0.57$	0.57	0.80	$F_{5,74} = 0.88$	0.50	0.75
	Day	$F_{1,205} = 24.43$	$1.60E^{-06}$	$8.61E^{-06}$	$F_{1,198} = 22.37$	$4.26E^{-06}$	$1.98E^{-05}$	$F_{1,191} = 22.72$	$3.69E^{-06}$	$1.79E^{-05}$
	Session	$F_{5,590} = 13.63$	$1.33E^{-12}$	$1.05E^{-11}$	$F_{5,573} = 11.60$	$1.09E^{-10}$	$8.06E^{-10}$	$F_{5,552} = 10.50$	$1.21E^{-09}$	$8.70E^{-09}$

	Genotype x Day	$F_{1,205} = 1.77$	0.19	0.38	$F_{2,199} = 0.68$	0.51	0.75	$F_{5,192} = 0.87$	0.50	0.75
	Genotype x Session	$F_{5,590} = 1.18$	0.32	0.57	$F_{10,574} = 0.68$	0.74	0.91	$F_{25,557} = 0.80$	0.74	0.91
	Session x Day	$F_{5,549} = 20.74$	5.26E^{-19}	5.67E^{-18}	$F_{5,533} = 17.42$	5.50E^{-16}	5.21E^{-15}	$F_{5,513} = 17.09$	1.20E^{-15}	1.05E^{-14}
	Genotype x Session x Day	$F_{5,549} = 0.65$	0.66	0.88	$F_{10,534} = 0.51$	0.88	0.97	$F_{25,517} = 0.49$	0.98	1.00
Waking EEG High Beta 20 – 30 Hz	Genotype	$F_{1,79} = 0.61$	0.44	0.70	$F_{2,77} = 0.44$	0.65	0.86	$F_{5,74} = 1.04$	0.40	0.66
	Day	$F_{1,178} = 5.65$	1.85E^{-02}	4.98E^{-02}	$F_{1,172} = 6.88$	9.49E^{-03}	2.78E^{-02}	$F_{1,165} = 6.57$	1.13E^{-02}	3.25E^{-02}
	Session	$F_{5,582} = 3.43$	4.58E^{-03}	1.45E^{-02}	$F_{5,568} = 2.94$	1.25E^{-02}	3.56E^{-02}	$F_{5,547} = 2.76$	1.79E^{-02}	4.87E^{-02}
	Genotype x Day	$F_{1,178} = 0.79$	0.38	0.64	$F_{2,172} = 0.90$	0.41	0.67	$F_{5,154} = 0.47$	0.80	0.91
	Genotype x Session	$F_{5,582} = 0.32$	0.90	0.97	$F_{10,569} = 1.20$	0.29	0.54	$F_{25,551} = 0.78$	0.78	0.91
	Session x Day	$F_{5,529} = 6.69$	4.64E^{-06}	2.11E^{-05}	$F_{5,515} = 5.74$	3.65E^{-05}	1.44E^{-04}	$F_{5,495} = 5.23$	1.08E^{-04}	4.13E^{-04}
	Genotype x Session x Day	$F_{5,529} = 0.53$	0.76	0.91	$F_{10,516} = 1.29$	0.23	0.44	$F_{25,497} = 0.87$	0.65	0.86

q-Values: FDR-corrected p-values. Note: The FRD correction is performed across all three genetic groups and therefore takes into account all 237 p-values shown in the table. Subscript F values represent numerator and denominator degrees of freedom, respectively. Red values are below the standard 5% alpha criteria.