Differential regulations of vestibulo-ocular reflex and optokinetic response by β- and α2-adrenergic receptors in the cerebellar flocculus

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Supplementary Table S1

Effects of various treatments on OKR gain at 1 Hz, 10°/sec peak screen rotation velocity

Drug	Side	Training	Pre	Post	Change	N	T-test	Dunnett
saline	contra	no	0.31±0.02	0.31±0.03	0.01±0.03	6	0.813	
		OKR-up	0.29±0.02	0.66±0.03	0.37±0.03	6	<0.001	
		VOR-up	0.33±0.02	0.69±0.05	0.36±0.04	6	<0.001	
		VOR-down	0.31±0.02	0.52±0.03	0.21±0.03	6	0.001	
	ipsi	no	0.31±0.01	0.31±0.02	0.00±0.02	6	0.870	
isoproterenol	contra	no	0.33±0.02	0.47±0.02	0.14±0.02	6	<0.001	0.012
		OKR-up	0.35±0.02	0.64±0.05	0.29±0.05	6	0.002	0.388
		VOR-up	0.31±0.02	0.69±0.05	0.38±0.05	6	0.001	0.981
		VOR-down	0.33±0.03	0.63±0.03	0.30±0.03	6	<0.001	0.154
	ipsi	no	0.31±0.02	0.44±0.03	0.13±0.03	6	0.005	0.002
propranolol	contra	no	0.32±0.02	0.28±0.03	−0.04±0.02	6	0.111	0.732
		OKR-up	0.35±0.02	0.42±0.03	0.07±0.03	6	0.095	< 0.001
		VOR-up	0.31±0.02	0.36±0.02	0.05±0.02	6	0.105	< 0.001
		VOR-down	0.29±0.03	0.36±0.02	0.07±0.02	6	0.045	0.016
	ipsi	no	0.27±0.02	0.27±0.01	0.00±0.02	7	0.985	0.994
UK14304	contra	no	0.32±0.02	0.27±0.02	−0.05±0.02	6	0.066	0.532
		OKR-up	0.33±0.02	0.46±0.04	0.13±0.04	6	0.017	0.001
		VOR-up	0.30±0.02	0.52±0.02	0.22±0.01	6	<0.001	0.026
		VOR-down	0.28±0.02	0.44±0.04	0.16±0.03	6	0.005	0.697
yohimbine	contra	no	0.30±0.02	0.42±0.03	0.12±0.03	7	0.010	0.034
		OKR-up	0.30±0.03	0.61±0.06	0.31±0.05	7	<0.001	0.607
		VOR-up	0.28±0.01	0.57±0.03	0.29±0.02	6	<0.001	0.419
		VOR-down	0.28±0.02	0.47±0.04	0.19±0.04	6	0.008	0.973
salbutamol	contra	no	0.35±0.05	0.51±0.07	0.15±0.04	6	0.008	0.006
timolol	contra	no	0.37±0.03	0.33±0.03	−0.04±0.03	7	0.234	0.628
DMSO	contra	no	0.32±0.03	0.34±0.02	0.02±0.02	6	0.494	1.000

Administration of saline, isoproterenol, propranolol, UK14304, yohimbine, salbutamol, timolol, or DMSO to the flocculus contralateral or ipsilateral to the recorded eye, with or without OKR, VOR-up or VOR-down training was performed. The effect of each treatment on OKR gain was examined between pre- and post-treatment with the paired t-test. The effect of each drug on OKR gain change in each training condition was compared with that of saline-administered control with Dunnett's test. P values are presented.

Supplementary Table S2

Effects of various treatment on VOR gain at 1 Hz, 10°/sec peak turntable rotation velocity

Drug	Side	Training	Pre	Post	Change	N	T-test	Dunnett
saline	contra	no	0.61±0.02	0.63±0.02	0.01±0.02	6	0.564	
		OKR-up	0.59±00.2	0.60±0.03	0.01±0.03	6	0.637	
		VOR-up	0.62±0.02	0.81±0.05	0.19±0.05	6	0.011	
		VOR-down	0.61±0.02	0.41±0.02	−0.20±0.02	6	<0.001	
	ipsi	no	0.71±0.02	0.72±0.04	0.01±0.03	6	0.821	
isoproterenol	contra	no	0.66±0.01	0.63±0.04	−0.04±0.04	6	0.415	0.695
		OKR-up	0.64±0.04	0.81±0.03	0.17±0.03	6	0.004	0.016
		VOR-up	0.66±0.04	0.82±0.05	0.16±0.04	6	0.013	0.959
		VOR-down	0.61±0.03	0.40±0.03	−0.21±0.03	6	0.002	0.999
	ipsi	no	0.72±0.04	0.77±0.04	0.05±0.06	6	0.441	0.717
propranolol	contra	no	0.64±0.03	0.51±0.02	−0.13±0.04	6	0.017	0.010
		OKR-up	0.62±0.03	0.52±0.04	−0.10±0.06	6	0.154	0.091
		VOR-up	0.58±0.04	0.71±0.04	0.13±0.04	6	0.029	0.768
		VOR-down	0.69±0.03	0.43±0.04	−0.26±0.03	6	<0.001	0.470
	ipsi	no	0.74±0.06	0.58±0.06	−0.15±0.04	7	0.005	0.031
UK14304	contra	no	0.65±0.04	0.49±0.04	−0.16±0.03	6	0.004	0.001
		OKR-up	0.65±0.02	0.65±0.03	0.00±0.01	6	0.949	0.995
		VOR-up	0.61±0.03	0.74±0.05	0.13±0.06	6	0.063	0.792
		VOR-down	0.62±0.03	0.49±0.04	−0.13±0.03	6	0.010	0.328
yohimbine	contra	no	0.65±0.04	0.69±0.04	0.04±0.02	7	0.053	0.990
		OKR-up	0.68±0.03	0.73±0.04	0.05±0.02	7	0.091	0.901
		VOR-up	0.64±0.04	0.85±0.03	0.21±0.04	6	0.002	0.994
		VOR-down	0.63±0.03	0.38±0.02	−0.25±0.03	6	<0.001	0.631
salbutamol	contra	no	0.52±0.05	0.56±0.05	0.04±0.02	6	0.085	0.993
timolol	contra	no	0.65±0.04	0.43±0.04	−0.23±0.04	7	0.001	< 0.001
DMSO	contra	no	0.58±0.04	0.61±0.04	0.02±0.01	6	0.161	1.000

Administration of saline, isoproterenol, propranolol, UK14304, yohimbine, salbutamol, timolol, or DMSO to the flocculus contralateral or ipsilateral to the recorded eye, with or without OKR, VOR-up or VOR-down training was performed. The effect of each treatment on VOR gain was examined between pre- and post-treatment with the paired t-test. The effect of each drug on VOR gain change in each training condition was compared with that of saline-administered control with Dunnett's test. P values are presented.

Supplementary Table S3

Effects of contralateral administration of propranolol or isoproterenol on OKR gain during screen rotation (0.5 Hz, 10°/sec peak rotation velocity; 1 Hz, 20°/sec)

Drug	Frequency	Peak velocity	Pre	Post	Change	N	T-test	Dunnett
saline	0.5	10	0.41±0.04	0.41±0.05	0.00±0.03	6	0.943	
	1	20	0.17±0.02	0.17±0.02	0.00±0.01	6	0.679	
isoproterenol	0.5	10	0.45±0.03	0.60±0.04	0.15±0.06	6	0.040	0.017
	1	20	0.17±0.01	0.21±0.02	0.04±0.01	6	0.042	0.044
propranolol	0.5	10	0.35±0.03	0.34±0.04	−0.02±0.02	6	0.380	0.946
	1	20	0.18±0.02	0.20±0.02	0.02±0.01	6	0.095	0.432

The effect of drug application on OKR gain was compared between before and after the administration with the paired t-test in each condition. The drug effect on OKR gain was also compared with that of saline-administered control with Dunnett's test in each rotation condition. P values are presented.

Supplementary Table S4

Effects of contralateral administration of propranolol or isoproterenol on VOR gain during turntable rotation (0.5 Hz, 10°/sec peak rotation velocity; 1 Hz, 20°/sec)

Drug	Frequency	Peak velocity	Pre	Post	Change	N	T-test	Dunnett
saline	0.5	10	0.29±0.03	0.28±0.03	−0.01±0.01	6	0.439	
	1	20	0.60±0.06	0.62±0.03	0.02±0.05	6	0.752	
isoproterenol	0.5	10	0.36±0.03	0.28±0.03	−0.08±0.04	6	0.114	0.118
	1	20	0.65±0.03	0.61±0.05	−0.04±0.04	6	0.407	0.568
propranolol	0.5	10	0.37±0.03	0.28±0.03	−0.10±0.01	6	<0.001	0.041
	1	20	0.66±0.03	0.49±0.05	−0.17±0.03	6	0.003	0.014

The effect of drug application on VOR gain was compared between before and after the administration with the paired t-test in each condition. The drug effect on VOR gain was also compared with that of saline-administered control with Dunnett's test in each rotation condition. P values are presented.

Supplementary Table S5

Effects of various treatments on OKR phase at 1 Hz, 10°/sec peak screen rotation velocity

Drug	Side	Training	Pre	Post	Change	N	T-test	Dunnett
saline	contra	no	29±2	29±1	0±3	6	0.977	
		OKR-up	27±3	18±1	-9±3	6	0.017	
		VOR-up	31±2	20±1	-11±2	6	0.002	
		VOR-down	28±1	13±2	-14±2	6	0.002	
	ipsi	no	34±3	37±2	3±2	6	0.163	
isoproterenol	contra	no	28±2	21±1	-7±1	6	0.004	0.683
		OKR-up	26±3	15±2	-11±3	6	0.024	0.906
		VOR-up	29±2	23±2	-5±3	6	0.120	0.260
		VOR-down	28±2	17±1	-12±2	6	0.001	0.903
	ipsi	no	38±1	30±1	-8±2	6	0.007	0.021
propranolol	contra	no	28±1	31±3	3±3	6	0.469	0.996
		OKR-up	29±1	20±2	-9±1	6	<0.001	1.000
		VOR-up	29±2	26±3	-3±2	6	0.110	0.087
		VOR-down	28±3	13±1	-15±4	6	0.013	1.000
	ipsi	no	34±3	39±5	5±3	7	0.187	0.837
UK14304	contra	no	27±1	33±1	6±2	6	0.031	0.829
		OKR-up	29±1	18±2	-11±2	6	0.002	0.926
		VOR-up	26±1	26±2	0±2	6	0.970	0.010
		VOR-down	30±3	19±2	-11±2	6	0.004	0.766
yohimbine	contra	no	30±1	28±2	-2±2	7	0.347	1.000
		OKR-up	28±1	15±1	-13±2	7	<0.001	0.515
		VOR-up	26±2	23±1	-3±3	6	0.371	0.071
		VOR-down	28±2	17±3	-11±3	6	0.013	0.878
salbutamol	contra	no	28±2	21±2	-7±3	6	0.077	0.675
timolol	contra	no	29±2	41±8	12±8	7	0.175	0.133
DMSO	contra	no	34±2	31±1	-3±2	6	0.200	0.994

Administration of saline, isoproterenol, propranolol, UK14304, yohimbine, salbutamol, timolol, or DMSO to the flocculus contralateral or ipsilateral to the recorded eye, with or without OKR, VOR-up or VOR-down training was performed. The effect of each treatment on OKR phase was examined between pre- and post-treatment with the paired t-test. The effect of each drug on OKR phase change in each training condition was compared with that of saline-administered control with Dunnett's test. P values are presented. A positive phase value indicates a delay of eye rotation relative to the screen rotation.

Supplementary Table S6

Effects of various treatments on VOR phase at 1 Hz, 10°/sec peak turntable rotation velocity

Drug	Side	Training	Pre	Post	Change	N	T-test	Dunnett
saline	contra	no	−29±2	−27±3	2±3	6	0.535	
		OKR-up	−22±2	−28±1	−7±2	6	0.034	
		VOR-up	−20±1	−18±2	1±1	6	0.471	
		VOR-down	−18±2	−33±4	−15±3	6	0.006	
	ipsi	no	−23±3	−24±2	−1±3	6	0.776	
isoproterenol	contra	no	−22±2	−34±3	−11±4	6	0.035	0.217
		OKR-up	−27±4	−31±2	−4±3	6	0.255	0.749
		VOR-up	−28±2	−29±4	−1±5	6	0.822	0.946
		VOR-down	−22±3	−35±4	−12±3	6	0.010	0.939
	ipsi	no	−25±4	−31±3	−7±3	6	0.112	0.328
propranolol	contra	no	−19±1	−17±1	2±1	6	0.155	1.000
		OKR-up	−25±2	−27±3	−2±2	6	0.494	0.372
		VOR-up	−24±3	−22±1	2±3	6	0.503	0.999
		VOR-down	−24±3	−26±2	−1±2	6	0.567	0.020
	ipsi	no	−20±3	−13±3	8±3	7	0.032	0.107
UK14304	contra	no	−22±1	−20±2	2±2	6	0.412	1.000
		OKR-up	−25±2	−26±2	−1±2	6	0.634	0.254
		VOR-up	−22±2	−19±2	3±1	6	0.054	0.982
		VOR-down	−21±3	−27±2	−6±3	6	0.070	0.170
yohimbine	contra	no	−18±1	−24±2	−6±2	7	0.037	0.692
		OKR-up	−17±2	−22±2	−5±2	7	0.047	0.926
		VOR-up	−24±1	−18±2	6±3	6	0.071	0.593
		VOR-down	−20±1	−26±5	−6±4	6	0.214	0.175
salbutamol	contra	no	−20±4	−48±9	−28±12	6	0.063	< 0.001
timolol	contra	no	−27±2	−22±3	5±2	7	0.062	0.998
DMSO	contra	no	−23±2	−19±2	5±1	6	0.026	0.999

Administration of saline, isoproterenol, propranolol, UK14304, yohimbine, salbutamol, timolol, or DMSO to the flocculus contralateral or ipsilateral to the recorded eye, with or without OKR, VOR-up or VOR-down training was performed. The effect of each treatment on VOR phase was examined between pre- and post-treatment with the paired t-test. The effect of each drug on VOR phase change in each training condition was compared with that of saline-administered control with Dunnett's test. P values are presented. A negative phase value indicates that the eye rotation occurs ahead of the screen rotation.

Supplementary Table S7

Effects of contralateral administration of propranolol or isoproterenol on OKR phase during screen rotation (0.5 Hz, 10°/sec peak rotation velocity; 1 Hz, 20°/sec)

Drug	Frequency	Peak velocity	Pre	Post	Change	N	T-test	Dunnett
saline	0.5	10	22±9	13±1	−8±9	6	0.391	
	1	20	29±1	20±2	−9±3	6	0.023	
isoproterenol	0.5	10	15±2	18±8	3±9	6	0.784	0.487
	1	20	28±3	30±7	2±10	6	0.851	0.361
propranolol	0.5	10	13±1	15±2	2±2	6	0.466	0.533
	1	20	30±1	27±3	−3±3	6	0.401	0.709

The effect of drug application on OKR phase was compared between before and after the administration with the paired t-test in each condition. The drug effect on OKR phase was also compared with that of saline-administered control with Dunnett's test in each rotation condition. P values are presented. A positive phase value indicates a delay of eye rotation relative to the screen rotation.

Supplementary Table S8

Effects of contralateral administration of propranolol or isoproterenol on VOR phase during turntable rotation (0.5 Hz, 10°/sec peak rotation velocity; 1 Hz, 20°/sec)

Drug	Frequency	Peak velocity	Pre	Post	Change	N	T-test	Dunnett
saline	0.5	10	−48±5	−55±9	−7±7	6	0.375	
	1	20	−12±1	−14±1	−2±1	6	0.093	
isoproterenol	0.5	10	−46±4	−62±4	−16±5	6	0.021	0.403
	1	20	−13±2	−28±4	−14±5	6	0.032	0.015
propranolol	0.5	10	−41±3	−50±4	−8±3	6	0.057	0.974
	1	20	−16±1	−19±1	−4±1	6	0.037	0.831

The effect of drug application on VOR phase was compared between before and after the administration with the paired t-test in each condition. The drug's effect on VOR phase was also compared with that of saline-administered control with Dunnett's test in each rotation condition. P values are presented. A negative phase value indicates that the eye rotation occurs ahead of the screen rotation.

Supplementary Table S9

Effects of contralateral administration of propranolol or isoproterenol on OKR gain during constant-velocity optokinetic stimulation of NT or TN direction

Drug	Period	Direction	Pre	Post	Change	N	T-test	Dunnett
saline	former	NT	0.35±0.03	0.38±0.03	0.02±0.01	6	0.096	
		TN	0.36±0.03	0.38±0.03	0.02±0.02	6	0.485	
		T-test (NT vs TN)	0.584	0.895	0.217			
	latter	NT	0.48±0.03	0.46±0.03	−0.01±0.02	6	0.374	
		TN	0.39±0.03	0.38±0.03	−0.01±0.02	6	0.930	
		T-test (NT vs TN)	0.003	0.025	0.985			
iso	former	NT	0.30±0.02	0.53±0.05	0.23±0.05	6	0.004	0.001
		TN	0.35±0.05	0.52±0.06	0.17±0.01	6	<0.001	0.014
		T-test (NT vs TN)	0.302	0.836	0.185			
	latter	NT	0.43±0.02	0.64±0.04	0.21±0.04	6	0.004	<0.001
		TN	0.34±0.04	0.48±0.06	0.14±0.03	6	0.005	<0.001
		T-test (NT vs TN)	0.006	0.032	0.216			
pro	former	NT	0.34±0.03	0.37±0.04	0.03±0.03	6	0.373	0.991
		TN	0.34±0.03	0.42±0.05	0.08±0.05	6	0.142	0.356
		T-test (NT vs TN)	0.997	0.151	0.245			
	latter	NT	0.43±0.03	0.44±0.04	0.01±0.02	6	0.763	0.943
		TN	0.35±0.02	0.32±0.03	−0.03±0.02	6	0.094	0.61
		T-test (NT vs TN)	0.046	0.012	0.177			

Mean gain values during the former and the latter 1 sec periods of the 2 sec stimulation were presented. The effect of drug application on OKR gain was compared between before and after the administration with the paired t-test. The drug's effect on OKR gain was also compared with that of saline-administered control with Dunnett's test. In addition, the directional difference was examined with the paired t-test in each condition. P values are presented.

Supplementary Table S10
Effects of contralateral administration of norepinephrine (NE) on OKR gain

NE	Additional drug	Pre	Post	Change	N	T-test	Dunnett
10 mM	no	0.34±0.02	0.47±0.04	0.14±0.05	6	0.049	0.204
	propranolol	0.34±0.02	0.33±0.06	−0.01±0.05	6	0.852	0.996
30 mM	no	0.34±0.01	0.34±0.02	0.00±0.02	6	0.937	1.000
	yohimbine	0.35±0.02	0.54±0.06	0.20±0.06	6	0.026	0.031

Administration of 10 mM NE with or without co-administration of propranolol, or that of 30 mM NE with or without co-administration of yohimbine was performed. The effect of each treatment on OKR gain was examined between before and after drug application with the paired t-test. The effect of each treatment on OKR gain change was also compared with that of saline-administered control with Dunnett's test. P values are presented.

Supplementary Table S11
Effects of contralateral administration of norepinephrine (NE) on VOR gain

NE	Additional drug	Pre	Post	Change	N	T-test	Dunnett
10 mM	no	0.57±0.03	0.56±0.02	−0.01±0.02	6	0.573	0.926
	propranolol	0.62±0.03	0.45±0.06	−0.17±0.04	6	0.009	< 0.001
30 mM	no	0.58±0.03	0.45±0.03	−0.12±0.04	6	0.024	0.008
	yohimbine	0.58±0.03	0.61±0.03	0.03±0.01	6	0.051	0.987

Administration of 10 mM NE with or without co-administration of propranolol, or that of 30 mM NE with or without co-administration of yohimbine was performed. The effect of each treatment on VOR gain was examined between before and after drug application with the paired t-test. The effect of each treatment on VOR gain change was also compared with that of saline-administered control with Dunnett's test. P values are presented.

Supplementary Table S12
Effects of contralateral administration of norepinephrine (NE) on OKR phase

NE	Additional drug	Pre	Post	Change	N	T-test	Dunnett
10 mM	no	29±2	27±3	−1±3	6	0.692	0.992
	propranolol	24±1	31±3	7±3	6	0.059	0.189
30 mM	no	31±1	26±3	−5±2	6	0.069	0.584
	yohimbine	27±2	22±2	−5±3	6	0.091	0.458

Administration of 10 mM NE with or without co-administration of propranolol, or that of 30 mM NE with or without co-administration of yohimbine was performed. The effect of each treatment on OKR phase was examined between before and after drug application with the paired t-test. The effect of each treatment on OKR phase change was also compared with that of saline-administered control with Dunnett's test. P values are presented. A positive phase value indicates a delay of eye rotation relative to the screen rotation.

Supplementary Table S13
Effects of contralateral administration of norepinephrine (NE) on VOR phase

NE	Additional drug	Pre	Post	Change	N	T-test	Dunnett
10 mM	no	−28±3	−30±5	−2±4	6	0.640	0.932
	propranolol	−23±3	−27±5	−3±6	6	0.580	0.858
30 mM	no	−20±1	−22±2	−2±2	6	0.452	0.951
	yohimbine	−23±3	−20±7	3±8	6	0.702	1.000

Administration of 10 mM NE with or without co-administration of propranolol, or that of 30 mM NE with or without co-administration of yohimbine, was performed. The effect of each treatment on VOR phase was examined between before and after drug application with the paired t-test. The effect of each treatment on VOR phase change was also compared with that of saline-administered control with Dunnett's test. P values are presented. A negative phase value indicates that the eye rotation occurs ahead of the screen rotation.