

Supplementary Material

Sedative properties of dexmedetomidine are mediated independently from native mice thalamic hyperpolarization-activated, cyclic nucleotide gated channel function at clinically relevant concentrations

Supplementary Table S1. Effects of dexmedetomidine on the resting membrane potential at different concentration groups (absolute values) after 30 minutes and 45 minutes of DEX wash in. There were no significant differences between control, 30 minutes, and 45 minutes of DEX (1, 10, and 100 μ M) exposure on the resting membrane potential. For multiple comparisons of repeated measures, Friedman test was used.

resting membrane potential [mV]								
DEX [μ M]	control		DEX 30 min		DEX 45 min		n	p
	Median	IQR	Median	IQR	Median	IQR		
1	-58.55	-61.12 – -55.77	-60.03	-62.78 – -58.41	-58.85	-61.86 – -56.85	11	0.219
10	-58.17	-60.23 – -57.13	-58.04	-61.44 – -56.14	-57.60	-61.25 – -56.17	10	0.368
100	-57.48	-58.47 – -56.91	-58.54	-60.5 – -56.97	-58.73	-59.68 – -57.11	10	0.067

Supplementary Table S2. Effects of dexmedetomidine (45 minutes) on the resting membrane potential at different concentration groups (absolute values). Wilcoxon-matched pairs signed rank test for statistical comparisons.

resting membrane potential [mV]						
DEX [μ M]	control		DEX		n	p
	Median	IQR	Median	IQR		
1	-58.55	-61.12 – -55.77	-58.85	-61.86 – -56.85	11	0.465
10	-58.17	-60.23 – -57.13	-57.60	-61.25 – -56.17	10	0.846
100	-57.48	-58.47 – -56.91	-58.73	-59.68 – -57.11	10	0.106

Supplementary Table S3. Effects of dexmedetomidine (45 minutes) on the input resistance at different concentration groups (absolute values). Wilcoxon-matched pairs signed rank test for statistical comparisons.

DEX [μ M]	input resistance [M Ω]				n	<i>p</i>
	control		DEX			
	Median	IQR	Median	IQR		
1	290.3	235.4–343.4	317.4	260.8–337.8	11	0.044
10	362.7	311.5–386.3	393.1	362.5–420.7	10	0.006
100	339.4	261.9–413.9	424.5	369.1–493.3	10	0.002

Supplementary Table S4. Effects of dexmedetomidine (45 minutes) on the action potential threshold at different concentration groups (absolute values). Wilcoxon-matched pairs signed rank test for statistical comparisons.

DEX [μ M]	action potential threshold [mV]				n	<i>p</i>
	control		DEX			
	Median	IQR	Median	IQR		
1	−38.22	−39.98 – −37.45	−40.28	−41.69 – −36.84	11	0.102
10	−38.64	−39.50 – −36.49	−39.38	−41.16 – −37.55)	10	0.232
100	−39.80	−40.97 – −39.27	−38.16	−38.98 – −33.25	10	0.002

Supplementary Table S5. Effects of dexmedetomidine (45 minutes) on the action potential at different concentration groups (absolute values). Wilcoxon-matched pairs signed rank test for statistical comparisons.

DEX [μM]	action potential frequency [Hz]				n	<i>p</i>
	control		DEX			
	Median	IQR	Median	IQR		
1	39.67	36.46–39.84	41.96	36.59–45.19	11	0.054
10	42.48	34.56–45.57	41.26	35.01–46.52	10	>0.999
100	42.08	39.75–45.30	27.44	21.61–33.66	10	0.002

Supplementary Table S6. Effects of dexmedetomidine (45 minutes) on $I_{h \text{ maximal}}$ (recorded at -133 mV) at different concentration groups (absolute values). Wilcoxon-matched pairs signed rank test for statistical comparisons.

DEX [μM]	I _h maximal [pA]				n	<i>p</i>
	control		DEX			
	Median	IQR	Median	IQR		
1	516	479–983	495	378–838	11	0.042
10	534	321–719	434	305–663	10	0.006
100	605	418–860	429	321–500	10	0.004

Supplementary Table S7. Effects of dexmedetomidine (45 minutes) on the half-maximal activation potential of HCN channels at different concentration groups (absolute values). Wilcoxon-matched pairs signed rank test for statistical comparisons.

half-maximal activation potential [mV]						
DEX [μ M]	control		DEX		n	<i>p</i>
	Median	IQR	Median	IQR		
1	-86.23	-87.32 – -84.81	-86.64	-87.63 – -84.65	11	0.898
10	-87.42	-88.70 – -86.22	-86.89	-88.47 – -85.29	10	0.695
100	-85.88	-88.15 – -83.99	-91.54	-93.22 – -88.07	10	0.004

Supplementary Table S8. Effects of dexmedetomidine (45 minutes) on the HCN activation time constant τ_{fast} at different concentration groups (absolute values). Wilcoxon-matched pairs signed rank test for statistical comparisons.

τ_{fast} [ms]						
DEX [μ M]	control		DEX		n	<i>p</i>
	Median	IQR	Median	IQR		
1	217.5	199.9–223.9	207.1	188.6–224.0	11	0.413
10	271.5	219.4–290.5	279.2	244.8–335.1	10	0.014
100	250.8	225.1–289.4	376.0	259.2–412.6	10	0.084

Supplementary Table S9. Effects of (45 minutes) on the HCN activation time constant τ_{slow} at different concentration groups (absolute values). Wilcoxon-matched pairs signed rank test for statistical comparisons.

DEX [μM]	τ _{slow} [ms]				n	p
	control		DEX			
	Median	IQR	Median	IQR		
1	1088	984.4–1329	1089	881.8–1190	11	0.765
10	1248	938.9–1482	1295	1041–1962	10	0.322
100	1227	1029–1608	941.8	735.4–1423	10	0.232

Supplementary Table S10. Effects of dexmedetomidine (45 minutes) on the voltage sag amplitude at different concentration groups (absolute values). Wilcoxon-matched pairs signed rank test for statistical comparisons.

DEX [μM]	voltage sag amplitude [mV]				n	p
	control		DEX			
	Median	IQR	Median	IQR		
1	85.07	71.68–89.16	84.90	74.20–87.41	11	0.577
10	91.29	78.67–96.41	87.33	80.76–95.77	10	0.492
100	71.22	65.70–90.50	85.72	68.19–93.15	10	0.014

Supplementary Table S11. Effects of dexmedetomidine (45 minutes) on the rebound burst delay at different concentration groups (absolute values). Wilcoxon-matched pairs signed rank test for statistical comparisons.

DEX [μ M]	rebound burst delay [ms]				n	<i>p</i>
	control		DEX			
	Median	IQR	Median	IQR		
1	29.0	27.0–30.5	29.5	26.5–32.0	11	0.419
10	28.1	24.9–29.8	29.0	25.3–33.1	10	0.719
100	30.4	27.9–31.9	36.5	35.4–39.5	10	0.006

Supplementary Table S12. Effects of dexmedetomidine (45 minutes) on the number of action potentials during rebound at different concentration groups (absolute values). Wilcoxon-matched pairs signed rank test for statistical comparisons.

DEX [μ M]	number of action potentials (n)				n	<i>p</i>
	control		DEX			
	Median	IQR	Median	IQR		
1	7.8	6.8–11.4	9.0	7.9–11.0	11	0.31
10	9.6	5.3–17.6	7.9	5.8–17.3	10	>0.999
100	10.5	7.8–17.3	4.0	2.9–8.3	10	0.002

Supplementary Table S13. Effects of sevoflurane (45 minutes) on the rebound burst duration at different concentration groups (absolute values). Wilcoxon-matched pairs signed rank test for statistical comparisons.

DEX [μM]	rebound burst duration [ms]				n	p
	control		DEX			
	Median	IQR	Median	IQR		
1	188.0	117.0–389.5	251.5	149.0–322.5	11	0.206
10	257.0	118.6–572.9	259.0	159.8–625.3	10	0.557
100	252.5	129.9–679.8	50.75	36.0–337.5	10	0.020