

Supplementary Table 1. Neurological pupil index

Time	EEG finding	L NPi	R NPi	L size	R size	Absolute difference in NPi	Absolute difference in size	If NPi >0.6, then abnormal pupil response (1=yes, 0=no)	L NPi reactivity grade (0=brisk, 1=sluggish, 2=fixed)	R NPi reactivity grade (0=brisk, 1=sluggish, 2=fixed)	Difference in pupillary grade between eyes (0=no, 1=yes)	Comment	Infusion
May 9, 2021 20:00	Focal motor seizures, no scalp correlate	0.5	0.6	5.94	5.87	0.1	0.07	0	1	1	0	None	
May 10, 2021 08:00	1.5 Hz LPDs+R, sharp wave morphology, right hemisphere (max temporal).	3.8	3.9	2.31	2.83	0.1	0.52	0	0	0	0	Midazolam, Levophed	
May 10, 21 12:00	1.5–2 Hz LPDs+R, right hemisphere (max temporal).	3.7	3.5	2.4	2.41	0.2	0.01	0	0	0	0	Midazolam, Levophed	
May 10, 21 16:00	1 Hz LPDs+R, right hemisphere (max temporal). EEG background is discontinuous.	3.6	4.2	2.36	3.24	0.6	0.88	0	0	0	0	Midazolam, Levophed	
May 10, 2021 20:00	1 Hz LPDs, sharp wave and spike morphology, R hemisphere (max temp)	4.1	3.4	2.39	2.33	0.7	0.06	1	0	0	0	Midazolam, Levophed	
May 16, 2021 12:00	0.6 Hz R hemisphere LPDs, sharp wave morphology. EEG background is discontinuous.	2.2	1.8	3.83	3.88	0.4	0.05	0	1	1	0	Heparin gtt (going forward)	
May 16, 2021 16:00	0.5–0.8 Hz R hemisphere LPDs, sharp wave morphology. EEG background is discontinuous.	2.9	2.5	3.77	3.96	0.4	0.19	0	1	1	0		
May 17, 2021 20:00	0.5 Hz R hemisphere LPDs, sharp wave/spike morphology. EEG background is discontinuous.	0.8	0.7	4.95	5.08	0.1	0.13	0	1	1	0		
May 17, 2021 22:49	0.8 Hz R hemisphere LPDs, sharp wave/spike morphology. EEG background is discontinuous	1.5	1	4.34	4.36	0.5	0.02	0	1	1	0		

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Supplementary Table 1. Continued

Time	EEG finding	L NPi	R NPi	L size	R size	Absolute difference in NPi	Absolute difference in size	If NPi >0.6, then abnormal pupil response (1=yes, 0=no)	L NPi reactivity grade (0=brisk, 1=sluggish, 2=fixed)	R NPi reactivity grade (0=brisk, 1=sluggish, 2=fixed)	Difference in pupillary grade between eyes (0=no, 1=yes)	Comment	Infusion
May 17, 2021 23:23	0.5 Hz R hemisphere LPDs, sharp wave/spike morphology. EEG background is discontinuous.	1	1.1	4.33	4.56	0.1	0.23	0	1	1	0		Ketamine, Levophed
May 18, 2021 04:00	0.5 Hz R hemisphere LPDs, spike morphology. EEG background is discontinuous.	0	0	2.24	2.31	0	0.07	0	2	2	0	Rhythmic pro-nation of the L arm, rhythmic movement in the left thumb and eye blinking, movements appeared to match LPDs on cEEG, 2 mg Ativan x 1 given without relief. Underwent CTP consistent with hyperfusion in the R temporal/occipital lobes concerning for ongoing focal status, started ketamine to achieve burst suppression.	Ketamine, Levophed
May 18, 2021 09:09	Burst suppression background, rare LPDs 0.5 Hz, sharp wave morphology R hemisphere	0	2.4	5.95	3.38	2.4	2.57	1	2	1	1		Ketamine, Levophed

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May 18, 2021 09:10	Burst suppression background, rare LPDs 0.5 Hz, sharp wave morphology R hemisphere	0	0	6.58	6.39	0	0.19	0	2	2	0	Repeat stat CTH w/o contrast; No acute intracranial abnormality or other significant interval change; Unchanged moderate prominence of the ventricular system.	Ketamine, Levophed
May 18, 2021 09:21	Burst suppression background, no LPDs	0	0	6.5	6.27	0	0.23	0	2	2	0		Ketamine, Levophed
May 18, 2021 09:46	Off EEG for imaging study	0.9	1	4.36	4.26	0.1	0.1	0	1	1	0		Ketamine, Levophed
May 18, 2021 10:37	0.7 Hz R hemisphere LPDs, spike morphology. EEG background is discontinuous.	0.8	0	6.61	6.14	0.8	0.47	1	1	2	1		Ketamine, Levophed
May 18, 2021 10:46	Burst suppression background, rare 0.3 Hz R LPDs	3.3	3.7	2.79	2.69	0.4	0.1	0	0	0	0		Ketamine, Levophed
May 18, 2021 11:06	Rare LPDs, background discontinuous/burst suppression	2.6	2.2	3.25	4.13	0.4	0.88	0	1	1	0		Ketamine, Levophed
May 18, 2021 12:32	Burst suppression, no LPDs	1.3	1.7	4.43	3.83	0.4	0.6	0	1	1	0		Ketamine, Levophed
May 18, 2021 13:39	Burst suppression, no LPDs	0.7	0	4.88	5.68	0.7	0.8	1	1	2	1		Midazolam, Ketamine, Levophed

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Supplementary Table 1. Continued

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May 18, 2021 16:00	Burst suppression, no LPDs	0	0	3.83	4.48	0	0.65	0	2	2	0		Ketamine, Levophed
May 18, 2021 20:00	Burst suppression, no LPDs	0.8	0.6	4.48	4.76	0.2	0.28	0	1	1	0		Midazolam, Ketamine, Levophed
May 19, 2021 00:00	Burst suppression, no LPDs	0	0	5.86	5.9	0	0.04	0	2	2	0		Midazolam, Ketamine, Levophed
May 19, 2021 04:00	Burst suppression, no LPDs	0.8	0.8	5.05	5.07	0	0.02	0	1	1	0		Midazolam, Ketamine, Levophed
May 19, 2021 08:00	Burst suppression, no LPDs	1.6	1.4	3.89	4.06	0.2	0.17	0	1	1	0		Midazolam 10 mg/hr, Ketamine 8 mg/kg/hr, Levophed
May 19, 2021 08:45	Burst suppression, no LPDs	1.3	1.7	4.15	4.03	0.4	0.12	0	1	1	0		Midazolam, Ketamine, Levophed
May 19, 2021 11:00	Burst suppression, no LPDs	1.9	2.5	3.55	3.28	0.6	0.27	0	1	1	0		Midazolam, Ketamine, Levophed
May 19, 2021 16:00	Burst suppression, no LPDs	0.6	0.7	4.79	5.37	0.1	0.58	0	1	1	0		Midazolam 10 mg/hr, Ketamine 2 mg/kg/hr, Levophed
May 19, 2021 18:22	Burst suppression, no LPDs	2.9	2.9	2.92	2.88	0	0.04	0	1	1	0		Midazolam, Levophed
May 19, 2021 20:00	Burst suppression, no LPDs	1.7	1.8	3.66	3.69	0.1	0.03	0	1	1	0		Midazolam, Levophed
May 20, 2021 00:00	Burst suppression, no LPDs	3.1	3.1	2.62	2.59	0	0.03	0	0	0	0		Midazolam (10 mg/hr), Levophed

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May 20, 2021 04:00	Burst suppression, no LPDs	2.1	2.6	2.65	2.57	0.5	0.08	0	1	1	0		Midazolam, Levophed
May 20, 2021 07:58	Burst suppression, occasional 0.3 Hz LPDs	0	0	5.92	6.11	0	0.19	0	2	2	0		Midazolam, Levophed
May 20, 2021 08:02	Burst suppression, no LPDs	0.8	0.7	5.36	5.47	0.1	0.11	0	1	1	0		Midazolam, Levophed
May 20, 2021 10:00	Burst suppression, occasional 0.3 Hz LPDs	0	0	2.67	2.65	0	0.02	0	2	2	0		Midazolam, Levophed
May 20, 2021 12:00	Burst suppression, occasional 0.3 Hz LPDs	3.3	3.1	2.67	3.15	0.2	0.48	0	0	0	0		Midazolam, Levophed
May 20, 2021 16:00	Burst suppression, rare T6 spikes	3.9	3.1	2.65	2.48	0.8	0.17	1	0	0	0		Midazolam, Levophed
May 20, 2021 20:00	Discontinuous EEG background; Frequent 0.5 Hz R LPDs, sharp wave, spike morphology	3.1	3.4	2.73	3.06	0.3	0.33	0	0	0	0		Midazolam (10 mg/hr), Levophed
May 21, 2021 00:00	Discontinuous EEG background; Frequent 0.5 Hz R LPDs, spike morphology	1.1	1.5	4.1	4.1	0.4	0	0	1	1	0		Midazolam, Levophed
May 21, 2021 08:31	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology	1.4	1.1	4.19	4.87	0.3	0.68	0	1	1	0		Midazolam, Levophed
May 21, 2021 04:00	Burst suppression, rare T6 spikes	1	0.8	5	5.2	0.2	0.2	0	1	1	0		Midazolam, Levophed
May 21, 2021 07:49	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology	3.7	3.5	2.66	2.77	0.2	0.11	0	0	0	0		Midazolam, Levophed

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Time	EEG finding	L NPI	R NPI	L size	R size	Absolute difference in NPI	Absolute difference in size	If NPI >0.6, then abnormal pupil response (1=yes, 0=no)	L NPI reactivity grade (0=brisk, 1=sluggish, 2=fixed)	R NPI reactivity grade (0=brisk, 1=sluggish, 2=fixed)	Difference in pupillary grade between eyes (0=no, 1=yes)	Comment	Infusion
May 21, 2021 10:57	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology.	0.7	0.9	5.38	5.53	0.2	0.15	0	1	1	0		Midazolam (15 mg/hr), Levophed
May 21, 2021 11:33	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology.	0.8	0.7	5.04	4.9	0.1	0.14	0	1	1	0		Midazolam, Levophed
May 21, 2021 12:00	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology.	0.9	0.6	5.12	5.32	0.3	0.2	0	1	1	0		Midazolam, Levophed
5/21/2021 16:00	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology.	3.2	0	2.26	2.37	3.2	0.11	1	0	2	1	L brisk, R fixed	Midazolam, Levophed
May 21, 2021 17:02	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology.	0.7	0.9	5	5.06	0.2	0.06	0	1	1	0		Midazolam (30 mg/hr), Levophed
May 21, 2021 20:00	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology.	0.5	0.5	5.69	5.71	0	0.02	0	1	1	0		Midazolam, Levophed
May 22, 2021 00:00	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology.	1.2	1.1	4.49	4.59	0.1	0.1	0	1	1	0		Midazolam, Levophed
May 22, 2021 04:00	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology.	1.6	1.8	3.94	4.18	0.2	0.24	0	1	1	0		Midazolam, Levophed
May 22, 2021 07:51	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology.	3.9	2.9	2.37	3.64	1	1.27	1	0	1	1		Midazolam, Levophed

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May 22, 2021 09:06	Burst suppression EEG background; 1 Hz LPDs+R run.	0	0.5	5.37	5.76	0.5	0.39	0	2	1	1		Midazolam, Levophed
May 22, 2021 11:58	Burst suppression EEG background; frequent 0.3 Hz R LPDs, spike morphology.	0.9	1.6	4.76	4.61	0.7	0.15	1	1	1	0		Midazolam, Levophed
May 22, 2021 16:26	Burst suppression EEG background; occasional 0.5 Hz R LPDs, spike morphology.	1.4	1.5	4.14	4.06	0.1	0.08	0	1	1	0		Midazolam (30 mg/hr)
May 22, 2021 19:36	Burst suppression EEG background; Occasional 0.3–0.5 Hz R LPDs, spike morphology.	1.4	1.4	4.56	4.84	0	0.28	0	1	1	0		Midazolam (30 mg/hr)
May 23, 2021 00:00	Burst suppression EEG background; Occasional 0.3–0.5 Hz R LPDs, spike morphology.	0.7	0.6	5.38	5.35	0.1	0.03	0	1	1	0		Midazolam (30 mg/hr)
May 23, 2021 04:00	Burst suppression EEG background; Occasional 0.3–0.5 Hz R LPDs, spike morphology.	0.9	1.1	4.67	5.16	0.2	0.49	0	1	1	0		Midazolam (30 mg/hr)
May 23, 2021 07:15	Burst suppression, rare T6 spikes	0.8	1.1	4.63	4.72	0.3	0.09	0	1	1	0		Midazolam (30 mg/hr)
May 23, 2021 09:26	Burst suppression, rare T6 spikes	1.4	1.4	4.21	4.6	0	0.39	0	1	1	0		Midazolam (30 mg/hr)
May 23, 2021 12:57	Burst suppression, rare T6 spikes	4	3.2	2.67	2.67	0.8	0	1	0	0	0		Midazolam (30 mg/hr)
May 23, 2021 16:00	Off EEG	1.9	2.1	3.87	3.88	0.2	0.01	0	1	1	0		Midazolam (30 mg/hr)

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Supplementary Table 1. Continued

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May 23, 2021 20:00	Discontinuous EEG background; Occasional 1 Hz R LPDs, spike morphology.	0.8	0.9	4.81	5.15	0.1	0.34	0	1	1	0	Midazolam (30 mg/hr)	
May 24, 2021 00:00	Burst suppression EEG background; Occasional 0.3–0.5 Hz R LPDs, spike morphology.	0.7	2.9	4.8	3.05	2.2	1.75	1	1	1	0	Midazolam (30 mg/hr)	
May 24, 2021 04:00	Burst suppression EEG background; Occasional 0.5–1 Hz R LPDs, spike morphology.	2.4	2.2	3.96	3.56	0.2	0.4	0	1	1	0	Midazolam (30 mg/hr)	
May 24, 2021 08:00	Burst suppression EEG background; Occasional 0.5–1 Hz R LPDs, spike morphology.	2.4	2.3	3.62	3.84	0.1	0.22	0	1	1	0	Midazolam (30 mg/hr)	
May 24, 2021 12:00	Burst suppression EEG background; Occasional 0.5–1 Hz R LPDs, spike morphology.	2.4	2.1	3.52	3.74	0.3	0.22	0	1	1	0	Midazolam (30 mg/hr)	
May 24, 2021 16:00	Burst suppression, no LPDs	0.5	0.5	6.01	6.04	0	0.03	0	1	1	0	Midazolam (28 mg/hr), Levophed	
May 24, 2021 20:00	Burst suppression, rare T6 spikes	1.6	3.2	3.78	3.8	1.6	0.02	1	1	0	1	Midazolam (26 mg/hr), Levophed	
May 25, 2021 00:00	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology.	2.1	3.3	3.7	3.43	1.2	0.27	1	1	0	1	Midazolam (22 mg/hr), Levophed	

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May 25, 2021 04:00	Burst suppression EEG background; Frequent 0.5 Hz R LPDs, spike morphology.	1	0.9	5.22	4.68	0.1	0.54	0	1	1	0	Midazolam (20 mg/hr), Levophed	
May 25, 2021 08:00	Burst suppression, no LPDs	0.7	0.9	5.67	5.76	0.2	0.09	0	1	1	0	Midazolam (20 mg/hr), Levophed	
May 25, 2021 12:00	Burst suppression, no LPDs	0.5	0.6	5.8	5.55	0.1	0.25	0	1	1	0	Midazolam (20 mg/hr), Levophed	
May 25, 2021 20:00	Burst suppression EEG background; Occasional 1 Hz R LPDs, spike morphology.	0.4	0.4	5.86	5.99	0	0.13	0	1	1	0	Midazolam (15 mg/hr), Levophed	
May 26, 2021 00:00	Burst suppression, no LPDs	0.7	0.5	5.82	5.85	0.2	0.03	0	1	1	0	Intermittently on low dose Levophed	
May 26, 2021 04:00	Burst suppression, no LPDs	0.6	0.5	6.08	6.1	0.1	0.02	0	1	1	0		
May 26, 2021 08:00	Burst suppression, no LPDs	1.3	1.3	4.27	4.58	0	0.31	0	1	1	0		
May 26, 2021 12:00	Discontinuous EEG background; Frequent 0.75 Hz R LPDs, spike morphology.	0.5	0.5	5.69	5.82	0	0.13	0	1	1	0		
May 26, 2021 20:00	Discontinuous EEG background; Frequent 0.75 Hz R LPDs, spike morphology.	3.7	3.4	3.1	3.88	0.3	0.78	0	0	0	0		
May 27, 2021 00:00	Discontinuous EEG background; Frequent 0.75 Hz R LPDs, spike morphology.	1.2	0.7	5.2	5.67	0.5	0.47	0	1	1	0		
May 27, 2021 04:00		1.4	0.9	4.7	4.85	0.5	0.15	0	1	1	0		

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May 27, 2021 08:00		2.1	1.1	4.49	4.92	1	0.43	1	1	1	0		
May 27, 2021 16:00		1.5	2.8	4.35	3.75	1.3	0.6	1	1	1	0		
May 27, 2021 20:00		1	0.7	5.01	5.54	0.3	0.53	0	1	1	0		
May 28, 2021 00:00		2.5	2.2	3.94	4.2	0.3	0.26	0	1	1	0		
May 28, 2021 04:00		3.8	3.6	3.13	3.33	0.2	0.2	0	0	0	0		
May 28, 2021 08:00		3.8	2.5	2.94	3.96	1.3	1.02	1	0	1	1		
May 28, 2021 20:00		1.9	1.3	3.96	4.17	0.6	0.21	0	1	1	0		
May 29, 2021 00:00		1.5	1.2	4	4.78	0.3	0.78	0	1	1	0		
May 29, 2021 04:00		3.2	3.3	2.25	2.51	0.1	0.26	0	0	0	0		
May 29, 2021 08:00		2.1	1.6	3.87	4.37	0.5	0.5	0	1	1	0		
May 29, 2021 12:00		2.5	1.8	3.8	4.18	0.7	0.38	1	1	1	0		
May 29, 2021 16:00		3.8	3.9	3.14	2.61	0.1	0.53	0	0	0	0		Discontinued Levophed
May 29, 2021 20:00		2.9	1.9	3.49	4.02	1	0.53	1	1	1	0		
May 30, 2021 00:00		2.7	2	3.86	3.9	0.7	0.04	1	1	1	0		
May 30, 2021 04:00		3.3	4.2	2.34	2.84	0.9	0.5	1	0	0	0		
May 30, 2021 08:00		2.2	1.3	3.83	4.35	0.9	0.52	1	1	1	0		
May 30, 2021 12:00		2.7	2.4	3.66	3.82	0.3	0.16	0	1	1	0		
May 30, 2021 20:00		2.2	2	4.11	4.44	0.2	0.33	0	1	1	0		

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May 31, 2021 00:00		2.8	1	4.01	4.87	1.8	0.86	1	1	1	0		
May 31, 2021 04:00		2.4	2.2	3.85	4.12	0.2	0.27	0	1	1	0		
Jun 1, 2021 08:32		2.4	2.4	3.81	4.08	0	0.27	0	1	1	0		
Jun 2, 2021 11:00		4.3	4.1	3.3	3.37	0.2	0.07	0	0	0	0		
Jun 2, 2021 15:00		2.2	1.5	3.9	4.33	0.7	0.43	1	1	1	0		
Jun 3, 2021 07:57		2	1.3	4.07	4.08	0.7	0.01	1	1	1	0		
Jun 3, 2021 12:00		4.3	3.7	3.05	3.02	0.6	0.03	0	0	0	0		
Jun 3, 2021 16:00		2.6	1.9	3.73	3.66	0.7	0.07	1	1	1	0		

Pupil reactivity was categorized into three groups: brisk (NPI >3.0), sluggish (NPI <3.0), and fixed (NPI=0) based upon prior validated guidelines by the NeuroOptics NPI-200 Pupilometer (Neuroptics Inc., Irvine, CA, USA). The rows are highlighted in blue when one or both pupils are fixed. We reviewed 106 time points throughout May–June 2021 hospital admission for a single patient admitted to our large academic neurosciences critical care unit (NCCU). The NPI is a proprietary number that purports to gauge the quality of the pupillary light reflex independent of pupillary diameter [10]. Throughout the NCCU course, pupillary response data included: left NPI range 0–4.3, size 2.2–6.6 mm; right NPI range 0–4.2, size 2.3–6.4 mm; left pupil fixed 9/106 (8%), sluggish 76/106 (72%), and brisk 21/106 (20%); right pupil fixed 10/106 (9%), sluggish 76/106 (72%), and brisk 20/106 (19%).

EEG, electroencephalogram; L, left; NPI, neurological pupil index; R, right; LPD, lateralized periodic discharge; cEEG, continuous EEG; CTP, CT; computed tomography; H, ***; w/o, ***.