Title: Processed electroencephalogram normative values in neonates

Presenting/First Author:
Georgia Georgostathi
Researcher in Vagelos Intergrated Program in Energy Research, University of Pennsylvania, Philadelphia, PA, USA.
ggeorgia@seas.upenn.edu

Co-authors:
Rachit Kumar, BS
Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA
Medical Scientist Training Program at the University of Pennsylvania, Philadelphia, USA

Ashley S. Hodges, MD
Fellow in Pediatric Anesthesiology and Critical Care
Department of Anesthesiology and Critical Care Children's Hospital of Philadelphia

Olivia Nelson, MD
Assistant Professor of Anesthesiology and Critical Care
Children's Hospital of Philadelphia
Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA

Shavonne Massey, MD, MSCE
Assistant Professor in Neurology
Division of Neurology, Children's Hospital of Philadelphia
Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA

Nicholas S. Abend, MD, MSCE
Associate Professor of Neurology, Pediatrics and Anesthesiology and Critical Care, Children's Hospital of Philadelphia
Perelman School of Medicine at the University of Pennsylvania

Alexis A. Topjian, MD, MSCE
Associate Professor of Pediatrics and Anesthesiology and Critical Care,
Children's Hospital of Philadelphia
Perelman School of Medicine at the University of Pennsylvania

Senior Author:
Ian Yuan, MD MEng
Assistant Professor of Anesthesiology and Critical Care
Children's Hospital of Philadelphia
Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA

Introduction:

Electroencephalogram (EEG) monitors brain electrical activity that can reflect anesthetic depth. However, intraoperative proprietary EEG indices (e.g., BIS and PSI) originally developed from healthy adult volunteers are not reliable in infants and neonates, a population particularly sensitive to the effects of anesthesia.[1] Whereas raw unprocessed EEG can reliably detect "excessive" anesthesia in neonates, interpreting raw EEG requires advanced training and practice.[2] Besides proprietary EEG indices and raw EEG, there are other non-proprietary processed EEG (pEEG) parameters that can be used to determine anesthetic levels. However, there are no normative values for these non-proprietary pEEG parameters in unanesthetized infants that can be used for comparison to neonates under anesthesia. This study aims to address this knowledge gap by deriving normative values for pEEG parameters in unanesthetized neonates in awake and asleep states. The secondary aim is to determine the best pEEG parameters to discriminate between the different states of consciousness.

Methods:

This retrospective study included normal EEG recordings (14-channel neonatal bipolar montage) from healthy neonates, as interpreted by neurology and annotated into awake *vs* quiet asleep *vs* active sleep states. Since most intraoperative EEG monitoring use frontal channels, only frontal channels Fp1-C3 and Fp2-C4 were analyzed. EEG processing was performed using Matlab with NEURAL, a publicly available and validated library of Matlab functions.[3] After band-filtering between 0.5-30hz and artifact removal using the built in-function, the pEEG parameters listed in table 1 were calculated across 5 frequency bands (δ1: 0.5-1hz; δ2: 1-4hz; θ: 4-8hz; α: 8-13hz; ß: 13-30hz) for each EEG file. Mean and standard deviation (SD) were calculated for each channel and state (awake, quiet sleep, and active sleep) and paired 2-tailed Student's t-test were used to compare pEEG between states.

Results:

EEG from 23 neonates (mean [stdev] adjusted age on day of recording: 40.9 [1.97] weeks) were analyzed. The mean [stdev] of SEF 50/90 are listed in table 2. SEF 50 but not SEF 90 was able to differentiate between Awake vs Quiet and Awake vs Active. The power ratio, entropy, and coherence for each frequency band are listed in table 3. Power ratio can best differentiate between Awake vs Quiet and Awake vs Active best δ1 and θ bands. Conversely, entropy can best differentiate between the same states in ß bands. Finally, left/right coherence can differentiate between Awake vs Active best in δ2 band. None of the pEEG were able to differentiate between Active vs Quiet sleep states.

Conclusion:

This retrospective study provides normative pEEG values in neonates that will allow future researchers to compare to pEEGs obtained in neonates under anesthesia or sedation and provide direction on selecting pEEG parameters and frequency bands to best differentiate different states of consciousness.

Table 1:

pEEG parameter	Definition	Changes with increased anesthetic depth
Spectral Edge Frequency 50	Frequency where 50% of the EEG power lies under.	Decreases
Spectral Edge Frequency 90	Frequency where 90% of the EEG power lies under.	Decreases
Power ratio (δ1,δ2,θ,α,ß)	% of power for each of 5 frequency band over total power	Increase in lower frequency bands
Coherence (δ1,δ2,θ,α,ß)	Synchrony between Left vs Right channels (0: no synchrony; 1: total synchrony)	Increases
Entropy (δ1,δ2,θ,α,ß)	Amount of randomness in EEG signals. (0: total order; 1: total randomness)	Decreases

Table 2:

			SEF 50 (hz)	SEF 90 (hz)
Fp1-C3	Awake	Mean	0.92	3.99
		Stdev	0.33	3.22
	Quiet Sleep	Mean	1.20	4.63
		Stdev	0.32	1.20
	Active Sleep	Mean	1.14	4.11
		Stdev	0.32	1.09
	Awake vs Quiet		**< 0.01**	0.38
	Awake vs Active		**0.03**	0.86
	Quiet vs Active		0.59	0.16
Fp2-C4	Awake	Mean	0.95	4.64
		Stdev	0.29	3.99
	Quiet Sleep	Mean	1.21	5.39
		Stdev	0.27	3.59
	Active Sleep	Mean	1.11	4.21
		Stdev	0.26	1.29
	Awake vs Quiet		**< 0.01**	0.52
	Awake vs Active		**0.05**	0.63
	Quiet vs Active		0.25	0.17

Table 3:

Power ratio			δ1 %	δ2 %	θ %	α %	ß %
Fp1-C3	Awake	Mean	0.51	0.39	0.06	0.02	0.03
		Stdev	0.18	0.12	0.04	0.01	0.03
	Quiet Sleep	Mean	0.39	0.47	0.10	0.02	0.02
		Stdev	0.10	0.08	0.04	0.01	0.01
	Active Sleep	Mean	0.39	0.49	0.08	0.02	0.02
		Stdev	0.15	0.13	0.03	0.01	0.01
	Awake vs Quiet		**<0.01**	**0.02**	**<0.001**	0.1	0.16
	Awake vs Active		**0.02**	**0.01**	**0.03**	0.28	0.14
	Quiet vs Active		0.93	0.57	0.09	0.52	0.98
Fp2-C4	Awake	Mean	0.47	0.42	0.06	0.02	0.03
		Stdev	0.14	0.10	0.03	0.01	0.03
	Quiet Sleep	Mean	0.37	0.48	0.10	0.02	0.03
		Stdev	0.09	0.06	0.04	0.01	0.04
	Active Sleep	Mean	0.39	0.49	0.08	0.02	0.02
		Stdev	0.13	0.11	0.03	0.01	0.01
	Awake vs Quiet		**<0.01**	**0.02**	**<0.001**	0.09	0.47
	Awake vs Active		0.06	**0.04**	**0.04**	0.28	**0.05**
	Quiet vs Active		0.6	0.72	0.08	0.53	0.49
Entropy							
Fp1-C3	Awake	Mean	0.93	0.84	0.96	0.98	0.98
		Stdev	0.06	0.09	0.02	0.01	0.02
	Quiet Sleep	Mean	0.98	0.90	0.96	0.98	0.94
		Stdev	0.03	0.04	0.01	0.01	0.03
	Active Sleep	Mean	0.97	0.89	0.96	0.98	0.95
		Stdev	0.04	0.06	0.01	0.01	0.02
	Awake vs Quiet		**<0.001**	**<0.01**	0.24	0.09	**<0.001**
	Awake vs Active		**<0.01**	**0.05**	0.34	0.49	**<0.001**
	Quiet vs Active		0.3	0.4	0.77	0.22	0.51
Fp2-C4	Awake	Mean	0.95	0.86	0.95	0.98	0.98
		Stdev	0.04	0.07	0.02	0.02	0.02
	Quiet Sleep	Mean	0.98	0.90	0.96	0.98	0.95
		Stdev	0.03	0.04	0.01	0.01	0.02
	Active Sleep	Mean	0.96	0.89	0.96	0.98	0.96
		Stdev	0.04	0.05	0.01	0.01	0.02
	Awake vs Quiet		**<0.01**	**<0.01**	0.06	0.91	**<0.001**
	Awake vs Active		0.2	0.07	0.06	0.95	**<0.001**
	Quiet vs Active		0.12	0.43	0.94	0.78	0.18
Coherence							
	Awake	Mean	0.35	0.36	0.27	0.3	0.33
		Stdev	0.25	0.20	0.19	0.27	0.24

Fp1-C3/ Fp2-C4	Quiet Sleep	Mean	0.41	0.48	0.33	0.28	0.21
		Stdev	0.18	0.16	0.15	0.15	0.15
	Active Sleep	Mean	0.46	0.56	0.4	0.34	0.39
		Stdev	0.19	0.18	0.25	0.32	0.35
	Awake vs Quiet		0.39	**0.03**	0.29	0.7	**0.04**
	Awake vs Active		0.11	**<0.001**	0.07	0.66	0.54
	Quiet vs Active		0.38	0.14	0.27	0.42	**0.04**

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2. Yuan I, Xu T, Kurth CD. Using Electroencephalography (EEG) to Guide Propofol and Sevoflurane Dosing in Pediatric Anesthesia. *Anesthesiology Clinics.* 2020;38(3):709-725.
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