

The Impact of Neuromuscular Blockade Reversal on Processed EEG-Derived Depth of Anesthesia: An Integrative Review

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INTRODUCTION

- Sudden arousal following neuromuscular blockade reversal (NMBR) (eg, moving, sucking, grimacing, coughing, increased blood pressure, tachycardia) puzzles clinicians
- Processed EEG (pEEG) monitors quantify depth of anesthesia (DoA) via computation of a dimensionless index value
- The link between NMBR and subsequent changes in pEEG values warrants exploration
- This integrative review explores the relationship between NMBR and DoA using the widely available bispectral index (BIS) monitor
- **PICO:** In patients undergoing general anesthesia and receiving rocuronium for neuromuscular blockade, what is the effect of NMBR using sugammadex compared to anticholinesterase on BIS values?

METHODS

- MEDLINE, PubMed, and EMBASE were systematically searched
- Keywords: *sugammadex, EEG, neuromuscular block**
- Limiters: English, general anesthesia
- Search yielded < 16 results
- Highest level evidence meeting inclusion criteria were 3 prospective cohort studies with randomization
- IRB/IACUC approval does not apply to this evidence-based project

REVIEW OF LITERATURE

- All studies¹⁻³ reported increases in BIS values following NMBR independent of NMBR agent used
- One study¹ compared sugammadex to neostigmine and pyridostigmine with maintenance using desflurane, while the other two studies^{2,3} compared sugammadex to neostigmine using total intravenous anesthesia (TIVA)
- Two studies^{1,3} maintained anesthesia throughout NMBR, while one study² stopped anesthesia prior to NMBR
- One study³ observed NMBR resulted in a significant increase in BIS values in those with reappearance of muscular activity on EMG while another study¹ observed NMBR resulted in significant increases in BIS and EMG across groups
- One study² observed NMBR resulted in both higher BIS and motor evoked potential values, with significantly higher values in the sugammadex group

Reversal of rocuronium-induced neuromuscular blockade is associated with a quantifiable impact on processed EEG monitoring

Unexpected arousal following neuromuscular blockade reversal requires further research

Author, Study Design	Anesthesia	Group (n)	BIS		EMG		Results	
			Pre-NMBR	Post-NMBR	Pre-NMBR	Post-NMBR		
Kim et al, ¹ 2019 RSBP	Inhalation: desflurane	NEO + GLYC (19)	41 [37-47]	61 [46-71]	27 [26-27]	40 [29-45]	BIS and EMG significantly increased post-NMBR in all 3 groups	
			MD 18, 95% CI 9-25, P < .001		MD 13, 95% CI 5-17, P = .001			
		SUG (20)	40 [34-46]	52 [41-70]	26 [26-27]	35 [27-49]	No differences in BIS and EMG values between drug groups	
			MD 14, 95% CI 5-26, P < .001		MD 9, 95% CI 1-19, P = .001			
PYR + GLYC (18)	42 [36-50]	58 [52-71]	27 [26-28]	37 [29-46]				
			MD 18, 95% CI 10-25, P = .001		MD 10, 95% CI 3-15, P = .001			
Biricik et al, ² 2019 RDBP	TIVA: remi-prop	SUG (30)	58.03 (5.5)	77.4 (4.7)	369.9 (29.9) ^a	465.3 (34.8)	Significantly higher BIS in SUG than NEO group, P = .023	
		NEO + ATRO (30)	57.6 (4.1)	74.8 (3.7)	354 (33.28)	431.3 (28.2)	Significantly higher MEP in SUG than NEO group, P = .001	
Dahaba et al, ³ 2012 RP	TIVA: remi-prop	No EMG activity (< 35 dB) ^b						No significant increase in BIS after SUG and NEO in subjects with no EMG activity
		SUG (13) ^c	49.3 (4.9)	51.9 (5.4)	NR	NR		
		NEO + GLYC (11)	52.3 (7.4)	53.3 (6.8)	NR	NR		
		High EMG activity (≥ 35 dB)						BIS increased significantly after SUG and NEO in subjects with high EMG activity, P < .05
		SUG (11)	50.1 (10.3)	61.7 (7.9)	NR	NR		
		NEO + GLYC (13)	51.9 (8.1)	63.9 (8.1)	NR	NR		

Table 1. Bispectral index and electromyogram readings pre- and post-administration of neuromuscular blocking reversal agents
 Abbreviations: ATRO, atropine; BIS, bispectral index; dB, decibels; CI, confidence interval; EMG, electromyogram; GLYC, glycopyrrolate; MD, mean difference; NEO, neostigmine; NMBR, neuromuscular blockade reversal; NR, not reported; PYR, pyridostigmine; RDBP, randomized, double-blind prospective; RP, randomized prospective; remi-prop, remifentanyl-propofol; RSBP, randomized, single-blind, prospective; SUG, sugammadex; TIVA, total intravenous anesthesia
^aMotor evoked potential values reported during spine surgery.
^bFrontal EMG reading post-NMBR < 35 dB allocated to no EMG activity group, ≥ 35 dB allocated to high EMG activity group. EMG readings for individual groups not reported.
^cBIS scores reported 5 minutes post-SUG administration and 15 minutes post-NEO administration.



GAPS IN KNOWLEDGE

- EMG frequencies (30-300 Hz) overlap EEG frequencies (0-50 Hz), suggesting that pEEG algorithms could confuse changes in EMG signaling with decreased DoA at NMBR
- It is not known what impact depth of NMB has on reversal as all studies maintained TOFC ≥ 1 at reversal
- It is not known what impact DoA (BIS ≤ 40) has on reversal as all studies maintained BIS > 40 at reversal
- It is not common practice in clinical anesthesia to maintain steady state anesthesia or prohibit stimuli during surgical closure and NMBR, so study results should be generalized with caution

RECOMMENDATIONS FOR PRACTICE

1. Clinicians cannot be assured that increases in BIS values reflect decreased DoA because NMBR may interfere with BIS monitoring; therefore, clinicians should combine BIS values with direct observation of the patient's arousal state
2. There is no difference between type of anesthetic technique (inhalation vs TIVA) and change in BIS value following NMBR
3. Elevated BIS values following NMBR affirm the necessity of anesthetic maintenance—whether by TIVA or inhalation agent—until full restoration of neuromuscular function to avoid potential episodes of awareness

CONCLUSIONS

- **PICOT answered:** In patients undergoing general anesthesia and receiving rocuronium for neuromuscular blockade, NMBR using sugammadex or an anticholinesterase increases BIS values
- Current evidence supports a link between NMBR and increased BIS values, with EMG contamination a likely explanation for this phenomenon
- Future research is needed to demonstrate that increased BIS values following NMBR result in clinically significant episodes of awareness
- BIS monitors should be applied with careful consideration, given the limitations of BIS values to accurately track DoA when NMBR agents are administered

REFERENCES

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