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Effect of sugammadex on processed EEG parameters in patients undergoing robot-assisted radical prostatectomy

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Abstract

Background: Sugammadex has been associated with increases in the bispectral index (BIS). We evaluated the effects of sugammadex administration on quantitative electroencephalographic (EEG) and electromyographic (EMG) measures.
Methods: We performed a prospective observational study of adult male patients undergoing robot-assisted radical prostatectomy. All patients received a sevoflurane-based general anaesthetic and a continuous infusion of rocuronium, which was reversed with 2 mg kg^{-1} of sugammadex i.v. BIS, EEG, and EMG measures were captured with the BIS Vista™ monitor.
Results: Twenty-five patients were included in this study. Compared with baseline, BIS increased at 4–6 min (β coefficient: 3.63; 95% confidence interval [CI]: 2.22–5.04; $P<0.001$), spectral edge frequency 95 (SEF95) increased at 2–4 min (β coefficient: 0.29; 95% CI: 0.05–0.52; $P=0.016$) and 4–6 min (β coefficient: 0.71; 95% CI: 0.47–0.94; $P<0.001$), and EMG increased at 4–6 min (β coefficient: 1.91; 95% CI: 1.00–2.81; $P<0.001$) after sugammadex administration. Compared with baseline, increased beta power was observed at 2–4 min (β coefficient: 93; 95% CI: 1–185; $P=0.046$) and 4–6 min (β coefficient: 208; 95% CI: 116–300; $P<0.001$), and decreased delta power was observed at 4–6 min (β coefficient: −526.72; 95% CI: −778 to −276; $P<0.001$) after sugammadex administration. Neither SEF95 nor frequency band data analysis adjusted for EMG showed substantial differences. None of the patients showed clinical signs of awakening.
Conclusions: After neuromuscular block reversal with 2 mg kg^{-1} sugammadex, BIS, SEF95, EMG, and beta power showed small but statistically significant increases over time, while delta power decreased.

Keywords: bispectral index; depth of anaesthesia monitors; electroencephalogram; frequency bands; spectral edge frequency; sugammadex

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Editor's key points

- Processed EEG index scores, such as the bispectral index (BIS), can increase after administration of sugammadex. Interpretation of this phenomenon is confounded by declining effect-site concentrations of anaesthetic drugs and increasing EMG activity occurring at the same time.
- In this prospective cohort study, anaesthetic administration was kept constant at around one minimum alveolar concentration while sugammadex 2.0 mg kg^{-1} was administered to reverse neuromuscular block from a train-of-four count of four. The BIS, EEG, and EMG were collected.
- BIS, spectral edge frequency 95 (SEF95), EMG and beta power increased, and delta power decreased, after administration of sugammadex. These changes were statistically significant but small. Adjustment of SEF95 and frequency band results for EMG did not change these results and none of the patients showed clinical signs of awakening.
- An increase in frontal cortical activity after sugammadex administration could be due to increasing signals generated by stretching muscular receptors that reach the brain by afferent pathways and induce arousal. Contamination of the BIS by EMG artifact remains a possibility.

Cortical brain activity monitoring has become common practice during general anaesthesia. The aim of this monitoring is not only to decrease the chance of intraoperative awareness, but also to individualise anaesthesia, assess cerebral repercussions of intraoperative events, and reduce the risk of neurological complications.[1–8] Depth of anaesthesia indices, usually scaleless numbers obtained from the processed EEG, are commonly used for this purpose. These indices are derived using complex mathematical algorithms that include several variables besides the EEG. Most of these algorithms are company-owned and not publicly disclosed.[9–11] The bispectral index (BIS) is among the most widely used and studied for processed EEG monitors.[12,13]

The EEG recordings from the BIS monitor may be affected by patient characteristics, clinical situations, and electrical interference from nearby devices.[14–18] The effect of drugs that do not cross the blood–brain barrier on the processed EEG, such as neuromuscular blocking and reversal agents, has been described recently.[19–21] Some anaesthetists have a clinical perception of patients waking up faster after receiving sugammadex administration and changes in the BIS suggesting increased cortical brain activity similar to anaesthesia emergence have been reported.[22–28] The dose of sugammadex, observation periods, and effect on cerebral parameters vary within these studies. It is also unclear whether these drugs have a direct effect on cortical activity, their peripheral effects cause cortical changes, or these changes are secondary to the increase in the EMG activity.[18–31]

The aim of this prospective observational study in adult males having robot-assisted radical prostatectomy was to analyse the effects of sugammadex administration on the EEG, EMG, and BIS. We used specific timestamps to standardise our findings, and an adjustment for EMG activity to moderate its impact in the other parameters analysed (spectral edge frequency 95 [SEF95] and frequency band data).

Methods

This prospective observational study (CUN-SUG-2018-01) was approved by Navarra's Institutional Review Board (EO18/7). Patients were recruited at the Clínica Universidad de Navarra from October 2018 to November 2021 (principal investigator: Iñigo Rubio; date of inclusion 18 July 2018). Male patients undergoing elective robot-assisted radical prostatectomy who agreed to participate and who signed the consent form were included. Exclusion criteria were refusal to participate, being scheduled for an anaesthetic that did not include rocuronium, sugammadex, or BIS Vista™ monitoring (Medtronic Inc., Minneapolis, MN, USA), and pre-existing relevant neurological diseases that could alter EEG recording, such as stroke, epilepsy, drug abuse, neuroleptic or benzodiazepine treatment, neuromuscular disorders, or moderate-to-severe vascular diseases.

Standard monitoring consisting of electrocardiogram, pulse oximetry, capnography, invasive arterial BP, and oesophageal temperature was applied. All data were registered and automatically stored on computers connected to the Carescape B650 monitor (GE Healthcare, Chicago, IL, USA).

Frontal EEG was recorded using a bilateral BIS Vista monitor. The monitor sensor is composed of six electrodes in a self-adhesive patch placed on the patient's forehead. In our study, these electrodes were placed according to international 10/20 system locations. Electrode LE was placed over Fp1, RE over Fp2, LT over F7, RT over F8, C over FPz, and G between Fpz and Fp1. In addition to the BIS, the BIS Vista monitor generates a density spectral array (DSA), SEF95, suppression ratio, burst count, and signal quality linked to EMG power. The exact algorithm is not publicly available, but reportedly uses three descriptors to generate the BIS: relative β ratio, SynchFastSlow, and burst suppression.[29] We downloaded the raw data from the BIS Vista monitor and used custom-made Matlab™ (MathWorks, Inc., Natick, MA, USA) scripts developed by our team to convert BIS Vista files into the Spike2™ data format for further analyses (in Supplementary Appendix S1).

The anaesthesia protocol included maintenance with sevoflurane and opioids, targeted to obtain a DSA with predominating alpha and delta activity, with low or suppression of activity in the beta band, maintaining SEF95 between 10 and 14 Hz (Supplementary Appendix S2). We monitored neuromuscular block depth using the train-of-four (TOF) and TOF ratio (DatexOhmeda M-NMT-00-01, GE Healthcare, Inc., Chicago, IL, USA, compatible with Carescape B650, GE Healthcare, Inc.). After an initial bolus of rocuronium (0.6–1.2 mg kg^{-1} i.v.), we administered a continuous rocuronium infusion starting with 0.3–0.4 mg kg^{-1} h^{-1} to obtain a TOF count between 1 and 2. This infusion was stopped in all patients once urethral suturing was complete. The dose of sugammadex was calculated according to recommendations for each TOF value,[31,32] and was administered once the surgery was completed. A steady sevoflurane minimum alveolar concentration (MAC) was maintained from 2 min before sugammadex administration until 6 min after sugammadex administration.

In addition to the data exported from the BIS Vista monitor, the HR, BP, pulse oximetry (SpO_2), capnography ($ETCO_2$), and MAC were also recorded. Clinical signs of awakening (eye opening, coughing, or limb movement) were noted.

We analysed 120-s blocks from the BIS Vista™ recordings at four time-intervals: baseline (2 min before sugammadex administration), 0–2 min (from sugammadex administration to 2 min after), 2–4 min (between the 2nd and 4th min after sugammadex), and 4–6 min (between the 4th and 6th min after sugammadex administration). These time periods were selected based on an expected median time of reversal of moderate neuromuscular block after sugammadex 2 mg kg^{-1} i.v. of between 1.3 and 1.7 min.[33]

Statistical analysis

We estimated a sample size of 24 patients for the detection of a standardised effect size of 0.8, considering a within-subject design with a two-sided test and assuming a power of 90%, a probability of type I error of 5%, and an expected dropout rate of 20%. Patient characteristics were summarised using means and standard deviations (SD), medians and interquartile ranges, and counts and percentages. Linear mixed-effects models were used to consider dependencies from the data, including patient and laterality levels. The adjustment for EMG was performed including the EMG variable as a covariate in the model. The residuals were assessed for normality by using QQ plots. Statistical significance was set at $P<0.05$. Statistical analyses were performed using Stata 14 software (StataCorp. 2015, Stata Statistical Software: Release 14; StataCorp LP, College Station, TX, USA).

Results

Of the 30 patients who agreed to participate, five were excluded because of failures in data export. Thus, 25 patients were included in the final analysis. Supplementary Table S1 presents the characteristics of the study population. Mean age was 65.4 (6.5) years. For the BIS, SEF95, and EMG parameters, a total of 200 measurements for each parameter over time were registered (eight per patient) from the right and left hemispheres. A total of 400 measurements (16 per patient) were registered for frequency bands over time from the frontal lobes.

The mean procedure duration was 266 (68) min. Mean rocuronium dose was 196 (59) mg. Before sugammadex administration, all patients had a TOF count of 4 and a TOF ratio <90%. All patients received 2 mg kg^{-1} sugammadex to achieve a TOF ratio >90%. No complications related to reversal were documented. All patients were admitted to the post-anaesthesia care unit and subsequently transferred to the hospital ward.

Changes in BIS, SEF95, and EMG over time after sugammadex administration are shown in Table 1. All these parameters increased over time after sugammadex administration. Compared with baseline, a statistically significant increase in BIS was observed in the 4–6 min after sugammadex administration (β coefficient: 3.63; 95% CI: 2.22–5.04; $P<0.001$) (Table 1). Right side mean BIS values increased from 46.5 (7.1) to 50.1 (10.2), while left side values increased from 46.1 (7.2) to 49.8 (9.8) (Table 1). Unadjusted SEF95 data showed a significant increase at 2–4 min (β coefficient: 0.29; 95% CI: 0.05–0.52; $P=0.016$) and 4–6 min (β coefficient: 0.71; 95% CI: 0.47–0.94; $P<0.001$) after sugammadex administration compared with baseline (Table 1). Mean SEF95 values at 2–4 min ranged from 15.0 (1.8) Hz to 15.2 (2.2) Hz and from 14.6 (2.0) Hz to 15.0 (2.3) Hz, while the values for 4–6 min ranged from 15.0 (1.8) Hz to 15.6 (2.4) Hz and from 14.6 (2.0) Hz to 15.4 Hz (2.4), on right and left sides, respectively (Table 1). SEF95 data adjusted for EMG showed parallel results at every time analysed (Table 2). EMG showed a statistically significant increase from baseline to 4–6 min (β coefficient: 1.91; 95% CI: 1.00–2.81; $P<0.001$) (Table 1). Right side mean EMG increased from 25.1 (1.4) dB to 27.0 (4.5) dB, while that of left side increased from 25.4 (2.4) dB to 27.2 (5.1) dB.

A summary of the bilateral frequency bands over time is presented in Supplementary Table S2. Figure 1 shows an example of the changes observed in the frequency bands of one of the study subjects. Table 2 shows the changes in the frequency bands over time after sugammadex administration in two ways. Model 1 is an unadjusted model that shows raw data, while model 2 is adjusted for EMG to eliminate possible contamination. When analysing unadjusted data, compared with baseline, a decrease in delta power over time was observed, specifically at 2–4 min (β coefficient: −223; 95% CI: −474 to 28; $P=0.082$) and at 4–6 min (β coefficient: −527; 95% CI: −778 to −276; $P<0.001$) (Table 2). The beta power increased

Table 1 Summary of BIS Index, SEF95 and EMG parameters over time according to right and left measures. BIS, bispectral index; CI, confidence interval; SD, standard deviation; SEF95, spectral edge frequency below 95%.

Parameter (units)			Time from sugammadex administration (min)			
			−2 to 0	0–2	2–4	4–6
BIS	Left, mean (SD)		46.1 (7.2)	45.9 (7.5)	46.3 (7.9)	49.8 (9.8)
	Right, mean (SD)		46.5 (7.1)	46.3 (7.7)	47.2 (8.2)	50.1 (10.2)
	Left and right values included	β-coefficient (95% CI)	Reference	−0.21 (−1.62 to 1.20)	0.42 (−0.99 to 1.83)	3.63 (2.22–5.04)
		P-value	–	0.766	0.561	<0.001
SEF95 (Hz)	Left, mean (SD)		14.6 (2.0)	14.8 (2.1)	15.0 (2.3)	15.4 (2.4)
	Right, mean (SD)		15.0 (1.8)	15.0 (1.9)	15.2 (2.2)	15.6 (2.4)
	Left and right values included	β-coefficient (95% CI)	Reference	0.09 (−0.15 to 0.32)	0.29 (0.05–0.52)	0.71 (0.47–0.94)
		P-value	–	0.464	0.016	<0.001
EMG (dB)	Left, mean (SD)		25.4 (2.4)	24.9 (1.3)	25.4 (1.6)	27.2 (5.0)
	Right, mean (SD)		25.1 (1.4)	24.9 (1.0)	25.2 (1.0)	27.0 (4.5)
	Left and right v alues included	β-coefficient (95% CI)	Reference	−0.31 (−1.22 to 0.60)	0.10 (−0.81 to 1.00)	1.91 (1.00–2.81)
		P-value	–	0.500	0.835	<0.001

Table 2 Changes in frequency bands over time after sugammadex administration. CI, confidence interval; model 1, unadjusted; model 2, adjusted for EMG.

Frequency band [Hz]			Time from sugammadex administration (min)			
			−2 to 0	0–2	2–4	4–6
SEF95	Model 1	β coefficient (95% CI)	Reference	0.09 (−0.15 to 0.32)	0.29 (0.05–0.52)	0.71 (0.47–0.94)
		P-value	–	0.464	0.016	<0.001
	Model 2	β coefficient (95% CI)	Reference	0.08 (−0.15 to 0.32)	0.29 (0.06–0.52)	0.74 (0.49–0.98)
		P-value	–	0.490	0.015	<0.001
Delta [1, 4]	Model 1	β coefficient (95% CI)	Reference	136 (−115 to 387)	−223 (−474 to 28)	−527 (−778 to −276)
		P-value	–	0.288	0.082	<0.001
	Model 2	β coefficient (95% CI)	Reference	127 (−124 to 377)	−220 (−470 to 31)	−468 (−730 to −206)
		P-value	–	0.322	0.085	<0.001
Theta [4, 8]	Model 1	β coefficient (95% CI)	Reference	65 (−113 to 242)	65 (−113 to 242)	65 (−113 to 242)
		P-value	–	0.476	0.474	0.167
	Model 2	β coefficient (95% CI)	Reference	63 (−114 to 241)	65 (−112 to 243)	−119 (−305 to 68)
		P-value	–	0.484	0.472	0.212
Alpha [8, 14]	Model 1	β coefficient (95% CI)	Reference	−43 (−296 to 209)	−56 (−308 to 196)	−47 (−299 to 205)
		P-value	–	0.736	0.665	0.716
	Model 2	β coefficient (95% CI)	Reference	−37 (−288 to 216)	−58 (−310 to 193)	−93 (−358 to 171)
		P-value	–	0.781	0.651	0.489
Beta [14, 3]	Model 1	β coefficient (95% CI)	Reference	49 (−43 to 141)	93 (1–185)	208 (116–300)
		P-value	–	0.297	0.046	<0.001
	Model 2	β coefficient (95% CI)	Reference	50 (−42 to 142)	93 (1–185)	201 (104–298)
		P-value	–	0.286	0.047	<0.001

over time compared with baseline. The increases in the beta power over time were statistically significant at 2–4 min (β coefficient: 93; 95% CI: 1–185; P=0.046) and at 4–6 min (β coefficient: 208; 95% CI: 116–300; P<0.001) (Table 2). The theta and alpha frequency band changes from the baseline were less apparent (Table 2). When analysing data adjusted for EMG, there were no substantial differences compared with unadjusted data (Table 2). Analyses on the non-averaged version of the EEG were no different to those obtained with the normalised version (see Supplementary Fig. S1, Table S3).

Figure 2a shows the association between SEF95 and BIS. Both SEF95 and BIS increased over time after sugammadex administration. The crude estimate of the relationship between these variables was statistically significant (β coefficient: 3.16; 95% CI: 2.67–3.65; P<0.001). This association did not change substantially after adjustment for time (β coefficient: 2.94; 95% CI: 2.44–3.45; P<0.001).

The association between EMG and BIS was statistically significant (β coefficient: 1.23; 95% CI: 1.09–1.38; P<0.001) (Fig. 2b). The EMG also increased over time. After adjusting for time, the association between EMG and BIS remained virtually unchanged (β coefficient: 1.14; 95% CI: 0.99–1.30; P<0.001).

Table 3 displays relative changes of haemodynamic, oximetry, and capnography parameters from baseline to 4–6 min after sugammadex administration. Differences between baseline HR values and 4–6 min values were statistically significant, although without clinical relevance (average percentage change: −1.99; 95% CI: −3.46 to −0.52). No relevant changes were observed in mean BP, $ETCO_2$, and SpO_2. No change was observed in sevoflurane MAC.

Discussion

In this study, under stable anaesthetic conditions, neuromuscular block reversal with 2 mg kg^{-1} sugammadex was associated with a small but significant increase in the BIS. Power in the beta band frequency increased and the power in the delta band frequency decreased. SEF95 values showed a statistically significant increase after sugammadex administration, which can be extrapolated as an increase in global cortical activity below 30 Hz.

As expected, activity at the neuromuscular junction increased with sugammadex, as measured by the EMG. This has been documented previously by several groups, who also reported a concomitant increase in BIS.[20,23–28] However, high variability in the magnitude of these changes was present, both within and between studies. Aho and colleagues[26] reported changes in mean BIS of up to 40 points after administration of either sugammadex or neostigmine. They categorised changes as ‘strong’, ‘weak’, or ‘no response’. They did not titrate dose by weight and did not record the time between drug administration and BIS changes. Kim and colleagues[20] and Dahaba and colleagues[25] observed similar increases in BIS in two different studies (14 and 11 points, respectively) after sugammadex administration, but they did not record the time interval. In our study, we chose three specific intervals (0–2, 2–4, and 4–6 min after drug administration) and evaluated BIS over time. Le Guen and colleagues[24] reported an increase of up to 14 points within 5 min of sugammadex administration. In their study, the group with the greater increase showed signs of awakening in accordance with the magnitude of change. This same scenario was also described in a case report.[27] In our study, the changes observed in the BIS were quite homogeneous, and, although

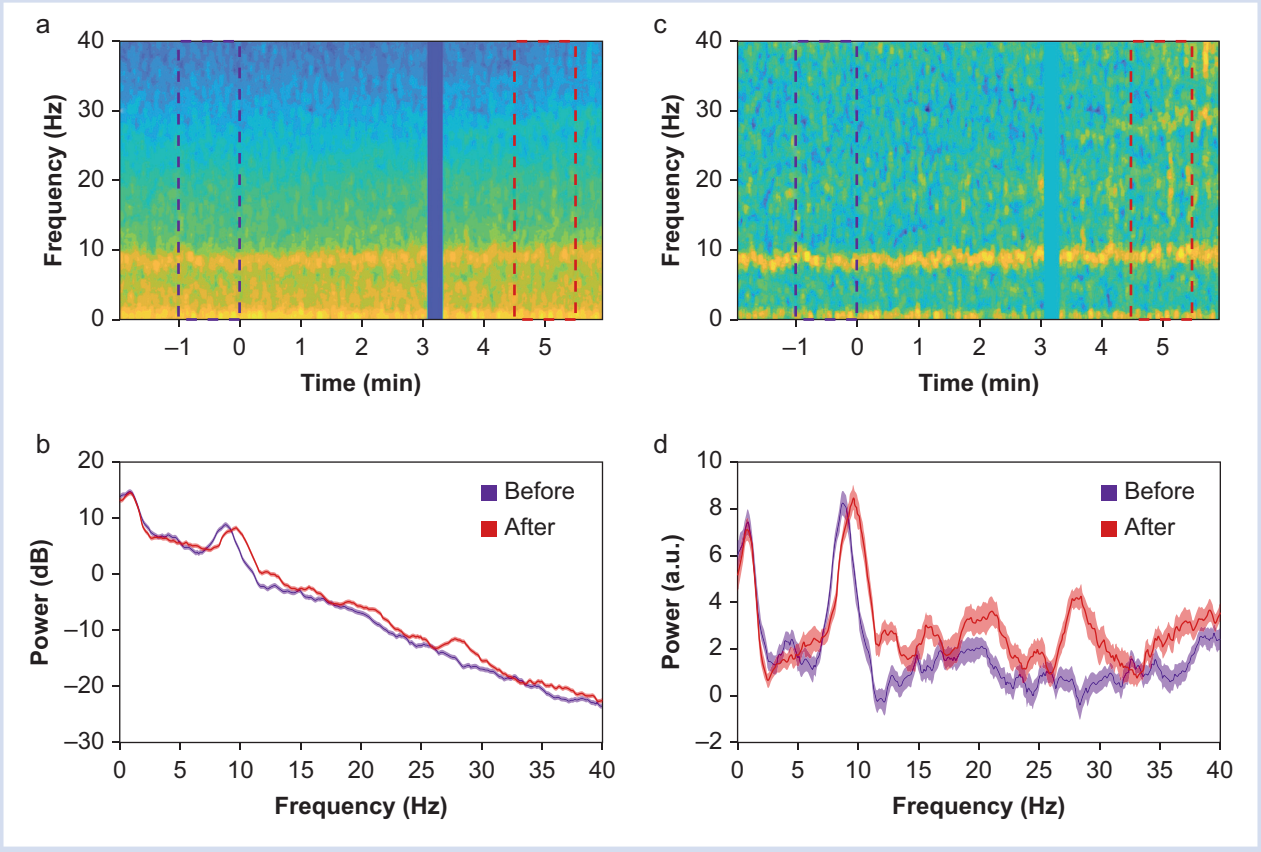

Fig 1. Example of changes in frequency ranges bands in one patient. Evolution of the EEG activity after sugammadex administration. (a) Time-frequency representation showing the evolution of the spectral content of the LT_EEG channel in a representative subject after sugammadex administration (t=0). (b) Power spectral density of the LT_EEG activity estimated within the [−1 to 0] and [4.5–5.5] min windows (marked by dashed rectangles in [a]). (c) Same representation as (a) after removing the $1/f^{\beta}$ trend of the LT_EEG data. (d) Same representation as (b) after removing the $1/f^{\beta}$ trend of the LT_EEG data in log-log scale. Both in (c) and (d) a linear fit of the 1/fβ (β=0.85) trend was computed and removed from the estimates in (a) and (b). Removal of 1/f trend allows a better appreciation of the evolution of the activity in the alpha and beta ranges. LT_EEG: EEG activity in LT electrode. 1/f: The power sistematically decreases with increasing frequency. 1/fβ: The relationship between power and frequency has a beta exponent which determines that the power decays more or less rapidly as the frequency increases.

small, were statistically significant over time. None of the patients showed any clinical signs of awakening during steady deep anaesthesia conditions. Sugammadex is usually administered under much lighter anaesthesia conditions at the end of surgery. We hypothesise that the previously reported perceptions of patients 'waking up' after receiving sugammadex may be explained by simultaneous lightening of anaesthesia. Although sugammadex administration at our measured depth of anaesthesia did not induce any clinical signs of awakening, a sugammadex-induced increase in global cortical activity under lighter anaesthesia could be the tipping point at which a patient regains consciousness.

The effects of sugammadex on cortical brain activity have not been studied in depth.[26–28,34,35] Stage III anaesthesia (targeted anaesthetic level for procedures requiring general anaesthesia)[36] DSA is typically characterised by beta activity (12–35 Hz) loss, with predominating delta (0.1–4 Hz) and alpha (8–12 Hz) activity, and theta oscillation (4–8 Hz) in a MAC-dependent manner. The SEF95 value was approximately 10–14 Hz in our study. Anaesthetic emergence is most commonly characterised by a gradual disappearance of slow activity, along with a rise and predominance of beta (12–35 Hz) and gamma (30–80 Hz) activity.[17,37,38] Both Chazot and colleagues[27] and Giuffrida and colleagues[34] reported that sugammadex administration was associated with an increase in global brain cortical activity, but they did not analyse its effect on the power of the different bands. Aho and colleagues[26] observed changes in beta and gamma bands after both sugammadex and neostigmine administration without weight-based dose titration, and associated this increase in the BIS to EMG contamination. Fassoulaki and colleagues[35] studied BIS and entropy changes after low to high doses of sugammadex (2–16 mg kg^{-1}) in the absence of neuromuscular blocking drugs, and did not find differences in BIS or entropy parameters, concluding that the administration of sugammadex in itself (i.e. not reversing a neuromuscular block) did not affect the BIS. In our study, sevoflurane MAC and vital signs were intentionally kept stable during the recording, and

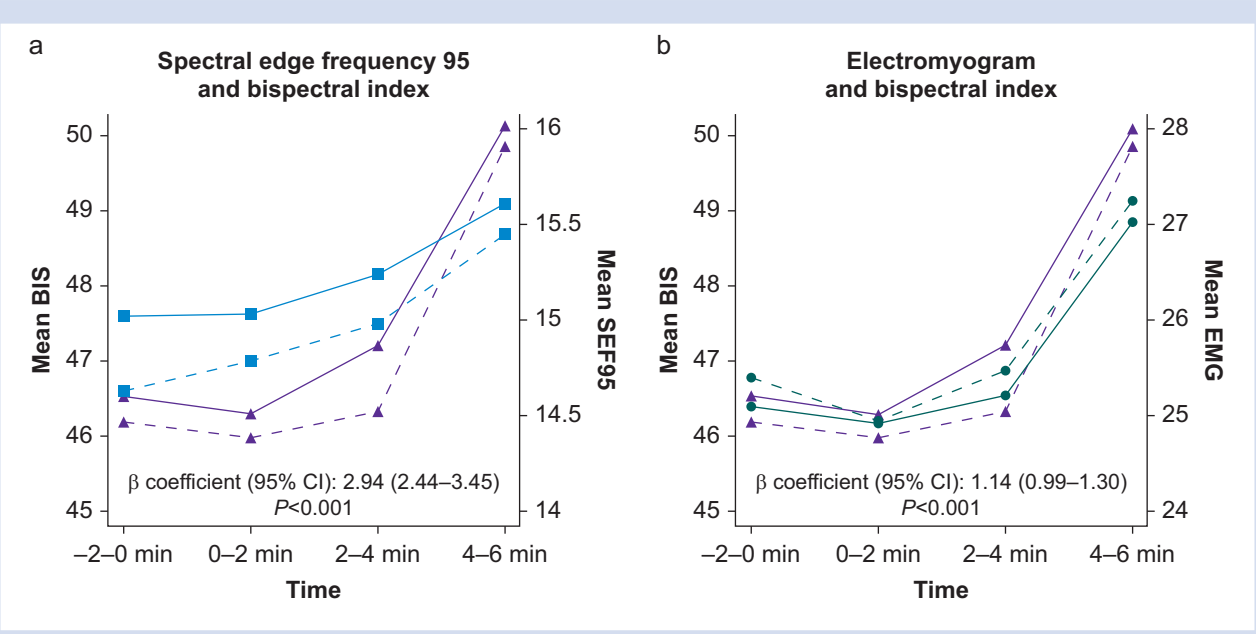

Fig 2. Time-adjusted association of spectral edge frequency 95 and electromyogram with bispectral index. Solid lines indicate right hemispheres, dashed lines left hemispheres. Red triangles indicate BIS means, blue squares SEF95 means, and black circles EMG means. BIS, bispectral index; CI, confidence interval; SEF95: spectral edge frequency 95.

Table 3 Relative change of haemodynamic, oximetry, and capnography parameters from baseline to 4–6 min after sugammadex administration. CI, confidence interval; MAC, minimum alveolar concentration.

Parameters	At sugammadex administration	6 min after sugammadex administration	Mean % change (95% CI)
HR (beats min^{-1})	70 (12)	69 (12)	−2.0 (−3.5 to−−0.5)
Mean arterial pressure (mm Hg)	68 (14)	68 (13)	−0.1 (−3.7 to 3.5)
Pulse oximetry (SpO_2)	97 (1)	97 (1)	0.1 (−0.2 to 0.3)
Capnography ($ETCO_2$)	34 (2)	34 (2)	−0.8 (−2.6 to 1.0)
Sevoflurane MAC	1 (0.07)	1 (0.07)	–

we observed an increase in beta activity after sugammadex administration, while delta activity decreased. Changes in the alpha and theta bands were smaller; these changes were compatible with a lighter anaesthesia depth pattern.

In our study, global cortical brain activity at 30 Hz (SEF95) increased after sugammadex administration. The SEF95 increase was closely related to the increase in the BIS. The pattern of increased beta power and decreased delta power observed in our study matches more closely to a light anaesthesia pattern rather than a global increase in cortical activity. Although we did not record enough activity, we were able to fully compare our own pattern to anaesthetic emergence patterns.[38]

There are several possible explanations for why this increase in frontal cortical brain activity is observed after sugammadex administration.[18,20,23–26,34] Firstly, sugammadex, besides acting to encapsulate rocuronium and vecuronium, may encapsulate other drugs such as propofol and remifentanil.[24,26,34] However, changes in the BIS have been observed with inhaled as well as intravenous agents. Another hypothesis is that EMG power increases after neuromuscular block reversal and thus interferes with beta and gamma activity, artificially inflating the BIS.[20,23,25,26] Lastly, the differentiation theory suggests that signals generated by stretching muscular receptors reach the brain by afferent pathways and induce arousal.[18,20,24,34] We consider that massive activation of these receptors after sugammadex administration could induce an increase in cortical brain activity. Our findings are in line with this theory. Contrary to traditional belief, there is evidence that EMG may also produce artifact frequencies below 30 Hz.[39] For this reason, we used an adjusted model for EMG to assess changes in each frequency band and the SEF95. Estimates did not change substantially following adjustment for EMG, suggesting that its impact is probably minimal. Low-dose sugammadex administration (2 mg kg^{-1}) provoked a lighter anaesthesia depth pattern characterised by an increase in beta activity and a decrease in delta activity, without clinical signs of awakening when administering sugammadex in deep anaesthesia stages.

In reversing rocuronium, sugammadex allows an increase in EMG activity. However, it remains unclear whether this

effect is merely an artifact of recording or if there is a wider effect over cortical brain activity.[18,20,23–25,28,34] Aho and colleagues[26] associated the increase in brain activity in different frequency ranges (13–30, 32–47, and 70–110 Hz) to an artifact caused by EMG recovery contamination. They found a positive correlation between EMG intensity (dB) and BIS change magnitude, but they could not find an explanation for the increase in the frequency range from 13 to 30 Hz.[26] Hayashi and colleagues[28] proposed that EMG is not contamination, but in fact, necessary for BIS indices to be over 80. The relationship between these parameters (EMG, BIS, and global cortical activity) remains unclear at this point.

Although it would have been interesting to look at signals above 45 Hz, we could not analyse them as the values became unreliable. Another limitation of our study is that our sample is homogeneous (in age, sex, and surgery), which limits the generalisability of our results. Another limitation of our study is that we only monitored the frontal lobe. It would be interesting to see what happens if we monitor EEG in areas with less underlying muscle, such as the occipital lobe. Finally, all patients had a TOF count of 4 at reversal, thus larger effects could be hypothesised with reversal of deeper neuromuscular block.

In conclusion, after 2 mg kg^{-1} of sugammadex administration and under steady anaesthesia, frontal EEG power distribution increased, as observed by changes in the BIS, beta activity, and SEF95. Although compatible with a lighter anaesthesia depth pattern, these results were not associated with clinical signs of awakening while maintaining a stable drug concentration.

Authors' contributions

Principal investigator: IR–B
Study design: CH–C, JMN–C, AM–S, IR–B
Patient recruitment: IR–B, CH–C, AM–S
Acquisition of data: IR–B, CH–C, AP, EC–A, OM, MA, AM–S
Analysis and interpretation of data: IR–B, MV, OM, MA, JMN–C
Statistical analysis: JMN–C
Writing the paper: IR–B, MV, JMN–C, AM–S
Critical revision, final revision, and approval: all authors.
All authors are accountable for all aspects of the work ensuring that questions related to accuracy or integrity are investigated and resolved.

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Declaration of interest

The authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

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