Bispectral Index and encephalogram monitoring in rats during dexmedetomidine infusion.

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Background and Goal of Study: Bispectral Index (BIS) monitoring is one of the most popular techniques for evaluating the depth of anesthesia in human. Moreover, BIS is becoming a useful tool for estimating the sedation level. Dexmedetomidine (Dex) shows preferable profiles for perioperative sedation, and studies are increasing; however, there is scarce reports studying the effect of Dex on BIS values in experimental animals. In the current preliminary study, we investigated the validity of BIS monitoring in awake and sedated rats using Dex.

Material and Methods: Male SD rats weighing 220-240 g were used. The rats were received brief anesthesia and were attached the 4 pierced electrodes on the head. Each rat was given 48-h recovery period. The electrodes were connected the leads and EEG signal was analyzed by Vista A-3000 (Nihon Kohden, Tokyo, Japan).

Study 1: The rats were administered Dex. The infusion rates were changed every 15 minutes and was randomly set at 0 (control), 20, 40 and 80 µg/kg/h. **Study 2:** The rats were infused Dex at 40 µg/kg/h. After the stabilization of BIS value, each animal was received gentle stimuli (patting). The BIS Index, spectral edge frequency 95% and amplitude were recorded after the equilibrium period. The results were analyzed using ANOVA and a *P* value less than 0.05 was considered as statistically significant.

Results and Discussion: Dex significantly reduced BIS values in a dose dependent manner (Table, Fig. 1.). In Study 2, the BIS value was temporarily increased immediately after the patting stimuli (Fig. 2.). The changes in BIS values indicated the sedation and anesthesia states of the rats.

Conclusion: We evaluated the changes in BIS values in awake, anesthetized and sedated rats. BIS monitoring might be useful and reliable tool for evaluating the effect of drugs modifying the activity of central nervous system in experimental animals.
References: Anesthesiology 2016, A4232)

Table. The dose of dexmedetomidine and the values of Bispectral Index, Spectral edge frequency and amplitude.

Dexmedetomidine infusion rate	Bispectral Index	Spectral edge frequency 95 (Hz)	Amplitude
0 (µg kg ⁻¹ h ⁻¹)	97.1 ± 0.8 [95.6 - 97.7]	23.6 ± 3.1 [20.3 - 29.0]	14.1 ± 3.0 [9.1 - 18.6]
20	81.7 ± 9.4 [62 - 97.7]	17.8 ± 5.3 [11.2 - 28.5]	16.9 ± 5.3 [8.8 - 28.1]
40	74.4 ± 9.1 [61.9 - 87.8]	16.6 ± 5.5 [11.5 - 28.5]	19.5 ± 6.3 [8.8 - 31.6]
80	60.1 ± 12.1 [38.5 - 87.5]	13.6 ± 3.8 [10.4 - 26.8]	20.2 ± 6.7 [9.2 - 34.4]

Data are expressed as mean ± S.D. and ranges. *: *P* < 0.05 between groups.

Fig. 1. The dot plots of the results. Each plots indicate the value at the infusion rate of dexmedetomidine. *: *P* < 0.05 between groups.

Conclusion: Although there is some limitations and inconsistencies, BIS monitoring might be applicable in rats during sedative state using dexmedetomidine. Spectral edge frequency, one of typical analysis of electroencephalogram, also showed decreasing during sedation in a dose dependent manner. Serial evaluation and numerical calculation of the depth of sedation might provide a possibility of evaluating detailed pharmacodynamic properties and interaction of drugs in laboratory animals in sedative state including sleeping period.

Conflict of interest: None throughout the study

Discussion: The results of current study suggested that the Bispectral (BIS) values of awakening and of sedative rats were correlate with the dose of dexmedetomidine. Generally, propofol anesthesia reduced the BIS value, however, some of results were inconsistent.

Publications concerning to the recording of BIS in animals were limited (Lab Anim 2012; 46: 85-94) and the studies were demonstrated below. There was no information for rats, on of the most popular experimental animal.

- Dog (isoflurane):** Vet Anaesth Analg 2011; 38: 536-43.
 - Pig (isoflurane, sevoflurane):** Am J Vet Res 2003; 64: 866-73.
 - Horse (isoflurane):** Am J Vet Res 2002; 63: 438-42.
 - Calf (isoflurane):** Acta Cir Bras 2015; 30: 67-72.
 - Goat (isoflurane):** Vet Res Commun 2000; 24: 361-70.
 - Cat (isoflurane):** Am J Vet Res 2003; 64: 1534-41.
 - Rabbit (etomidate, propofol, isoflurane):** J Am Assoc Lab Anim Sci 2014; 53: 74-80.
 - Dolphin (propofol):** Anesth Analg 2006; 103: 626-32.
 - Chicken (isoflurane):** Am J Vet Res 2008; 69: 1254-61.
- Another study (Br J Anaesth 2012; 109: 782-9) demonstrated that a increase in electro-encephalographic gamma activity suggested awakening from **isoflurane** anesthesia in **rats**, but BIS was not evaluated..

Fig2. The typical change in the value of Bispectral Index during dexmedetomidine infusion (40 µg kg⁻¹ h⁻¹). Gentle patting stimuli temporarily increased the value of Bispectral Index (yellow arrow) . The stimuli raised the value of BIS Index by 17.2 ± 6.3 (mean ± S.D.) from the base line.