J Anesth (2014) 28:601–605
DOI 10.1007/s00540-013-1780-8

ORIGINAL ARTICLE

The effects of stellate ganglion block on the electroencephalogram in rats

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Received: 8 May 2013 / Accepted: 17 December 2013 / Published online: 10 January 2014

Abstract
Purpose It is reported that the sympathetic nervous system may play an important role in the arousal response. The present study evaluated the effect of stellate ganglion block (SGB) on electroencephalogram (EEG) activity in rats.
Materials and methods Adult male Sprague–Dawley rats were divided into two groups: SGB ($n = 10$) or intramuscular (IM, $n = 10$) injection was performed with 0.2 ml 0.25 % bupivacaine. The spectral edge frequency 95 % (SEF 95 %), median frequency (MF), beta to theta ratio (BTR), and beta to delta ratio (BDR) were estimated 30 min before bupivacaine injection and 15, 20, 25, 30, 45, 55, and 100 min after SGB or IM injection.
Results Ipsilateral ptosis occurred in all the rats that underwent SGB but did not occur in the IM group. Significant decrease of the 95 % SEF value, MF, BTR, and BDR was observed from 15 to 45 min after SGB compared with those of the IM group, respectively ($p < 0.05$).
Conclusions SGB with 0.2 ml 0.25 % bupivacaine significantly decreased EEG activities in rats. These results suggest that SGB can induce a sedative effect in rats. Further studies are required to investigate the behavioral tests for sedative effects of SGB.

Keywords Electroencephalogram · Sympathetic nerve system · Stellate ganglion block

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Introduction

The stellate ganglion block (SGB) is a technique to block the sympathetic nerve distribution in the head and neck region and the upper limbs, and thus it has been tried in treating patients with various diseases including headache [1] and complex regional pain syndrome [2]. Recently, SGB was found to effectively treat anxiety in patients with combat-related posttraumatic stress disorder (PTSD) and night awakenings in breast cancer survivors [3, 4]. The well-known mechanism of action of SGB is through vasodilatation within its territory of innervations. However, the successful treatment of many diseases with SGB cannot always be explained by just one mechanism of action. It is reported that the sympathetic nervous system may play an important role in the arousal response. For example, an adrenergic hormone agonist can increase electroencephalogram (EEG) indices of arousal [5–7]. Therefore, we hypothesized that SGB might induce the sedative effect. In this study, we evaluated the effect of SGB on EEG activity in rats.

Materials and methods

Animals

Twenty adult male Sprague–Dawley rats (280–320 g) were used in the experiments. All the animal experiments were

performed in accordance with the National Institutes of Health guidelines on animal care.

EEG electrode implantation

Ten days before starting the experiments, epidural screw electrodes (tip diameter, 1.0 mm) for EEG recording were implanted under 2–3 % isoflurane anesthesia. The body temperature was kept at a constant 37 °C using a heating pad. After the rats had been placed in a stereotaxic apparatus, the incision site was anesthetized with 2 % lidocaine, incised, and the periosteum and the skull surface were cleaned. Four gold-layered stainless steel screws were inserted into the bone over the bilateral frontal (2.5 mm anterior and 1.25 mm lateral to bregma) and parietal bones (5 mm posterior and 1.25 mm lateral to bregma), without perforation the dura mater, and two stainless steel screws, which served as reference and ground electrodes, were inserted into the interparietal bone over the cerebellum. The electrodes with connecting pins were fixed over the skull with dental acrylic.

Injection of local anesthetics

SGB or intramuscular (IM) injection of 0.2 ml 0.25 % bupivacaine was performed under 2–3 % isoflurane anesthesia. The duration of anesthesia was 5 min in all rats, and immediately after local anesthetic injection, rats were returned to the monitoring cage. The rats were randomized into the two groups:

IM group ($n = 10$): 0.2 ml 0.25 % bupivacaine was injected into the left buttock area.

SGB group ($n = 10$): The animal was placed in the right lateral decubitus position. The lower part of the cervical vertebra was fixed between the left first and third fingers of the physician's left hand while palpating the C7 process with the second finger. An insulin injector was inserted laterally toward the vertebral body surface. When contact was made, the injectate (0.2 ml 0.25 % bupivacaine) was given after negative aspiration [8]. All rats were observed for ptosis on the left side as an indicator of successful SGB, and the duration of ptosis was recorded by an observer who was blinded to intervention.

EEG recordings

On the day of the experiment, habituation was allowed for 30 min in a recording cage, and the rats were allowed to move freely. The ambient temperature in the recording cage was maintained at 23 ± 1 °C. The baseline values of EEG were established for 30 min before bupivacaine injection. Then, the values of EEG were estimated at 15, 20, 25, 30, 45, 55, or 100 min after SGB or IM injection with 0.2 ml 0.25 % bupivacaine. The average EEG values were calculated for 1-min segments of continuous EEG data.

The four-channel EEG signals over the frontal and occipital cortices were recorded monopolarly with respect to the reference electrode. EEG signals from the frontal and parietal cortices and vibration signals were recorded via a Bioelectric Amplifier (model 3500; A-M System, WA, USA). The signals were amplified EEG signals with 10,000× and vibration signals with 10× gains, and filtered EEG signals with 1–100 Hz and vibration signals with 1–100 Hz. Signals were digitized at a rate of 1 kHz by an AD converter (DAQ 6015; National Instrument, CA, USA), averaged with five consecutive samples, and acquired at a rate of 200 Hz with a home-made LabView program (National Instrument). The raw EEG signal was inspected before analysis and sections with artifacts were removed.

EEG analysis

The EEG data were analyzed by quantitative EEG analyzing a home-made MATLAB (R2010b; Natick, MA, USA). Artifact-free 1-min EEG signals at 15, 20, 25, 30, 45, 55, and 100 min after SGB or IM using bupivacaine were used to quantify the EEG. The main frequency band of concentrated energy among EEG bands is from 1 to 35 Hz. The raw EEG has usually been described in terms of frequency bands: gamma (greater than 30 Hz), beta (13–30 Hz), alpha (8–12 Hz), theta (4–8 Hz), and delta (less than 4 Hz). Power spectral density was calculated at each frequency band. The 48 epochs of 2.5 s (1.25-s overlap) were converted to power spectra using a fast Fourier transform algorithm and then averaged to power spectra. To analyze these data for estimation of sedative index, we used spectral edge frequency 95 % (SEF 95 %) and median frequency (MF) [9–12]. In addition, beta to theta ratio (BTR) and beta to delta ratio (BDR) parameters were extracted to measure the level of sedation [13].

Statistical analysis

All results are expressed as mean (SEM). A p value < 0.05 was considered significant. Data were subjected to the Student's t test for intergroup comparison.

Results

Ptosis

The rats recovered from the general anesthesia within 5–10 min. Ipsilateral ptosis was observed in all the animals in the SGB but did not occur in the IM group. The ptosis lasted for 38 (±8.2) min (Fig. 1).

EEG activity

There were no significant differences in the baseline 95 % SEF, MF, BTR, or BDR values between the two groups. Significant decrease of the 95 % SEF, MF, BTR and BDR value was observed from 15 to 45 min after SGB, compared with the IM group ($p < 0.05$) (Fig. 2).

Fig. 1 Ptosis of the *left* eye after stellate ganglion block

Discussion

This study demonstrated that SGB with 0.25 % bupivacaine 0.2 ml significantly decreased SEF 95 %, MF, BTR, and BDR values, compared with the IM group, in rats.

Beta-adrenoceptors are present in various parts of the reticular activating system, particularly the medial septal region of the basal forebrain [5]. Infusion of β-adrenoceptor agonists into this region elicits enhancement of behavioral and EEG indices of waking in animals and, conversely, infusion of β-adrenoceptor antagonists decreases EEG indices of arousal [5]. Similarly in humans, infusion of isoprenaline or epinephrine causes clinical signs of arousal associated with an increase in EEG activity [6, 7]. Epinephrine infusion increases bispectral index and Observer's Assessment of Alertness/Sedation scores in patients

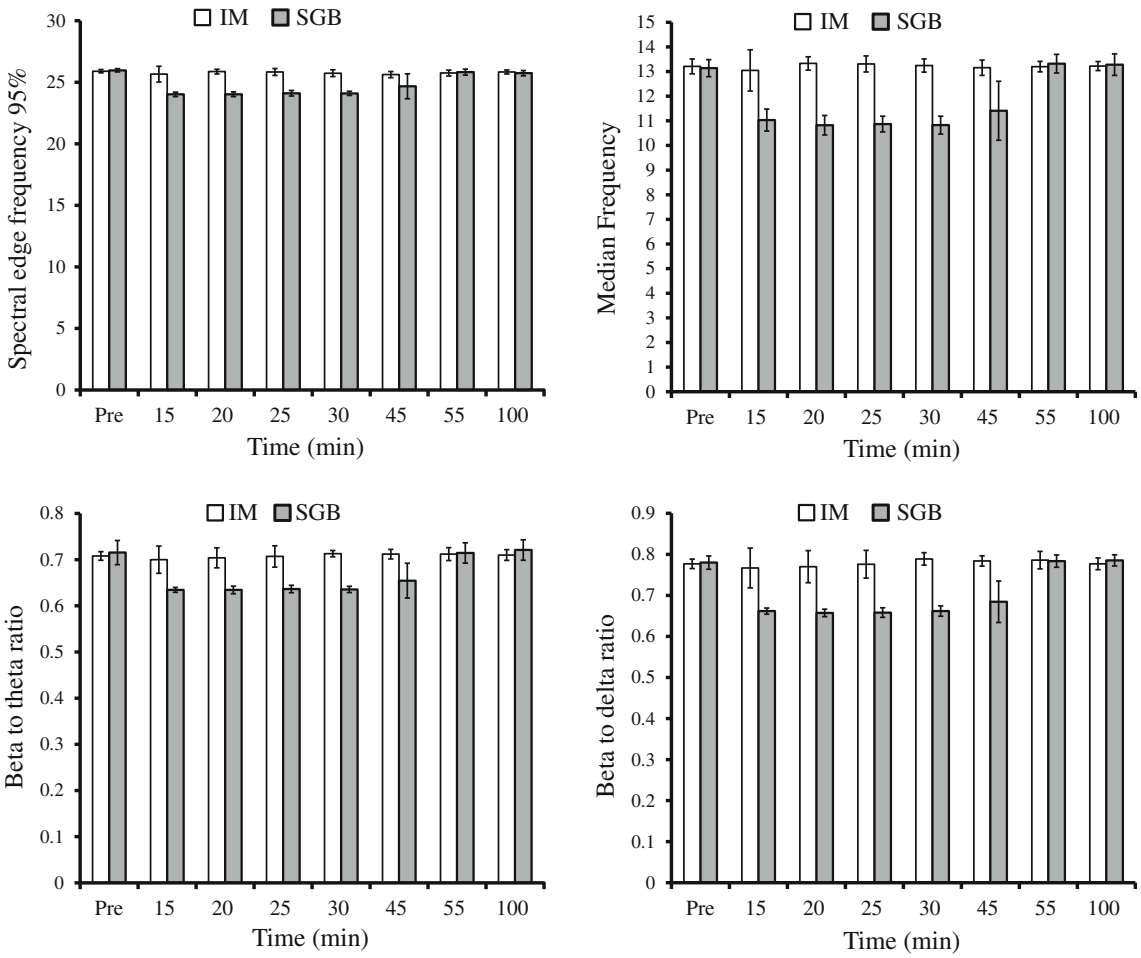

Fig. 2 Changes in the level of spectral edge frequency 95 % (SEF 95 %), median frequency (MF), beta to theta ratio (BTR), and beta to delta ratio (BDR) after stellate ganglion block (SGB) or intramuscular (IM) group with 0.25 % bupivacaine 0.2 ml. Data are presented as mean (SEM) ($n = 10$ each group). *$p < 0.05$ vs. IM group

undergoing sedation with propofol [7]. Additionally, EEG activity is significantly correlated with plasma norepinephrine concentrations [14]. The stellate ganglion is a sympathetic ganglion that is located anteroinferiorly to the transverse process of the seventh cervical vertebra: it has extensive neuronal connections to the hypothalamus, amygdala, infralimbic, insular, and ventromedial temporal cortical regions [15]. SGB is used to relieve pain in the head and upper extremity pain disorders mediated by the sympathetic nervous system [1, 2]. Its mechanism of action has been explained by mainly neural inhibition in its sphere of innervation. This mechanism cannot completely explain the therapeutic effect of SGB on many diseases. The extensive neuronal connection of stellate ganglion suggests that SGB has additional mechanisms of action. It was suggested that SGB could decrease adrenal hormone in the plasma [16] or the brain [17]. Recently, it was reported that SGB was effective to treat panic and anxiety symptoms with PTSD [3]. It was found that an increased level of norepinephrine could contribute to the anxiety symptoms associated with PTSD [18]. SGB could decrease brain norepinephrine or allow the normal melatonin rhythm to be reestablished, which in turn leads to a reduction of the symptoms of PTSD [17, 19].

The 95 % SEF and MF have been widely used to measure sedation depth [9–12], and BDR and BTR are suggested as sensitive parameters to estimate the depth of sedation and anesthesia [13]. In the present study, the values of four parameters significantly decreased from 15 to 45 min after SGB, compared with the IM group. Ptosis in the injected side is one of the signs after SGB. In the present study, ptosis only occurred in the SGB group and lasted 38 min after block. This result is consistent with previous reports [8, 20]. The extent of ptosis is approximately consistent with the duration of EEG changes. These results suggest that SGB can influence the level of sedation. It has been known that inhaled anesthetics modify EEG activities and also influence autonomic nerve system [21]. In the present study, we want to clarify the EEG change by SGB treatment alone in rats. Therefore, we recorded the EEG activity after recovery from anesthesia. There are some limitations in this study. First, SGB decreased EEG activity, but we did not perform behavioral tests for sedative effects of SGB in rats. Therefore, another study is needed using behavioral tests to assess the sedative effect of SGB in rats. Second, the human consciousness depends upon close interaction between specialized neuronal circuits of the brain and may be different from that of animals. It is uncertain whether the results of this study can be extrapolated to humans. Therefore, further studies are needed to investigate the effect of SGB on EEG activity and consciousness in humans.

In conclusion, SGB with 0.2 ml 0.25 % bupivacaine significantly decreased EEG activities such as 95 % SEF, MF, BTR, and BDR values compared with IM injection in rats. Further studies are required to investigate for the sedative effects of SGB.

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