Brain Stimulation 6 (2013) 812–816

Contents lists available at SciVerse ScienceDirect

Brain Stimulation

journal homepage: www.brainstimjrnl.com

Vagal Sensory Evoked Potentials Disappear Under the Neuromuscular Block – An Experimental Study

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ARTICLE INFO

Article history:
Received 25 September 2012
Received in revised form
25 February 2013
Accepted 9 March 2013
Available online 17 April 2013

Keywords:
Evoked potentials
Transcutaneous vagal nerve stimulation
Neuromuscular block

ABSTRACT

Background: Transcutaneous vagal nerve stimulation is a promising treatment modality in patients suffering mood disorders and chronic pain, however, the mechanisms are still to be elucidated. A recently developed technique of EEG responses to electrical stimulation of the inner side of the tragus suggests that these responses are far field potentials, generated in the vagal system – Vagal Sensory Evoked Potentials (VSEP).
Objective: To reproduce the VSEP technique free from myogenic artifacts.
Methods: Fourteen ASA I–II patients scheduled for elective surgery in standardized Total Intravenous Anesthesia (TIVA) were enrolled. Transcutaneous electrical stimulation was applied to the inner side of the right tragus. Averaged EEG responses were recorded from the electrode positions C4-F4 and T4-O2 before and after induction of TIVA, during the maximal effect of the non-depolarizing muscle relaxing agent, cis-atracurium (C-AR) and after recovery from C-AR under TIVA.
Results: Typical response curves with P1, N1 and P2 peaks could be reproduced in all patients before and after anesthesia induction. The response curves disappeared during the C-AR action and re-appeared after recovery from C-AR under TIVA.
Conclusion: The disappearance of the scalp responses to electrical tragus stimulation under the neuromuscular block suggests a muscular origin of these potentials.

Introduction

Vagal nerve stimulation (VNS) is recommended by the Food and Drug Administration as an adjunctive therapy for epilepsy and medication-resistant major depression [1]. VNS is promising as a potential treatment for sleep and anxiety disorders, cognitive deficits of the Alzheimer's disease and chronic pain [2,3]. The invasive VNS approach, using implanted battery-powered generators, has several disadvantages: it requires repeated surgical intervention for the implantation of the stimulator and electrodes, battery replacements or a dysfunction of the electronic equipment [4]. An alternative method of transcutaneous vagal nerve stimulation, recently shown to produce a mood enhancing effect in healthy volunteers [5] and antinociceptive effects in patients with chronic pelvic pain [6], is based on anatomical data on cutaneous representation of the vagal nerve. The auricular branch of the vagal nerve supplies the external acoustic meatus and the concha auricle [7]. Experimental data suggest that cutaneous stimuli of this region are transported via the auricular branch of the vagal nerve into the medulla oblongata and to the nuclei tractus solitarii [8], whereas the stimulation of peripheral regions of the auricle (helix) is mainly transmitted to the spinal ganglia of the cervical nerves [9].

Recently Fallgatter et al. demonstrated that the electric stimulation of the inner side of the tragus (the area of afferent vagal innervation) caused changes in the averaged EEG signal in a time interval of 10 ms after stimuli application [10]. The reproducible pattern of 3 waves: P1, N1 and P2 could be evoked only during stimulation of vagally innervated regions of the auricle, but not during stimulation of the helix and the lobule (regions innervated from the cervical plexus) of the auricle. Analogous to the early-evoked acoustic brain stem potentials, the authors concluded that

Financial disclosure: The study was funded by Department of Neuroscience, University Medicine of Greifswald.
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http://dx.doi.org/10.1016/j.brs.2013.03.005

they must have originated in parts of the vagal system and called these responses Vagal Sensory Evoked Potentials (VSEP) [10].

Usually, early-evoked brain stem potentials are stable to the pharmacological effects of various anesthetics and neuromuscular blocking drugs [11,12]. On the other hand, the recordings of evoked potentials during electrical stimulation of the afferent trigeminal arc in awake, healthy volunteers and patients are often "contaminated" by muscle responses, which may be improved by pharmacological agents during general anesthesia [13].

Regarding these facts, our investigation sought to achieve the recordings of previously described VSEP, elicited from the inner side of the tragus of the auricle, free of artifacts in patients under general total intravenous anesthesia and a neuromuscular blockade with the use of non-depolarizing muscle relaxant agents.

Methods

Design of the investigation and participants' selection criteria

This prospective experimental investigation was performed from March–May 2010 at the holding area of the Department of Anesthesiology of Greifswald University Hospital. The local ethics committee approved the design of the study and informed consent was obtained from each participant. Fourteen patients with physical status I–II according to the American Society of Anesthesiologists (ASA) classification, scheduled for elective extracranial surgery under general anesthesia (TIVA), requiring administration of muscle relaxant agents, were enrolled. No patients were included, who had a history of neurologic or psychiatric disease, local infection at the site of EP recording or EP stimulation or had implanted devices for electrical stimulation (e.g., cardiac pacemaker).

Recording of evoked potentials

On the evening before surgery, the enrolled patients were provided detailed information about the investigation and the positions of the recording electrodes C4-F4 and T4-O2 were marked on the scalp (Fig. 1), in accordance with the standard 10/20 electrodes system of the International Federation of Societies for Encephalography and Clinical Neurophysiology [14]. All investigations took place the following day between 8 a.m. and 4 p.m. The stimulation, recording and averaging of EEG responses were performed using a Nihon Kohden MEB 9200. When the patient arrived in the holding area, the standard monitoring for anesthesia was started and silver disc EEG electrodes (Nihon Kohden, Japan) were attached to the previously marked positions C4-F4 and T4-O2 (Fig. 1) using the adhesive Elefix Paste (Nihon Kohden). A self-adhesive electrode placed in the middle of the right temple served as grounding. To optimize the recording conditions, the skin at the marked positions had been prepared with abrasive "Skin Pure" Preparation Gel (Nihon Kohden) to maintain the impedances under the electrodes below 2 kΩ during the registration.

Stimulation was applied to the inner side of the right tragus [10] and to the concha of the auricle using a self-manufactured electrode consisting of 2 stainless steel straps, wrapped with wool fiber and stapled to a 9 × 9 mm piece of silicon rubber (Fig. 2). The silicon rubber's thickness was 2.1 mm; the cross section of each steel strap 0.75 × 0.35 mm and the length was 8 mm. The distance between straps was 5 mm. Each strap was soldered to conductor wire, connected to a stimulation block of Nihon Kohden MEB 9200. The wool was moistened with 0.9% NaCl solution before each experiment to achieve optimal conductivity for comparable stimulation conditions. Afterward, the stimulation electrode was tightly fixed, using commercially available anti-noise earplugs, made from polyurethane foam. Stimulation and acquisition parameters were chosen in accordance with the methodology of previous investigations [11,15]. Electrical square impulses with 0.1 ms duration with a frequency of 0.5 Hz and an intensity of 8 mA were applied. Using

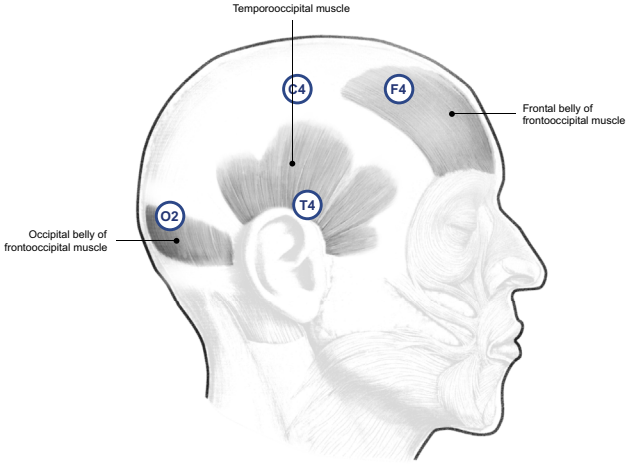

Figure 1. Positions of the recording electrodes C4-F4 and T4-O2 in accordance with the standard 10/20 electrodes system of the International Federation of Societies for Encephalography and Clinical Neurophysiology [14]. Please, note that O2 and F4 electrodes are located over the frontooccipital muscle; T4 electrode is located over temporoparietal muscle; further explanation in Discussion section. (With permission modified from Schünke, Schulte, Schumacher, Voll, Wesker "PROMETHEUS - Kopf, Hals und Neuroanatomie", Georg Thieme Verlag, 2009.)

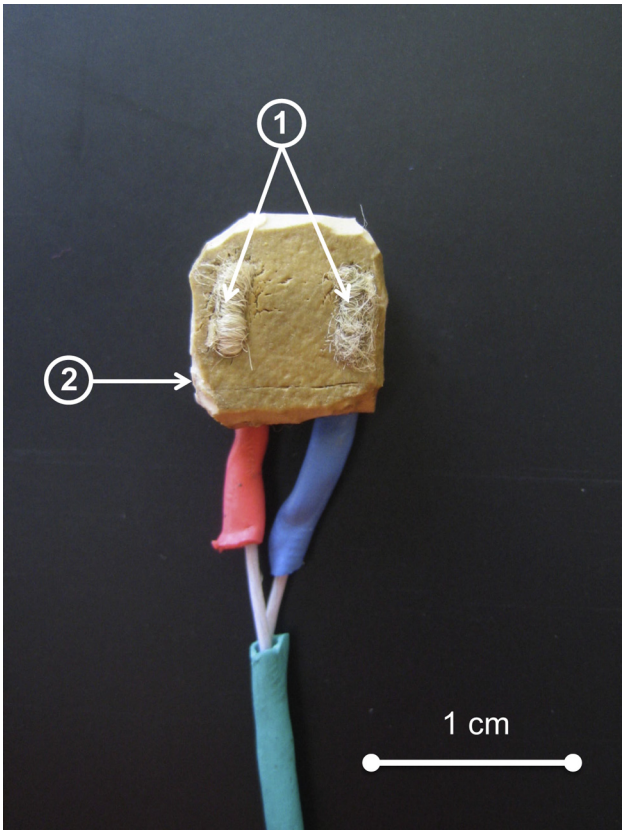

Figure 2. Self-manufactured electrode, consisting of wool-wrapped steel wires (1) stapled to a piece of silicon rubber (2) with the anode and cathode placed about 5 mm apart. Before each experiment the wool was moistened with 0.9% NaCl solution to achieve optimal conductivity for comparable stimulation conditions.

a band-pass filter of 0.1 Hz–1 kHz, 100 artifact-free impulses were averaged, the analysis time was 20 ms.

General anesthesia procedure

The scalp responses to the auricular stimulation were recorded before and after induction of TIVA, during the maximal effect of non-depolarizing muscle relaxing agent, cis-atracurium (C-AR) and after recovery from C-AR under anesthesia. After the first registration of scalp responses, anesthesia was induced intravenously with propofol (2–3 mg/kg) and fentanyl (2–3 μg/kg). The airway was secured with a laryngeal mask and the lung ventilation was mechanically controlled to keep end-tidal carbon dioxide at 4.5–5.3 kPa. Anesthesia was maintained with propofol (4–8 mg/kg/h) to achieve a deep anesthesia, monitored using the Bispectral Index (BIS). When BIS achieved values between 35–50, the second recording of scalp responses was performed. Then cis-atracurium (0.1 mg/kg) was used to facilitate the trachea intubation and a third recording was performed during the sufficient neuromuscular blockade, measured as Train-of-Four index (TOF) 0–1. TOF represents the electrical current stimulation pattern, consisting of four twitches at 2 Hz. TOF index describes the number of identifiable responses following a TOF stimulation pattern. In the absence of neuromuscular blockade all four responses are of equal amplitude. Loss of the 4th response represents a 75–80% neuromuscular blockade. The disappearance of all 4 responses can be associated with a block of about 98–100% [16]. The last recording of scalp responses was performed after recovery from neuromuscular blockade at the TOF value of 4, while still under general anesthesia at BIS values of 35–50. The heart rate and blood pressure had been maintained within 20% and the body temperature within 1°C from baseline level. The patients did not receive any other analgesics, antiemetic agents or vasopressor drugs during the registration of scalp responses.

Outcome measures and statistics

The peak latencies and peak-to-peak amplitudes of recorded scalp responses were measured by positioning the cursor at the peaks of the responses and analyzed using a repeated measures ANOVA with 2 within subject factors: TIME (3 time points) and LEAD (C4-F4 and T4-O2). Post-hoc contrasts or the factor TIME were tested separately for both leads using Bonferroni adjustment for multiple comparisons. *P* values less than 0.05 were considered statistically significant.

Results

Fourteen patients (5 females) aged from 26 to 54 (median 46) years finished the study. The demographic and clinical characteristics of the patients studied, are presented in Table 1.

The scalp responses, with identifiable waves P1, N1 and P2, could be reproduced in all patients before and after anesthesia induction and after recovery from neuromuscular block (Fig. 3).

The scalp responses disappeared during the neuromuscular block using C-AR at TOF values 0–1. In a search for scalp responses to stimulation, the electrode was applied to different locations at the concha of the ear, however without the expected scalp response. The scalp responses re-appeared after recovery from the neuromuscular blockade at TOF 4 still under TIVA in all studied patients. In 2 patients, a stimulation-synchronous twitching of scalp muscles was observed after anesthesia induction and after recovery from C-AR.

Exploratory analysis revealed that the latencies of P1 (ANOVA for factor TIME yielded $F_{2,12} = 29.96$ with $P < 0.001$) and N1 ($F_{2,16} = 17.36$; $P < 0.001$) waves after recovery from neuromuscular block were prolonged in comparison to baseline. The amplitudes of the recorded scalp responses from positions T4 to O2 were larger than those from C4-F4 (ANOVA for factor LEAD yielded $F_{1,6} = 14.29$ with $P = 0.009$, Table 2).

Patients did not describe the stimulation as painful or unpleasant before the induction of anesthesia. No changes in heart rate or blood pressure, ascribed to vagal activation, were registered during electrical stimulation of the inner side of the tragus in this investigation.

Table 1
Patients' characteristics.

Nr	Age (years)	Gender	BMI (kg/m^{-2})	ASA	Premedication	Type of surgery	Duration of surgery (min)
1	53	f	26.6	1	Y	Axillary adenectomy	108
2	44	f	23.2	1	Y	Lymph node biopsy (breast cancer)	29
3	41	f	24.8	2	Y	LBS	148
4	42	m	27.3	1	Y	Posterior interosseal nerve release	194
5	53	m	19.5	1	N	LBS	72
6	50	m	29.0	2	N	LBS	130
7	30	m	27.9	1	N	Implantation of cervical disc	165
8	38	f	30.1	1	Y	Mobilization of cubital joint	10
9	54	m	26.9	2	Y	LBS	47
10	47	m	30.8	2	N	SA	103
11	49	m	26.7	1	Y	SA	95
12	29	m	27.5	1	Y	SA	124
13	51	f	31.9	2	Y	LBS	92
14	26	m	30.6	2	Y	SA	51

BMI = body mass index; ASA = physical status according to the classification of American Society of Anesthesiologists; SA = shoulder arthroscopy; LBS = low back surgery; premedication was provided with midazolam 0.05 mg/kg.

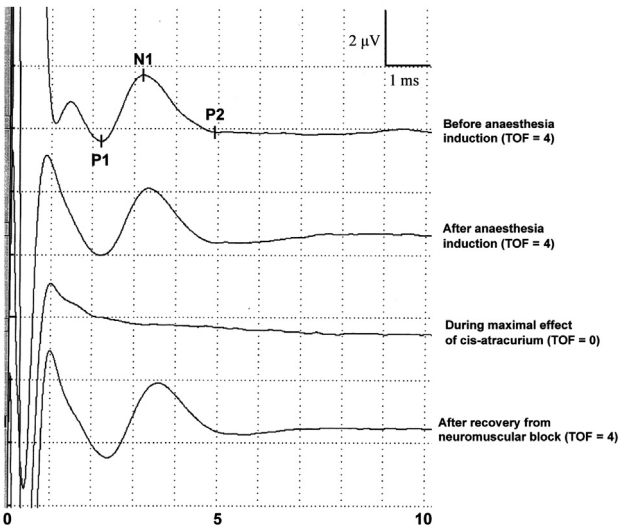

Figure 3. Typical traces of scalp responses of a single patient with identifiable waves P1, N1 and P2, evoked by electrical stimulation of inner side of the right tragus. This pattern could be reproduced in all patients before and after anesthesia induction and after recovery from neuromuscular block. Note that typical waves of scalp responses disappeared during the neuromuscular block using cis-atracurium at "Train-of-Four" (TOF) values 0–1 and re-appeared after recovery from the neuromuscular blockade at TOF 4 under anesthesia.

Table 2
Latencies and amplitudes of scalp responses to transcutaneous electrical stimulation of right tragus.

	Peaks	Leads	Time points of scalp response registration			*P* value[a]	
			Before anesthesia induction (T1)	After anesthesia induction (T2)	Recovery from neuromuscular block (T3)	T1 vs. T3	T2 vs. T3
Latency (ms)	P1	T4O2	**1.62 ± 0.62**	**1.62 ± 0.66**	**1.77 ± 0.59**	0.009	0.018
		C4F4	**2.07 ± 0.64**	2.12 ± 0.59	**2.19 ± 0.63**	0.048	n.s.
	N1	T4O2	**2.51 ± 0.76**	2.60 ± 0.78	**2.72 ± 0.74**	0.004	n.s.
		C4F4	**3.23 ± 1.19**	3.45 ± 1.28	**3.62 ± 1.40**	0.025	n.s.
	P2	T4O2	4.69 ± 1.59	4.85 ± 1.77	4.82 ± 1.52	n.s.	n.s.
		C4F4	4.64 ± 1.98	4.83 ± 2.37	4.92 ± 2.47	n.s.	n.s.
Amplitude (μV)	P1-N1	T4O2	6.70 ± 4.09	7.42 ± 3.89	5.08 ± 3.53	n.s.	n.s.
		C4F4	2.32 ± 1.44	2.94 ± 2.31	2.34 ± 1.84	n.s.	n.s.
	P1-P2	T4O2	7.92 ± 5.94	7.35 ± 5.76	6.95 ± 8.24	n.s.	n.s.
		C4F4	1.15 ± 1.03	2.14 ± 1.66	1.44 ± 0.93	n.s.	n.s.
	N1-P2	T4O2	**14.99 ± 8.78**	**15.17 ± 8.73**	**12.59 ± 8.47**	n.s.	n.s.
		C4F4	**1.25 ± 0.73**	**1.35 ± 1.01**	**0.82 ± 0.59**	n.s.	n.s.
	P value[a] T4O2 vs. C4F4		0.045	0.006	0.003		

Values are mean ± SD; the values with statistically significant difference are in bold.
[a] *P* values Bonferroni adjusted.

Discussion

The purpose of this investigation was to record the artifact-free vagal sensory evoked potentials (VSEP), elicited from the inner side of the tragus of the auricle, which had been previously described in several experimental and clinical studies [10,15,17,18].

In our investigation, we succeeded in reproducing the scalp responses (SR) with previously described waveform and latency in patients while awake and after the induction of a general anesthesia. However, these SR disappeared during the neuromuscular blockade using the non-depolarizing muscle relaxant agent, cisatracurium. This fact suggests a muscular origin of SR, elicited from the inner side of the tragus in this investigation.

The latencies of the SR obtained in our investigation concord with the values previously measured [10,17]. The amplitudes in our investigation were larger than previously described, varying between 1.25 ± 0.73 in C4F4 leads to 14.99 ± 8.78 in T4O2 (mean ± SD, μV) before anesthesia induction (Table 2). The difference in the amplitude size between our and previous studies could possibly be explained by the fact that Fallgatter et al. used an artifact criterion of 40 μV, thus excluding the responses with larger amplitude values [10]. The highest amplitude of SR in the occipital regions T4–O2, which had also been registered previously, supports the hypothesis of scalp muscle contribution, corresponding to muscle distribution on the head.

Our findings concord with the anecdotal observations in clinical neurophysiological research. Hammond et al. studied SR, evoked by implanted stimulators of the left vagal nerve in 9 patients with intractable seizures [19]. The investigation of the field distribution of these SR, using 16 scalp EEG leads, suggested that the response, within 12 ms after stimulation, had been myogenic in origin. This suggestion was confirmed by the disappearance of these SR after the neuromuscular blockade with the short-term non-depolarizing muscle relaxant agent, vecuronium [19].

So far, there is no direct proof that these SR are of a vagal origin, which had been previously suggested [10]. Regarding the partially overlapping innervation of the auricle [7,20], these potentials could also be responses to the stimulation of trigeminal or facial nerves. Thus, Leandri et al. found that a complex of three waves (W1–3) recorded after invasive infraorbital nerve stimulation, which appeared within 4 ms after stimulation, was of neurogenic origin, whereas a biphasic SR, appearing within 10 ms after stimulation of the upper lip, was clearly related to muscle activity of the orbicularis oris muscle. This response was supposed to reflect the far field activity of this muscle, which was evoked by stimulus intensities as low as 4 mA [21]. In another clinical investigation, the negative deflection, occurring at about 3 ms after stimulation of the facial nerve at the stylomastoid foramen, had neurogenic origin, since it appeared also during general anesthesia with a neuromuscular blockade. In contrast, the following wave at 5–6 ms was myogenic, since it disappeared under a neuromuscular blockade during general anesthesia [22]. The author suggested that this second potential could be a far field reflection of mimic muscles, supplied by the facial nerve.

However, the recording of evoked potentials under direct vagal nerve stimulation is in principle possible, as was recently shown by Usami et al. [23]. In their study, the stimulation of the vagal nerve on the neck in patients, who received the implanted vagal nerve stimulator for drug-resistant epilepsy, elicited scalp responses, which did not disappear after systemic administration of muscle relaxing agents.

In our investigation, the occipitofrontal muscle, innervated by branches of the facial nerve and the parietotemporal muscle, innervated by the trigeminal nerve (Fig. 1), could have been involved in the generation of myogenic scalp potentials. Excluding the possibility of direct muscle stimulation (maximal stimulation intensity of 8 mA several centimeters away from the muscles' bellies), we hypothesize that the muscular activity could have been elicited via direct activation of efferent fibers of the facial (stimulation site is near the stylomastoid foramen, where the facial nerve leaves the skull) and of the posterior auricular nerve, which crosses behind the ear (to the posterior ear muscles and the occipital belly of the occipitofrontal muscle). An experimental investigation with pharmacological blockade of the afferent arc of vagal nerve on the skin of the external ear using local anesthetics might further elucidate the origin of scalp responses under auricular stimulation.

The limitations of the study include the recording of SR using only few leads on the one side of the scalp and single area (only auricle) of stimulation. The standard multiple-leads EEG recording would allow the use of the field distribution approach for studying the origin of SR.

In summary, the disappearance of the scalp responses, elicited by electrical tragus stimulation under a neuromuscular block, suggests a muscular origin of this phenomenon. We currently do not know with certainty, which mechanisms and muscles account for these responses. Further studies are in progress to elucidate this question.

Acknowledgments

The authors thank Vasyl Gizhko of the Department of Experimental Physics at the University of Kiev, Ukraine, for his design and tests of the stimulation electrode, Professor Thomas Kohlmann

from the Department of Community Medicine, University Medicine of Greifswald for his statistical advice and Vasili Maslak, a freelance 3D computer graphics specialist, for his preparation of Figure 1 and the patients, who participated in this investigation.

References

[1] George MS, Nahas Z, Borckardt JJ, Anderson B, Burns C, Kose S, et al. Vagus nerve stimulation for the treatment of depression and other neuropsychiatric disorders. Expert Rev Neurother 2007;7:63–74.
[2] Groves DA, Brown VJ. Vagal nerve stimulation: a review of its applications and potential mechanisms that mediate its clinical effects. Neurosci Biobehav Rev 2005;29:493–500.
[3] Multon S, Schoenen J. Pain control by vagus nerve stimulation: from animal to man... and back. Acta Neurol Belg 2005;105:62–7.
[4] Hatton KW, McLarney JT, Pittman T, Fahy BG. Vagal nerve stimulation: overview and implications for anesthesiologists. Anesth Analg 2006;103:1241–9.
[5] Kraus T, Hösl K, Kiess O, Schanze A, Kornhuber J, Forster C. BOLD fMRI deactivation of limbic and temporal brain structures and mood enhancing effect by transcutaneous vagus nerve stimulation. J Neural Transm 2007;114:1485–93.
[6] Napadow V, Edwards RR, Cahalan CM, Mensing G, Greenbaum S, Valovska A, et al. Evoked pain analgesia in chronic pelvic pain patients using respiratory-gated auricular vagal afferent nerve stimulation. Pain Med 2012;13:777–89.
[7] Peuker ET, Filler TJ. Nerve supply of the human auricle. Clin Anat 2002;15:35–7.
[8] Nomura S, Mizuno N. Central distribution of primary afferent fibers in the Arnold's nerve (the auricular branch of the vagus nerve): a transganglionic HRP study in the cat. Brain Res 1984;292:199–205.
[9] Satomi H, Takahashi K. Distribution of the cells of primary afferent fibers to the cat auricle in relation to the innervated region. Anat Anz 1991;173:107–12.
[10] Fallgatter AJ, Neuhauser B, Herrmann MJ, Ehlis A-C, Wagener A, Scheuerpflug P, et al. Far field potentials from the brain stem after transcutaneus vagus nerve stimulation. J Neural Transm 2003;110:1437–43.
[11] Banoub M, Tetzlaff JE, Schubert A. Pharmacologic and physiologic influences affecting sensory evoked potentials: implications for perioperative monitoring. Anesthesiology 2003;99:716–37.
[12] Sloan TB. Nondepolarizing neuromuscular blockade does not alter sensory evoked potentials. J Clin Monit 1994;10:4–10.
[13] Leandri M, Parodi CI, Zattoni J, Favale E. Subcortical and cortical responses following infraorbital nerve stimulation in man. Electroencephalogr Clin Neurophysiol 1987;66:253–62.
[14] Jasper H. The ten twenty electrode system of the International Federation. Electroencephalogr Clin Neurophysiol 1958;10:371–5.
[15] Polak T, Markulin F, Ehlis A-C, Langer JBM, Ringel TM, Fallgatter AJ. Far field potentials from brain stem after transcutaneous vagus nerve stimulation: optimization of stimulation and recording parameters. J Neural Transm 2009;116:1237–42.
[16] Lee CM. Train-of-4 quantitation of competitive neuromuscular block. Anesth Analg 1975;54:649–53.
[17] Fallgatter AJ, Ehlis A-C, Ringel TM, Herrmann MJ. Age effect on far field potentials from the brain stem after transcutaneus vagus nerve stimulation. Int J Psychophysiol 2005;56:37–43.
[18] Polak T, Ehlis AC, Langer JBM, Plichta MM, Metzger F, Ringel TM, et al. Non-invasive measurement of vagus activity in the brain stem – a methodological progress towards earlier diagnosis of dementias? J Neural Transm 2007;114:613–9.
[19] Hammond EJ, Uthman BM, Reid SA, Wilder BJ. Electrophysiologic studies of cervical vagus nerve stimulation in humans: II. Evoked potentials. Epilepsia 1992;33:1021–8.
[20] Gray H. Anatomy of the human body. X. The organs of the senses and the common integument. The external ear. Lea & Febiger; 1918. 146.
[21] Leandri M, Parodi CI, Favale E. Early evoked potentials detected from the scalp of man following infraorbital nerve stimulation. Electroencephalogr Clin Neurophysiol 1985;62:99–107.
[22] Rödel R. Central nervous system evoked potentials in peripheral antidromic stimulation of the n. facialis. Laryngorhinootologie 1997;76:660–2.
[23] Usami K, Kawai K, Sonoo M, Saito N. Scalp-recorded evoked potentials as a marker for afferent nerve impulse in clinical vagus nerve stimulation. Brain Stimul 2012. doi:pii: S1935–861X(12)00161-1. 10.1016/j.brs.2012.09.007.