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Determination of Somatosensory Evoked Potentials(SEPs) by Posterior Tibial Nerve Stimulation in Dogs

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개에서 뒤쪽 경골신경자극에 의한 Somatosensory Evoked Potentials(SEPs)의 측정

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요 약 : 이 실험은 소형견종에 대한 정상 SEPs의 범위를 알아내기 위해 실시되었다. 임상증상이 정상인 28두를 대상으로 자극점에서 channel 1 까지의 P1(LP1), channel 1 까지의 N1(LN1), 자극점에서 channel 2 까지의 P1(TP1), channel 2 까지의 N1(TN1)의 절대잠복기와 'LP1-TN1' 의 파간잠복기를 알아내기 위해서 실시하였다. 이번 실험에서 LP1, LN1, TP1, TN1의 절대잠복기(absolute latency)의 평균값은 2.69±0.31 msec, 4.91±0.49 msec, 4.64±0.39 msec, 5.21±0.42 msec 이었다. LP1과 TN1 사이의 파간절대잠복기의 평균값은 2.52±0.19 msec 이었다. 측정치들을 속도로 변환하였을 경우 다음과 같았다. 즉, LP1, LN1, TP1, TN1 그리고 'LP1-TN1' 에서의 속도의 평균값은 각각 93.11±8.58 m/sec, 50.99±5.36 m/sec, 80.18±5.69 m/sec, 71.31±4.79 m/sec 그리고 49.50±3.58 m/sec 이었고, 71.66 m/sec, 37.59 m/sec, 65.95 m/sec, 59.33 m/sec, 40.55 m/sec의 최저속도를 초과하였을 때 정상범위로 간주하였다. LP1, LN1, TP1, TN1 까지의 절대잠복기와 자극전극에서 측정전극까지의 거리 사이에는 상관관계가 있었다. LP1, LN1, TP1, TN1의 상관계수는 각각 0.621, 0.494, 0.577, 0.618 이었다. 요추에서 기록된 SEPs 값은 LP1의 상관계수가 LN1 보다 높았으며, 흉추에서 기록된 SEPs 값은 TN1의 상관계수가 TP1 보다 높았다. LP1과 TN1의 파간잠복기와 channel 1과 2의 거리차이와의 상관계수는 0.561이다. 따라서 LP1, LN1, TP1, TN1 그리고 'LP1-TN1' 들의 최저속도를 이용하여 척수 손상 여부를 판단할 수 있다고 생각된다.

Key words : 개, 감각유발전위(somatosensory evoked potentials), 잠복기

Introduction

Somatosensory evoked potentials (SEPs) are the potentials elicited by stimulation of peripheral nerves and recorded at various sites along the sensory pathways. In recent years, SEPs have been increasingly used to evaluate the function of peripheral sensory pathways[18], and studied in patients with neurologic diseases since the early 1950s. However, it was only in the early 1970s that EPs began to have definite clinical utility[1].

The cortically recorded SEPs are usually impossible to recognize against the continuous background of electroencephalography (EEG) activity, because the SEPs are small in amplitude. Therefore, a signal-averaging technique should be used to cancel the randomly occurring 'EEG waves' and to record the summated 'time-locked signals'[11].

The most useful clinical utility of evoked potentials (EPs) are their ability to demonstrate abnormal sensory system function when the history and neurologic examination are equivocal. The second utility is the ability to reveal the presence of clinical unsuspected malfunction in the sensory system when demyelinating

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disease is suspected. The third is the ability to help define the anatomic distribution of disease process. The fourth is the ability to monitor the changes objectively over time in a patient's status1.

Responses to evoked potential could be recorded with either surface or needle electrodes over the scalp, spine, and peripheral nerve fibers in the limb[3,11,18].

Changes in the morphology and in the degree of dispersion of the response may also reflect a lesion of the somatosensory pathways. SEPs studies would be helpful in evaluating patients with suspected root lesions[18].

Assessment of spinal cord diseases has largely been dominated by the clinical neurologic examination in combination with the imaging study. Spinal cord imaging modalities include myelography, computer tomography (CT) and magnetic resonance imaging (MRI), all of which provide anatomic information about the spinal cord and surrounding structures. In contrast, electrophysiologic tests such as motor evoked potentials (MEPs) and somatosensory evoked potentials (SEPs) provide functional information on the central motor and sensory pathway, therefore, they should be considered complementary to the clinical examination and imaging study[5].

In veterinary medicine, the normal range of SEPs in toy breed dogs has not been reported yet. This experiment was performed to find out its normal range.

Materials and Methods

Experimental animals

Clinically healthy twenty eight dogs (3.0-4.3 kg and 2-5 years) were used regardless of their sexes to determine the normal SEP range by hindlimb stimulation. SEPs were recorded sixty two times in twenty eight dogs.

Anesthesia

Thiopental sodium (15 mg/kg, Penthotal sodium®, Joongwei, Korea) was intravenously injected to induce the anesthesia after premedication of acepromazine maleate (0.01 mg/kg, Sedaject®, Samwoo, Korea) and isoflurane (AErane®, Ilsung, Korea) was used to maintain anesthesia.

Apparatus for experiments

'MEM-7102'(Nihon kohden, Japan) model was used to measure the SEPs and the subdermal 'platinum needle electrode'(Grass, USA) was applied on the two channels.

Condition of SEPs stimulation

The posterior tibial nerves were stimulated with needle electrodes. The nature of the stimulation was electro-stimulation. Stimulation was conducted with 0.2 msec, 2 Hz and 4 mA. The supramaximal stimulation intensity was used at least three times of the response threshold. SEPs were averaged over 100 times in each recording.

SEPs measurement

The SEPs were measured on two channels. The channel 1 was located on the subdermal region between the 5th and 6th lumbar vertebra and the channel 2 was positioned between the 11th and 12th thoracic vertebra.

The latencies / distances from the electro-stimulating point on the posterior tibial nerve to channel 1, and from the channel 1 to channel 2 were measured.

The electro-stimulating point was the medial region between the distal part of tibia and calcaneal tuberosity (Fig 1).

In channel 1 and 2, the first upward beginning point (positive peak) was named as 'LP1' and 'TP1', respectively, and second point was 'LP2' and 'TP2'. The first downward beginning point (negative peak) was marked as 'LN1' and 'TN1', the second was 'TN2',

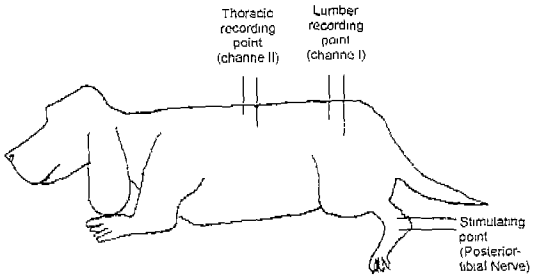

Fig 1. Diagram indicating the method used for recording spinal - evoked potentials in dogs. The reference electrodes of channel 1 and 2 were positioned 5 cm laterally from each recording electrodes.

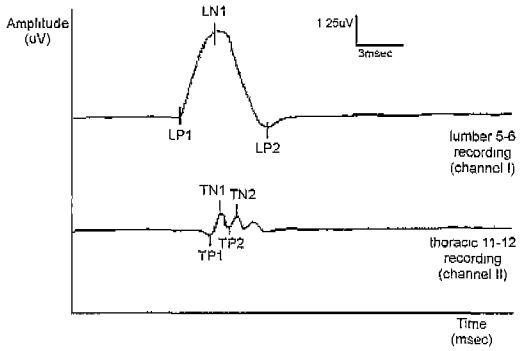

Fig 2. Schematic diagram of lumbar recording (channel I) and thoracic (channel II) by stimulating the posterior tibial nerves. The amplitude of LP1 and LN1 (between L5 and L6) was larger than that of TP1 and TN1 (between T11 and T12).

respectively (Fig 2.).

Conversion of latency to velocity

The measured potentials were converted to the velocity to compare the latencies. The limits of normal range were 'mean± 2.5S.D.'. The velocity of the two points was calculated by use of the following equation :

$$\text{Velocity (m/sec)} = \frac{distance(cm)\ of\ two\ points}{latency(msec)\ differences} \times 10$$

Statistical analysis

The correlation coefficients and regression equations between the distances and the latencies of LP1, LN1, TP1, TN1, and 'LP1-TN1' were calculated by SPSS® (ver 9.0).

Results

Distance and latency of somatosensory evoked potentials measured in normal toy breed dogs were as follows.

Mean latency of SEPs and mean distance

Mean absolute latencies of LP1, LN1, TP1, and TN1 were 2.69± 0.31 msec, 4.91± 0.49 msec, 4.64± 0.39 msec and 5.21± 0.42 msec, respectively. Mean distances from stimulating point to channel 1 and channel 2 were 24.9± 1.94 cm and 37.1± 2.71 cm, respectively. On the other hand, mean inter-wave latency from LP1 to TN1 was 2.52± 0.19 msec, and mean distance from channel 1 to channel 2 was 12.2 ± 1.00 cm.

Correlation coefficient and regression equation

Correlation coefficient between absolute latency and distance from the electro-stimulating point to LP1 was 0.621 ($P<0.01$, 2-tailed).

The regression equation in this case was 'Y = 0.102X+0.155' [X = distance(cm), Y = latency (msec)] (Fig 3).

Correlation coefficient between absolute latency and distance from the electro-stimulating point to LN1 was 0.494 ($P<0.01$, 2-tailed).

The regression equation in this case was 'Y = 0.125X+1.81' [X = distance(cm), Y = latency (msec)] (Fig 4).

Correlation coefficient between absolute latency and distance from the electro-stimulating point to TP1 was 0.577 ($P<0.01$, 2-tailed).

The regression equation in this case was 'Y = 0.0851X+1.49' [X = distance(cm), Y = latency (msec)] (Fig 5).

Table 1. Mean latency, velocity of somatosensory evoked potentials and mean distance.

	LP1	LN1	TP1	TN1	LP1-TN1
latency (msec)	2.69±0.31*	4.91±0.49	4.64±0.39	5.21±0.42	2.52±0.19
distance (cm)	24.9±1.94		37.1±2.71		12.2±1
velocity (m/sec)	93.11	50.99	80.18	71.31	49.5
standard deviation	8.58	5.36	5.69	4.79	3.58
range of velocity (mean±2.5 S.D.)	71.66-114.56	37.59-64.39	65.95-94.40	59.33-83.28	40.55-58.45

LP1 : latency from stimulating point to P1 of channel 1, LN1 : latency from stimulating point to N1 of channel 1
TP1 : latency from stimulating point to P1 of channel 2, TN1 : latency from stimulating point to N1 of channel 2
*mean± SD

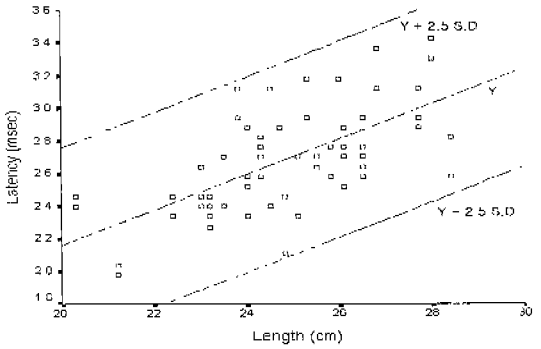

Fig 3. Correlation and regression analysis between the absolute latencies of LP1 and distance from the stimulating point to lumbar recording electrode.

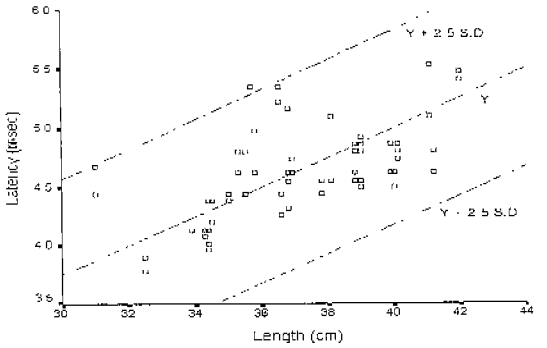

Fig 5. Correlation and regression analysis between the absolute latencies of TP1 and distance from the stimulating point to thoracic recording electrode.

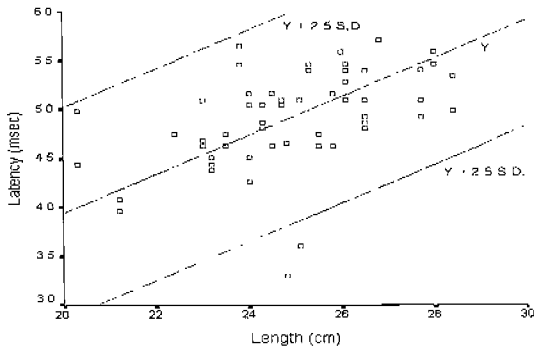

Fig 4. Correlation and regression analysis between the absolute latencies of LN1 and distance from the stimulating point to lumbar recording electrode.

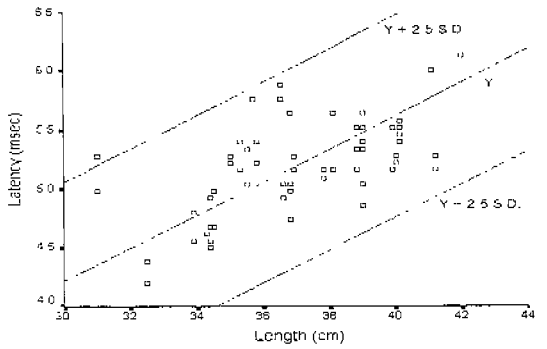

Fig 6. Correlation and regression analysis between the absolute latencies of TN1 and distance from the stimulating point to thoracic recording electrode.

Correlation coefficient between absolute latency and distance from the electro-stimulating point to TN1 was 0.618 ($P<0.01$, 2-tailed).

The regression equation in this case was 'Y = 0.0970X+1.62' [X = distance(cm), Y = latency (msec)] (Fig 6).

Correlation coefficient between the 'LP1-TN1' interwave latency and distance from the channel 1 and channel 2 recording site was 0.561 ($P<0.01$, 2-tailed).

The regression equation in this case was 'Y = 0.115X+1.08' [X = distance(cm), Y = latency (msec)] (Fig 7).

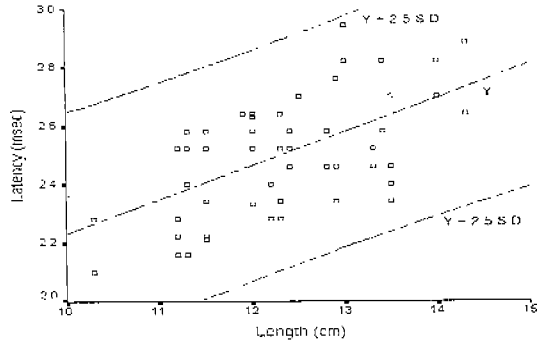

Fig 7. Correlation and regression analysis of 'LP1-TN1' interwave latencies and the distance from channel 1 to channel 2.

Discussion

Nerve conduction velocity (NCV) is an expression of the physiological or pathophysiological state of the neurons. There are three kinds of studies on the nerve conduction, those are the motor nerve conduction test, the sensory nerve conduction test, and the mixed

nerve conduction test[11].

The motor nerve conduction of a peripheral nerve was tested by stimulating the nerve with a single supramaximal stimulus at each of two proximal points along the course of the peripheral nerve, then the compound muscle action potential (CMAP) with a surface electrode were recorded from the muscle innervated by connected nerve[6,7,11,18].

The sensory nerve conduction of a peripheral nerve was tested either orthodromically or antidromically[17]. In orthodromic method, the sensory nerve conduction was tested by stimulating the distal part of the nerve and recording the compound nerve action potential (CNAP) directly over the proximal part of the nerve. When the stimulating and recording electrodes were switched, this was called antidromic stimulation[11].

The mixed nerve conduction of a peripheral nerve was tested by stimulating the distal part of the nerve (sensory and motor fibers) and recording the CNAP directly over the proximal part of the nerve. The methods of testing, measuring amplitude, and calculating velocity were identical to the orthodromic method of sensory nerve conduction. The only difference is that the mixed nerve fibers are being stimulated[10,11].

NCV is determined by dividing this distance by the conduction time, and it is limited to nerves that are accessible to stimulation. It is possible to get NCV of the median, ulnar, and radial nerves in the upper extremities, and of the sciatic, femoral, posterior tibial, and perineal nerves in the lower extremities[2,11]. In this experiment, the orthodromic sensory nerve conduction (SEP) was recorded by posterior tibial nerve stimulation.

Latency in EP work is usually stated in milliseconds (msec). The term 'latency' most commonly refers to the time interval between the stimulus and a specific point on the EP waveforms. This time interval is also called 'absolute latency' or 'implicit time'. In EPs studies, the waveform peak is most commonly used as the measurement point. The time separation between two peaks is termed 'interwave latency' or 'interpeak latency'. In this experiment, the normal lower limits of velocities in LP1, LN1, TP1, TN1 and 'LP1-TN1' were 71.66 m/sec, 37.59 m/sec, 69.95 m/sec, 59.33 m/sec and 40.55 m/sec, respectively. Therefore, the recorded velocities under these values could be regarded as spinal cord dysfunction.

Amplitude in EPs work is usually stated in microvolts. The measuring of amplitude has been most useful when used in comparison with the same measure on the other side of the subject when subjects serve as their own controls[1]. However, amplitude was not considered in this experiment, because the range of amplitude was very diverse.

The latencies of the individual component and the intervals between different components such as height or limb length were examined[18], therefore, the latency and hindlimb length were recorded together in this experiment. The average distances in 'stimulating point - lumbar recording channel', 'stimulating point - thoracic recording channel', and 'lumbar recording channel - thoracic recording channel' were 24.9± 1.94 cm, 37.1± 2.71 cm, and 12.2± 1.00 cm, respectively.

Evoked potentials and MRI are largely complementary tests. The former provides a 'view' of functional anatomy, whereas the latter mainly registers structure. Clinical studies have reported frequent cases where one test has missed a lesion detected by the other. For example, MRI may fail to catch a small lesion in the brain stem revealed by abnormal short latency EPs[16]. Evoked potential tests provide sensitive, quantitative extensions of the clinical neurologic examination. Sometimes the absence of a wave or an abnormal configuration on its potential field also provides useful information[1].

The standard deviation used as the limit of normality must include at least 98% of the population being tested, therefore, most laboratories use 2.5(98.8%)S.D. or 3(99.7%)S.D.[1]. It is completely incorrect to use 2.0 or less S.D. multiples to define the upper limit of normal for the purpose of clinical interpretation. In this experiment, 'mean± 2.5S.D.' was calculated to judge spinal cord dysfunction.

If the EPs are not recorded, one must consider whether the EPs are absent because of a conduction defect in the patient, or because of technical errors. If some EP waveforms are clearly seen, while others being poorly seen or absent, then this is unlikely to be due to a technical errors[1].

It is important to use the same parameters because many environmental factors have significant effects

on EPs latencies and amplitudes. One of the greatest problems encountered by clinical neurophysiologists in the operating room is that various anesthetic agents affect on sensory evoked signals[8]. Premedication agents, such as narcotic analgesics and sedatives have been studied for their potential effect on SEPs. At premedication doses, these agents have little or no effect on the EPs[8]. In this experiment, acepromazine was used as premedication.

The decrease in the response amplitude and an increase of latency in the scalp-recorded potentials have been observed at induction doses of thiopental. The cervical potentials are relatively resistant to thiopental at these doses[9]. In this experiment, there were no significant changes in SEPs after injection of thiopental.

The successful monitoring could be performed with the halogenated agents[3,8]. In this experiment, isoflurane was used to maintain the anesthesia, and SEPs were recorded within 30 minutes in order not to affect on SEPs waveforms in each case.

Continuous infusion of narcotics provides stable recordings, whereas bolus injections can affect both the evoked potentials and the wake-up test[13,14]. Kalkman *et al*[4]. recommended an alfentanil-propofol anesthetic technique for signal enhancement. SEPs in response to tibial nerve stimulation were recorded from the scalp of 31 normal mixed breed dog[15] and SEPs and MEPs were recorded in 111 clinical cases[12].

This experiment was performed to determine the normal range of SEP latency in toy breed dogs, but the normal range of SEP latency in cervical and cortical region, in middle-size and large breed dogs was not ascertained. Therefore, the further experiments of SEPs in other region and other breed dogs are thought to be needed.

Conclusion

The normal ranges of lumbar and thoracic SEP latencies in toy breed dogs were as follows.

The mean latencies from stimulating point to P1 of channel 1 (LP1), to N1 of channel 1 (LN1), to P1 of channel 2 (TP1), to N1 of channel 2 (TN1) and 'LP1-TN1' were 2.69± 0.31 msec, 4.91± 0.49 msec, 4.64± 0.39 msec, 5.21± 0.42 msec, and 2.52± 0.19 msec, respectively. The mean distances in 'stimulating point - lumbar recording channel', 'stimulating point - thoracic recording channel', and 'lumbar recording channel - thoracic recording channel' were 24.9± 1.94 cm, 37.1 ± 2.71 cm, and 12.2± 1.00 cm, respectively.

The correlations coefficient of LP1, LN1, TP1, and TN1 were 0.621, 0.494, 0.577, 0.618, respectively. In lumbar recording electrode, the correlation coefficient of LP1 was higher than that of LN1, and TN1 coefficient was higher than that of TP1 in thoracic recording electrode. The correlation coefficient between distance and latency from TN1 to LP1 was 0.561. The latency of 'LP1-TN1' would be possible to use as a factor of spinal cord dysfunction.

These latency and distance were conversed to velocity. The mean velocities of LP1, LN1, TP1, TN1 and 'LP1-TN1' were 93.11± 8.58 m/sec, 50.99± 5.36 m/sec, 80.18± 5.69 m/sec, 71.31± 4.79 m/sec and 49.5± 3.58 m/sec, respectively. The normal lower limits of velocity in LP1, LN1, TP1, TN1 and 'LP1-TN1' were 71.66 m/sec, 37.59 m/sec, 65.95 m/sec, 59.33 m/sec and 40.55 m/sec, respectively.

It is considered that normal lower limits of SEPs velocity might be helpful to evaluate the spinal cord dysfunction.

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