maintained by an additional intravenous administration of ketamine chloride (10 mg/kg) and pancuronium bromide. Lactated Ringer's solution was administered i.v. during the procedure (10 ml/kg per hour). Arterial blood pressure was monitored continuously by use of a catheter inserted into a femoral artery. Since several dogs developed cardiac shock over 42°C, dobutamine was administered intravenously to keep the blood pressure within normal values.

An electrocardiogram was also registered during the whole procedure, and blood gas was simultaneously analysed. The arterial pO2 was maintained above 90 mmHg, the pCO2 between 30 and 45 mmHg, and the pH between 7.35 and 7.45.

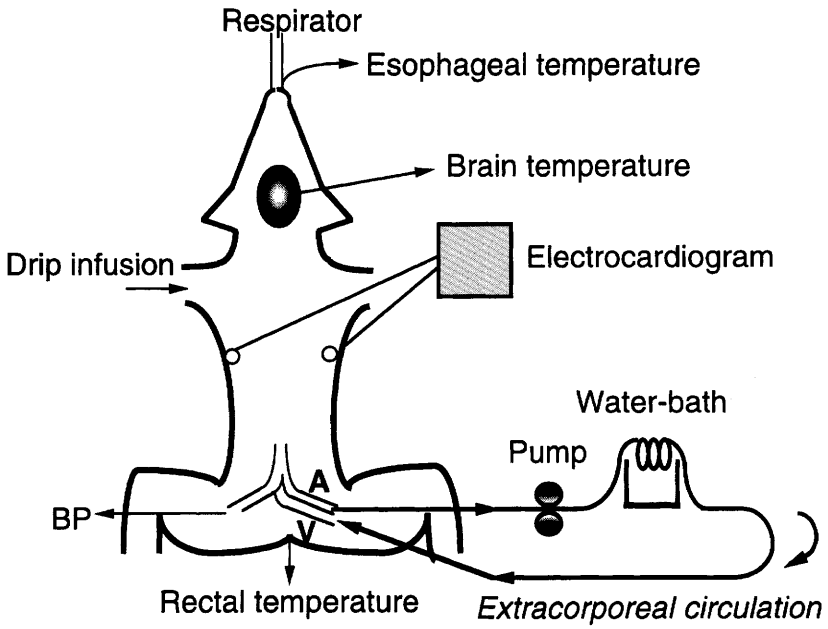

Fig. 1. A schematic illustration of an animal model with an extracorporeal circuit apparatus for whole-body hyperthermia and whole-body hypothermia.

Table 1. Summary of serial SCEP data during the whole-body hyperthermia

Time (min)	Esophageal Temp. (°C)	Spinal canal Temp. (°C)	N 1 Amp.	N 1 Lat.	N 2 Lat.
0	34.0	33.9	48.0	2.66	3.76
10	35.3	35.0	46.7	2.62	3.66
20	36.3	35.9	41.3	2.54	3.56
30	37.2	36.9	40.4	2.46	3.46
45	38.2	38.1	34.6	2.36	3.30
57	39.4	39.1	35.3	2.31	3.18
78	40.4	40.0	28.3	2.24	3.08
88	41.3	40.9	26.7	2.20	2.96
100	42.2	41.9	25.2	2.15	2.84

A representative case is shown. The first component was defined as a N1 and the second one as a N2 by the book.
temp., temperature; Amp., amplitude; Lat., latency.

At the end of each experiment, the animal was injected with a lethal dose of sodium pentobarbital and potassium chloride solutions. The experiments were conducted with permission of the Committee on the Guidelines for Animal Experimentation of Niigata University.

Whole-body hyperthermia, whole-body hypothermia

Whole-body hyperthermia was induced by heating the blood in a coiled tube of an extracorporeal circuit, using a femoral arteriovenous shunt[2,9]. Heparin at a dose of 200 units/kg was administered intravenously before the procedure. The arterial part of the circuit was led through a blood pump to set the circuit flow at 100-150 ml/min. The circuit had a capacity of 100 ml, including a coiled tube to be immersed in a waterbath (Thermo minder; Mini 80; Taiyo Co., Japan). The temperature of the waterbath was set at 50-58°C to raise the temperature of the blood. In contrast, cold water (10-15°C) was used to lower the temperature of the blood. A schematic illustration of an extracorporeal circuit is shown in Fig. 1.

Thermometry

Copper-constantan thermocouples were placed into each thoracic and lumbar epidural space after partial laminectomies to measure the temperature of the spinal canal. A brain thermistor was placed in the

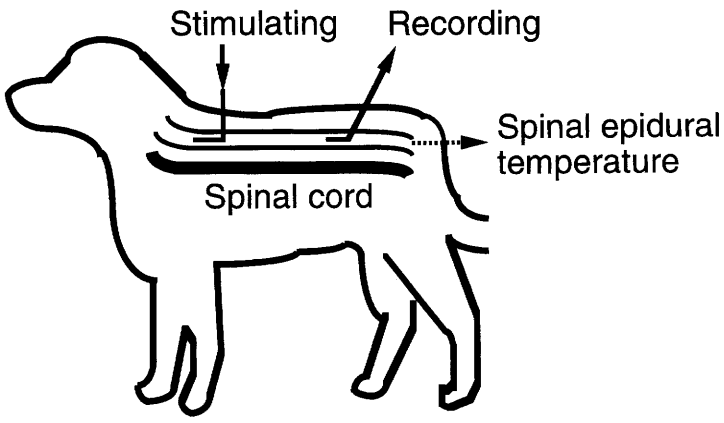

Fig. 2. A schematic illustration of SCEP recordings.

Table 2. The effect of whole-body hyperthermia on conduction velocity of the spinal cord which was calculated from changes in SCEP

	N	Latency (msec)	Conduction velocity (m/sec)
N1 (first component)			
34.0°C	4	2.37±0.13	97.4±5.6
37.0°C	7	2.17±0.11	106.2±5.5
41.0°C	7	1.98±0.10	116.2±6.3
42.0°C	3	1.92±0.14	120.2±8.3
N2 (second component)			
34.0°C	4	3.34±0.14	69.0±3.0
37.0°C	7	2.96±0.10	77.7±2.6
41.0°C	7	2.68±0.08	85.8±2.7
42.0°C	3	2.57±0.04	89.5±1.2

Values are mean±SD (n=7). Values are corrected, with the distance between stimuli and recordings estimated at 23 cm.

right parietal lobe through a small burr hole in the cranium. At the same time, the temperatures of the esophagus and the rectum were monitored on a telethermometer (SDT-5), and a standard mercury thermometer registered waterbath temperature.

SCEP recording

For recording the SCEP, two bipolar tube-type electrodes were both introduced into the dorsal epidural space through partial laminectomies. One electrode was placed at the level of L2 for recording, and the other at the level of T3 for stimulation (shown in Fig. 2). Stimulation was made with a Neuropack 4 mini (Nihon Kohden, Tokyo, Japan), which emitted rectangular waves of 0.2 msec in duration whose stimulation intensity was supramaximal. The recording device was also a Neuropack 4 mini. The filter range was 20 to 3,000 Hz. The analysis time was 10 msec with an average of 50-100 responses. Latency and amplitude of the responses were measured. Regarding the latency, the value corrected as the stimuli-recording distance was 23 cm, which was the average of all experimental dogs. We studied the first and second components of the SCEP, which always appeared clearly. The first component was defined as a N1 and the second one as a N2 by the book[2~5].

Data was presented as the mean and standard deviation (mean±SD).

RESULTS

We first confirmed that the temperature of the spinal epidural space was the same as that of the spinal cord during whole-body hyperthermia in this model. All differences among temperatures in all regions of the body measured were always within 0.1°C in our experiments. Arterial blood pressure and pulse rates were maintained to within normal values throughout the whole procedure.

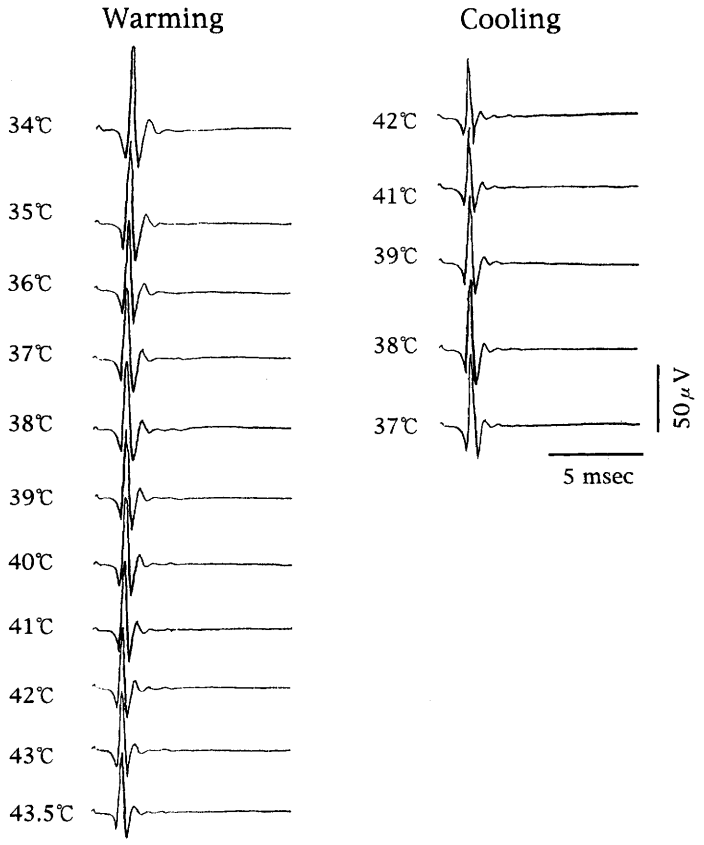

Fig. 3. Serial recordings of a representative case during whole-body hyperthermia. Both latencies and amplitudes of N1 and N2 reduce gradually with an increase in the temperature on one hand, and return with a decrease in the temperature on the other.

SCEP changes with an increase of the temperature

This method efficiently raised the spinal epidural temperature to 43°C easily and accurately. Both esophageal and rectal temperatures were also increased with elevation of the spinal canal temperature. Fig. 3 shows serial recordings of a representative case when the spinal canal temperature was increased. Serial SCEP data for the representative experiment is summarized in Table 1. The relationship between the spinal canal temperature and the SCEP latencies is shown in Fig. 4. At 42.0°C and below, the reductions in latencies were similar in N1 and N2 with an increase in the temperature. An increase in the temperature caused the latencies to reduce gradually, and the conduction velocity of the two potentials increased (Table 2).

Although we studied the values of amplitude in similar fashion, their changes did not significantly

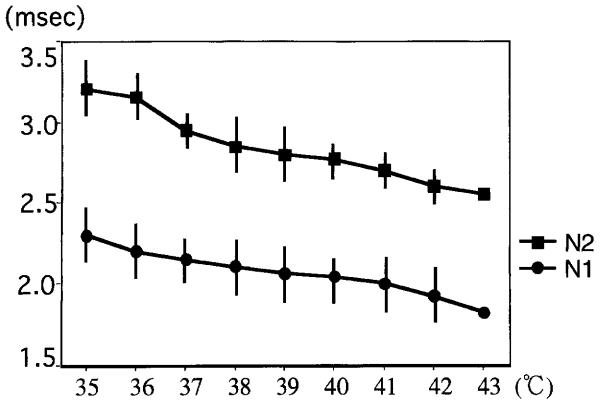

Fig. 4. The relationship of the spinal canal temperature to SCEP latencies. The reductions in SCEP latencies are similar in N1 and N2 with an increase in the temperature.

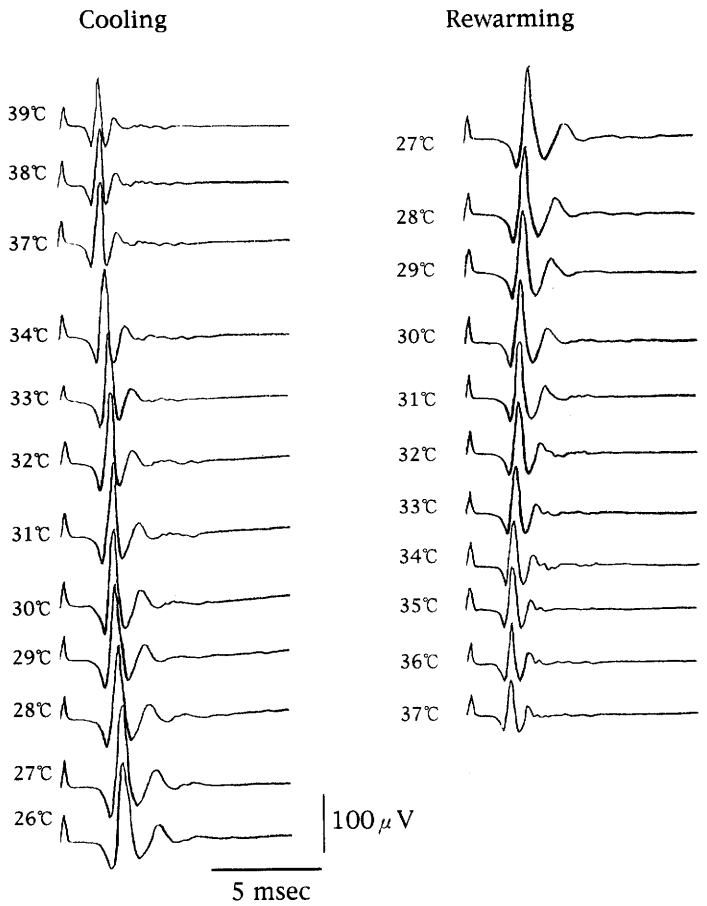

Fig. 5. Serial recordings during whole-body hypothermia. Latencies of N1 and N2 prolong and those amplitudes increase gradually with a decrease in the temperature.

differ because of high variations between each individual.

SCEP changes with a decrease in the temperature

Our method successfully brought about an easy and accurate decrease in the spinal canal temperature to 26°C, at which cardiac function was maintained normally in this study. The rectal temperature also fell when the temperature of spinal epidural space was decreased during whole-body hypothermia. Fig. 5 shows a series of responses recorded at altered spinal canal temperatures. The most striking features of these responses were the prolongation of both absolute latencies and the increase in their amplitudes while the temperature was decreasing.

DISCUSSION

SCEP

There is no doubt that the SCEP is a useful monitor of the spinal cord function, especially the function of its white matter. The response consists mainly of two components which appear within 10 msec following electrical stimuli. Of these two waves, the first is considered to be associated with the activity from fiber tracts of the lateral fasciculus, and the second is considered to be associated with the activity from fiber tracts of the posterior fasciculus[3,4]. Although numerous experimental reports concerning the SCEP and the heat sensitivity of the spinal cord have been published, most have focused only on regional effects through a localized hyperthermia by the use of an RF wave or microwave[7-11]. However, an RF wave or microwave system for hyperthermia must be turned off to avoid the interference noise generated during recording of the SCEPs. Moreover, it is always difficult to grasp the thermal distribution during local heating of the spinal cord due to a lack of uniformity of temperatures, rendering it difficult to evaluate the SCEP change at an altering spinal cord temperature. Concerning this point, the whole spinal cord was maintained at a uniform temperature in our model.

Little research has been carried out on the comprehensive effects of heat on the whole spinal cord[1,6]. The authors examined the SCEP on the canine spinal cords to estimate the tolerable temperature of the spinal cord. Our data revealed that, within the range of 26-43°C, an increase in the temperature led to a shortening of wave latencies and a decrease in amplitudes. On the other hand, a decrease in the temperature caused the reverse phenomenon. This SCEP change can be explained by physiological changes in the action potential and the nerve conduction of the spinal cord when the temperature is varied. The SCEP is believed to be independent of synaptic transmission, and our basic data supports this hypothesis.

Our canine model might be suitable for the analysis of various kinds of evoked potentials other than the SCEP when a localized hyperthermia is applied to the spinal cord. In our experiments, latency changes in the SCEP seemed to be more reliable than amplitude ones for obtaining estimates of the spinal cord temperature. A canine model with an extracorporeal circulation should allow a study of the precise effect of a varying body temperature on evoked potentials.

Whole-body hyperthermia and hypothermia as new tactics to study evoked potentials and to obtain a complete grasp of thermal distribution

Our method using an extracorporeal circulation to change the temperature of the body -- including the central nervous system (CNS), -- is considered to be a highly adjustable and safe method because it effected a uniform temperature for the whole spinal cord. No method to study the relationship between temperatures and evoked potentials has been established. The model used in this study represents a more sophisticated method to accomplish this task than those which have been previously performed. This model has an advantage of easily and reliably maintaining uniform temperature throughout the CNS, while allowing a grasp of the thermal distribution. On the other hand, it has the disadvantage of employing a large animal, which raises two problems: the animal's welfare, and the complications of carrying out the whole procedure. Moreover, even in this model, the cardiac output and the blood flow of the spinal cord are not always stable during the body temperature changes. To evaluate the circulatory function more precisely, more sophisticated methods must be developed in the future.

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