Somatosensory Evoked Potentials in Rats with Acute Uremia

Fumio KANDA, Kenji JINNAI, Kazuo TADA and Takuo FUJITA

The effects of acute renal failure (ARF) on somatosensory evoked potentials (SEPs) were studied in rats. With the increase in blood urea nitrogen caused by the ligation of bilateral ureters, both a significant augmentation of amplitudes of the SEP and an increase in the SEP latencies were observed. The nerve conduction velocities of peripheral nerves were unchanged. Thus a kind of cortical irritability and a lesser degree of damage in the peripheral nervous system are characteristics in ARF.

**Key words:** Acute renal failure, Nerve conduction velocity, SEP, Central nervous system

Peripheral neuropathy and encephalopathy are widely known as complications of uremia. A decrease in motor and sensory conduction velocities is commonly observed in chronic renal failure (CRF), even if clinical symptoms are not present, and encephalopathy seems to be more common than peripheral neuropathy in acute renal failure (ARF) (1, 2). Many electrophysiological investigations using electroencephalography (EEG) revealed a significant increase in slow waves in EEG characterizing ARF (3). There have been, however, few reports as to the relationship between acute uremia and somatosensory evoked potentials (SEPs). We studied the changes in the SEP in rats with ARF produced by the ligation of bilateral ureters.

**MATERIALS AND METHODS**

**Subjects**

Male Wistar rats weighing 200 to 300 g were used in this study.

**Electrode implantation**

Two silver needle electrodes were implanted under chloral hydrate anesthesia (320 mg/kg ip). The reference electrode was placed 6.5 mm anterior to the bregma on the midline, the recording one was on the primary somatosensory cortex (4.0 mm to the left of the bregma (4, 5)). Both electrodes were inserted a depth of 1.0 mm beneath the surface of the cortex, held in a place with dental cement and anchored to the skull with a stainless steel screw.

**SEP recording**

The SEP was recorded at least one week after the electrode implantation, and a 1500 EMG system II (DISA Elektronik A/S, Denmark) was used. Under ether anesthesia, the rats were immobilized in the prone position and their heads were fixed in a holder. Body temperature of rat was monitored with a Thermistor Type NPV (Shibaura Electronics Co., Ltd., Japan) inserted into the rectal colon during a recording of the SEP, and was kept between 36.0 and 38.0°C using a Nikon Incubator NP-2 (Nikon Co., Ltd., Japan). Two stimulating electrodes (26-gauge stainless steel needles) were inserted, one each into the first and forth digital footpad of the right forepaw. A square wave stimulus pulse of 0.2 ms in duration and 5.0 mA in intensity was derived at a rate of 2 pulses per second. The band pass of the amplifier measured 10 to 1000 Hz, and 256 samples were averaged. The SEP studies were started after the rats awoke from anesthesia. The first
Fig. 1. Somatosensory evoked potentials recorded at the 7th cervical vertebra (upper trace) and in the primary somatosensory cortex (lower trace) in awake rat by stimulation of the contralateral forepaw. In both recordings, the reference electrode was placed 6.5 mm anterior to the bregma. Central conduction time (CCT) is represented by an interpeak latency between \( N_{\text{cervix}} \) and \( N_1 \), and SEP amplitude is measured as voltage between \( P_1 \) and \( N_{max} \). Calibration: 20 \( \mu \)V (upper trace) and 50 \( \mu \)V (lower trace). The positive peak was named “\( P_1 \)” and the largest negative peak was named “\( N_{max} \)”. Several peaks were shown in the rising flank of the \( N_{max} \) as shown in Fig. 1, and the most stable peak was named “\( N_1 \)”.

To estimate the peripheral conduction time, stainless steel needle electrode was inserted at the seventh cervical vertebra. The latency of the first negative peak, named “\( N_{\text{cervix}} \)”, indicates the peripheral conduction time and interpeak latency between \( N_{\text{cervix}} \) and \( N_1 \) appears to represent the central conduction time (CCT). Details of the SEP in the rat were reported elsewhere (6, 7).

**Surgical procedures**

The rats were separated into two groups.

Uremic rats — Ten rats were given anesthesia with ether and were placed on a board in a supine position. A straight incision was made over the midline of the abdominal wall and bilateral ureters were exposed. Then the ligation of both ureters was performed (8).

Control rats — Additional ten rats were subjected to sham operation consisting of simple abdominal incision.

In both groups, blood sampling and the study of SEPs were performed before and 24 hours after the surgery. The concentrations of blood urea nitrogen (BUN) were measured with RaBA-SUPER SYSTEM (Chugai Pharmaceutical Co., Ltd., Japan). In statistical analysis, unpaired t-test was used for a comparison between the uremic rats and control rats, and paired t-test was used for between before and after the surgery in each group.

**RESULTS**

The mean values and the standard deviations of the serum concentrations of BUN before the surgery in the control rats and in the uremic rats were 20.5±3.0 and 19.0±3.9 mg/dl, and those at 24 hours after the surgery were 21.9±4.7 and 123.1±12.7 mg/dl, respectively. Before the surgery, the SEPs were not different in latencies or in amplitudes between the two groups (Fig. 2-4). The effects of uremia on peak latencies of the somatosensory evoked potentials in rats. There is a significant increase of \( N_1 \) latency in uremic rats (●), but \( P_1 \) or \( N_{\text{cervix}} \) latency is not affected. Control rats (○) show no changes. Horizontal bar represents the mean value.
SEP in Rat with Acute Uremia

Changes in the latencies of SEP before and after the surgery were shown in Fig. 2 and those in central conduction time (CCT) between the Ncervix and N1 were in Fig. 3. Latencies of the N1 and the CCT were prolonged in the uremic rats (N1: 8.02 ± 0.39 to 8.59 ± 0.33 ms; p < 0.005, CCT: 5.70 ± 0.32 to 6.02 ± 0.40 ms; p < 0.01), while latencies of the Ncervix and of the P1 were not changed (Ncervix: 2.31 ± 0.13 to 2.42 ± 0.10 ms; p > 0.05, P1: 4.90 ± 0.35 to 5.02 ± 0.35 ms; p > 0.1). Latencies of the Ncervix, P1, N1, and CCT in the control rats were 2.22 ± 0.16 to 2.27 ± 0.13 ms; p > 0.2, 4.81 ± 0.46 to 4.91 ± 0.46 ms; p > 0.1, 8.01 ± 0.45 to 8.14 ± 0.63 ms; p > 0.2, and 5.73 ± 0.32 to 5.77 ± 0.40 ms; p > 0.5, respectively. Probably because of the small number of rats, there were no statistical differences in the N1 latency (p > 0.05) nor in the CCT (p > 0.1) between the two groups after the surgery. The amplitudes of the P1-Nmax before and after the surgery were shown in Fig. 4. There was a significant augmentation of the amplitude of the P1-Nmax in the uremic rats (116.8 ± 51.5 to 274.0 ± 117.4 μV; p < 0.002). The mean value of amplitudes of the P1-Nmax in the uremic rats was greater than that in the control rats after the surgery (124.4 ± 42.8 μV; p < 0.05).

**DISCUSSION**

According to our previous studies on the SEP in awake rats (6, 7), the P1 originated from the medial lemniscus and the N1 was the potential from the primary somatosensory cortex. The Ncervix appeared to be equivalent to the N13 in the human cervical SEP. The latencies of those evoked potentials were similar to those in the anesthetized rats reported by Wiederholt et al (9). The Nmax indicates summation of polysynaptic evoked potentials from the primary somatosensory cortex and represents the function of the cerebral cortex, because the Nmax were rather unstable in its latency or in its amplitude under various conditions, such as anesthesia (6, 7, 10, 11). The central conduction time (CCT) which indicates the conduction velocity along the central sensory pathway, therefore, is not represent by the interpeak latency of Ncervix-Nmax, but by that of Ncervix-N1.

Electrophysiological studies on uremia have been conducted more intensively in patients with chronic renal failure (CRF) than in those with acute renal failure (ARF). Many authors have reported a decrement of peripheral nerve conduction velocity and a normal or a slightly delayed intracranial conduction time in patients with CRF, and these abnormalities have been found even in patients maintained on hemodialysis (12–15). While the conduction...
velocities decreases mainly in the peripheral nervous system, the central nervous system appears to be also affected functionally in CRF. Lewis et al reported that longer latency and larger amplitude in long latency SEP were observed in patients with long-standing uremia compared to an age matched control group (16). In addition, abnormalities both in visual evoked potentials (VEP) (17, 18) and in electroencephalogram (EEG) (19, 20) have been observed in patients with CRF.

In patients with ARF, despite striking abnormalities in the EEG (3), the nerve conduction velocity is unaffected (21). A normal nerve morphometry in acute uremic patients has recently been reported (22). Thus, in ARF, a profound encephalopathy is not uncommon, whereas the peripheral nervous system is damaged to a lesser degree (1). There have been no detailed studies, however, concerning the effect of acute uremia on the SEP. In the present study, increased interpeak latencies and augmented amplitudes of the SEP without prolongation of the peripheral conduction velocity in acute uremic rats suggest that ARF affects mainly the central nervous system rather than the peripheral nerve. Furthermore, normal latency of the P1 in uremic rats indicates that prolongation of the CCT in ARF depends not on dysfunction of the medial lemniscus but on that of the thalamus and/or the thalamo-cortical projection.

An augmentation of SEP amplitude might indicate a neuronal hyperexcitability of the cerebral cortex or a decrease in the cortical suppression of the reticular system of the brain-stem in uremia (23). Myoclonus, convulsion or tetany is not uncommon in uremia and those symptoms probably signifies both central and peripheral neuronal irritability (1). We have also reported an augmentation of SEP amplitude in rats (6) as well as patients (24) with hypocalcemia indicating a hyperexcitability of the central nervous system.

In acute uremia, there are many factors which have possibilities of effects on the central nervous system. Further studies on these factors in acute uremia seems to be necessary.

REFERENCES


