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Somatosensory evoked potentials in patients with hypocalcaemia after parathyroidectomy

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Summary. The effects of hypocalcaemia on somatosensory evoked potentials (SEPs) were studied in five patients after parathyroidectomy. Despite normal latencies the mean value of amplitudes of the SEPs in hypocalcaemic patients was greater than that in normocalcaemic subjects. Recovery functions of the SEPs showed a significant decrease in hypocalcaemic patients at interstimulus intervals of about 10 ms compared with those in normocalcaemic patients and in normal volunteers. Recovery functions appear to be a valid indicator of synaptic efficacy, especialy for evaluation of the reduction in conduction efficacy of the central nervous system in hypocalcaemia.

Key words: Parathyroidectomy – Hypoparathyroidism – Hypocalcaemia – Somatosensory evoked potentials – Recovery functions

Introduction

Calcium ions play an important role in the regulation of the excitability of the central and peripheral nervous systems. With low serum calcium concentrations various neurological symptoms may occur. The cardinal syndrome associated with hypocalcaemia is commonly referred to as tetany, which can be broadly characterized by paraesthesias, muscle cramps, carpopedal spasms, and convulsions [2]. Central nervous manifestations in hypocalcaemia are less common, but almost every type of seizure has been described.

Many have investigated the electroencephalogram (EEG) in patients with hypocalcaemia: the occurrence of bursts of high voltage paroxysmal slow waves associated with spikes and sharp waves is known to be characteristic of the EEG findings in hypocalcaemia [14]. There have been, however, few reports dealing with the relationship between the serum calcium concentration and somatosenory evoked potentials (SEPs).

In order to show the possible effects of hypocalcaemia on the central nervous system, the SEP and SEP recovery functions were studied in patients with hypocalcaemia after parathyroidectomy for primary hyperparathyroidism or malignant tumour of the thyroid gland.

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Subjects and methods

Subjects

Hypocalcaemic group. Five patients (4 females, 1 male) were studied. Their ages ranged from 54 to 66 years and their serum calcium concentrations from 6.2 to 8.6 mg/dl (normal range: 9.0~10.0 mg/dl).

Normocalcaemic group. Ten patients (9 females, 1 male), aged between 49 and 74 years, were studied as age-matched controls: 5 had osteoporosis, 3 urinary tract stone, and 2 mild essential hypertension. None of these patients showed any neurological complications, such as cerebral infarction, cervical spondylosis or peripheral neuropathy.

Normal volunteers. Twenty healthy volunteers (10 males, 10 females), ranging from 20 to 26 years in age, were also studied.

Methods

The subjects lay on an electrically shielded bed in a room at a temperature of 25 ± 1°C and were asked to relax and keep their eyes open during the whole examination. The 1500 EMG system II (DISA Elektronik A/S, Denmark) was used.

Somatosensory evoked potentials. The right median nerve was stimulated at the wrist with a constant current square wave (0.1 ms duration, 2 Hz repetition rate). Stimulus intensity was adjusted to 10% above the threshold for the motor response of the thenar muscles (4.0~11.0 mA). The three recording electrodes, made from silver discs, were placed on the skin at the right Erb's point, at the spinous process of the seventh cervical vertebra, and at the left parietal somatosensory area (2 cm posterior to and 7 cm to the left of the vertex). The reference electrode was placed on the forehead (Fpz). Additionally, peripheral nerve action potentials were recorded at the elbow. The bandpass extended from 10 to 1000 Hz and 256 samples were averaged. Peak latencies ($\overline{N9}$:Erb's point; $\overline{N13}$:C7 vertebra; $\overline{N20}$:parietal scalp) and interpeak latencies [central conduction time (CCT):$\overline{N13}$-$\overline{N20}$] were evaluated directly on the screen by cursor. The amplitude between $\overline{P15}$ and $\overline{N20}$ and that between $\overline{N20}$ and $\overline{P25}$ were calculated on the basis of paper records.

SEP recovery functions. Recovery functions of the SEP ($N\overline{20}$-$P\overline{25}$) were obtained with various interstimulus intervals: 2.0, 2.5, 3.0, 4.0, 5.0, 6.0, 8.0, 10, 12, 15, 20, 25, 30, 40, 50, 60, 80, 100, 120, 150, 200, 250, 300, and 400 ms. Stimulus pairs were given, ranging from 500 to 750 ms apart, depending on the interstimulus intervals used. Conditioning and test stimuli were of the same intensity. Percentages of the ratio of amplitude of the test SEP (t-SEP) to that of the conditioning one (c-SEP) were calculated: (t-SEP/c-SEP) × 100. The test SEP, superimposed on the conditioning one, was obtained by subtracting the single stimulated SEP from the paired stimulated one with intervals of 60 ms or less. Mann-Whitney's U-test was used to calculate differences between these groups.

Results

Somatosensory evoked potentials

The peak latencies and CCT in the three groups are summarized in Table 1. There were no significant differences between these groups. Though the mean CCT value in the hypocalcaemic patients may appear to be slightly longer than that in the normal volunteers, there were no statistically significant differences between these two groups. Both amplitudes of $P\overline{15}$-$N\overline{20}$ and $N\overline{20}$-$P\overline{25}$ were significantly greater in the patients with hypocalcaemia compared with those in the normocalcaemic patients and in the normal volunteers, as shown in Fig. 1.

Table 1. Peak latencies and interpeak latencies of somatosensory evoked potentials in hypocalcaemic patients, normocalcaemic patients and normal volunteers

	$N\overline{9}$ (ms)	$N\overline{13}$ (ms)	$N\overline{20}$ (ms)	CCT (ms)
Hypocalcaemic patients ($n = 5$)	9.0 8.1~9.8	12.6 11.2~13.9	18.9 16.9~20.4	6.4 5.7~7.0
Normocalcaemic patients ($n = 10$)	9.1 8.5~9.6	13.0 12.0~13.8	19.1 18.4~20.7	6.1 5.2~7.2
Normal volunteers ($n = 20$) (mean ± SD)	9.0±1.6	12.6± 1.4	18.4± 1.8	5.8±0.8

For each group of patients, the upper row is mean peak latency and the lower row is lower and upper range of latency

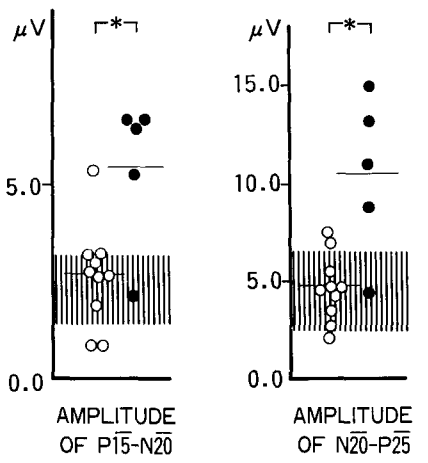

Fig. 1. Amplitudes of somatosensory evoked potentials in hypocalcaemic patients (●) and normocalcaemic patients (○). *Horizontal bar* represents the mean value of each group. The *hatched areas* represent the mean ± SD range in the normal volunteers. ✻ $P < 0.05$, significant differences between hypocalcaemic patients and normocalcaemic patients

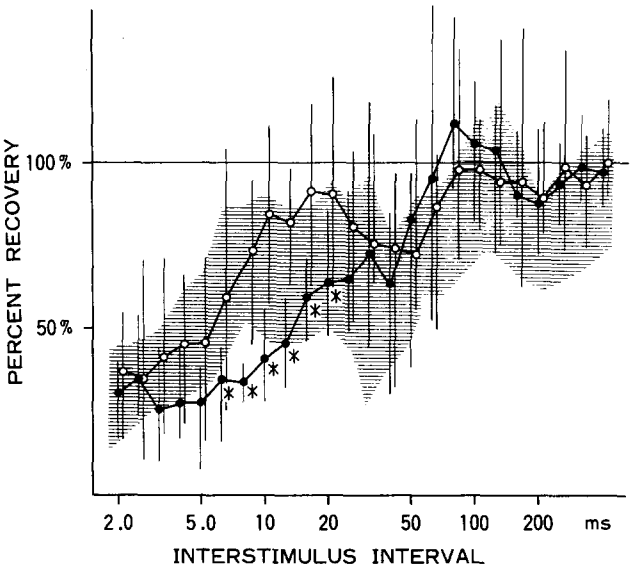

Fig. 2. Recovery functions of somatosensory evoked potentials (SEPs) in hypocalcaemia patients (●) and normocalcaemic patients (○). Each *point* represents the mean value of percentages of the ratio of amplitudes of the test SEP to that the conditioning one and a *vertical bar* represents upper and lower range of the percentages. The *hatched area* represents the mean ± SD range in normal volunteers. ✻ $P < 0.05$, significantly different from normocalcaemic patients

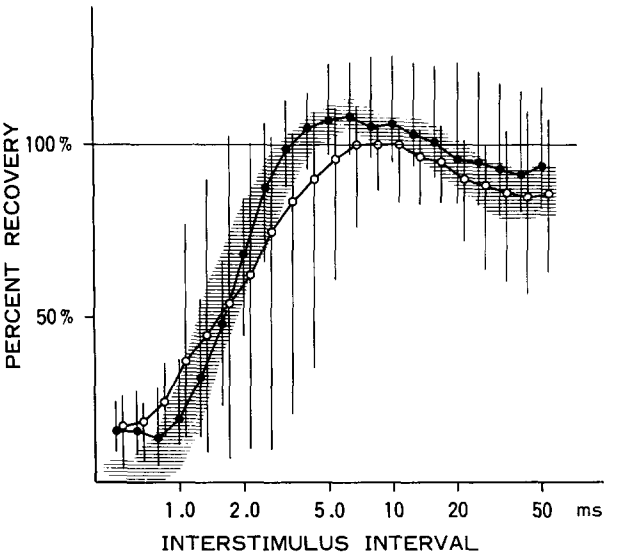

Fig. 3. Recovery functions of the peripheral nerve action potentials (NAPs) in hypocalcaemic patients (●) and normocalcaemic patients (○). Each *point* represents the mean value of percentages of the ratio of amplitudes of the test NAP to those of the conditioning one, and a *vertical bar* represents upper and lower range of the percentages. There were no significant differences between the two groups in any of the interstimulus intervals. The *hatched area* represents the mean ± SD range in normal volunteers

SEP recovery functions

In the normal volunteers, as the interstimulus intervals increased, the amplitude of the test SEP ($N\overline{20}$-$P\overline{25}$) was partly recovered at intervals of about 10 ms, somewhat reduced between 20 and 50 ms, and then subsequently recovered before 400 ms. Recovery functions of the SEP in the normocalcaemic patients were no different from those in the normal volunteers. In the hypocalcaemic patients, however, recovery functions of the SEP significantly decreased in comparison with those in the normocalcaemic patients at intervals ranging from 6 to 20 ms, as well as with those in the normal volunteers (Fig. 2). Recovery functions of the peripheral nerve action potentials were not significantly different between the hypocalcaemic patients and the normocalcaemic patients; full recovery was achieved well before an interstimulus interval of 5 ms (Fig. 3).

Discussion

Despite the familiaity of neural hyperexitability in hypocalcaemic patients, there have been few detailed studies concerning the effect of hypocalcaemia on cerebral evoked potentials. In 1971, Buchsbaum and Henkin [1] reported an association of low serum calcium concentrations with greater amplitude and shorter latency visual evoked potentials (VEPs) compared with high serum calcium concentrations. In view of the lack of effect of intravenous administration of parathyroid extract on the VEP latency or amplitude, they emphasized the serum calcium concentration as the significant variable in their study. Watanabe et al. [16], however, reported normal VEPs and auditory evoked potentials in most of the severely hypocalcaemic newborns and failed to find any correlation between peak latencies and serum calcium concentrations. Recently, auditory brain-stem responses (ABRs) were investigated by Pratt et al. [6] in patients with hypocalcaemia caused by renal failure. The prolongation of peak and interpeak latencies in hypocalcaemia was augmented on an increased stimulus rate. Because it was suggested that the increased stimulus rate was sensitive to impaired synaptic efficacy, they proposed that calcium might be an important factor influencing synaptic transmissions in ABR generators.

The first SEP study in hypocalcaemia was performed by Smits et al. [12] in patients with primary hypoparathyroidism. Despite normal latencies of specific complexes (N20, P45) reflecting the spinothalamocortical projection, delayed latencies of non-specific complexes (P100, P200), were observed which seemed to be a reflection of the diffuse spread of sensory information over the cortex. Those patients had shown mental deterioration, striocerebellar symptoms and calcification in the cerebrum, suggesting a possible involvement of factors other than hypocalcaemia in the changes in SEP. None of our patients showed cerebral calcification or neurological complications except for "tetany".

Normal latency and augmented amplitude of the SEP in the hypocalcaemic patients in the present study suggest the influence of hypocalcaemia not on the conduction velocities, but on the excitability of the central nervous system (CNS). Furthermore, the recovery functions of the SEP were reduced more profoundly in the hypocalcaemic patients than those in the normocalcaemic patients, but there were no differences in the recovery functions of the peripheral nerve action potentials between the two groups. The reduction in the recovery functions of the SEP is thus apparently not influenced by any changes through the peripheral nervous system in hypocalcaemia.

The signifcance of recovery functions of the SEP has been investigated in detail by Shagass and Schwarts [10], who reported a less early recovery in the patients with psychotic depressive syndromes than in the non-patient group. They also studied the effects of different states of alertness on SEP recovery functions, concluding that the probably reflected generalized changes in excitability of the CNS on the recovery change [8]. In addition, many authors have reported facilitation of recovery functions of the SEP which seemed to be a reflection of hyperexcitability of the CNS in patients with myoclonus [3, 11, 13, 15]. Furthermore, experimental studies have revealed a reduction in the recovery functions of the SEP with low doses of pentobarbital introducing a functional block of the brain-stem reticular system; higher doses, however, would exert a depressent effect directly on the thalamic relay nuclei, followed by a marked reduction in amplitude of the SEP [5, 9]. Summarizing these studies, recovery functions of the SEP can largely be a reflection of synaptic efficacy in the thalamus, probably influenced by the brain-stem reticular system [5, 9] and other components of the CNS [8, 10]. In the present study, the decrease in the recovery functions in hypocalcaemic patients may reflect the reduction in conduction efficacy of sensory pathways through the CNS in hypocalcaemia.

The opposite effects of calcium ions have long been known in neuronal excitability and synaptic transmission. Decreases in external calcium concentration give rise to a decrease in the transmembrane potential difference, consequently causing an increase in neuronal excitability [2]. On the other hand, in synapses calcium ions have a facilitatory and essential role in the release of transmitter [7]. Decima [4] reported an absence of the monosynaptic spinal reflex in hypocalcaemia, which was restored after intravenous injection of calcium ions. Such contradictory effects of hypocalcaemia on neuronal excitability and synaptic efficacy might explain our findings of an augmentation of the amplitude of the SEP with a reduction in the SEP recovery functions in patients with hypocalcaemia.

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