Neurophysiologic study of patients with Parkinson's disease and patients with persistent pain after spinal surgery

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【Background】

Pain is a common non-motor symptom of Parkinson's disease (PD), occurring in 40 to 85 % of patients with PD [1-3]. Pain is one of the most troublesome symptoms of PD, and is associated with reduced health-related quality of life. PD has been shown to exhibit abnormal central pain processing, although underlying mechanisms are not fully understood.

In general, it is difficult to evaluate the degree of pain objectively, while pain-related evoked potentials have been considered to be one of the reliable objective assessments of pain processing. Pain-related evoked potentials may be recorded by laser, heat and mechanical stimulations. Recently, Inui et al. [4] recorded evoked potentials induced by epidermal electrical stimulation using a thin needle electrode, which can specifically activate the Aδ fiber-mediated pain mechanism.

【Objective】

The aim of this study is to investigate dysfunction of the central pathway of pain in patients with PD and patients with persistent pain after spinal surgery using pain-related evoked potentials induced by intra-epidermal electrical stimulation.

Table 1 Subject

	Age(year)	Gender(M/F)
Normal Controls (n=12)	59.6±10.7	7/5
PD with pain (n=15)	64.3±9.0	7/8
PD without pain (n=8)	63.4±9.5	4/4
Patients with persistent pain (n=6)	69.5±7.5	3/3

Data are presented as mean ± S.D.

Table 2 Clinical characteristic of PD

	PD with pain	without pain
Duration(years)	4.9±3.1	6.8±3.4
Hoehn-Yahr stage	3.3±0.4	3.4±0.7
UPDRS	43.5±14.7	52.0±25.3
SDS	42.9±7.9*	34.3±6.3
MMSE	29.3±1.0	28.9±2.1
L-dopa (mg/day)	330±168.8	431.3±171.0

*p<0.05 compared to PD patients without pain.
UPDRS: Unified Parkinson's Disease Rating Scale
SDS: Self-rating Depression Scale (Zung)
MMSE: Mini Mental State Examination

Table 3 Patients with persistent pain after surgery

case	Diagnosis (after surgery)	Gender	Age	Parts of pain
①	Lumber herniated intervertebral disc	male	73	Left upper leg, both lower legs
②	Lumber herniated intervertebral disc	male	70	both lower legs
③	Lumber herniated intervertebral disc	female	68	both lower legs
④	Lumber pseudo arthrosis	female	70	both lower legs
⑤	Cervical herniated intervertebral disc	male	65	both upper, lower legs
⑥	Cervical ossification of posterior longitudinal ligament	female	71	both upper, lower legs

【Methods】

Pain-related evoked potentials induced by Intra-epidermal electrical stimulation

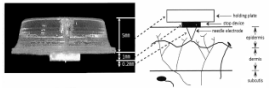


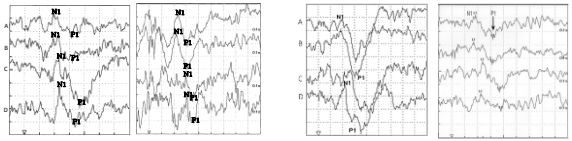
Fig. 1 Picture of a needle (left) and a schematic drawing of its insertion in the epidermis (right) by Inui et al. [4]

To produce a pain stimulus, intra-epidermal electrical stimulation, which selectively stimulates Aδ fibers, was applied to the second digit on each of the 4 limbs.
A pushpin-type needle electrode with a needle tip 0.2 mm in length was used.
The stimulus was a square-wave pulse.
Interval was 3 - 10 sec (at random). Duration was 0.5ms.
Intensity was 0.12 - 0.6 mA (3 times the pain threshold for each subject).

- Evoked potentials were recorded from the vertex (Cz) and referenced to a linked earlobe electrode of the International 10-20 system.
- The impedance for each electrode was < 5kΩ.
- 5 responses were collected and averaged per trial, and 2 trials were recorded.

The protocol of our study was approved by the Ethics Committee of Hyogo College of Medicine, and written informed consent performed from controls or patients.

【Results】



PD patient with pain (male,53ys) | PD patient without pain (female,73ys) | Control subject (male,70ys) | Patient with persistent pain (male,65ys)

Fig. 2 Pain-related evoked potentials in a control subject and patients.
A: right hand, B: left hand, C: right leg, D: left leg

Major negative (N1) and positive (P1) deflections were observed after each stimulation. N1/P1 amplitude was measured between N1 and P1 peaks. Note the reduced N1/P1 amplitude in patients with PD and a patient with persistent pain compared with a control subject.

Table 4 N1/P1 amplitudes and N1, P1 latencies in controls and patients

		N1/P1 amplitude(μV)	N1 latency(ms)	P1 latency(ms)
Normal Controls	upper limbs	35.8±12.4	189.6±15.2	299.8±18.2
	lower Limbs	31.2±9.8	231.9±33.2	347.7±24.5
PD with pain	upper limbs	25.2±9.9*	202.1±29.6	313.3±35.2
	lower Limbs	24.5±9.8*	242.3±29.7	354.3±37.0
PD without pain	upper limbs	23.2±7.7*	198.1±21.8	297.1±23.4
	lower Limbs	20.2±8.2*	232.1±36.8	324.7±36.6
Patients with persistent pain				
	upper limbs	19.5±7.1*	176.9±31.2	296.6±29.2
	lower Limbs	20.0±7.5*	231.5±30.2	348.1±38.2

*p<0.01 compared to normal controls.

【Discussion】

The N1/P1 amplitudes were significantly lower in PD patients with or without pain and patients with persistent pain after surgery compared with controls. Although the precise origin of the N1/P1 complex remains uncertain, there is evidence that several brain structures devoted to the processing of nociceptive input, including the cingulate cortex and the insula [5,6], contribute to N1/P1 complex generation. The N1/P1 reduction in patients with PD might reflect nigrostriatal impairment leading to dysfunction of inhibitory control exerted by the basal ganglia on the areas of the CNS devoted to pain stimulation. In addition, there was no difference in N1/P1 amplitudes between patients with PD and patients with persistent pain after surgery. These results may show the existence of abnormal central processing of pain in PD patients with or without pain, as well as patients with persistent pain after spinal surgery.

【Conclusion】

The present results may show the existence of abnormal central processing of pain in PD patients with or without pain, as well as patients with persistent pain after spinal surgery.

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