

## SHORT REPORT

## Central motor and sensory conduction in X-linked recessive bulbospinal neuronopathy

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### Abstract

**Central conduction was studied in 12 patients with X-linked recessive bulbospinal neuronopathy (XBSN) using percutaneous electrical cortical, cervical and lumbar stimulation and somatosensory evoked potentials (SEPs). The central motor conduction time from the motor cortex to the cervical and lumbar segments of the spinal cord was normal in XBSN. SEPs, however, were abnormal or central sensory conduction time was prolonged in patients with XBSN. These results are consistent with the clinicopathological findings of XBSN in which the primary sensory neurons are involved as well as the lower motor neurons in the CNS, whereas the upper motor neurons are well preserved.**

Progressive bulbar and spinal muscle atrophy with X-linked recessive trait is characterised by adult-onset slowly progressive motor neuron symptoms such as proximal neurogenic muscular atrophy with contraction fasciculation, bulbar signs and endocrinological abnormalities such as gynaecomastia, testicular failure and impaired glucose tolerance.<sup>1-3</sup> Since primary sensory neurons have recently been shown to be affected as well as lower motor neurons, this disease is now designated as X-linked recessive bulbospinal neuronopathy.<sup>4-6</sup> Pathological studies have demonstrated that the descending motor pathways in the pyramidal tract are well preserved, whereas axons in the posterior column of the spinal cord are involved in a distally-accentuated manner. However, the electrophysiological aspects of these changes have not yet been studied. We investigated both the descending motor and ascending somatosensory pathways in the central nervous system in this disease, using percutaneous transcranial electrical stimulation of the brain and somatosensory evoked potentials.

### Patients and methods

We studied twelve male patients with X-linked recessive bulbospinal neuronopathy (XBSN) ranging in age from 39 to 70 years. The duration of disease ranged from two to 29 years. All except one had a family history of a similar disease. Postural finger tremor was the initial symptom in 9 patients. In 3 patients, the

illness started with gait disturbance. Contraction fasciculation was noted in all patients. Muscle atrophy and weakness were predominant in the proximal portion of the extremities, especially in the upper limbs. Mild dysphagia and dysarthria were present in all patients. Deep tendon reflexes were diminished in most patients. One patient had experienced cerebral thrombosis resulting in left hemiparesis, and examination showed an extensor plantar response in the left foot. There was mild sensory impairment in the lower extremities in 6 patients. Gynaecomastia was also a common symptom, and was seen in 9 patients. Electromyographic changes such as reduced interference patterns, high amplitude potentials (greater than 6 mV), polyphasic units, positive sharp waves and fasciculation potentials were common in all patients.

To study the descending pathways, stimulation was carried out with a capacitive discharge device (Digitimer D 180) which produces a maximum output voltage of 750 V with time constants of 50  $\mu$ s and 100  $\mu$ s. Ag/AgCl surface electrodes with a diameter of 1 cm were used for stimulation and EMG recordings. To stimulate the hand motor area of the cerebral cortex the cathode was applied to the vertex and the anode was applied 7 cm laterally on a line from the vertex to the external auditory meatus. For cervical stimulation the anode was placed in the midline over the C6 spinous process and the cathode was placed over the T1 spinous process. The recordings were made by the electrodes in pairs about 3 cm apart over the thenar eminence. When the anterior tibial muscle was being studied, the anode for scalp stimulation was placed at the vertex and the cathode was placed 5 cm anterior to the vertex. For lumbar stimulation, the anode was positioned in the midline over the L1 spinous process and the cathode was positioned over the L3 spinous process. Recordings were made on the middle of the anterior tibial muscle on both sides. Signals were amplified, filtered (band pass 20 Hz-3 kHz), and stored with an electromyograph (Nihon Koden MEM 4104) for further investigation. The patients were instructed to contract the examined muscles very slightly when the scalp stimulation was delivered so that the shortest conduction time was obtained each time. The time from scalp stimulation to the onset of evoked EMG activity in the thenar muscle contralateral to the anode was taken as the cortical latency. The time from cervical

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Received 15 March 1991  
and in revised form 1 July  
1991.

Accepted 11 July 1991

stimulation to the onset of EMG activity was taken as the cervical latency. The difference between cortical and cervical latencies in the same muscle was designated as the central motor conduction time from the cerebral cortex to the cervical segment of the spinal cord (C-CMCT). The central motor conduction time from the cortex to the lumbar segment of the spinal cord (L-CMCT) was estimated by subtracting the latency to onset of the anterior tibial muscle EMG activity after lumbar stimulation (lumbar latency) from the latency to onset of EMG activity after scalp stimulation (cortical latency). L-CMCT was studied in 10 patients.

In all patients somatosensory evoked potentials (SEPs) were obtained by separate stimulation of the median nerve on both sides at the wrist, and were recorded from the contralateral parietal scalp (2 cm posterior to C3 or C4 by International 10-20 system) and from the posterior neck at the level of the C5 spinous process. A common reference electrode was placed on the forehead (2 cm posterior to Fpz). Electrical stimulation was applied at 3 Hz with pulses of 0.1 ms duration, and an intensity approximately 20% above the motor

threshold. One thousand sweeps were averaged and stored with the same electromyograph used in the study of central motor conduction. The filter was set at 20 Hz (low cut) and 3 kHz (high cut). The difference in latency between N19 of the cortical SEPs and N13 of the cervical SEPs was taken as the central sensory conduction time from the cervical region to the somatosensory cortex (C-CSCT). In 10 patients, SEPs performed by stimulation of the tibial nerve were recorded from the parietal scalp (2 cm posterior to Cz) and from the back at the level of the T12 spinous process. The reference electrodes were placed on the forehead (2 cm posterior to Fpz) for the parietal scalp and at the level of the T10 spinous process for the back. The tibial nerves on both sides were separately stimulated at the ankle with 0.2 ms pulses at 2 Hz. The intensity was approximately 50% above the motor threshold. One thousand sweeps were averaged and stored. The filter was set as for the median nerve stimulation. The latencies of the first positive peak of the cortical SEPs (P36) and of the first negative peak of the lumbar SEPs (N19) were measured. The difference in latency between P36 and N19 was taken as the central sensory conduction time from the lumbar region to the somatosensory cortex (L-CSCT).

The results were compared with CMCT and CSCT of 13 age matched normal volunteers. None of the subjects had had epileptic seizures, heart attacks or abnormal ECG findings. Informed consent was obtained from all subjects.

## Results

### 1) Central motor conduction time

In the normal controls C-CMCT ranged from 3.9 to 6.9 ms. The mean C-CMCT was 5.1 ms with a standard deviation (SD) of 0.69 ms. L-CMCT ranged from 11.0 to 15.0 ms with mean of 12.9 ms and SD of 1.24 ms in the normal controls. Generally, either C-CMCT or L-CMCT in XBSN was no longer than in controls, ranging from 3.2 to 5.9 ms for C-CMCT and from 10.2 to 15.6 ms for L-CMCT. No patient's values were more than 3 SD outside the control mean, except for one patient who had experienced a stroke with left hemiparesis, in whom an action potential could not be evoked in the left thenar muscle by scalp stimulation and the L-CMCT in the left anterior tibial muscle was prolonged (17.6 ms). The calculated mean C-CMCT was 5.2 ms (SD; 0.80 ms), and the mean L-CMCT was 13.7 ms (SD; 1.69 ms), excluding the paretic patient. There was no difference in C-CMCT or L-CMCT between the controls and the patients with XBSN.

### 2) Somatosensory evoked potentials (SEPs)

SEPs were obtained by median nerve stimulation in all patients except for one patient with stroke-associated left hemiparesis as shown in the table. In patient 4 cortical SEPs were not recorded after left median nerve stimulation. The latency of N19 was slightly longer in

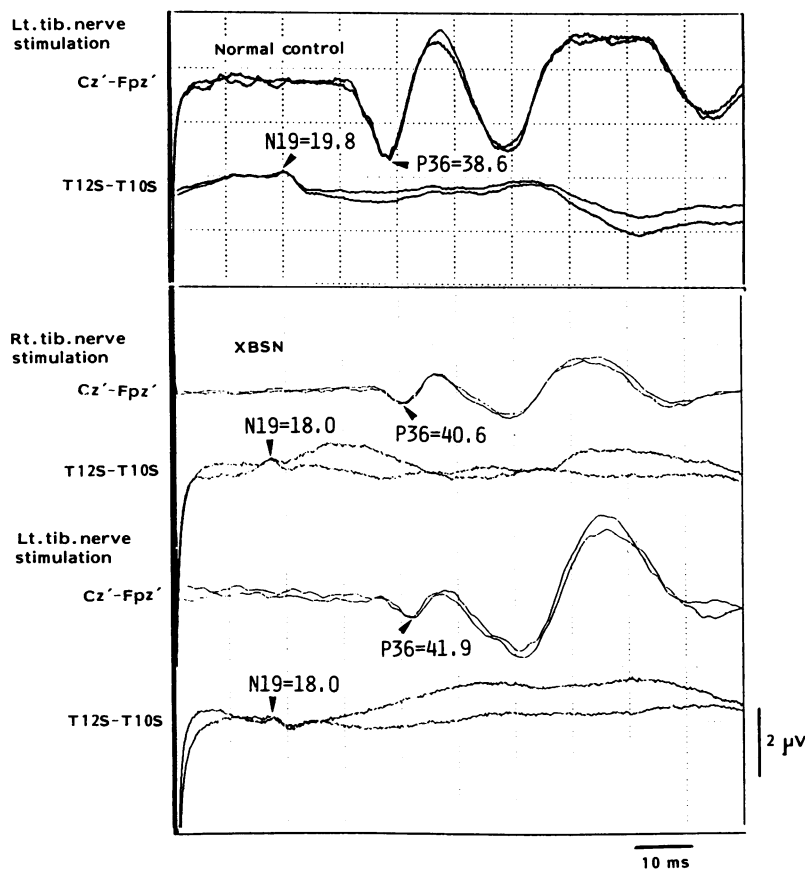


Figure Somatosensory evoked potentials (SEPs) after tibial nerve stimulation in a normal control subject (43 year old male) and in a patient with XBSN (Case 10). Arrows indicate the latencies of P36 and N19. P36 is prolonged on both sides in the patient. Since the latencies of N19 are normal, the estimated L-CSCT in the patient was prolonged on both sides.

Cz' and Fpz': 2 cm posterior to Cz and Fpz of the international 10-20 system. T12S and T10S: T12 and T10 spinous processes. Rt: right; Lt: left.

Table 1 Central sensory conduction time in X-linked recessive bulbospinal neuronopathy

Patient	Sex	Age	Side	Median nerve stimulation			Tibial nerve stimulation		
				Cortical N19 (ms)	Cervical N13 (ms)	C-CSCT (ms)	Cortical P36 (ms)	Lumbar N19 (ms)	L-CSCT (ms)
1	M	47	R	19.6	13.8	5.8	NE	NE	—
			L	19.7	13.8	5.9	NE	NE	—
2	M	62	R	22.0	14.4	7.6	48.7	NE	—
			L	22.7	15.6	7.1	NE	NE	—
3	M	69	R	22.6	14.4	8.2	ND	ND	—
			L	21.4	15.4	6.0	ND	ND	—
4*	M	59	R	21.8	14.0	7.8	ND	ND	—
			L	NE	14.4	—	ND	ND	—
5	M	51	R	20.6	14.4	6.2	42.2	NE	—
			L	20.1	14.3	5.8	40.4	19.6	20.8
6	M	70	R	25.8	15.4	10.4	NE	NE	—
			L	25.3	16.5	8.8	NE	NE	—
7	M	56	R	19.6	14.0	5.6	43.7	23.6	20.1
			L	19.6	14.3	5.3	46.4	23.8	22.6
8	M	39	R	18.9	13.5	5.4	NE	21.2	—
			L	18.8	13.2	5.6	NE	NE	—
9	M	41	R	18.1	12.5	5.6	36.9	20.3	16.6
			L	18.5	12.8	5.7	39.3	19.2	20.1
10	M	55	R	18.7	13.2	5.5	40.6	18.0	22.6
			L	18.7	12.6	6.1	41.9	18.0	23.9
11	M	59	R	18.7	12.6	6.1	34.8	20.1	14.7
			L	18.2	12.9	5.3	35.1	18.7	16.4
12	M	58	R	19.3	13.6	5.7	40.5	NE	—
			L	19.4	13.5	5.9	39.6	NE	—
Mean				20.4	14.0	6.4	40.8	20.3	19.8
SD				2.14	1.03	1.31	4.01	2.08	3.19
Normals (N = 11, 18 sides)		Mean		18.9	13.2	5.7	37.1	20.5	16.5
		SD		1.01	1.07	0.39	2.12	2.50	1.47
		(Mean + 3 SD)		21.9	16.4	6.9	43.4	28.0	20.9

NE: not evoked or not detected; ND: not done.

\*Patient 4 had a stroke resulting in left hemiparesis.

XBSN than in normal controls (table). The measured C-CSCT was also prolonged in 4 patients. Obvious abnormalities were frequently seen in the SEPs after tibial nerve stimulation. The figure shows SEPs in a normal control subject and in a patient with XBSN. P36 in the cortical SEPs was sometimes undetectable. The latency of P36 was prolonged (longer than 43.3 ms) in 2 of the patients whose cortical SEPs could be recorded. Lumbar SEPs could not be recorded on at least one side in 5 patients, but the latency of N19 was normal in the patients whose lumbar SEPs were recorded. L-CSCT either could not be estimated or was prolonged in 9 out of 10 patients.

### Discussion

Recent advances in techniques for percutaneous electrical and magnetic stimulation have made it possible to investigate the descending pathways in the central nervous system without using surgical procedures.<sup>7-9</sup>

Early studies have demonstrated that the conduction time in the corticomotoneuronal pathway is prolonged in multiple sclerosis,<sup>10</sup> several types of myelopathy,<sup>11</sup> cerebrovascular disorders<sup>12</sup> and motor neuron disease (MND).<sup>13,14</sup> In most of these disorders, the corticospinal pathway is pathologically involved. The conduction time is normal in Huntington's disease, essential tremor and Parkinson's disease in which the corticospinal tract is spared.<sup>15</sup> These findings suggest that if the CMCT is intact, at least the fastest fibres in the corticospinal tract are not involved, although a significantly prolonged CMCT does not always indicate prolonged corticospinal conduction.<sup>16</sup> Our results strongly suggest

that the corticospinal tract (upper motor neurons) in XBSN is functionally well preserved. They also confirm previous pathological reports that there are no obvious morphological changes in the pyramidal tracts in this disease.<sup>2-4</sup>

Since the electrical stimulation delivered to the cervical and lumbar vertebrae will excite the motor root at a site immediately proximal to the spinal cord,<sup>17-20</sup> CMCT in this study must include synaptic delay in the anterior horn and a very short conduction in the ventral root as well as the conduction from the motor cortex to the anterior horn of the spinal cord. However, CMCT in this study was normal in XBSN, even though the anterior horn cells and ventral roots were severely damaged.<sup>2,3,6</sup> Relatively long cervical and lumbar latencies in a few cases of XBSN may be caused by severe anterior root involvement; however, CMCT is almost completely preserved if the corticospinal tract is spared, even though lower motor neurons are involved. Furthermore, it has been suggested that the fastest descending fibres in the central nervous system are not impaired in XBSN, whereas it is well documented that in MND the large myelinated fibres are depleted in the corticospinal tract.<sup>21</sup>

In contrast, SEPs were frequently abnormal and CSCT was prolonged in most cases of XBSN. Although some authors have reported that SEPs are abnormal in MND,<sup>22-24</sup> the abnormality of SEPs and the prolongation of CSCT in XBSN were more obvious. The absence of lumbar SEPs may be caused by a peripheral sensory nerve lesion. Nevertheless, the prolongation of CSCT in XBSN indicates an abnormality in the sensory pathways, including those in the central nervous system. Recently, morphological investigations have

demonstrated degeneration of the distal portion of the central rami of primary sensory neurons in the spinal cord<sup>6,25</sup> in XBSN. In fact, some patients, showed mild sensory disturbances in their legs. The abnormalities in SEPs, especially those measured by tibial nerve stimulation in this study, correspond well with the clinical and morphological findings. The changes in SEPs may also show subclinical features, because CSCT was significantly prolonged even in patients without sensory symptoms.

We conclude that the results of these electrophysiological studies are consistent with the clinico-pathological findings in XBSN. These physiological studies may be helpful in diagnosing XBSN in its early stage or in cases without information on family history.

This work was supported by a grant from the Research Committee of CNS Degenerative Diseases, the Ministry of Health and Welfare of Japan.

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