Single fibre electromyography in central core disease

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SUMMARY Single fibre electromyography in the extensor digitorum communis muscle was studied in five patients with central core disease. The average number of muscle fibre action potentials belonging to the same motor unit was higher in patients than in healthy subjects of the same age. The increase in motor unit fibre density is consistent with increased terminal innervation ratio described in other papers about central core disease.

Central core disease was first described by Shy and Magee (1956) in five patients of the same family. Hypotonia, non-progressive myopathy with proximal weakness, occasionally facial impairment, and skeletal deformities such as congenital hip dislocation, pes cavus, and kyphoscoliosis, are the main clinical manifestations. Cases without muscular weakness and with only pes cavus have also been described (Telerman-Toppet *et al.*, 1973).

Electromyographic study has been described as normal, myopathic (Mrozeck *et al.*, 1970), or neurogenic with polyphasic potentials of long duration and increased voltage (Isaacs *et al.*, 1975). Nerve conduction velocities are normal (Isaacs *et al.*, 1975; Bethlem, 1977) or slowed (Hooshmand *et al.*, 1971).

The results of the electromyographic and recent muscle biopsy studies (Telerman-Toppet *et al.*, 1973; Isaacs *et al.*, 1975; Cöers *et al.*, 1976) indicate a neurogenic basis for the disease (Engel and Warmolts, 1973; Telerman-Toppet *et al.*, 1973; Isaacs *et al.*, 1975; Bethlem, 1977).

In this paper we present the results of single fibre electromyographic study in five patients with central core disease.

Method

Single fibre EMG was performed according to the technique described by Ekstedt (1964), Ekstedt and Stålberg (1973), and Stålberg and Ekstedt (1973).

Medelec MS6 equipment was used. A special

electrode (Medelec SF25) with a recording area of 25 μm diameter was inserted into the right extensor digitorum communis muscle (EDC) during slight voluntary contraction. A delay line of 20 ms and a low frequency limit of 500 Hz were used to reduce activity recorded from distant fibres. Action potentials were recorded on a photo-sensitive film and displayed on a storage oscilloscope.

The fibre density of the motor unit was studied according to the technique of Stålberg and Thiele (1975), determining the average number of muscle fibres belonging to the same motor unit with action potential exceeding 200 μV and within the uptake area of the electrode. The average number was calculated for 20 random and different electrode positions.

The jitter interval of the double or complex potentials was calculated manually (Ekstedt *et al.*, 1974) from superimposed recording. Mean range of five (MR5) or ten (MR10) was measured and the conversion factor (0.49 or 0.37 respectively) applied to calculate the mean consecutive differences (MCD) of the interpotential interval values. In normal subjects MCD varies between 5 and 50 μs (Ekstedt *et al.*, 1974).

Subjects

Three males and two females, belonging to two families and aged 13 to 43 years (mean age 22 years), were investigated (Table 1). The diagnosis of central core disease was based on the findings of muscle biopsy. Cases 1, 2, and 3 were siblings. Case 5 was the father of case 4 (Table 1).

The main clinical features of the patients are

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Table 1 Main features in five patients with central core disease. Cases 1, 2, and 3 are siblings. Cases 4 (son) and 5 (father) belong to another family

Case	Age (yr)	Sex	Delayed motor development	Facial weakness	Proximal weakness	Distal weakness lower limbs	Tendon jerks	Deformities
1	14	M	+	+	+	+	↓	Pes cavus
2	17	F	+	+	++	+	↓	Pes cavus
3	24	F	+	+	+++	+	↓	Pes cavus
4	13	M	+	—	+	—	↓	Kyphoscoliosis
5	43	F	?	—	+	—	↓	—

shown in Table 1. All the cases had hypotonia and delay in motor milestones during infancy.

The muscle biopsy samples showed the typical findings described in this disease. One or several cores were seen in the centre of the muscle fibres. The cores were present only in the type 1 fibres, except in case 2 where they were also present in a few type 2 fibres. The proportion of type 1 fibres with cores varied from 15% (case 4) to 100% (case 1). A normal mosaic of type 1 and 2 fibres was seen in case 4. The other patients showed a type 1 fibre predominance. In case 5, 90% of the fibres were of type 1. Splitting of the fibres was also observed.

The control group consisted of 20 healthy subjects, 11 males and nine females, aged from 8 to 43 years (mean age 21 years). All the control subjects had no history, signs, or symptoms of neuromuscular diseases. Clinical examination was normal.

Results

The mean value of the motor unit fibre density in EDC was 1.51 fibres per recording area (SD=0.091; SE=0.02) in control subjects (range: 1.35–1.65) (Fig. 1).

The jitter in the control group was calculated from 92 potentials. The mean value of the MCD was 29.3 μ s (SD=10.38; SE=1.09) with a range from 9.2 to 53.6 μ s. Only three measurements were over 50 μ s (51.8, 51.8, and 53.6 μ s) (Fig. 2).

In normal subjects, single muscle fibre potentials were recorded in 55.3% of the random electrode insertions. In 38.3% of the points, potentials from two fibres were registered. Only in 6.3% of the insertions were potentials belonging to three or four fibres of the same motor unit observed (Fig. 3).

The mean value of the motor unit fibre density in five patients with central core disease was 2.22 fibres per recording area. Individual values are shown in Table 2 and Fig. 1. All the values are above the normal limits for healthy subjects.

In central core disease the jitter was measured in 31 complex potentials. The mean value of the MCD was 28.6 μ s, with a range from 9.2 to 48.1 μ s (Figs. 2 and 4). All the values are within the normal limits for healthy subjects of the same age. No impulse blocking was observed. The highest values of the jitter usually correspond to late components of a complex potential with three, four or more fibres.

In central core disease single potentials were

Fig. 1 Fibre density mean value (full line) and two standard deviations above and below the mean (interrupted lines) in control subjects (○) (20 healthy subjects, 8–43 years, mean age 21 years), and patients with central core disease (●) (five patients, aged 13–43 years, mean age 22 years). Mean value in control subjects=1.51±0.091, and in patients with central core disease=2.22.

Fig. 2 Jitter. MCD values. Mean value in control subjects (92 potentials): $29.3 \mu s \pm 10.38$. Mean value in central core disease (31 potentials): $28.6 \mu s$. ● = individual values in central core disease. Full line indicates mean value in control subjects, and interrupted lines two standard deviations above and below the mean.

Fig. 3 Percentage of random electrode insertions in which potentials from one, two, three, four, or more fibres are registered. □ = control subjects, ▨ = patients with central core disease.

Table 2 Fibre density of the motor unit and terminal innervation ratio in different reports. The results of the present study are included under fibre density in central core disease

Disease	Terminal innervation ratio*	Fibre density	References
Amyotrophic lateral sclerosis	1.80	3.3	Cöers <i>et al.</i> , 1973b; Cöers and Telerman-Toppet, 1977; Stålberg <i>et al.</i> , 1975
Syringomyelia	2.11	4.7	
Progressive spinal muscular atrophy	2.27	5.3	
Duchenne dystrophy	1.12	3.1	Cöers and Telerman-Toppet, 1977; Stålberg and Eksted, 1973
Central core disease	1.32	2.05	Isaacs <i>et al.</i> , 1975
	1.43	1.90	Cöers <i>et al.</i> , 1976
		2.00	
		2.65	
		2.50	

*Normal = 1.1 ± 0.05 (Cöers *et al.*, 1973a).

recorded only at 6% of the points. Potentials belonging to two fibres (63% of points), to three or four fibres (23%), and multiple potentials with more of four fibres (2%) were more frequent than in control subjects (Fig. 3).

Discussion

The patients in this series had clinical features and morphological changes consistent with central core disease. Results of clinical and morphological studies in three of these cases and conventional EMG in the same patients have been published previously (Pascual Castroviejo *et al.*, 1974; López-Terradas, and Conde, 1979).

Single fibre EMG can provide information about the pathology of the motor unit when no definite signs of abnormality are found in the conventional EMG. We could not find any reported results of this technique applied to the congenital myopathies.

Fig. 4 Normal jitter in two potential pairs in central core disease. (A) 24 years MCD (R_{10}) = 22.2 μ s (B) 43 years MCD (R_{10}) = 29.6 μ s. Potentials are registered at two different sweeps. In A (right) and B (top), only the second potential of the pair is seen.

The average of the motor unit fibre density per recording area of the electrode and the values of the MCD in our normal subjects are similar to those published by Stålberg and Thiele (1975) and Ekstedt *et al.* (1974).

Our patients with central core disease showed an increase in the values of the motor unit fibre density when we compared them with healthy subjects of the same age. Double and complex potentials with three, four, or more fibres belonging to the same motor unit were more frequent in central core disease than in normal subjects. The jitter was only measured in some potentials, with normal results. High but normal jitter (near 50 μ s) was observed in late components of some complex potentials. These values suggest that patients with central core disease have, in general, stable neuromuscular transmission.

Motor unit fibre density increases in different diseases. The highest values are observed in lower motor neurone disorders, such as amyotrophic lateral sclerosis, progressive spinal muscular atrophy, and syringomyelia (Stålberg *et al.*, 1975), but density is also high in myopathies, especially in Duchenne muscular dystrophy (Stålberg and Ekstedt, 1973). Increased fibre density indicates that the muscle fibres belonging to the same motor unit are increased per recording area of the electrode. It is usually the result of reinnervation and, in the EMG, generally corresponds to polyphasic and high amplitude action potentials and, possibly, to late components of the motor unit

potentials. These late components are the result of collateral sprouting with reinnervation of previously denervated muscle fibres (Borenstein and Desmedt, 1973). In the first phases of reinnervation, late components have an increased jitter and intermittent blocking. Afterwards, the neuromuscular transmission is more secure and the late components have a fixed latency (Borenstein and Desmedt, 1973). This theory is consistent with the results of single fibre EMG. (Stålberg *et al.*, 1975).

In our patients, increased motor unit fibre density was accompanied by an increased percentage (7% to 20%) of motor unit potentials with late components (López-Terradas and Conde, 1979). In normal subjects, only a maximum of 3% of the motor unit potentials show late components at 9–16 ms from the main component (Nissen-Petersen *et al.*, 1969).

Increased motor unit fibre density and motor unit potentials with late components are a striking feature in myopathies, especially in Duchenne dystrophy (Stålberg and Ekstedt, 1973; Stålberg *et al.*, 1974; Desmedt and Borenstein, 1973; 1976). Desmedt and Borenstein suggest that collateral innervation is also present in muscular dystrophy.

Study of the terminal innervation ratio (Cöers and Woolf, 1959; Cöers *et al.*, 1973a) shows that in normal subjects the mean is 1.1. In neurogenic atrophy the terminal innervation ratio is increased (Cöers *et al.*, 1973b), indicating an increased amount of branching. Although the motor unit fibre density is also increased in Duchenne dys-

trophy, the terminal innervation ratio is normal in this disease (Cöers and Telerman-Toppet, 1977). Obviously, increased peripheral branching is not the only cause of increment in the fibre density of the motor unit. In Duchenne dystrophy, it is observed that small clusters of regenerating muscle fibres receive innervation (Swash and Schwartz, 1977), split fibres (Aloisi *et al.*, 1974; Schwartz *et al.*, 1976), and a separate part of a fibre divided by segmental necrosis, which develops extra-junctional acetylcholine receptors (Katz and Miledi, 1964) and receives new innervation from unemployed axons (Cöers and Telerman-Toppet, 1977), can explain late components of the motor unit potentials and increased fibre density of the motor unit without an increased terminal innervation ratio.

In central core disease necrosis of the fibres is not a striking feature, whereas increased terminal innervation ratio was found by Isaacs *et al.* (1975) and Cöers *et al.* (1976). The increased motor unit fibre density in central core disease is less than the values observed in progressive diseases of the lower motor neurone (Table 2), but similar to those described in mild or moderately severe axonal neuropathies (Thiele and Stålberg, 1975). Increased terminal innervation ratio is well correlated with increased fibre density of the motor unit in lower motor neurone diseases (Stålberg *et al.*, 1975), and other processes such as in psychotic patients (Crayton *et al.*, 1977). In our series of cases of central core disease, the average value of the motor unit fibre density was increased by 46%, and the terminal innervation ratio was increased by 20–30% in the cases of Isaacs *et al.* (1975) and Cöers *et al.* (1976).

We think that the single fibre EMG study in our patients provides information about the motor unit in central core disease. We have previously commented that the EMG in central core disease is contradictory, since both myogenic and neurogenic changes are described (Mrozeck *et al.*, 1970; Hooshmand *et al.*, 1971; Isaacs *et al.*, 1975). Motor unit fibre density and terminal innervation ratio are consistent with a possible neural aetiology of the disease (Engel and Warmolts, 1973; Bethlem, 1977), since an increment of both parameters is only described in neuropathies. The process affects type 2 fibres, which disappear progressively and possibly suffer a transformation from type 2 to type 1 with predominance and cores in the latter (Telerman-Toppet *et al.*, 1973). Reinnervation of type 2 by type 1 fibres could explain the disappearance of type 2 fibres with the predominance of type 1 (Telerman-Toppet *et al.*, 1973), the collateral

branching with increased terminal innervation ratio (Isaacs *et al.*, 1975; Cöers *et al.*, 1976), the increased percentage of late components of the motor unit potentials, and the increment in motor unit fibre density.

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