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Nucleo-cytoplasmic Ratio in Ageing Skeletal Muscle

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Summary. In order to investigate possible changes in the nucleo-cytoplasmic ratio of the muscle fibres during ageing, samples of quadriceps femoris from 15 normal individuals whose age ranged from 17 to 82 years were studied (autopsy material). The mean lesser diameter and the number and size of the muscle fibre nuclei were calculated using a planimetric technique. It was found that nucleo-cytoplasmic ratio increased significantly after the age of 60 years. This was due to a decrease in the mean fibre size whilst the number and the size of myonuclei remained unchanged. The resemblance of this finding to denervation atrophy changes is noted.

Key words: Ageing – Skeletal muscle – Karyometry

Introduction

During normal fetal development, tissue growth is due to an increase in both the size and the number of cells. Cells may increase in size but only to a genetically determined limit which is characteristic for that tissue. This increase is accompanied by an increase in nuclear size in order to maintain an almost constant nucleo-cytoplasmic ratio. The relative constancy of this ratio in all tissues indicates the fundamental importance of nucleo-cytoplasmic interactions for the maintenance of normal cell metabolism.

Striated muscle consists of multi-nucleated muscle fibres and along with the syncytiotrophoblast of the placenta is regarded as one of the two syncytial tissues of the mammalian body (Muir 1970). The nucleo-cytoplasmic ratio during normal muscle ageing in this exceptional tissue does not appear to have been documented.

The elucidation of possible changes in the nucleo-cytoplasmic ratio would be helpful in understanding not only normal muscle ageing but also the muscle response to disease processes.

Material and Methods

Samples from left quadriceps femoris were taken at autopsy from 15 individuals within 5 to 30 h of death. According to their age they were divided in three groups. In group-A (3 males, 1 female), the age range was 17 to 30 years, in group-B 31 to 60 years (3 females, 1 male) and in group-C the 4 males and 3 females were more than 60 years. All persons had died suddenly, most of them in road accidents, and the remainder from cerebro-vascular accidents or heart attack. No signs or symptoms of any neuro-muscular disease were detected in their previous history. The clinical data of the examined persons are shown in Table 1.

Frozen sections 10 μm in thickness stained with haematoxylin and eosin were examined. The mean muscle fibre size was measured by the "lesser fibre diameter" method of Dubowitz and Brooke (1973). Muscle nuclear size was estimated by measuring the areas of at least 100 myonuclei closely apposed to transversely sectioned muscle fibres in 6–8 fields, using a planimetric technique, at a final magnification of X 1000 (Vassilopoulos et al. 1977). Finally the number of sarcolemmal nuclei per muscle fibre was computed. Nuclei residing in the connective tissue and centrally placed myonuclei were excluded. The nucleo-cytoplasmic ratio was calculated in each case.

Table 1. Clinical data of individuals studied

	Case	Age (years)	Sex	Cause of death	Past history
Group-A	1	26	M	R.A.[a]	–
	2	26	F	R.A.	–
	3	25	M	R.A.	–
	4	17	M	R.A.	–
Group-B	5	56	F	C.V.A.[b]	Cardiac myxoma
	6	54	M	C.V.A.	–
	7	54	F	C.V.A.	Mild diabetes
	8	32	F	C.V.A.	–
Group-C	9	82	F	H.A.[c]	–
	10	73	M	H.A.	–
	11	71	M	C.V.A.	Bronchitis
	12	70	M	C.V.A.	Mild diabetes
	13	66	M	Burns	–
	14	62	F	C.V.A.	–
	15	61	F	R.A.	Bronchitis

[a] Road accident
[b] Cerebrovascular accident
[c] Heart attack

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Table 2. Age range, mean fibre size and karyometric data for the three age groups studied (the results are expressed as mean ± 1 SD)

	Age (years)	Fibre size (μ)	Muscle fibre nuclei		Nucleo-cytoplasmic ratio
			Number	Nuclear size (μ^2)	
Group-A	17–30	42.3 ± 4.0	2.9 ± 1.0	14.8 ± 0.8	0.96 ± 0.19
Group-B	31–60	34.1 ± 7.9	2.1 ± 0.03	14.1 ± 2.8	0.87 ± 0.09
Group-C	>60	31.6 ± 3.9	2.4 ± 0.2	15.8 ± 2.5	1.19 ± 0.22

Results

The results of this study are summarised in Table 2. It can be seen that the muscle fibre size was reduced in group B and C. As for the myonuclei their number per muscle fibre and their size did not appear to vary between these groups. As a consequence of the above changes, the nucleo-cytoplasmic ratio was found to be significantly increased in group-C ($P<0.05$ from group-A and $P<0.01$ from group-B). This increased ratio suggested that as age progresses more nuclei correspond to a certain amount of cytoplasm.

Discussion

The results of the present study confirm (for groups A and B) the well documented finding that muscle fibre size remains fairly constant during adult life (Cheek 1968; Brooke and Engel 1969; Sissons 1974). As the number and size of nuclei also remains constant, no changes in the nucleo-cytoplasmic ratio are observed during adult life.

However, a significant increase in nucleo-cytoplasmic ratio in the advanced age group was observed in this study, and the results showed this increase to be due to a reduction in muscle fibre size. The latter finding is in agreement with the observed changes (decrease in both size and number of muscle fibres) in aged muscle (Moore et al. 1971; Adams et al. 1973; Manta 1978; Papapetropoulos et al. 1981).

The observed pattern of muscle changes (reduction of muscle fibre size with maintenance of the number and size of nuclei unchanged) resembles the changes found in neurogenic atrophy.

The muscle weakness and atrophy of advanced age have been studied from both neuro-physiological and histo-pathological points of view. In a neuro-pathological investigation Campbell and McComas (1970) considered that the muscle atrophy of ageing is probably the result of progressive loss of motor neurones. Tomlinson et al. (1969) in a histo-pathological study of skeletal muscle of people with presenile dementia and advanced age people also found certain similarities with neurogenic atrophy. Certain signs of denervation such as fibre type grouping and angulated fibres in aged muscle have been observed in previous studies (Manta 1978; Papapetropoulos et al. 1981). The histo-pathological changes of elderly muscular atrophy as Jennekens et al. (1971) suggested, are indistinguishable from those found in dernervation and may be due to a progressive loss of anterior horn cells in the spinal cord.

The participation of motor neurons in the pathogenesis of muscle ageing seems to be rather unequivocal. Nevertheless the whole matter is certainly far more complicated since the muscle, apart from its functional dependence on the nerve, is under the influence of other factors such as trophic, hormonal, hypoxaemic and many others. The investigation of these factors is necessary in order to elucidate the pathogenesis of muscle ageing.

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