Spinobulbar muscular atrophy (SBMA) is a slowly progressive disorder with post-adolescent onset, characterized by degeneration of lower motor neurons, which results in proximal muscle weakness and muscle atrophy. Severe muscle cramps are often observed before any other symptoms. Weakness of the bulbar muscles causes dysphagia and dysarthria. Other signs, such as gynaecomastia, testicular atrophy and reduced fertility, due to mild androgen insensitivity, are also characteristic of the disease (Bingham 1995, Guidetti 1996). SBMA is inherited in an X-linked recessive manner. Only males are affected and their daughters are obligatory carriers.

SBMA belongs to polyglutaminopathies – a group of disorders caused by expansions of CAG repeats, which results in increasing the number of glutamine residues in the corresponding protein. Abnormal length of the polyglutamine tract alters protein conformation and leads to its aggregation and dysfunction. Several genes with CAG repeat expansion have been recognized as responsible for a number of neurodegenerative disorders: Huntington’s disease (HD), spinocerebellar ataxias (SCA1, 2, 3, 6, 7 and 17) and dentatorubral pallidoluysian atrophy (DRPLA) (Andrew 1997)

The molecular defect that causes SBMA is an expansion of CAG repeats in the first exon of the androgen receptor (AR) gene, located in Xq11-q12 and composed of 8 exons. A polymorphism of the CAG repeats is observed, as their number in healthy people ranges from 9 to 34 repeats and the most common alleles contain 18 to 25 repeats (McLean 1996, Bingham 1996). The ranges of CAG repeat number in the AR gene differ slightly between populations. Among Scandinavian populations, the ranges are: 15–29 in Finnish, 17–29 in Swedish and 18–27 in Danish control groups (Lund 2000). Edwards et al. (1992) reported ranges of CAG repeat number in four hu-

The aim of this study was to characterize the CAG repeat polymorphism in the AR gene in a Polish control group and to determine the CAG repeat number among patients with SBMA.

DNA samples were obtained from leukocytes of peripheral blood of 150 unrelated healthy individuals (100 males and 50 females), representing the control group, and of 60 male patients suspected of SBMA as well as their family members (four daughters, two mothers, one sister and one mother’s sister).

Analysis of CAG repeats in the AR gene was performed by a standard PCR reaction with specific primers labelled with the γATP ³²P radioisotope or with the fluorescent 6-FAM (La Spada 1991). The number of CAG repeats was determined by comparison with the internal standard TAMRA 500.

The CAG repeat number observed in 200 alleles from the control group ranged from 16 to 30. The frequency and distribution of particular alleles of the AR gene are not significantly different from those observed in other Caucasian populations (Figure 1 and Table 1). The most frequent allele in the Polish group was 22 CAG, whereas the most frequent alleles observed in whites, blacks and Asian populations were 21 CAG, 18 CAG and 22 CAG, respectively (Edwards 1992).

The diagnosis of SBMA was molecularly confirmed in 21 male patients from 19 families. The pathogenic CAG number ranged in them from 43 to 51 repeats. Male hemizygotes presented only one allele with an expanded CAG repeat region, whereas eight female carriers presented one normal allele and one allele in the pathogenic range of 44 to 47 CAG repeats.

The pathogenic range described previously as 36–66 CAG repeats (Andrew 1997) is much wider than the range of 43–51 CAG repeats detected in our material, but the difference is most probably due to the small size of the Polish SBMA group.

| Table 1. Statistical evaluation of distribution of the CAG repeats number in AR gene in Polish control group composed of 150 healthy individuals (200 alleles) |
|-----------------------------------------------|---|---|---|---|---|---|---|
| N                | Mean (SD) | Median | Mode | Skewness (SE) | Kurtosis (SE) | Perc. 25 | Perc. 50 | Perc. 75 |
| Values           | 200        | 22.25 (2.73) | 22.00 | 20 | 0.41 (0.17) | -0.2 | 0.34 | 20 | 22 | 24 |
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REFERENCES


