Congenital and Childhood Myotonic Dystrophy type 1
- the impact on central nervous system, visual and motor function

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin vid Göteborgs Universitet kommer att offentligen försvaras i föreläsningssal 1, Drottning Silvias barn- och ungdomssjukhus, Göteborg
Fredagen den 24 april 2009, klockan 9.00
av

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Avhandlingen baseras på följande delarbeten


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**Background and aims:** Myotonic dystrophy type 1 (DM1) is an autosomal dominant multisystemic disorder, caused by an expanded CTG repeat on chromosome 19. The disorder can present both in children and adults. The overall purpose of this study was to gain further insight on neuropsychiatric and neurocognitive aspects, vision and motor function in individuals with congenital and childhood DM1. Further to correlate the size of the CTG repeat expansion, inheritance and the onset form with the clinical findings.

**Methods:** Fifty-nine children and adolescents with DM1 were included. Based on age at onset and presenting symptoms, the individuals were divided into four groups; severe and mild congenital, childhood and classical DM1. In study I and IV, the results were compared with healthy age and gender-matched controls. Measurement of muscle strength, motor function and contractures was performed. According to the DSM-IV criteria, neuropsychiatric diagnoses were assigned on the basis of all available information. The intellectual level was assessed using the Griffiths Mental Developmental Scale or the Wechsler Scales, and adaptive skills using the Vineland Adaptive Behaviour Scales. The ophthalmological examination included best corrected visual acuity, refraction, slit-lamp biomicroscopy, indirect ophthalmoscopy and flash visual evoked potentials (VEP).

**Results:** Motor function and muscle strength was significantly reduced in children with DM1 compared with healthy controls, but there was great variation regarding the degree of muscle weakness. Forty-nine percent had an autism spectrum condition (ASC) and autistic disorder was the most common diagnosis, present in 35% of the affected individuals. A large majority of the participants had learning disability, usually in the moderate to severe range. Almost all participants showed poor adaptive skills. The ophthalmological study shows a higher prevalence of low visual acuity and refractive errors compared with the controls. No true cataract was found. Subtle non-specific fundus changes were present in addition to VEP pathology. The frequency of ASC increased with increasing CTG repeat expansions. Motor function, intellectual level, visual acuity and adaptive skills presented lower values in individuals with larger CTG repeat expansion size. Maternal inheritance had a negative impact on intellectual and adaptive functioning. The more severe the form of DM1, the more reduced the motor function and visual acuity, and the higher the frequency of ASC and learning disability.

**Conclusions:** DM1 in childhood shows great variability regarding symptoms and age at onset. At the individual level, the size of the CTG repeat expansion cannot predict the DM1 form. No clear genotype-phenotype correlations were found, although the largest expansions were present in the severe congenital group. In everyday life, it appears that individuals with DM1 primarily suffer from their CNS-related symptoms, such as cognitive deficits, neuropsychiatric problems and visual dysfunctions, rather than their neuromuscular symptoms.

**Key words:** myotonic dystrophy type 1, children, muscle strength, motor function, autism spectrum conditions, learning disability, adaptive skills, visual impairment, hyperopia

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