Complex I and ATP content deficiency in lymphocytes from Friedreich's ataxia

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Friedreich's ataxia (FRDA) is an inherited recessive disorder characterized by progressive neurological disability and heart abnormalities. A deficiency in the protein frataxin causes this disease. Frataxin deficiency leads to progressive iron accumulation in mitochondria, excessive free radical production and dysfunction of respiratory chain complexes. The expansion (GAA) repeat in the first intron causes decreased frataxin expression by interfering with transcription. Activity of mitochondrial respiratory chain complex I (measured as NADH ferricyanide reductase) and intracellular ATP measurement was performed on lymphocytes of FRDA patients (n=12) and control subjects (n=25). Our findings showed that complex I activity and intracellular ATP were significantly reduced (P=0.001) in patients compared with controls and we found a strong correlation between complex I activity and intracellular ATP content in FRDA patients (r=0.93; P<0.002). 8.6 and 9.0 kb deletions in mtDNA were detected in 9 patients out of 12 (75%) by multiplex polymerase chain reaction (PCR) and southern blot analysis. This study suggested that a biochemical defect in complex I activity and ATP production, which may be due to iron accumulation in mitochondria, could be involved in age of onset of FRDA.

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