Rare window on spinal muscular atrophy genetics

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Caused by a mutation of the SMN gene, spinal muscular atrophy (SMA) is an infantile and juvenile neurodegenerative disorder where motor neuron loss causes progressive paralysis. A new study published in the open access journal *BMC Medicine* details the first research focused on human muscle tissue atrophied due to a genetic condition, and sheds light on two distinct mechanisms at work in different forms of SMA.

A research team from Italy, led by Gerolamo Lanfranchi, analyzed muscle biopsies and genomic DNA from peripheral blood of four SMA I and five SMA III patients from the Neuromuscular Bank organised by Corrado Angelini at the University of Padova, to investigate which other muscle genes, other than the SMN defect, played a role in atrophy. They used microarray and quantitative real-time PCR to study at transcriptional level the effects of a defective SMN gene in skeletal muscles affected by the two forms of SMA: the most severe, type I (infantile), and the milder type III (juvenile).

SMA type I is also known as severe infantile SMA or Werdnig-Hoffmann disease. Manifesting rapidly in infants, babies diagnosed with type I SMA do not generally live past one year of age. SMA type III represents a milder form of the disorder. It has a later onset and affected patients may be able to walk but later lose this ability.

The two forms of SMA gave distinct expression signatures. The SMA III muscle transcriptome is close to normal, whereas in SMA I gene expression is significantly altered. Genes implicated in signal

transduction were up-regulated in SMA III whereas those involved in energy metabolism and muscle contraction were consistently down-regulated in SMA I.

"Our work indicates that SMA I and III muscles are in different phases: the 'prolonged' atrophic condition typical of the SMA I muscle and the coexistence of atrophy and hypertrophy in SMA III muscle," says Lanfranchi.

Previous studies have investigated transcriptional changes in mouse or rat muscle atrophied due to physiopathological conditions, but this is the first to use human tissue affected by a genetic atrophic condition.

More information: ifferent atrophy-hypertrophy transcription pathways in muscles affected by severe and mild spinal muscular atrophy , Caterina Millino, Marina Fanin, Andrea Vettori, Paolo Laveder, Maria Luisa Mostacciuolo, Corrado Angelini and Gerolamo Lanfranchi, BMC Medicine (in press), www.biomedcentral.com/bmcmed/

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